

# Tinnitus Retraining Therapy Trial

**Manual of Procedures**  
version 1.8

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## **Chapter 1** **Significance and Background**

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### **1.0 Introduction**

Tinnitus is the perception of sound in the absence of a corresponding external sound. Patients who seek intervention for tinnitus report subjective sensations of ringing, buzzing, roaring, whistling and/or hissing sounds. There is a distinction between subjective tinnitus and objective tinnitus. Objective tinnitus may be caused by abnormal blood flow within or around the ear, or by some anatomical abnormality or pathophysiology of the neurological, immunological, or auditory systems. Subjective tinnitus is the perception of sound for which there is no apparent cause. The subjective tinnitus sound may appear to originate in the ear or within the head, but there is no objective evidence of corresponding cochlear activity. The mechanism underlying subjective tinnitus is not known but may involve both peripheral and central sites of origin.

At some time or another, virtually everyone experiences some degree of tinnitus. Fortunately, for most people, tinnitus is either transient or of such low level that the individual either is unaware of it (in most situations) or deems it to be unobtrusive. The vast majority of persons with tinnitus report no distress associated with their tinnitus and require no professional help. However, in some individuals the impact of tinnitus can be severely debilitating, impairing their

well being and ability to lead a normal lifestyle. It is the severely impaired tinnitus patients who will be the study participants in this project.

### 1.1 Epidemiology of Tinnitus

Tinnitus is a complicated and unpredictable phenomenon. At least seven major epidemiological studies have been conducted over the past 40 years. Investigators of these studies report prevalence rates of continuous subjective tinnitus among adults between 10.1 and 14.5% (David and Rafaie, 2000). The majority of the tinnitus patients report no distress due to the condition, but about 2% of these patients are severely debilitated by their tinnitus condition and require professional help for the treatment of tinnitus. Thus, it is estimated that as many as 5 million Americans suffer tinnitus of such severity that it significantly impacts their work, normal daily activities, and/or sleep (Dobie, 1999; Jastreboff and Jastreboff, 2000).

#### 1.1.1. Tinnitus in the General Population

There are many factors that have been associated with the prevalence of tinnitus (see Table 1). High-frequency hearing loss has been recognized as a major predictor for tinnitus. Increasing age has also been related to an increase in the prevalence of tinnitus.

**Table 1**  
**Factors Related to Prevalence of Tinnitus**

<b>Tinnitus Frequency</b>	
Prolonged spontaneous tinnitus	Affects 10 to 15% of adults
Occasional tinnitus	Affects 22 to 32% of adults
<b>Hearing Impairment</b>	
High frequency hearing impairment in the worst ear (major predictor)	Prolonged spontaneous tinnitus
Profound hearing impairment	Severe tinnitus annoyance
Slight hearing impairment	Slight tinnitus annoyance
The greater the air-bone gap...	The higher the possibility of reported tinnitus for a given hearing impairment
<b>Otologic History</b>	
History of chronic suppurative otitis media and discharge from ears	Most likely to have unilateral tinnitus
Meniere Disease	Show greater sensitivity to tinnitus than any other etiological group

**Table 1**  
**Factors Related to Prevalence of Tinnitus**

<b>Age ("The prevalence of hearing impairment and tinnitus increases with age."</b>	
18 to 44 years of age	2% (prevalence of tinnitus)
45 to 64 years of age	5% (prevalence of tinnitus)
65 to 74 years of age	9% (prevalence of tinnitus)
Elderly versus younger patients	Study results from elderly have shown that tinnitus pitch and loudness were lower than that seen in the younger patients
<b>Gender</b>	
Females versus Males	Some evidence of slightly higher prevalence of tinnitus amongst females, but men tend to seek treatment for the problem more than women.
<b>Socioeconomic and Occupational Group</b>	
Office workers versus general laborers	Professionals and office workers are more likely to report tinnitus than those persons in labor class.
<b>Site of Tinnitus</b>	
Left versus Right Ear	Some evidence of slightly higher prevalence of tinnitus reported in the left ear vs right ear in unilateral cases
Bilateral tinnitus or tinnitus in the head	Reported more often than unilateral tinnitus
<b>Noise (Excessive noise is known to be a major factor causing hearing loss and tinnitus)</b>	
High lifetime exposure to noise	21% (prevalence of tinnitus)
Low lifetime or no significant exposure to noise	8% (prevalence of tinnitus)
Regular exposure to gun shots	14% (prevalence of tinnitus)
Low exposure to gun shots	8% (prevalence of tinnitus)
<b>Miscellaneous Factors</b>	
Smoking	Preliminary research has suggested smoking can result in an increased incidence of hearing loss, especially in the high frequencies – possibly increasing the rate of tinnitus among smokers
Coffee	It is unclear whether caffeine is related in any way to tinnitus
Alcohol	It has been suggested by some researchers that alcohol may have an adverse effect on existing tinnitus
<b>Children</b>	
Estimated incidence	6 to 29%, but largely unknown
Tinnitus and hearing loss	Tinnitus associated with hearing loss in children is often intermittent

Other factors remain less certain, including gender and ear effects. Some research suggests women may have as high, if not a slightly higher prevalence of tinnitus than do men (Davis and Rafaie, 2000). This distribution has not been seen at the University of Maryland or the University of Oregon tinnitus centers, where women present for treatment of debilitating tinnitus in smaller numbers than do men. Of 1,543 tinnitus patients seen at the University of Maryland

Tinnitus and Hyperacusis Center (between 1991-2003), 63% were men and 37% were women. Meikle (Meikle, 1977) described 1,630 tinnitus patients as 71% men and 29% women (entered into their archive between 1981 and 1994).

The most commonly reported locations for tinnitus are “bilateral” or “in the head.” In cases of unilateral tinnitus it is still debatable whether one ear is affected more often than the other. Not surprisingly, increased rates of lifetime noise exposure have also been associated with an increased prevalence of tinnitus. The effects of smoking, coffee, and alcohol have also been explored. No conclusive tie between these habits and the prevalence of tinnitus has been found.

Socio-economic and occupational group effects also have been determined to be positive predictive factors because of associated higher noise exposures on the job or in leisure activities (e.g., hunting with firearms). In addition, specific pathological conditions are characterized by a higher occurrence and greater severity of tinnitus, including conditions associated with acoustic trauma and Meniere's disease, but also ototoxicity and presbyacusis (Spoendlin, 1987). Although there are many causes for tinnitus, exposure to hazardous noise is the most widely associated cause of tinnitus-related complaints (Axelsson and Barrenas, 1992).

The prevalence of tinnitus among children and adolescents is unclear but is perhaps two-fold greater among children with hearing loss (both conductive and sensorineural) than among normal-hearing children. Research has suggested that between 6 to 36% of normal hearing children experience tinnitus, with only about 3% self-reporting the problem (Kentish *et al.*, 1999). Coles (1997) suggested some factors that may explain why the problem of tinnitus may not be as apparent in children as it is in adults: 1) Children might consider tinnitus as being a “normal” condition if it is present since early life; 2) Children are less prone to the anxiety suffered by adults regarding the medical implications of tinnitus; 3) Children's complaints of tinnitus may be ignored by adults. Children with primary otologic complaints and/or hearing loss have been described to suffer tinnitus in greatest numbers (Davis and Rafaie, 2000). Graham (1981) related that 40% of a sample of hearing-impaired children reported tinnitus to be disturbing, causing confusion on audiology, reluctance to wear hearing aids, and behavioral problems. Gabriels (1995) also found that approximately one-third to one-half of her sample of children with tinnitus suffered from sleep disturbance, concentration problems, and sound sensitivity in the ear with the reported tinnitus. Others estimate percentages as high as 75% of children sampled with significant hearing losses may have tinnitus. Thus, tinnitus can be a problem for children; however, inconsistencies within population make identification of the problem and treatment considerably more difficult than for adults. In fact, most tinnitus treatment centers see few if any children for primary tinnitus problems. Perhaps the largest sample of children now in treatment for tinnitus is in Poland. Bartnik (2004) reports that in their national tinnitus treatment center about 1-2% of the patients receiving treatment for tinnitus are children or adolescents. Thus, children either self-reporting or requiring treatment for tinnitus appear to be

vanishingly rare in comparison with the large numbers of tinnitus sufferers undergoing treatment among the adult population.

### **1.1.2. Tinnitus in the Military Population**

The incidence and prevalence of tinnitus among U.S. military personnel is not known, but is likely much higher than that among the overall population because of increased exposure to loud noise (Humes *et al.*, 2005). In fact, it has been established that noise-induced hearing loss is the most prevalent occupationally related health hazard among United States Army troops (Walden *et al.*, 1975). Despite increased hearing conservation efforts in the military, the problem in recent years has increasingly been compounded by training exposures to weapons systems that have greater fire power with higher and more hazardous noise levels (Ohlin, 1992). The enormity of the problem is highlighted by a 1993 estimate that approximately 500,000 U.S. Army military and civilian personnel were exposed to hazardous noise levels (U.S. Army Environmental Hygiene Report, 1993). Recently, Henry *et al.* (2004) estimated the prevalence of chronic tinnitus among military veterans in the Veterans Administration (VA) Medical System alone to be between 2.7 and 4 million Americans.

Studies of military personnel suffering acoustic trauma in connection with military weapons reveal that tinnitus is significantly related to degree of hearing loss (Hamberger and Liden, 1951), although tinnitus is also frequently reported by individuals with audiometrically normal hearing sensitivity. Indeed, tinnitus may be the only symptom following acute acoustic trauma and may be permanent and severe despite audiometrically normal thresholds. One of the difficulties in establishing these epidemiological statistics and a causal relation with noise exposure is that the onset of tinnitus does not always coincide with a specific incident of acoustic trauma and, in fact, may not appear until years after the causal incident (Axelsson and Barrenas, 1992).

Estimates of tinnitus incidence or prevalence among military personnel from other nations vary considerably and depend on which population was studied. For example, a Finnish study reported an incidence of about 25% in 418 conscripts who suffered acoustic trauma from hand-held firearms and large caliber weapons or explosions (Ylikoski and Ylikoski, 1994). These incident cases suffered prolonged tinnitus up to a year following the noise exposure, and about 8% continued to suffer distressing tinnitus over their lifetime. Among Finnish officers, 32% (220 of 669) experienced tinnitus and 17% (118 of 669) suffered distressing tinnitus continuously. Salmivalli (1967) reported that 16% of military personnel with normal hearing sensitivity and 56.0% of those with severe hearing loss suffered from tinnitus. Similar estimates have also been reported for Israeli soldiers (Roth *et al.*, 1989). The important point is that it is reasonable to expect that a substantial proportion of the roughly 1 million active U.S. military personnel will be exposed to conditions that make them more susceptible to tinnitus than the civilian population.

Because we expect the prevalence of tinnitus is likely higher among U.S. military personnel than among the civilian population, the adverse consequences of tinnitus should reasonably be greater in the military. Significant correlations have been reported in the military population between tinnitus and depression and between tinnitus and sleep disturbances. These disturbances are appreciably higher than among normal controls (Alster *et al.*, 1993).

### **1.2 Natural History of Subjective Tinnitus**

The natural course for subjective tinnitus is not known. Estimates differ regarding the post-onset time period required to assume stability and permanence for tinnitus. For example, Vernon (1996) recommends a two-year period of stability before concluding that tinnitus is permanent, whereas Dobie (2002) suggests that tinnitus lasting more than a year is unlikely to resolve. On the other hand, the effects of tinnitus on quality of life appear more apt to be diminished rather than exacerbated with a longer period of post-onset follow-up.

### **1.3 Health Care Costs Associated with Tinnitus**

Fiscal costs to the military and VA Medical System are significant because of increased compensation claims for tinnitus, especially since 1999, when Federal regulations were modified and eased for tinnitus-related compensation claims. Indeed, VA compensation is staggering for service-related tinnitus as either a primary disability or a secondary disability to hearing loss. Since 2001, tinnitus has been the most common service-related disability. As of September 2003, 242,610 veterans were on file for tinnitus-related compensation claims. Altogether, their total compensation costs for these service-related tinnitus benefits exceeded 285 million dollars in 2003 (Henry *et al.*, 2004). This monetary value does not include costs for medical or audiological assessment of the tinnitus problem or its management. Diagnostic evidence for tinnitus and attendant validity of an individual's compensation claim is especially difficult, time-consuming, and expensive. This difficulty is due to the subjective nature of the tinnitus, the variable onset of the tinnitus, and the uncertain relation between the tinnitus and associated hearing loss. This problem is compounded by the lack of comprehensive tinnitus treatment and therapy programs for managing military patients and dependents, as well as veterans in the VA Medical System for whom minimal services are available for tinnitus management (Henry *et al.*, 2004). The paucity of good educational and training programs for the clinical management of tinnitus patients and the critical need for proven intervention methods continue to limit progress in tinnitus treatment in the military.

### **1.4 Management of Subjective Tinnitus**

Most of the past clinical approaches to patients with debilitating tinnitus have been based on the idea that tinnitus is due to a problem in the auditory periphery (mainly the cochlea), or that the reaction to tinnitus is due to depression and anxiety. Therapeutic approaches for suspected

cochlea disorders have attempted to suppress or isolate the tinnitus cochlear generator using diverse methods such as tinnitus masking or sectioning of the auditory nerve. Suffice it to say that, to date, there is no reliable method for eliminating (curing) the tinnitus source (Parnes, 1997).

Psychotropic drugs and/or behavioral counseling have been used to treat the assumed tinnitus-associated anxiety and depression. Cognitive-behavioral treatments have been successful for about 50% of tinnitus patients using this intervention (see Henry and Wilson, 1999). Consequently, the role of cognitive psychology in the treatment of tinnitus has been enthusiastically promoted in clinical psychology. Cognitive therapy asserts that thoughts, beliefs, and assumptions cause feelings. Negative feelings associated with tinnitus are challenged, as the clinical focus is on reduction of distress caused by tinnitus. Thus, cognitive psychologists assert that improvements are mediated by cognitive changes. The use of habituation to help tinnitus patients was first proposed in clinical psychology (Hallam *et al.*, 1984). The psychological habituation approach, which focuses on reassurance, relaxation, and attention distraction techniques (Jakes *et al.*, 1986), usually has not produced significant, sustained improvements for most tinnitus patients, and it often requires continual therapy to prevent relapses (Jastreboff and Jastreboff, 2000).

In a comprehensive review of 69 clinical trials for medical and non-medical tinnitus interventions, Dobie (1999) reported that “None of the medical or non-medical treatments studied to date has been shown to eliminate tinnitus more frequently than a placebo, or even to provide replicable long-term reduction in the impact of tinnitus on everyday life, in excess of placebo effects” (p.1208). In 2002, Dobie reported again that there continues to be no proven or definitive treatment for tinnitus. Unsuccessful non-medical approaches have included electrical stimulation, acupuncture, ultrasound, hypnosis, biofeedback, behavioral modification, psychotherapy, counseling, ginkgo biloba, and masking with noise. Indirect efforts to help patients cope, such as biofeedback and hypnotherapy may improve the patient’s reaction to tinnitus (Jastreboff *et al.*, 1998). Several therapies such as magnets, hyperbaric oxygen, herbal preparations, cranio-sacral therapy have not been evaluated in controlled studies to verify anecdotal claims of benefit for tinnitus.

## **1.5 Tinnitus Retraining Therapy (TRT)**

Tinnitus retraining therapy (TRT) is a non-medical intervention that uses directive counseling (DC) and low-level sound therapy (ST) to habituate the patient’s associated negative emotional reactions (annoyance) to tinnitus, its perception (awareness) and, ultimately, its impact on the patient’s life (Gold *et al.*, 2000). In the absence of other known effective interventions, TRT has grown in popularity world-wide and is increasingly becoming the standard-of-care in this country and abroad for treating severe disabling tinnitus (see Hazell, 1999).

### **1.5.1 Description of TRT**

TRT is based on a neurophysiological model of tinnitus described by Jastreboff (1990). An updated description of TRT and the implementation of the current form of the neurophysiological model of tinnitus were recently described by Jastreboff and Hazell (2004). The model evolved from attempts to reconcile discordant observations in the tinnitus literature. First, the majority of tinnitus patients report no distress due to the condition (McFadden, 1982); it is a severely debilitating disease in 1 to 2% of the general population (Jastreboff and Jastreboff, 2000). Further, there is also little or no good evidence that the distress reported by severely affected tinnitus patients has any correlation with their subjective reports of tinnitus sensation (documented by psychoacoustic measures such as tinnitus loudness, pitch, and maskability)(Jastreboff, 1995). In fact, it is not uncommon to find that a pair of tinnitus patients with similar psychoacoustic profiles may report vastly different distress levels. Jastreboff (1990) surmised from these and other observations that any tinnitus model must include abnormal processing of the tinnitus signal at sites within the nervous system beyond the cochlea and auditory nerve (auditory periphery).

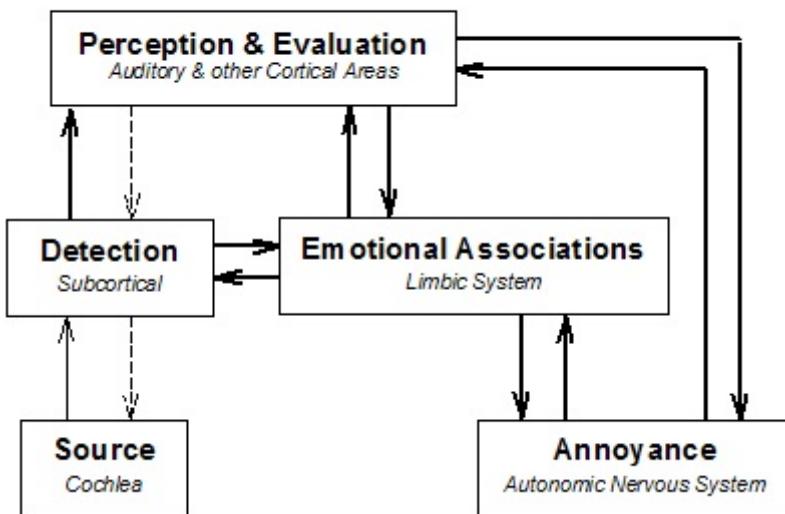
The block diagram shown in Figure 1 depicts Jastreboff's neurophysiological model of tinnitus, which provides a theoretical framework for habituation-based TRT (Jastreboff *et al.*, 1996) . The five stages include the following:

- Auditory periphery, usually considered the primary site where tinnitus-related neuronal activity originates;
- Subcortical auditory structures responsible for detection of the peripherally generated tinnitus activity;
- Cortical centers, involved in the perception (awareness) and evaluation of the tinnitus code;
- Limbic system; and
- Autonomic neural structures, which contribute to the negative emotional reactions (annoyance, distress) and exacerbated physiological responses to the tinnitus code.

In this model, if the patient is aware of the tinnitus, but experiences no strong negative emotional reaction to it, then only stages 1 to 3 are involved. The additional activation of stages 4 and 5 explain the inordinate distress experienced by tinnitus patients as well as the increased stress, anxiety, loss of well being, sleep problems, and general annoyance to the tinnitus. Patients who experience activation of all stages are those who ostensibly seek professional care and are candidates for TRT.

Support for this model comes from functional imaging techniques showing increased activation of the limbic system and cortical areas, which are normally associated with emotion, in tinnitus patients (Lockwood *et al.*, 1998; Mirz *et al.*, 1999, 2000). This increased activation, represented in Figure 1 by the emboldened arrows (coding the relative strength of the activation along the pathways connecting the various stages), is influenced by the magnitude of the patient's negative emotional reactions to the tinnitus. As the strength of reaction increases, the patient focuses greater attention on the tinnitus, which in turn enhances subcortical detection of the tinnitus (Jastreboff *et al.*, 1996). This enhancement, in turn, exacerbates the activation of the limbic and autonomic systems, setting up a vicious cycle of sustained, enhanced activation within one or more of the feedback loops shown in Figure 1. Ultimately, in severe cases, the tinnitus-induced reactions within feedback loops containing the limbic and autonomic neural structures take on properties of a conditioned (learned) reflex.

**Figure 1**  
**Jastreboff's Neurophysiological Model of Tinnitus**



The first component of TRT, directive counseling (DC), is believed to neutralize the negatively associated emotional reactions to the tinnitus (Gold *et al.*, 2000). DC is considered an important and necessary first step to habituate the negatively learned response to the tinnitus signal. During the treatment course, the learned response is gradually extinguished as the tinnitus stimulus ceases to have relevance in the patient's life.

The other treatment component in the model that is believed to be crucial to TRT success is ST (Gold *et al.*, 2000). This element is based on physiological evidence that diminished cochlear stimulation (due to disease or pathological processes) increases neuronal sensitivity within the auditory pathway (Boettcher and Salvi, 1993; Gerken, 1993). Jastreboff and Jastreboff (2000) argue that this centrally mediated compensation, or gain, within the auditory pathway amplifies tinnitus activity from the auditory periphery that otherwise would be undetectable. Several lines of evidence suggest that this gain mechanism is adaptable via plastic central auditory processes, which are sensitive to and partly controlled by the acoustic input to the auditory periphery

(Formby *et al.*, 2000; Gold *et al.*, 1999; McKinney *et al.*, 1999b). This property motivates the use of ST as a key component in the intervention for severe disabling tinnitus.

According to Jastreboff *et al.* (1996), ST facilitates the habituation of both the tinnitus-induced negative reactions and perception by decreasing the perceived contrast between the background neuronal activity and the tinnitus-related neuronal activity. Habituation of tinnitus perception (awareness) is facilitated because (1) the tinnitus is made more difficult to resolve in background noise and (2) the auditory gain mechanism is reset by the increased ambient background noise to which the patient is exposed. This resetting further decreases the contrast between the tinnitus and the overall spontaneous neuronal background activity. Habituation of the negative emotional reactions (annoyance) to the tinnitus is facilitated by ST because, with diminished detection in the background noise, the patient's focus and perseveration on the tinnitus is concomitantly diminished and the conditioned reflex is extinguished between the subcortical structures and limbic/autonomic neural structures. Habituation of the sensation of tinnitus may also occur in some patients (perhaps 20%)(Sheldrake *et al.*, 1996), but this finding is unusual in our clinical experience and requires verification in a controlled clinical trial of TRT.

TRT has been pioneered and refined over the past decade at the University of Maryland Tinnitus and Hyperacusis Center (UMTHC) (Gold *et al.*, 2000). Based upon 15 years of clinical experience with TRT at UMTHC, the process of habituation is incremental (Gold *et al.*, 2000), with successful treatment effects usually seen within 6 months to 1 year (although necessary treatment for an optimum response to TRT may take longer for some patients). The final goal of TRT is for tinnitus to cease to have an impact in the patient's life. However, even with a high level of habituation of the reaction to the tinnitus and the awareness of it, TRT is not a cure for tinnitus. After undergoing TRT, patients usually continue to hear the tinnitus when they focus their attention on it. Tinnitus pitch and loudness may be the same at the beginning and end of treatment, and the tinnitus sensation may not be significantly changed (Jastreboff and Jastreboff, 2000).

### **1.5.2. Preliminary Uncontrolled Studies of TRT**

Retrospectively analyzed data from among the first 500 patients seen at the UMTHC were reported in 1996 by Jastreboff *et al.* (1996). Data on the effectiveness of tinnitus habituation were gathered from 100 of these patients: 63% received DC and were fitted with sound generators (SGs); 16% received DC and were fitted with hearing aids, and 21% received DC alone. Assessment of effectiveness of treatment was evaluated using a patient questionnaire to assess tinnitus habituation, effects of tinnitus on the patient's life, and the level of tinnitus-induced annoyance at initial appointment and after at least 6 months of treatment. Improvements were seen in 83% of patients fitted with bilateral SGs, 70% of patients treated with hearing aids, but in only 18% of patients treated with DC alone. Similar data were reported in a second series of 124 patients, where 82% (n=102) received full TRT and 18% (n=22) received a single session of DC

(Jastreboff, 1996). Significant improvements in tinnitus condition were noted in 79% (n=81) of the group receiving full TRT, while only 18% of patients (n=4) showed improvements after a single session of counseling.

In a subsequent analysis of 152 patients, Jastreboff (1998) evaluated patient improvement using the following considerations:

- Is the patient performing activities that were prevented or interfered with previously?
- Is there a change in the level of annoyance to the tinnitus?
- Is there a change in the percentage of time when the patient is aware of tinnitus?

Improvement was defined by an appropriate change of at least 20% in 2 of the above 3 issues. Among 152 patients treated for at least 6 months at UMTHC, 129 (85%) received full treatment involving both DC and ST (i.e., SGs or hearing aids) and 105 (81%) of these patients showed significant improvement in their tinnitus.

In a more recent retrospective analysis of TRT treatment outcomes, UMTHC evaluated treatment progress through questionnaires administered at initial and follow-up visits or through telephone interviews (Jastreboff and Jastreboff, 2000). Among a sample of 263 patients, 90% participated in full TRT, while 10% received one session of DC, but did not use ST as prescribed. Combined results from all 263 patients revealed that 75% were significantly improved by treatment, as judged by indices for tinnitus awareness and annoyance, and negative effect on quality of life; each index was decreased to about half of the corresponding pretreatment value.

In summary, preliminary evidence from UMTHC, based upon analyses of various uncontrolled patient samples who received full or partial TRT as part of their treatment for tinnitus, consistently supports the therapeutic benefits of the full TRT protocol. DC alone does not appear to be sufficient in and of itself as a successful treatment for tinnitus among patients at UMTHC.

Prospective studies show similar results. Berry *et al.* (2001) prospectively followed 19 tinnitus patients who had received TRT at UMTHC for 6 months. They evaluated change in subjective self-assessment of life-effect ratings using the Tinnitus Handicap Inventory (THI). The THI is a widely-used validated psychometric outcomes measure that addresses problem areas for patients with tinnitus (Newman *et al.*, 1996). The 25-item questionnaire is scored on three subscales that target emotional, functional, and catastrophic problems associated with the tinnitus. A total score is also derived from the THI that provides an overall index of the tinnitus handicap (life impact). Berry *et al.* reported significantly higher baseline THI scores than

corresponding scores obtained after six months with TRT. The resulting scores represent significant improvements in the patients' assessments of their tinnitus problems after 6 months of TRT.

In recent years a growing body of clinical evidence from other sites has accumulated to support the efficacy of TRT. In part, because of the apparent success of this intervention and the associated publicity, "TRT... has become the non-medical management of this decade" for treating severe tinnitus (Jacobson, 2000). This guarded recognition of TRT is reflected in the opening address at the Fifth International Tinnitus Seminar in 1995, by the respected tinnitus expert Ross Coles, who stated, " I am firmly of the opinion that it works and is, in fact, by far the largest step forward in management of tinnitus that has yet been achieved. What I am not sure of though is the mechanism. It could be that the sound generator is nothing more than a placebo, with additional benefit coming from repeated counseling and natural adaptation. But even if that were the case, I would be happy to use it in this way, because I believe in it and therefore can honestly do so" (Coles, 1996, p. 8).

In 1999, at the Sixth International Tinnitus Seminar held in Cambridge, UK, fully one quarter of the more than 100 presentations were concerned with the management of tinnitus using TRT and related therapy (Hazell, 1999). In virtually every one of these presentations, the clinical successes of TRT or its components were heralded in managing tinnitus and hyperacusis. A review of these and other recent studies routinely reveals that when the TRT protocol is closely followed, typical rates of clinical success, as judged by a minimum of 20% change in two or more impact-on-life scales, approach or exceed 80% improvement across the various study populations (e.g., Jastreboff, 1998; Bartnik *et al.*, 1999; Heitzman *et al.*, 1999; Herraiz *et al.*, 1999; McKinney *et al.*, 1999a; Sheldrake *et al.*, 1999). These successes have been reported by multiple centers around the world and, in the continuing absence of controlled clinical trials of TRT, have been promoted as providing "evidence by consensus" for the validity and efficacy of TRT (Jastreboff and Jastreboff, 1999). The Jastreboffs contend that the appropriate test of the validity and efficacy of TRT will be a meta-analysis of studies from multiple sites using TRT. They also propose that "a randomized trial with some agreeable controls..." is not necessary because "...the validity of this study, time frame and the sample of patients will be questionable and face many ethical issues..." (Jastreboff and Jastreboff, 2000, p.91). The known ascertainment bias inherent in case series and the open doubts about the treatment efficacy of TRT among professionals actively involved in the treatment and management of tinnitus patients are in contrast with the Jastreboffs' perspective that a randomized controlled clinical trial of TRT is unnecessary.

### **1.5.3 TRT Trials**

Despite the many reported successes of TRT, it remains a highly controversial intervention. This controversy stems in large part from the fact that there still are no published controlled

clinical trials to test the efficacy of TRT (Coles, 1996; Wilson *et al.*, 1998; Baguley, 1999; Leal and Milne, 1998; Kroner-Herwig *et al.*, 2000). Moreover, there have been no rigorous efforts to control for the treatment effects of DC and ST, and the relative contributions of these components to the success of the intervention are not known (Wilson *et al.*, 1998). Because the mechanisms underlying TRT are as yet unknown, skeptics suggest that its apparent success may be due simply to placebo effects arising from the patient's (1) "positive" counseling experience and (2) expectation that the sound instruments used in ST "will" facilitate improvement in his or her condition (Coles, 1996; Tyler, 1997; Wilson *et al.*, 1998), or that ST may simply help the tinnitus patient to cope better with, or to acclimate more quickly, to his or her condition (Coles, 1996; Dineen *et al.*, 1997). Thus, there is a real and timely need to establish the efficacy of TRT.

One of the best-conducted studies to date was that of McKinney *et al.* (1999a). The goals of this longitudinal observational study were to evaluate the treatment effects and permanence of TRT and the relative treatment effects of the DC and ST components of TRT. They enrolled 186 patients with primary complaints of tinnitus alone or tinnitus with hearing loss. They treated 182 of these patients with TRT or TRT components, for one year; 159 were followed for an additional year after treatment. Participants were sequentially assigned to six subgroups based on their hearing status and need for hearing aids. Three of the subgroups are relevant here. Patients in these subgroups had normal hearing sensitivity or only high-frequency hearing loss. The subgroups included patients who: were treated with (1) DC only (n=54), (2) DC and a low-level (barely audible) sound generators (LLNG) (n=35), and (3) full TRT (DC in combination with a higher level sound generators (HLNG)) (n=36). The output sound level for the HLNG was set to be just below that at which the external noise and tinnitus became difficult to resolve from one another.

Comparison of subgroups 2 and 3 tested the placebo effect of ST inasmuch as the sound output from the LLNG in group 2 was just audible and probably ineffective as an intervention. In contrast, the HLNG used in group 3 was set at the recommended volume level in the TRT protocol (i.e, the "mixing point," which is the level that just blends with the tinnitus and reduces the contrast between the tinnitus-related neuronal activity and the patient's spontaneous neuronal background) (Jastreboff, 1998). Comparisons of groups 3 and 1 tested the incremental contribution resulting from the use of HLNG as a supplement to DC. Outcomes were psychoacoustic (pitch match, loudness discomfort level (LDL), minimum masking level (MML)) and questionnaire data collected from each participant at the start of treatment and at 6, 12 (end of treatment) and 24 months.

The key findings were that 72% of patients receiving DC only, 67% of patients receiving DC + LLNG, and 83% of patients receiving full TRT demonstrated improvements of  $\geq 40\%$  on two or more of the four self-report questionnaire scales (annoyance, quality-of-life, loudness, and percent awareness) after 12 months of treatment. Psychoacoustic indices for MML decreased and those for LDL increased for each patient group over the treatment period. The respective

changes are in the direction predicted for the re-calibration of an adaptive chronic auditory gain process (Gold *et al.*, 1999; McKinney *et al.*, 1999b; Jastreboff and Jastreboff, 2000). Notably, the largest changes were obtained in patients receiving full TRT for whom the change in MML was roughly twice as great (i.e., approximately 16 dB versus 8 dB) as that for other patient subgroups.

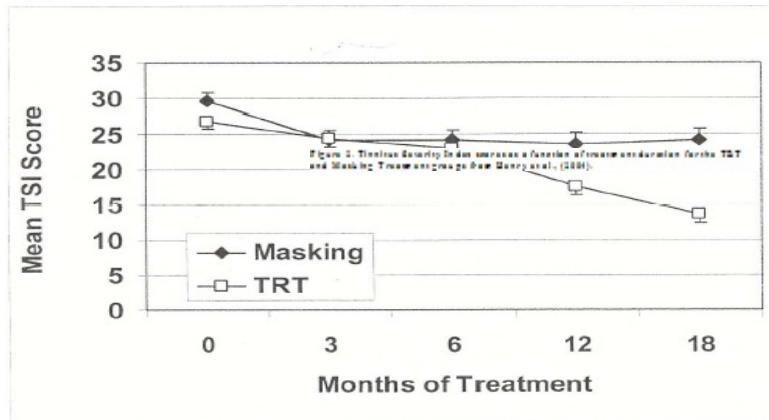
Questionnaire data collected at 12 months after termination of full TRT treatment showed either a stable treatment effect or further improvements in habituation of the tinnitus. The investigators concluded that (1) the observed treatment effect is greater than that which could be reasonably expected for a placebo, (2) DC is probably the most important component of TRT, and (3) ST from bilateral sound generators provides an incremental benefit when in combination with DC. These investigators also observed sizable treatment effects after 6 months into the TRT protocol. This finding differs from Jastreboff's (1998) early reports that the successful treatment of patients with severe tinnitus may require up to 18-24 months of TRT. The latter treatment duration also is consistent with our clinical experience with debilitated patients at the UMTHC (Gold *et al.*, 2000).

Herraiz, Hernandez, Plaza, and de los Santos (2005) also reported on the efficacy of TRT which was compared with that obtained for tinnitus patients receiving partial TRT implemented without ST and improvements obtained over the treatment period of one year by a waiting list control group. The study design was described as a prospective non-randomized clinical essay. The primary finding was that 82% of the patients who received full TRT reduced their THI scores on average by 16% (48% to 32%) over 12 months of treatment, which was statistically more effective than the improvements obtained by either of the other two groups. Herraiz, Hernandez, Toledano, and Aparicio (2007) subsequently reported greater improvements for tinnitus sufferers should be expected for those with more severe problems and that ST with SGs was mandatory for obtaining optimum benefit from TRT.

Two recent randomized clinical trial studies of TRT have been described. Tyler (2004) conducted a pilot study in which he randomly assigned about 60 patients to one of three treatments: (1) full TRT, including DC and “mixing point” ST via bilateral sound generators; (2) DC and complete noise masking of the tinnitus via sound generators; and (3) DC alone. The treatment patients were evaluated before treatment and at 12 and 18 months after the start of treatment. Tyler reported that the degree of tinnitus handicap was reduced in about 80% of the treatment patients, with no obvious differences among the three treatment groups. To date, neither methodological details of the study nor the results have appeared in a peer-reviewed publication, perhaps because of problems that Tyler mentioned related to participant attrition and treatment non-compliance. Tyler's pilot study provided him with data that led to an on-going NIH-funded clinical trial of TRT in which he is now comparing “mixing point” ST with other treatment conditions that use either partial or full masking of the tinnitus in combination with counseling (Tyler, 2005).

In the second of these preliminary reports, Henry *et al.*, (2004) described a controlled prospective study in which they compared the clinical efficacy of masking and TRT protocols for treatment of tinnitus. A sample of 124 veterans with severe tinnitus was randomly assigned to one of the two treatment protocols. A Study Audiologist conducted all audiological and tinnitus evaluations, and obtained outcome data. The TRT treatment was performed independently by a second clinician, and the Masking treatment was performed by a third clinician. In addition to baseline measurements, follow-up treatment measurements were conducted at 3, 6, 12, and 18 months. Self-administered (written) questionnaires included the Tinnitus Severity Index, the Tinnitus Handicap Inventory, and Tinnitus Handicap Questionnaire. Treatment patients completed the questionnaires and were interviewed by the Study Audiologist using TRT Interview forms at each clinic visit. One hundred and eleven veterans (53 in the Masking protocol; 58 in the TRT protocol) completed their 18-month treatment protocols.

Group mean scores from the Tinnitus Severity Index (TSI), a 48-point (maximum) index, are shown in Figure 2 for the two treatment groups as a function of treatment visit. Henry *et al.* report that these data are reasonably representative of results obtained across the different outcome instruments. Each treatment group experienced similar improvements through 6 months of treatment. At the 12- and 18-month visits, however, the TRT treatment group showed significantly greater improvement relative to the Masking treatment group. Henry *et al.* also noted that, on average, both groups reported awareness of their tinnitus to drop from over 70% of their waking hours at the start of treatment to 32 and 19% for the Masking and the TRT treatment groups, respectively, at the end of the treatment. Henry *et al.* concluded that veterans in both groups experienced significant habituation to their tinnitus, with the TRT treatment group showing the greatest effect. Henry *et al.* (2006) also noted that differences in the TRT and Masking treatment groups were most evident for those patients who had severe problems at onset of treatment and were less evident for patients with mild and moderate tinnitus problems. This latter observation is consistent with similar findings reported by Heraiz *et al* (2007).



**Figure 2. Tinnitus Severity Index scores as a function of treatment duration for the TRT and Masking Treatment groups from Henry et al., (2004).**

## 1.6 Rationale, Motivation, and Overview of the TRTT

Despite the apparent successes of TRT in observational studies (and now in the above-mentioned preliminary clinical trials), a limited review of TRT studies (Sheldrake *et al.*, 1996; McKinney *et al.*, 1996) by the Wessex Institute in 1998, was critical of methodological shortcomings in these studies (see Leal and Milne, 1998). Most of these criticisms continue to be valid now. They pointed out problems in the selection of validated outcome measures and psychometric instruments. They also noted the lack of prospective studies, double-blind designs, randomized treatment assignment, and placebo controls. The Wessex Institute report concluded that the available literature simply could not support the validity of TRT in light of current methodological weaknesses, and ended with the statement, “There is clearly a need for properly controlled research trials into the effectiveness of retraining therapy.”

In the same year, a second, independent review focused on the perceived shortcomings of the DC component of TRT and on the necessity to have trained psychologists perform the counseling (Wilson *et al.*, 1998). The reviewers, clinical psychologists who are proponents of cognitive and behavioral therapy for the management of severe tinnitus, echoed the Wessex Institute’s criticisms. They noted that “Methodological limitations in the research which has been published to date preclude any claims about the efficacy of TRT at the present time. It is suggested that randomized, controlled studies, which include no-treatment and placebo conditions need to be undertaken. Studies are required in which the efficacy of the counseling and white sound components can be clearly isolated.” (Wilson *et al.*, 1998, p. 273). Thus, although many clinicians now view TRT to be the most promising non-medical intervention for disabling tinnitus, skeptics such as Wilson *et al.* (1998) continue to call for controlled randomized trials.

In 2004, the Washington State Department of Labor and Industries undertook a review of the literature to assess the available evidence of the effectiveness of TRT (Cochrane, 2005). This study concluded that the lack of baseline measurements, comparison groups, predetermined outcome measurements, and patient homogeneity in past studies precludes any conclusion about TRT efficacy at this time. This study further suggested that TRT should continue to be considered investigational and controversial in the absence of prospective trials. Finally, Phillips and McFerran recently completed a Cochrane systematic review of TRT. They included only one trial, limiting their review to randomized trials that explicitly followed the TRT protocol. They found only one trial (Henry *et al.* 2006). They reported that although this trial found that TRT was more effective than masking, more research is needed (Phillips *et al.* 2010). Accordingly, we will conduct a randomized clinical trial of TRT that will satisfy these legitimate scientific criticisms.

**Table 2. Studies Evaluating Effectiveness of TRT or TRT-like Therapy using Tinnitus Questionnaire (TQ) Scores**

Author	Group	Therapy	No.	TQ Score at Baseline	TQ Score at Follow-up	Months Follow-up
Haerkotter, 2001	“severe”	TRT-like counseling only	26	48.5±12.4	23.9±12.5	6
	“severe”	TRT-like with sound generator	28	53.7±12.3	29.5±14.3	6
	less severe	counseling only	33	25.5±8.6	10.6±7.3	6
	less severe	counseling with sound generator	28	28.8±10.5	13.6±6.2	6
Zachriat, 2003	all	TRT	30	44.5±12.7	29.1±16.0	12
Schnieder, <i>et al.</i> , 1999	TF>40	TRT-like (habituation and intensive counseling)	16	56 (est from graph)	35 (est from graph)	6
Goebel and Hiller, 1999	TF>40	TRT	10	47±9	39±12	6-12 weeks
		sound generator only	16	56±9	55±13	
Kroener-Herwig <i>et al.</i> , 1999	all	wait list control	20	38.7±13	35.9±14	6-12 weeks
		education	20	36.3 graph	28 (graph)	
Delb, <i>et al.</i> , 2002	all	wait list control	13	48.1±17.6	47.4±20.1	3
		TRT-like (with hearing aid)	17	49.1±20.0	36.8±14.9	6
		TRT-like (with sound generator)	33	49.5±13.8	35.3±17.2	6
von Wedel, <i>et al.</i> , 2000	NR	counseling	49	47.2	42.8	12
		counseling and hearing aid or sound generator	51	48.6	36.8	12
		TRT	51	49.1	32.4	12
Schmitt and Kroener-Herwig, 2002	TF>25;	TRT	31	44 (graph)	32 (graph)	12
		education	23	43 (graph)	38 (graph)	4
Biesinger, <i>et al.</i> 1997*	TF>52	TRT	42	56.4±	42.3±	12
Goebel <i>et al.</i> , 1999	TF>40	TRT	10	47.2±9	39.7±12	4
		sound generator	16	55.7±9	55.3±13	4
Haerkotter <i>et al.</i> , 1999	TF>40	TRT	16	34.9±11	17.2±8	1

\* in Goebel and Hiller, 1999

Another problem in assessing the efficacy of any treatment for tinnitus is the selection of an appropriate outcome measure (i.e, how is treatment improvement measured?) The early trials considered by Wilson *et al.* (1998) and by Leal and Milne (1998) in their reviews and, subsequent ones described by others, used many different types of outcome measures to monitor “improvement.” In preparation for this project, we completed a literature review looking at trials that evaluated TRT, TRT-like, or TRT components by looking at change in the score of the Tinnitus Questionnaire (TQ), which is a well-validated instrument (Gobel and Hiller, 1998). Shown in Table 2 is a sample of different studies that have looked at the change in TQ score by treatment group.

Ongoing trials as of September 2008 and listing in clinicaltrials.gov includes both Phase I (NCT00124800, C. Bauer, PI) and Phase II (NCT00578058, R. Tyler, PI) trials, as well as a multi-site VA trial (NCT0036908, J. Henry, PI). This latter trial is an extension of the single-site VA trial by Henry *et al.*, (2004; 2006).

We will conduct a randomized, double-blind, placebo-controlled, multi-site clinical trial of TRT, the TRT Trial (TRTT), funded by the National Institute of Deafness and Other Communication Disorders, as a Phase III trial. We will conduct this trial in military clinical centers, which offer a diverse participant group for whom there is more likely to be a higher prevalence of noise-induced tinnitus than in the general population. Completion of a successful clinical trial of TRT at multiple U.S. military medical centers will be an important first step toward the development of a comprehensive program for the management of tinnitus in the military. Military clinical centers treat a broad range of tinnitus patients, including active duty and retired military personnel and their dependents. This breadth of patients to sample in the TRTT ensures balance across age, gender and ethnic groups. Study Participants will include functionally normal-hearing individuals who suffer severe tinnitus. They will be patients at participating military Clinical Centers staffed by the U.S. Air Force (Wilford Hall Medical Center, Lackland Air Force Base, San Antonio, Texas and David Grant Medical Center, Travis Air Force Base, Fairfield, California), Navy (Naval Medical Center, San Diego, California and Portsmouth Naval Medical Center, Norfolk, Virginia; Camp Pendleton Naval Hospital, Camp Pendleton, California), Army (Madigan Army Medical Center, Tacoma, Washington; Fort Rucker, Fort Rucker, Alabama; and Fort Campbell, Army Medical Center, Fort Campbell, Kentucky), and combined Army and Navy (Walter Reed National Military Medical Center, Bethesda, Maryland) . This unique involvement of multiple military clinical sites in the TRTT provides a large and diverse study population which is ideal for sampling, the efficacy of TRT in a broad age range of men, women, children, and minorities from across the United States.

We hypothesize that:

- TRT is an efficacious therapeutic intervention for severe disabling tinnitus;

- Both the DC and ST components are essential to the success of TRT;
- Elimination of either component part of the treatment will reduce the therapeutic benefit from TRT; and
- Beneficial effects of TRT will be greater than that for TRT implemented with placebo ST, which in turn will be greater than that achieved for the standard of care (SC) treatment for tinnitus in the military.

The primary research questions that the TRTT will seek to address are: Is TRT an efficacious intervention for disabling tinnitus? If so, then what are the dynamics of the treatment? What are the contributions from each component of TRT to its success? Are both components of TRT essential for achieving the primary effects of the intervention? What are the mechanisms that underlie these effects? Our goals are:

- To evaluate the efficacy of TRT and its component parts in habituating (decreasing) the perceived magnitude (sensation), perception (awareness), and negative emotional reactions (annoyance) to tinnitus, and to measure TRT treatment effect on the impact of tinnitus on each patient's quality of life;
- To characterize and monitor the temporal courses of the habituation effects (if any) during the TRT intervention, by comparing the resulting dynamics with those measured for SC in the military or the habituation effects measured for a partial TRT intervention administered with the placebo ST component;
- To determine the existence and scope of a sustained benefit(s) of TRT or that from either of the TRT components;
- To determine the relative contributions of the TRT components;
- To predict indices of successful treatment using statistical models; and
- To identify target groups for whom TRT is most likely to provide the greatest benefit.

The TRTT will be conducted to evaluate the efficacy of the DC and ST components of TRT within the context of a large-scale randomized clinical trial for the following reasons:

- TRT offers a comprehensive management protocol, including diagnostic (medical and audiological), educational, and treatment components, that is designed to habituate tinnitus annoyance and awareness (Gold *et al.*, 2000);

- In most clinics where TRT has been applied, about 80% of the TRT-managed patients have demonstrated reduced impact of tinnitus on their lives (Hazell, 1999);
- TRT is one of the few interventions for tinnitus (if not the only one) that is theory based and model driven (Jastreboff *et al.*, 1996);
- TRT is a gentle, flexible, noninvasive treatment that does not interfere with hearing and communication nor require frequent office visits. In many cases, follow-up counseling can be performed over the telephone and office visits are minimal (Gold *et al.*, 2000); and
- After medical intervention is ruled out (for otologic disease or for a psychiatric disorder), almost all tinnitus patients qualify for treatment, independent of the etiology. Thus TRT appears to offer an intervention strategy with broad general applicability (Jastreboff and Jastreboff, 2000).

Standard TRT calls for DC (and follow-up reinforcement counseling) combined with ST to facilitate habituation of the tinnitus (Jastreboff and Jastreboff, 2000). DC is a structured educational protocol that the clinician uses to provide TRT theory and related information to the patient. Both the DC and ST components appear to be beneficial in maximizing the success of TRT in the treatment of tinnitus, but Jastreboff (2000) believes that DC may be the more important component because he proposes that negative thoughts about the tinnitus must first be eliminated for the habituation process to begin. The DC component provides education of the patient about tinnitus in the context of Jastreboff's neurophysiological model (Jastreboff *et al.*, 1996). Ostensibly this instruction "demystifies" the patient's uncertainty about his or her tinnitus condition and neutralizes associated negative emotional reactions to the tinnitus. DC also addresses related questions and concerns about the tinnitus and provides an opportunity to discuss treatment options. Ultimately, the role of DC is to influence conscious levels of thought and appropriate changes in thinking about the tinnitus, leading to diminished associated emotional responses.

The important objective of ST is ultimately to enrich the tinnitus patient's sound environment so that the tinnitus habituation process, which has been initiated by DC, can be facilitated. ST, which is intended to modify auditory processing at subconscious levels, can be implemented in different ways (Gold *et al.*, 1996b). The standard approach is to use low-level SGs that produce a relatively soft broad-band noise. The bilateral ear-worn devices are fitted so as not to occlude the ear canals nor prevent normal communication. The sound level is set at "the mixing point", that point where the sound just begins to blend, but not mask the tinnitus signal. Patients are instructed to use the SGs throughout the waking day to achieve maximum benefit from ST. Alternative methods that ostensibly may achieve the same objective for ST are: amplified sound from hearing aids for hearing-impaired tinnitus patients and augmented environmental sound

(e.g., fans, soothing music, etc.) to enrich the patient's acoustic environment. For some tinnitus patients, ST from an enriched acoustic environment (with music or pleasant background sound) is sufficient after receiving DC. For them, the use of ear-worn sound devices is unnecessary for a successful intervention.

There have been numerous and repeated calls for a randomized controlled study of TRT for treating severe tinnitus (Coles, 1996; Leal and Milne, 1998; Wilson *et al.*, 1998; Baguley, 1999; Kroener-Herwig *et al.*, 2000). The TRTT would seem especially timely for treatment of military populations with debilitating tinnitus. Tinnitus now goes virtually untreated with the current SC in the military, because of the lack of a validated intervention. This void is undoubtedly disheartening both for patients and for clinicians.

Participants will be randomly assigned to full TRT treatment or to permutations of the components, including DC versus SC, and DC with ST from conventional SGs versus DC with ST from placebo SGs. If the TRTT outcome data support the efficacy of TRT, or any component of TRT, then all patients not receiving optimal therapy will be offered the opportunity to receive that treatment.

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## References:

Alster J, Shemesh Z, Ornan M, Attias J. Sleep disturbances associated with chronic tinnitus. *Biol Psychiatry*. 1993. 34:84-90.

Axelsson A, Barrenas ML. Tinnitus in noise-induced hearing loss. In: Dancer AL, Henderson D, Salvi RJ, Hamernik RP (ed). Noise-Induced Hearing Loss, Baltimore Mosby, p. 269-276, 1992.

Baguley DM. Chairman's introduction to Plenary 4: Tinnitus retraining therapy- tinnitus and the nature of evidence. *Proceedings of the Sixth International Tinnitus Seminar*. London, UK. 1999.

Bartnik G, Fabijanska A, Rogowski M. Our experience n treatment of patients with tinnitus and/or hyperacusis using the habituation method. *Proceedings of the Sixth International Tinnitus Seminar* (p. 415-7). London, UK. 1999.

Bartnik G. 2004. (Personal communication).

Berry JA, Gold SL, Frederick EA, Gray WC, Staecker H. Patient-based outcomes in primary tinnitus patients undergoing tinnitus retraining therapy. Presented at the Trilological Society, Southern Section, Marco Island, FL, Jan, 2001.

Boettcher FA, Salvi RJ. Functional changes in the ventral cochlear nucleus following acute acoustic overstimulation. *J Acoust Soc Am*. 1993. 94:2123-34.

Cacace, AT. The limbic system and tinnitus. In Snow JB (ed) Tinnitus: Theory and Management. London, UK, BC Decker, pp. 162-170, 2004.

At <http://www.clinicaltrials.gov> (accessed August 30, 2008)

Cochrane Collaboration summary review of Tinnitus Retraining Therapy

Coles R. Placebo effects and placebo treatment. *Proceedings of the Fifth International Tinnitus Seminar* (p. 6-8). Portland, OR. 1995.

Coles R. Tinnitus. In Kerr AG (ed), Scott-Brown Otolaryngology Volume 2, Chapter 18. London. Butterworth Heinemann.1997.

Davis A, Rafaie E. Epidemiology of Tinnitus. In R. Tyler (ed), Tinnitus Handbook (p. 1-23). San Diego, CA. Singular Press. 2000.

Delb W, D'Amelio R, Boisten CJ, Plinkert PK. [Evaluation of the tinnitus retraining therapy as combined with a cognitive behavioral group therapy]. 2002. *HNO* 50:997-1004.

Dineen R, Doyle J, Bench J. Managing tinnitus: a comparison of different approaches to tinnitus management training. *Br J Audiol*. 1997. 31:331-44.

Dobie RA. A review of randomized clinical trials in tinnitus. *Laryngoscope*. 1999. 109:1202-11.

Dobie RA. Medico-legal aspects of tinnitus. *Proceedings of the Seventh International Tinnitus Seminar* (p 272-6). Perth, Australia. 2002.

Formby, C. Hyperacusis and Related Sound Tolerance Complaints: Differential Diagnosis, Treatment Effect, and Models, *Seminars in Hearing*, 28(4), 2007.

Formby C, Gold S, Frederick E. Hyperacusis: a plastic disorder of chronic auditory gain? Abstracts of the 23<sup>rd</sup> Midwinter Meeting of the Association for Research in Otolaryngology, p. 218. 2000.

Gerken GM. Alteration of central auditory processing of brief stimuli: a review and a neural model. *J Acoust Soc Am*. 1993. 93:2038-49.

Gabriels, P. Children with Tinnitus. In G. Reich & J. Vernon (ed), *Proceedings of the Fifth International Tinnitus Seminar* (p. 270-5). Portland, OR. 1995.

Goebel G, Rübner D, Steppurat F, Hiller W, Heuser J, Fichter MM. Controlled prospective study of tinnitus retraining therapy compared to tinnitus coping therapy and broad-band noise generator therapy. *Proceedings of the Sixth International Tinnitus Seminar* (p. 302 – 6). London, UK. 1999.

Goebel G, Hiller W. Quality management in the therapy of chronic tinnitus., *Proceedings of the Sixth International Tinnitus Seminar* (p. 357–63). London, UK. 1999.

Gold SL, Formby C, Gray WC. Celebrating a decade of evaluation and treatment: the University of Maryland Tinnitus & Hyperacusis Center. *Am J Audiol*. 2000. 9:69-74.

Gold SL, Frederick EA, Formby C. Shifts in dynamic range for hyperacusis patients receiving tinnitus retraining therapy (TRT). *Proceedings of the Sixth International Tinnitus Seminar* (p. 297-301). London, UK. 1999.

Gold, S.L., Gray, W.C., He, S., and Jastreboff, P.J., Selection and Fitting of Noise Generators and Hearing Aids for Tinnitus Patients. In Reich, G.E. & Vernon, J.A. (eds): *Proceedings of the 5th International Tinnitus Seminar*, American Tinnitus Association, Portland OR, pp. 312-314, 1996.

Gold SL, Gray WC, Jastreboff PJ. Audiological evaluation and follow up. *Proceedings of the Fifth International Tinnitus Seminar* (p. 485-7). Portland, OR. 1995.

Graham, JM. Pediatric tinnitus. *Journal of Laryngology and Otology*, 1981. 95 (Suppl. 4), 117-20.

Haerkötter C, Hiller W. Combining elements of tinnitus retraining therapy (TRT) and cognitive-behavioral therapy: does it work? *Proceedings of the Sixth International Tinnitus Seminar* (p. 399 – 402). London, UK. 1999.

Haerkötter C. Kognitive verhaltenstherapie bei chronischen tinnitus: Evaluation neurer Ansätze. Eine Studie zu potentiellen Therapieeffekten verbesserter Edukation und apparativer Versorgung mit therapeutischem Rauschgeneratoren. Dissertation zur Erlangung des akademischen Grades Doktor der Sozialwissenschaften in der Fakultät für Sozial -und Verhaltenswissenschaften der Eberhard-Karls-Universität Tübingen. 2001. At  
<http://w210.ub.uni-tuebingen.de/dbt/volltexte/2001/268/pdf/HAER>

Hallam RS, Rachman S, Hinchcliffe R. Psychological aspect of tinnitus. In: Rachman S. (Ed) Contribution to Medical Psychology. Vol 3. Oxford, Pergamon Press, p. 31-4. 1984.

Hamberger CA, Liden G. The prognosis in hearing injuries following acoustic shot traumata. *Acta Otolaryngol* 1951. 39:160-5.

Hazell JWP. The TRT method in practice. *Proceedings of the Sixth International Tinnitus Seminar* (p. 92-8). London, UK. 1999.

Hazell JWP, Wood SM, Cooper HR, Stephens, SDG, Corcoran AL, Coles RRA *et al.* A clinical study of tinnitus maskers. *Br J Audiol*. 1985. 19:65-146.

Humes, L.E., Joellenbeck L.M., Durch J.S. Noise and Military Service: Implications for Hearing Loss and Tinnitus. Washington, DC: The National Academics Press, 2005.

Kentish R. C., Crocker, S.R. & McKenna, L. Children's experience of tinnitus. *Proceedings of the Sixth International Tinnitus Seminar* (p. 220 – 3). London, UK. 1999.

Heitzmann T, Rubio L, Cardenas MR, Zofio E. The importance of continuity in TRT patients: results at 18 months. *Proceedings of the Sixth International Tinnitus Seminar* (p. 118-24). London, UK. 1999.

Henry J.A., Schechter MA, Zaugg TL, Griest TL, Jastreboff, PJ et al. Outcomes of Clinical Trial: Tinnitus marking versus tinnitus retraining therapy. *J Am Acad Audiol* 2006. 17:104-132.

Henry JA, Schechter MA, Regelin RT, Dennis KC. Veterans and tinnitus. In: Snow JB (ed.) Tinnitus: Theory are Management. Lewiston, NY: BC Decker, Inc., p. 337-355.

Herraiz C, Hernandez FJ, Machado A, De Luca P, Tapia MC. Tinnitus retraining therapy: our experience. *Proceedings of the Sixth International Tinnitus Seminar* (p. 483-4). London, UK. 1999.

Herraiz C, Hernandez FJ, Plaza G, de los Santos G. Long-term clinical trial of tinnitus retraining therapy. *Otolaryngol Head Neck Surg* 2005. 133(5): 774-779.

Jacobson GP. Editorial in Special Issue on tinnitus. *J Am Acad Audiol*. 2000. 11: preface.

Jakes SC, Hallam RS, Rachman S, Hinchcliffe R. The effects of reassurance, relaxation training and distraction on chronic tinnitus sufferers. *Behav Res Therapy*. 1986. 24:497-507.

Jastreboff PJ, Phantom auditory perception (tinnitus): mechanisms of generation and perception. *Neurosci Res* 1990. 8:221-54.

Jastreboff PJ. Tinnitus as a phantom perception: theories and clinical implications. In: Vernon J, Miller AR (eds). Mechanisms of Tinnitus. Boston, Allyn & Bacon. p. 73-94. 1995.

Jastreboff PJ. Clinical implications of the neurophysiological model of tinnitus. *Proceedings of the Fifth International Tinnitus Seminar* (p. 500-7). Portland, OR. 1995.

Jastreboff PJ. Tinnitus. In: Current Therapy in Otolaryngology- Head and Neck Surgery. Sixth Edition. Gates GA (ed). St Louis, Moby-Year Book Inc. p. 90-5. 1998.

Jastreboff PJ, Gray W.C., Gold SL. Neurophysiological approach to tinnitus patients. *Am J Otol*. 1996. 17:236-40.

Jastreboff PJ, Gray W.C., Madhouse DC. Tinnitus and Hyperacusis. In Otolaryngology Head and Neck Surgery Volume Four, Third Edition. Cummings *et al.* (ed). St Louis, Moby , p 3198-22. 1998.

Jastreboff PJ, Hazell J.P. A neurophysiological approach to tinnitus: clinical implications. *Br J Audio* 1993. 27:7-17.

Jastreboff PJ, Jastreboff MM. Tinnitus Retraining Therapy (TRT) as a method for treatment of tinnitus and hyperacusis patients. *Am J Acad Audio* 2000. 11:162-77.

Jastreboff PJ, Jastreboff MM. How TRT derives from the neurophysiological model. *Proceedings of the Sixth International Tinnitus Seminar* (p. 87-91). London, UK. 1999.

Kroner-Herwig B, Easer G, Frenzel A, Fritsche G, Schilkowsky G. Results of an outpatient cognitive-behavioral group treatment for chronic tinnitus. *Proceedings of the Sixth International Tinnitus Seminar* (p. 369 – 72). London, UK. 1999.

Leal P, Milne R. Tinnitus retraining therapy. Development and Evaluation committee report No. 83. The Wessex Institute for health Research and Development. At <http://www.epi.bris.ac.uk/rd>

Lockwood AH, Salvi RJ, Coad ML *et al.* The functional neuroanatomy of tinnitus: evidence for limbic system links and neural plasticity. *Neurol* 1998 50:114-20.

McFadden D. Tinnitus: Facts, Theories, and Treatments. Washington , DC, National Academy Press. 1982.

McKinney CJ, Hazell J.P., Graham RL. Retraining therapy- outcome measures. *Proceedings of the Fifth International Tinnitus Seminar* (p. 524-5). Portland, OR. 1995.

McKinney CJ, Hazell J.P., Graham RL. An evaluation of the TRT method: *Proceedings of the Sixth International Tinnitus Seminar* (p. 99 – 105). London, UK. 1999a.

McKinney CJ, Hazell J.P., Graham RL. Changes in loudness discomfort level and sensitivity to environmental sound with habituation based therapy. *Proceedings of the Sixth International Tinnitus Seminar* (p. 499 – 501). London, UK. 1999b.

Meikle, M.B. Electronic access to tinnitus data: The Oregon Tinnitus Data Archive. *Otolaryngol Head Neck Surg* 1997. 117, 698-700.

Mirz F, Gjedde A, Ishizu K, Pedersen CB. Cortical networks subserving the perception of tinnitus - a PET study. *Acta Otolaryngol Suppl* 2000. 543:241-3.

Mirz, Pedersen V, Ishizu K, Johannsen P, Ovesen T, Stodkilde-Jorganse H, Gjedde A. Positron emission tomography of cortical centers of tinnitus. *Hear Res* 1999. 134:133-44.

Newman CW, Jacobsen GP, Spitzer JB. Development of the tinnitus Handicap Inventory. *Arch Otolaryngol Head Neck Surg* 1996. 122:143-8.

Ohlin DW. Fifteen years revisited: the prevalence of hearing loss among selected U.S. Army branches (Hearing Conservation Special Study No. 51-01-PM82-93) Aberdeen Proving Ground, Md: Us Army Environmental Hygiene Agency. 1992.

Parnes SM. Current concepts in the clinical management of patients with tinnitus. *Eur Arch Otorhinolaryngol* 1997. 254:406-9.

Phillips JS, McFerran D. Tinnitus Retraining Therapy (TRT) for tinnitus. *Cochrane Database of Systematic Reviews*. 2010. Issue 3 Art o. CD007330 DO I: 10.1002/14651858.CD007330.pub2.

Roth Y, Kronenberg J, Lotem S, Leventon G. Blast injury of the ear. *Harefuah* 1989. 117:297-301.

Salmivalli A. Acoustic trauma in regular army personnel: clinical audiological study. *Acta Otolaryngol Suppl* 1989. 222:1-85.

Schmitt C, Kroner-Herwig B. Comparison of tinnitus coping training and TRT: Are they superior to education? *Proceedings of the Seventh International Tinnitus Seminar* (p 272-6). Perth, Australia. 2002.

Schneider E, Hocker KM, Lebisch H, Pilgramm M. Does systematic noise stimulation improve tinnitus habituation? *Proceedings of the Sixth International Tinnitus Seminar* (p. 391 – 3). London, UK. 1999.

Sheldrake JB, Hazell J.P., Graham RL. Results of tinnitus retraining therapy. *Proceedings of the Sixth International Tinnitus Seminar* (p. 292-6). London, UK. 1999.

Sheldrake JB, Jastreboff PJ, Hazell J.P. Perspectives for total elimination of tinnitus perception. *Proceedings of the Fifth International Tinnitus Seminar* (p. 531-6). Portland, OR. 1996.

Tyler RS. Perspectives on tinnitus. *Br J Audio* 1997. 31:381-6.

Tyler RS. Cited in *Tinnitus Today*, American Tinnitus Association, Portland, OR. p.12, September 2004.

Tyler RS. Personal communication, 2005.

Vernon JA. Attempts to relieve tinnitus. *J Am Audio Soc* 1977. 2:124-61.

Von Wedel H, von Wedel UC. [An assessment of tinnitus retraining therapy]. *HNO* 2000. 48:887-901

Walden BE, Prosek RA, Worthington DW. The prevalence of hearing loss with selected U.S. Army branches (Interagency No. IAO 4745). Washington, DC. US Army Medical Research and Development Command. 1975.

Wilson PH, Henry JL, Anderson HG, Hallam RS, Lindberg P. A critical analysis of directive counseling as a component of tinnitus retraining therapy. *Br J Audio* 1998. 32:273-86.

Ylikoski ME, Ylikoski JS. Hearing loss and handicap of professional soldiers exposed to gunfire noise. *Scand J Work Environ Health*. 1994. 20:93-100.

Zachriat C. Vergleichende Evaluationsstudie zur Wirksamkeit des Tinnitus-Bewältigungs-Trainings und der Tinnitus-Retraing-therapie. Dissertation zur Erlangung des Doktorgrades der Mathematisch-Naturwissenschaftlichen Fakultäten der Georg-August-Universität zu Göttingen. 2003. At <http://webdoc.sub.gwdg.de/diss/2003/zachriat/zachriat.pdf>

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## Chapter 2

### Research Plan

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#### **2.1 Purpose/Objectives of the Trial**

The primary objective of the Tinnitus Retraining Therapy Trial (TRTT) is to assess the efficacy of Tinnitus Retraining Therapy (TRT) as a treatment for severe debilitating tinnitus. TRT is an habituation-based intervention that uses directive counseling (DC) and low-level sound therapy (ST) to facilitate habituation of the awareness of tinnitus, its annoyance, and impact on the patient's life.

Millions of Americans experience varying levels of distress from tinnitus, but tinnitus is severely disabling for as many as 2-5 million individuals. In the absence of a cure for debilitating tinnitus and with no proven intervention shown conclusively to ameliorate the symptoms or distress caused by tinnitus, TRT has become the therapeutic intervention "of this decade." TRT, however, remains highly controversial and requires validation in a rigorous, controlled clinical trial.

The TRTT is a randomized, double-blind, placebo-controlled, multi-center, clinical trial for individuals with intolerable tinnitus. The TRTT will include persons with functionally adequate hearing sensitivity who do not need to use hearing aids. Eligible Study Participants will be randomized to one of three treatment arms to compare the efficacy of full TRT versus the standard of care in the military (SC). The trial design will also contrast the treatment effects of DC in combination with ST as implemented in TRT with conventional low-level sound

generators (SGs) versus placebo SGs. In addition, the TRTT will evaluate the efficacy of DC by comparing individuals randomized to DC and placebo SGs versus SC.

The TRTT will be conducted at flagship Air Force, Navy, and Army Medical Centers with active-duty and retired military personnel and their dependents. The likely higher incidence of noise-induced tinnitus than in the general population and the great diversity of this study population makes the U.S. Armed Forces an ideal study group for a clinical trial of TRT.

The primary outcome to be measured in the TRTT will be change in scores on the Tinnitus Questionnaire (TQ) longitudinally assessed between baseline and follow-up (i.e., at 3, 6, 12 and 18 months following treatment). Secondary outcomes include change in other tinnitus repeated-measures self-report tinnitus questionnaires, changes in the sub-scales of the TQ, and change in the Digit Symbol Substitution Task (DSST), EuroQOL, and audiological data.

The primary questions we ask in the TRTT include:

- 1) Is treatment for intolerable tinnitus with TRT more efficacious than SC, which is the usual and customary care in the military Clinical Centers, for habituating the tinnitus sensation, its awareness, annoyance, and impact on the patient's life as measured by change in the TQ?
- 2) What are the contributions of DC and ST from conventional SGs to TRT treatment?
  - Are the treatment benefits for conventional SGs greater than those for placebo SGs?
  - Is DC used in TRT more effective than SC?
- 3) What is the time course of the treatment effect for each treatment group?
- 4) Can successful treatment for any treatment group be predicted by responses on baseline psychological questionnaires or by demographic groups ?
- 5) Does successful treatment depend on initial severity of the tinnitus condition as measured by the TQ at baseline?

The specific aims of the study are to:

- Develop and maintain a collaborating structure of Clinical Centers and related coordinating and resource centers for the purpose of performing the randomized trial of TRT;

- Enroll eligible patients into the study at Clinical Centers;
- Collect data on patients before, during, and at the end of treatment using a standard set of procedures and forms;
- Assemble data for the comparison of randomized treatment groups;
- Perform analyses of randomized treatment groups to assess the effect of treatment on the subjective impact of tinnitus on a participant's life;
- Perform analyses to assess other outcomes associated with treatment, including tinnitus self-report questionnaires, cognitive and quality of life questionnaires, audiological measures, and psycho-acoustic indices for secondary outcomes.
- Characterize the epidemiologic features of patients with severe tinnitus; and
- Predict indices of successful treatment and identify target groups for whom treatment is most likely to provide the greatest benefit by using statistical models and methods in the analyses of various demographic and outcome measures data.

## **2.2 Design of the Study**

The TRTT involves participants with debilitating tinnitus and functionally normal hearing who would not routinely use or benefit from hearing aids. Participants will be randomized to one of three treatment groups. The goal is to enroll 76 participants per treatment group for a total of 228 Study Participants. Individuals meeting the eligibility criteria will have an equal probability of being randomized to one of the three treatment groups. The randomized schedule will be stratified by Clinical Center. Within each stratum, allocations will be balanced across treatment groups within blocks of consecutive patients. Blocks will be randomly permuted multiples of 3.

Details of the treatment protocols are provided in Chapter 11, 12, and 13. Scheduled study follow-up visits are the same for all treatment groups. These visits will be at 3, 6, 12, and 18 months following the initial treatment visit, and annually thereafter until study close-out. Details of patient visits and examinations are provided in Chapter 10.

### **2.2.2 Choice of Study Population**

Specific medical, audiological, and psychological criteria for inclusion into, or exclusion from, this randomized trial have been developed. These criteria are described in Chapter 4. The main feature of the study population is that patients have severely debilitating subjective tinnitus with onset of symptoms at least one year prior to treatment (See Chapter 5 for details of enrollment.) The Clinical Center study team, including a Study Otolaryngologist, a Clinical Coordinator, at least two Study Audiologists, and a Data System Operator, will be responsible for accepting or rejecting patients for participation into the TRTT.

Examinations, tests, and interviews will provide the following information:

Inclusion:

- Evidence of debilitating subjective tinnitus;
- Evidence that the onset of tinnitus occurred at least one year prior to enrollment in a treatment group; and
- Evidence of achieving good patient follow-up.

Exclusion:

- Evidence of concurrent disease that might be medically or surgically manageable and lead to resolution of tinnitus;
- Evidence of concomitant litigation or financial claims related to tinnitus other than customary Veterans Administration claims upon retirement from the Military; or
- Conditions that might interfere with the patient carrying out the evaluation procedures at baseline or during follow-up.

Clinicians in military medical centers, who have been made aware of this study and who have expressed support for it, will refer willing patients who meet the eligibility criteria. If the TRTT is to achieve its stated goal of recruiting adequate numbers of patients for the study within the allocated time period of the TRTT, then a concerted effort will be needed. A major thrust at the outset of the study will focus on patient and referring clinician recruitment. In subsequent years of recruitment, we will develop and maintain liaisons with Clinical Center and referring military clinicians to facilitate patient recruitment. Although the study is designed to produce comparable treatment groups, subtle variations in the characteristics of those individuals enrolled in the

treatment groups may affect the generalizability of the results. Thus referral of all eligible patients is sought.

### **2.2.3 Outcome Measures**

The primary outcome to be measured in the TRTT is the difference in scores on the Tinnitus Questionnaire (TQ) between baseline and follow-up, assessed longitudinally, at 3, 6, 12, and 18 months of treatment. Our primary objective is to test the hypothesis that TRT (DC and conventional SG) will significantly reduce the severity of debilitating tinnitus compared with SC, as currently offered to tinnitus patients in the military Clinical Centers. This longitudinal analysis assumes a linear treatment effect over time. We will also compare the difference in TQ score at 18 months (end of treatment) for individuals assigned to TRT with those assigned to SC as a secondary analysis.

The secondary objectives of the TRTT are to investigate the efficacy of each of the TRT components; DC, and ST with conventional SGs. We will investigate whether ST using conventional SGs is more effective in treating Study Participants with debilitating tinnitus compared with placebo SGs given that both groups are assigned to DC. Similarly, we will investigate whether DC is more effective in treating Study Participants with debilitating tinnitus compared with SC, when DC is combined with placebo SGs. The outcomes will be the same as for the primary outcome, i.e., longitudinally assessed change in TQ score over 18 months, the end of treatment.

Secondary outcome data will include change in the sub-scales of the TQ, and change in scores for additional tinnitus questionnaires, including:

- Tinnitus Handicap Inventory;
- Tinnitus Functional Index; and
- Visual analogue scale of the TRT Interview.

Additional secondary outcomes will include change in the:

- Digit Symbol Substitution Task; and
- EuroQol.

Additional secondary measures include change in pure-tone and speech audiometry, loudness discomfort level, and psychoacoustic measures of tinnitus properties for pitch and loudness. The procedures for obtaining these and other measurements are described in Chapters 6, 7, and 9.

We will also evaluate the impact of change in tinnitus severity on outcomes related to the participant's health by assessing change from baseline in the following:

- Hearing handicap Inventory; and
- Beck Depression Inventory Fast Screen.

### **2.3 Sample Size Calculations**

The sample size for the studies is based on the minimum differences (effect size) to be detected between the mean change in TQ score from baseline to follow-up by treatment group. Based on a literature survey (see Chapter 23) and conversations with Drs. Hallam, who developed the TQ, and Hiller, who has extensively used the TQ, we estimate that the minimal clinically significant effect of treatment is a change of 10 points on the global score of the TQ, or a change between 9 to 11 points on the Emotional Distress.

We chose to use a type I error or  $\alpha$  of 0.05 and a two-sided test, spending  $\alpha$  among the three major comparisons for an analyses at one time point only (i.e, at the end of treatment at 18 months). These assumptions allow for a conservative estimate, since the primary outcome will be longitudinally assessed over 18 months. With these assumptions, we estimate that with 228 Study Participants and allowing for 10% attrition, we will have greater than 95% power to detect a difference of 10 points in the TQ score of Study Participants assigned to TRT (DC + SG) compared with SC. In addition, we will have 80% power to detect a 7 point difference in the component group comparisons, (i.e, comparison of DC with SC for individuals assigned to DC and placebo SGs, and comparison of conventional with placebo SGs for individuals assigned to DC). These sample sizes will also have sufficient power to account for an equivalent point change in the "Emotional Distress" sub-scale and also for the longitudinal analyses.

### **2.4 Analysis of Results**

Analysis of data pertaining to study procedures and treatment efficacy will be carried out by the Data Coordinating Center (DCC) staff throughout the recruitment and follow-up phases of the study. Reports will be generated for the Steering Committee (STC) and the Data and Safety Monitoring Board (DSMB). Data related to treatment efficacy, including consideration of any adverse effects, will be provided initially to the DSMB, but not to the STC. If there is evidence

prior to the planned end of the study that one or more of the treatments is significantly superior (or inferior) to the others, then the DSMB may recommend that randomization be discontinued. Any such recommendation would be forwarded by the DSMB to the STC for implementation. At the end of the study, analyses relating to treatment efficacy for the treatment groups will be provided to the STC, as well as to DSMB.

The DCC statisticians will work closely with the DSMB and clinical investigators to insure that appropriate statistical analyses of the primary and secondary outcome measures are carried out. Analyses will be performed based on the principle of intention to treat, i.e., in the analysis Study Participants will be included in the group to which they were randomized, regardless of whether they adhered to the treatment. Repeated measures analyses will compare treatment groups using Generalized Estimating Equations (GEE) by modeling outcomes as a function of treatment assignment, time and potentially influential baseline variables. Additional comments on the statistical considerations of the study are provided in Chapter 23.

The consistency of the study results will be examined in this study. For example, some of the secondary outcomes measures to be evaluated are related to basic hearing function and sound tolerance, and these factors may interact with tinnitus to affect the primary outcome measures. The data obtained in the study will be analyzed to assess whether the changes noted for various outcomes are consistent with current knowledge about their relations with one another and with the tinnitus condition. It is expected that this study will add to our understanding of the relation among various measures obtained from the severely debilitated tinnitus patients enrolled in this study.

## **2.5 Methods to Control Bias**

The most important elements in controlling bias are:

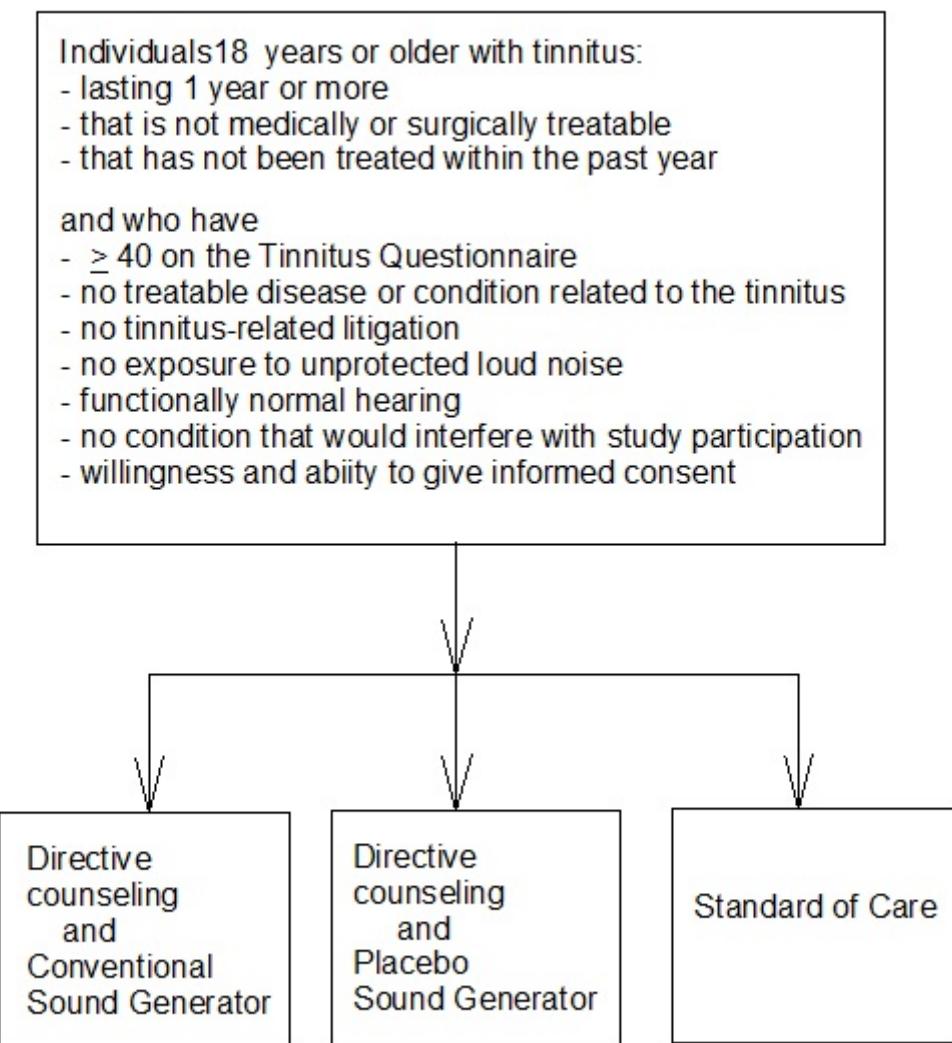
- Application of objective criteria in evaluating eligibility and study outcomes;
- Use of standard data collection procedures and forms;
- Randomization of eligible patients to study treatment;
- Use of a double-blind placebo to control for treatment effects from ST; and
- Intention-to-treat analysis.

The existence of procedures for randomization, use of a placebo SG, implementation of objective criteria for outcomes and standard data collection protocols and forms are critical for

controlling, but cannot completely eliminate all bias. The detection of bias by monitoring the factors and variables listed above is one of the responsibilities of the Quality Assurance Committee (QAC) outlined in Chapter 3 and 16. If this Committee believes that one or more of the functioning Clinical Centers is failing to adhere to the quality standards required for the successful completion of the study, then the QAC will submit a report of the circumstances to the STC and a recommendation for the appropriate action.

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**Figure 1**  
**Study Participant Entry in the TRTT**



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## Chapter 3

### Organizational Structure

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### 3.1 Introduction

Leadership in the Tinnitus Retraining Treatment Trial (TRTT) is shared by the Study Chair and the Director of the Data Coordinating Center (DCC):

- The Chair's Office will be responsible for the overall scientific and administrative aspects of the trial and delivery of all clinical treatments. Responsibilities of the Chair's Office will include clinical training and quality assurance in performing TRT, TRT components, and the Standard of Care (SC) treatments, and the various medical, audiological, and psychoacoustic tests. Technical questions with regard to treatment and complications will be directed to this office.
- The DCC oversees scientific aspects of the study design, and serves as the focus of study communications, training and certification of clinical staff in trial procedures, protocol interpretation, data processing, data analysis, and quality assurance activities. The DCC will also be responsible for evaluating adherence to protocol of all data.

The National Institute on Deafness and Other Communication Disorders (NIDCD) of the National Institutes of Health funds the TRTT and serves as the Project Office with a designated representative to the study.

General Hearing Instruments, Inc. provides the sound therapy devices.

The Clinical Centers are responsible for patient recruitment, treatment administration, and follow-up.

The study management structure consists of four functional primary standing committees and the Full Investigative Group, as follows:

- Steering Committee (STC);
- Executive Committee (EC);
- Quality Assurance Committee (QAC);
- Data and Safety Monitoring Board (DSMB); and
- Full Investigative Group (FIG).

The function of each committee is described in the sections that follow.

### **3.2 Functioning centers and their responsibilities**

The study operations are carried out by the following Centers, each of which serves an important, distinct role:

- Study Chair's Office;
- DCC;
- NIDCD Project Office; and
- Nine Clinical Centers, located at Military sites.

The specific functions of each of the centers are described in detail in the following sections.

### **3.2.1 Chair's Office**

Location: University of Alabama, Tuscaloosa, Alabama

Director: Craig Formby, PhD

The Chair's Office is responsible for the overall scientific and administrative conduct of the trial. Specific duties include:

- Supervision of the overall study by integrating the activities of the DCC and Clinical Centers;
- Coordination of the subcontract to Military Clinical Centers;
- Resolution of all technical and scientific questions with regard to clinical treatment issues and complications;
- Preparation of training materials related to the treatment options;
- Organization and conduct of Clinical Center training sessions for audiologists and physicians;
- Development and implementation of quality assurance measures used to monitor treatment protocol in TRTT Clinical Centers jointly with the DCC;
- Monitoring and supervision of Clinical Center activities, Study Audiologists and Otolaryngologists;
- Arrangements for the STC, EC, QAC, and the FIG meetings;
- Preparation and distribution of meeting minutes to the appropriate Committee members;
- Surveillance of the published literature on treatment of tinnitus and TRT, with prompt reporting of critical information;
- Interpretation of scientific data and outcomes measures; and
- Preparation of scientific manuscripts and meeting presentations together with the DCC and Clinical Center Directors.

Study personnel at the Chairman's Office include the Study Chair, TRT and SC Training/Protocol Monitors, Otolaryngologist Training Coordinator, and Administrative Assistant/Meeting Coordinator and Business Manager.

### **3.2.2 Data Coordinating Center**

Location: Center for Clinical Trial, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Director: Roberta Scherer, PhD

The responsibilities of the DCC are to provide expertise for the study in the design and operation of the trial, including all activities related to data processing, training, quality assurance and control, data analyses, and paper writing activities. The DCC will:

- Provide expertise in study design and operation;
- Provide representation to the STC, EC, DSMB, QAC, and FIG;
- Provide arrangements for DSMB meetings;
- Prepare, maintain, and distribute study documents such as the Manual of Procedures and data collection forms, in collaboration with other study investigators;
- Prepare and maintain a web-based up-to-date address, telephone, and email directory of the TRTT investigators and study staff;
- Prepare training materials related to the trial and train Clinical Center Staff in study methods and procedures, especially with regard to data collection;
- Coordinate certification of Clinical Center staff;
- Coordinate communication among Clinical Center staff;
- Provide expertise in study design and operation;
- Supervise the TRTT data collection, processing, and analysis procedures;
- Respond to day-to-day problems regarding data collection and protocol administration at the Clinical Centers;

- Generate randomization schedules for each Clinical Center;
- Review data transmitted by Clinical Centers, visually and electronically, for completeness, accuracy, and consistency;
- Resolve data errors or problems with Clinical Centers;
- Develop a web-based data system to receive and process data forms, audiological information, and materials related to treatment quality assurance;
- Develop and implement quality control monitoring programs for data processing;
- Develop and maintain a storage system for all study documents and materials;
- Develop and implement a data storage system with security and backup features for all study data;
- Develop and implement quality assurance measures to monitor treatment protocol in TRTT Clinical Centers in collaboration with the Chair's Office;
- Coordinate study meetings and prepare and distribute meeting materials prior to each meeting;
- Analyze study data including analysis relative to the DSMB and the objectives and aims of the trial and the observational study;
- Serve as the official TRTT archive;
- Maintain computerized master file of edited study data;
- Provide facilities and staff to carry out analyses designed to monitor performance of the TRTT Clinical Centers, including patient recruitment and eligibility;
- Work with other study investigators in the preparation of scientific reports for publication;
- Prepare all necessary reports for NIDCD and all study committees; and
- Prepare a public use data set of TRTT data.

Staff at the DCC during the five years of the trial include the Director of the DCC, Biostatistician, Director of Information Management, Co-Investigator, Database Programmer, Statistical Programmer/Analyst, Project Coordinator, Research Assistant, and Administrative Assistant.

### **3.2.3 National Institute on Deafness and Other Communication Disorders Project Office**

The National Institute on Deafness and Other Communication Disorders (NIDCD) Project Office is responsible for assigning a Project Officer to the study. Gordon Hughes, MD, is the NIDCD Project Officer. His responsibilities include:

- Serving as a voting member of the Steering and Executive Committees and as a non-voting member of the Data and Safety Monitoring Board;
- Serving as liaison between the sponsor and the TRTT;
- Providing administrative and fiscal advice;
- Participating in site visits to Clinical Centers; and
- Participating in the design and analysis of the TRTT.

### **3.2.4 General Hearing Instruments, Inc.**

General Hearing Instruments, Inc.(GHI), located in New Orleans, Louisiana, will provide the digital sound therapy (ST) devices for the TRTT. Both the conventional and the placebo sound generators will be manufactured and supplied by GHI. President of GHI, Mr. Roger Juneau will oversee the manufacturing and quality control, and supply acoustic output characteristics of all devices used in the TRTT. GHI will work in coordination with the Study Chair and the DCC to facilitate custom device production and timely return of the completed devices for the double-blind randomized ST assignment for each Study Participant at their Clinical Center. GHI also will provide the necessary software to download and analyze each Study Participant's ST usage pattern and sound exposure history at follow-up visits. This information will be used to assess ST compliance and for counseling of non-compliant participants.

### 3.2.5 Clinical Centers

#### 3.2.5.1 Military Clinical Centers

Nine sites of the United States Armed Forces will serve as Clinical Centers. The Air Force, Army, and Navy will each provide Clinical Center sites for the TRTT. Each center has a Clinical Center Director, who is responsible for supervising activities at that center:

##### **Air Force Clinical Centers**

David Grant Medical Center (DGMC)  
Travis Air Force Base  
Fairfield, California

Wilford Hall Medical Center (WHMC)  
Lackland Air Force Base  
San Antonio, Texas

##### **Army Clinical Centers**

Madigan Army Medical Center  
Tacoma, Washington

Fort Campbell  
Clarksville, Tennessee

Fort Rucker  
Fort Rucker, Alabama  
Lyster Army Health Clinic

US Army Aeromedical Center

##### **Navy Clinical Centers**

Naval Hospital Camp Pendleton (NHCP)  
Camp Pendleton, California

Naval Medical Center Portsmouth (NMCP)  
Portsmouth, Virginia

##### **Director**

Maj. Cynthia Eades, MS  
Flight commander, Audiology Clinic  
(retired)

Col. Ben Sierra-Irizarry, AuD  
Director, Communications Research  
and Training

##### **Director**

Maj. David Pedersen, MS, AuD  
Chief, JBLM Hearing Program

LTC. Amy A. Blank, AuD  
Chief, Army Hearing Program Fort  
Campbell

Col Lynnette Bardolf, PhD  
Interim DDCS, Chief, Audiology;  
Clinical and Research Audiologist

Maj. Scott McIlwaine, MS, Aud  
Acoustics Branch Chief

##### **Director**

Priscilla George, AuD  
Division Head, Audiology

George Conley, MD  
Dept Otolaryngology Head and Neck  
Surgery

Naval Medical Center San Diego (NMCSD)  
San Diego, California

Cynthia Kirby, AuD  
Head Audiology Division

**Navy and Army Clinical Center**

Walter Reed National Military  
Medical Center (WRNMMC)  
Bethesda, Maryland

**Director**

Shoshannah Kantor, Au.D.  
Integrated Occupational and  
Environmental Medicine Department

### **3.2.6.2 Clinical Center Responsibilities**

The Clinical Centers will complete both Clinical Center and personnel certification procedures prior to initiation of recruitment activities. Altogether clinics are expected to recruit 228 Study Participants, with follow-up continuing for a minimum of 18 months with extended annual follow-up to study close-out. The number of Study Participants per clinic varies depending on when the clinic entered the study as a participating site.

In addition, all TRTT Clinical Centers have the following responsibilities:

- To recruit prospective referral sources and participants leading to fulfillment of planned target enrollment goals;
- To carry out the patient education and consent process;
- To enter information about all patients screened for eligibility, the outcome of their screening, and if ineligible, the reason for ineligibility in the TRTT web-based data system;
- To obtain treatment assignments from the TRTT website for eligible and willing patients and to adhere to those assignments;
- To make the necessary preparations for providing the assigned treatment prior to randomization;
- To follow the treatment protocol for each patient and complete the data collection forms describing treatment in a timely fashion;
- To follow the recruited randomized patients using specified follow-up procedures;
- To perform data management activities, including proper completion of data collection forms;

- To transmit information on data collection forms to the DCC using the TRTT website on a regular basis;
- To respond to requests for clarification or correction of data by the DCC promptly and accurately;
- To attend training sessions conducted by the Chair's Office and DCC for quality assurance, training, certification and re-certification of personnel;
- To undergo certification and re-certification procedures designed to maintain the quality of study activities;
- To participate in meetings of the FIG;
- To be visited by the site visit teams at least twice over the course of the Study and to provide requested information or demonstrations.

Clinical Center staff include at least two Study Audiologists, a Clinical Coordinator, a Study Otolaryngologist, and a Data System Operator. The Center Director may hold any of these positions, but would typically be either a Study Audiologists or Study Otolaryngologist.

### **3.3 Functioning committees and their responsibilities**

Committees whose functions serve the entire study have members drawn from the participating centers. The Data and Safety Monitoring Board will also have members from the outside community. The committees include the following:

Steering Committee (STC);

Executive Committee (EC);

Quality Assurance Committee (QAC); and

Data and Safety Monitoring Board (DSMB).

The function of each committee is described in the sections that follow.

### **3.3.1 Steering Committee (STC)**

The following individuals are permanent voting members of the TRTT STC:

- Study Chair, who chairs the STC;
- Director of the DCC;
- Biostatistician;
- Six Clinical Center Directors; and
- the NIDCD Project Officer.

Other members of the DCC may be non-voting members of the Steering Committee.

The responsibilities of the Steering Committee include:

- Review and approval of the procedures for the conduct of the trial, including: recruitment and treatment procedures, data collection procedures and forms, data management and analysis procedure, and the study handbooks and manuals;
- Resolution of technical issues that arise during the execution of the trial;
- Receipt and action on advice from DSMB concerning the continuation and conduct of the trial, including recommendations concerning premature termination because of evidence of beneficial or harmful results;
- Appointment or termination of subcommittees related to the trial, (e.g., subcommittees on data analysis, quality control, training, and publication);
- Review of study progress (including recruitment) and action to correct deficiencies;
- Approval of major changes to the Manual of Procedures;
- Review and approval of all ancillary studies;
- Resolution of operational problems brought to the Committee by Directors of the Clinical Centers, the DCC, or the Study Chair;

- Priority setting; and
- Overseeing publication of study findings.

The STC meets face-to-face two times during Years 01, and once per year in subsequent years in conjunction with the FIG meetings. Telephone conference call meetings will be held monthly during the intervals between face-to-face meetings.

### **3.3.2 Executive Committee (EC)**

The members of the EC are:

- Study Chair;
- Director of the DCC; and
- NIDCD Project Officer.

All members of the Executive Committee serve for the duration of the trial, provided they continue in their designated capacities.

The Executive Committee is chaired by the Study Chair. The responsibilities of this Committee include:

- Training and certification of Clinical Centers;
- Implementation of decisions made by the STC;
- Action on matters affecting day-to-day operations of the trial;
- Performance of executive functions for the trial, including scheduling meetings and preparing agenda;
- Coordination of the preparation of progress reports; and
- Performance of other functions assigned by the STC.

The EC meets by conference telephone call, monthly, throughout the trial. Face-to-face meetings may occur in place of conference calls and may also occur on an *ad hoc* basis.

Additional meetings may be arranged to coincide with scheduled DSMB or STC meetings and may be called by any one of the members.

### **3.3.3 Data and Safety Monitoring Board (DSMB)**

The DSMB has the responsibility for monitoring ethical aspects of the study and statistical analyses of study data, as they are collected, for evidence of harmful or beneficial treatment effects. The members of this committee are appointed by NIDCD. Its composition may include:

- DSMB Chair, chosen from among the DSMB appointed members;
- Three additional voting members not affiliated with the study, including at least one person from the fields of otolaryngology, epidemiology, and biostatistics;
- One non-health professional representing ethical concerns regarding the patients (e.g., clergy, lawyer);
- One consumer representative; and
- Non-voting members from TRTT (Study Chair, Director of the DCC, Biostatistician, Project Coordinator, and the NIDCD Project Officer).

The current DSMB members are

- Jay F. Piccirillo, M. D. , Chair, Washington University School of Medicine;
- Judy R. Dubno, Ph.D. , Medical University of South Carolina;
- James A. Henry, Ph.D., National Center for Rehabilitative Auditory Research, VA Medical Center; and
- Jennifer Schumi, Ph. D., Statistics Collaborative, Inc.

Specific responsibilities of the DSMB include:

- Provision of advice to the STC on operational procedures that would improve the quality of the trial;
- Review and approval of the treatment protocol;

- Review of the data collected throughout the trial for evidence of adverse or beneficial treatment effects;
- Development and implementation of stopping rules used to decide whether to discontinue the trial upon evidence of beneficial or adverse treatment effects; and
- Provision of advice to the investigators of TRTT and the NIDCD on the design, organization, and conduct of the trial.

This committee is the only committee provided with evidence of treatment effects while the study is still in progress. Any recommendation for a protocol change, based on accumulated data, will be forwarded to the STC for implementation.

The DSMB meets twice in Year 01, with at least one meeting taking place prior to the start of randomization, and twice yearly in succeeding years to review reports prepared by the DCC. Additional meetings will be scheduled as needed or at the request of a single member of the DSMB because he or she has concerns regarding data contained in an interim report.

### **3.3.4 Quality Assurance Committee (QAC)**

Membership in the QAC includes:

- Study Chair;
- Director of the DCC;
- Training/Protocol Monitors;
- Project Coordinators; and
- Rotating Clinical Coordinator, serving for one year, selected annually by the QAC.

Quality assurance measures are particularly important when the study protocol is being interpreted by a number of Clinical Centers. The QAC is set up to provide measures of quality control by:

- Assessing the quality of operations in Clinical Centers through participation in site visit teams and evaluation of site visit reports;

- Monitoring of protocol implementation in TRTT Clinical Centers through review of performance data developed and implemented jointly by the Chair's Office and the DCC;
- Meeting on an *ad hoc* basis to discuss Clinical Centers found to be in violation of the study protocol;
- Responding to issues raised by the STC concerning Clinical Center performance;
- Making recommendations to the DSMB concerning actions to be taken toward Clinical Centers found to be repeatedly in violation of the TRTT protocol; and
- Forming a liaison between the Clinical Centers and the DCC.

The QAC meets twice a year in Year 01, and annually at FIG meetings thereafter for discussion of accumulating data, prepared by the DCC. Additional meetings are scheduled as needed.

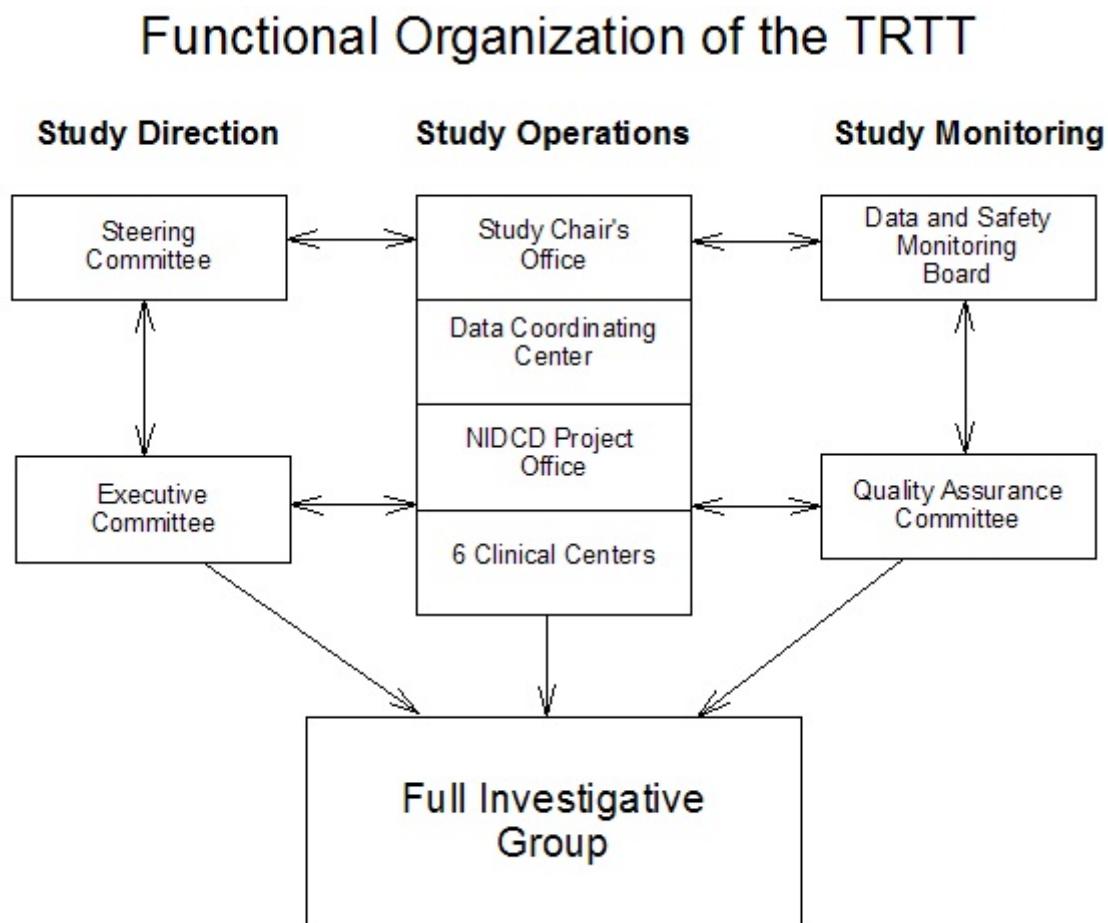
### **3.3.5 Full Investigative Group (FIG)**

The FIG is comprised of all Clinical Center personnel and staff members of the DCC and Chair's Office, and the NIDCD Project Officer.

This group meets at least annually through the course of the trial, in conjunction with STC meetings, in order to discuss the trial progress, in terms of recruitment, quality control, patient followup, re-certification, and other issues of common concern.

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Figure 1. Functional organization of the TRTT



## **Chapter 4** **Inclusion and Exclusion Criteria**

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### **4.1 Introduction**

The TRTT Steering Committee (STC) is responsible for defining and refining the inclusion and exclusion criteria for eligibility to identify suitable study participants with subjective tinnitus for inclusion in the TRTT. To be eligible for enrollment, each participant must satisfy all of the inclusion criteria. The Baseline Eligibility Visits of the study are primarily devoted to screening those individuals who might fit the TRTT profile for eligibility.

The Clinical Coordinator and the Study Audiologist conduct the eligibility review during the Baseline Eligibility Visits and evaluate the potential Study Participant. Individuals who are considered eligible, but who cannot commit themselves to an eighteen month schedule of clinic visits should be refused entry into the TRTT. Persons who are eligible may be denied enrollment at the discretion of the Clinical Center Director. Any individual who is found to be ineligible is returned to the referring clinician or is treated as a non-study patient. The exclusion criteria are summarized in Table 1.

### **4.2 Inclusion Criteria**

All of the following conditions must be satisfied for an individual to be eligible for enrollment into the TRTT:

- Age of patient at the Randomization Visit must be greater than or equal to 18 years;

- Diagnosis of subjective tinnitus that interferes with the patient's daily activities and confirmed by a score of 40 or greater on the Tinnitus Questionnaire;
- Functionally normal hearing, defined by audiometric thresholds  $\leq$  30 dB HL at and below 2,000 Hz and  $\leq$  40 dB HL at 4,000; no or minor hearing loss for which hearing aids would not normally be prescribed or would be refused.
- The patient must understand and sign the informed consent statement allowing the baseline eligibility visit examinations and randomization.

#### **4.3 Pending Criteria**

Some individuals may not be eligible for the TRTT because of criteria that may change over time. The presence of any of the following provisional criteria may temporarily exclude an individual from being randomized:

- Tinnitus of less than 12 month's duration;
- Treatment for tinnitus within previous 12 months, including psychological or psychiatric care, medications, tinnitus masker, bio-feedback, acupuncture, gingko biloba, or other treatment(s) designed to treat subjective tinnitus;
- Use of a cancer chemotherapeutic drug within previous 12 months; or
- Treatment for head or brain trauma (i.e., concussion, blunt trauma, blast injury, or skull fracture) 24 months before being screened or enrolled, or presence of head or brain injury requiring treatment.

Although ineligible at the time the criterion is present, these individuals may be re-evaluated for eligibility once the pending criterion no longer applies. (See Chapter 5, Study Participant Entry and Baseline Eligibility Visits.)

#### **4.4 Exclusion Criteria**

##### **4.4.1 General Exclusion Criteria**

Individuals will be ineligible for participation in the TRTT if any of the following general exclusion criteria are met:

- Unable to understand the English language well enough to complete questionnaires and benefit from counseling;
- Not eligible for medical care at a Department of Defense Clinical Center;
- Refusal to give consent;
- Inability or unwillingness of patient to comply with study requirements;
- Unwillingness of audiologist to randomize the patient to treatment due to the presence of any condition, professional, physical, mental or social, which is likely to affect the patient returning for follow-up visits on schedule or which is likely to impair his or her performance on the functional tests, including a history of alcoholism or drug addition, or systemic disease that might affect survival during the duration of the study or impair his or her ability to return for follow-up or to perform the tests.

#### **4.4.2 Non-medical Tinnitus-Related Exclusion Criteria**

Non-medical tinnitus related characteristics will be elicited from potential TRTT Study Participants during screening or while assessing the tinnitus history. Individuals who fulfill any of the following exclusion criteria are not eligible for the TRTT:

- Routine exposure to unprotected hazardous noise; or
- Pending tinnitus-related financial claims or litigation other than customary Veterans Administration claims upon retirement from the Military.

#### **4.4.3 Medical Exclusion Criteria**

A screening medical examination, including adequate history, physical examination, and appropriate laboratory tests should be obtained and interpreted by the Study Otolaryngologist and/or Study Audiologist. Medical criteria are designed to exclude individuals who might be unable to complete two years of follow-up because of medical conditions. The medical history will also identify those potentially eligible Study Participants who have objective tinnitus or who have a medically or surgically treatable disease process related to their tinnitus. These processes may either cause or contribute to the severity of the tinnitus or threaten the individual's health.

Any individual will be ineligible for participation in the TRTT if he or she reports any of the following during the history:

- Treatment for head or brain trauma 24 months before being screened or enrolled.  
Any of the following conditions may have resulted in the current tinnitus:
  - Concussion;
  - Blunt trauma;
  - Blast injury; or
  - Skull fracture.

If the tinnitus is still present at 24 months after treatment for the head trauma has concluded, the individual may be re-evaluated for eligibility for the TRTT. If the individual is diagnosed at the Baseline Eligibility Visit with head or brain trauma requiring treatment, then s/he is not eligible for the TRTT until 24 months after treatment has ended.

- Requirement for the continued, regular use of an ototoxic drug, including the following:
  - Aminoglycoside antibiotic;
  - Quinine, or quinine derivative drug; or
  - More than 325 mg of aspirin per day.
- Use of a cancer chemotherapeutic drug within the previous 12 months.

If the tinnitus is still present at 12 months after the individual has stopped taking a cancer chemotherapeutic drug, then the individual may be eligible for the TRTT.

Any individual with an uncontrolled or inadequately controlled medical problem will be excluded. Individuals with any of these conditions may not be available for long term follow-up and include the following conditions:

- Uncontrolled diabetes. Individuals with uncontrolled diabetes will not be eligible for the TRTT. In general, the physician should use his or her best judgment in determining whether a potential Study Participant has uncontrolled diabetes; however, an individual with a blood glucose level consistently over 200 mg/dl or a HBA1c above 8% will be ineligible.
- Uncontrolled hypertension. Individuals with a resting supine systolic blood pressure  $>160$  mm Hg or a diastolic blood pressure  $>100$  mm Hg despite adequate conventional oral antihypertensive therapy are ineligible for the TRTT.

An individual will be ineligible for participation in the TRTT if any of the following medical conditions, which suggest or indicate that he or she has treatable tinnitus, are present:

- Clinical evidence of a tumor that may contribute to the tinnitus, including the following:
  - Acoustic neuroma (or vestibular schwannoma);
  - Cerebellopontine angle tumor;
  - Skull base tumor; or
  - Any tumor that the examining physician believes is responsible for the tinnitus, based on his or her best clinical judgment.
- Clinical evidence that the tinnitus is due to an ear disorder, such as
  - Chronic otitis media, as evidenced by ear pain, fever, decreased hearing, redness, and bulging of the eardrum;
  - Otosclerosis;
  - Uncontrolled allergies creating fluid in sinus cavities; or
  - Eustachian, middle ear, or inner ear disease or pathology that may be related to the tinnitus, based on the best clinical judgment of the examining physician.
- Presence of Meniere's disease as assessed by best clinical judgment;
- Clinical evidence that the tinnitus is due to a vascular disorder, such as
  - Aberrant ear, head, or neck blood vasculature; or
  - Glomus tumors of the temporal bone.
- Clinical evidence of any neurological condition which may be related to the tinnitus, including, but not limited to, the following:
  - Multiple sclerosis; or
  - Any ear-related demyelinating or neurological disease.
- Clinical evidence of any immunological condition that may be related to the tinnitus, including, but not limited to, the following:
  - Lyme disease; or
  - Ear autoimmune disease.
- Clinical evidence of any other medical condition that may be related to the tinnitus, including, but not limited to, the following:
  - Perilymphatic fistula;
  - Malocclusion or temporomandibular joint disease;
  - Facial weakness or paralysis; or
  - Vertigo or dizziness.

- Any laboratory test that suggests an etiology for the tinnitus that is treatable, including, but not limited to, the following:
  - Abnormal thyroid stimulating hormone (TSH) or thyroid hormone (T3 or T4) level;
  - Positive fluorescent treponomal antibody (FTA) test;
  - Positive Lyme titer;
- Any imaging study (MRI, ultra CT, SPECT, MRA, lumbar puncture, or angiogram) result that suggests a treatable condition that may be related to the tinnitus.

#### **4.4.4 Audiological Exclusion Criteria**

An individual will be ineligible for participation in the TRTT if he or she does not have functionally normal hearing sensitivity, defined as hearing thresholds  $\leq$  30 dB HL at and below 2000 Hz and  $\leq$  40 dB HL at 4000. An individual that requires or wears hearing aids will not be eligible.

An individual will be ineligible if diagnosed with objective tinnitus based on any of the following conditions:

- Evidence of objective tinnitus as shown by one or more prominent spontaneous otoacoustic emissions, defined as the presence of a spontaneous otoacoustic emission spike that is 3 or more times larger than the measured variation in amplitude across the remaining frequency range and/or if the emission corresponds in pitch to the tinnitus pitch. Such evidence of objective tinnitus will make an individual ineligible for the TRTT; or
- Evidence of pulsatile somatosounds, suggesting the presence of abnormal vasculature or high blood pressure contributing to the tinnitus.

In addition, results from audiological tests may suggest a treatable condition that may be related to the tinnitus. Individuals for whom the following tests are abnormal should be carefully evaluated to determine whether a treatable cause of tinnitus is present:

- Pure-tone thresholds reflecting a treatable conductive hearing impairment;
- Abnormal acoustic immittance reflex test;
- Abnormal auditory brainstem response.

If a treatable cause of tinnitus is found to be present based on any of these audiological tests, then the individual is ineligible for TRTT.

In addition, if an individual presents with significant hyperacusis such that it would become an ethical dilemma, in the best clinical judgement of the Study Audiologist, to randomize to, and treat, this individual to the standard of care, s/he would not be eligible.

Lastly, if the individual reports the presence of fluctuating hearing loss such that study results would not be reliable, s/he will not be eligible for the TRTT.

#### **4.4.5 Mental Health Exclusion Criteria**

Because tinnitus may affect an individual psychologically or emotionally, Study Audiologists should carefully consider whether an individual with a recent or active mental health condition will be able to participate fully in the TRTT or complete all follow-up visits. The need to care for an individual's mental health should take precedence over participation in the TRTT.

An individual will be ineligible to participate in the TRTT if he or she:

- Is unable to participate fully in the trial or complete all followup visits because of an active or ongoing mental health condition, as assessed by best clinical judgment;
- Is feigning tinnitus or hearing loss, as assessed by best clinical judgment.

The above conditions are not intended to be an exhaustive list of exclusion criteria, nor would it be possible to compose a complete list. Each investigator is expected to use good judgement in selecting Study Participants with tinnitus that is not currently treatable by medical or surgical means, is willing to undergo the assigned study treatment regimen, and is likely available for long-term followup. The time and expense that this may require are considerable, but if Study Participants drop out of the trial, serious bias may occur in the study results. Therefore, it is imperative that every investigator screen potential Study Participants very carefully and eliminate those individuals with a poor prognosis for a good follow-up over the course of the TRTT.

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**Table 4.1**  
**Tinnitus Retraining Therapy Trial**  
**Exclusion Criteria**

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- Age less than 18 years;
- Unable to understand the English language well enough to complete questionnaires and benefit from counseling;
- Not eligible for medical care at a Department of Defense Clinical Center;
- Score of less than 40 on the Tinnitus Questionnaire;
- Tinnitus of less than 12 month's duration;
- Treatment for tinnitus within previous 12 months, including psychological or psychiatric care, medications, tinnitus masker, bio-feedback, acupuncture, gingko biloba, or other treatment(s) designed to treat subjective tinnitus;
- Pending tinnitus-related financial claims or litigation other than customary Veterans' Administration claims upon retirement from the Military;
- Routine unavoidable exposure to unprotected hazardous noise;
- Use of a cancer chemotherapeutic drug within previous 12 months;
- Requirement for the continued, regular use of an ototoxic drug, such as aminoglycoside antibiotic, quinine, or quinine derivative drugs, or aspirin at more than 325 mg per day;
- Treatment for head or brain trauma (i.e., concussion, blunt trauma, blast injury, or skull fracture) 24 months before being screened or enrolled, or presence of head or brain injury requiring treatment;
- Inability to participate fully in the study and complete all follow-up visits because of an active or ongoing mental health condition, as assessed by best clinical judgment;
- Hearing impairment, defined by audiometric thresholds > 30 dB HL at and below 2,000 Hz and > 40 dB HL at 4,000;

- Required use of hearing aids;
- Presence of fluctuating hearing loss, as reported by the individual, at a level that would interfere with the reliability of testing, based on the best clinical judgment of the examining physician;
- Evidence of objective tinnitus as shown by one or more prominent spontaneous otoacoustic emissions, defined as the presence of a spontaneous otoacoustic emission spike that is 3 or more times larger than the measured variation in amplitude across the remaining frequency range and/or if the emission corresponds in pitch to the tinnitus pitch.
- Evidence of pulsatile somatosounds suggesting presence of abnormal vasculature or high blood pressure contributing to the tinnitus;
- Evidence from audiological testing of a treatable etiology of the tinnitus , such as conductive hearing impairment as shown by pure-tone thresholds, abnormal acoustic immittance, abnormal stapedial reflex test; or abnormal auditory brainstem response;
- Evidence or history of feigning tinnitus or hearing loss, as assessed by best clinical judgment;
- Presence of significant hyperacusis that, based on best clinical judgement, cannot ethically be randomized to, or treated, in the standard of care treatment arm.
- Clinical evidence that the tinnitus is due to an ear disorder, such as chronic otitis media, as evidenced by ear pain, fever, decreased hearing, redness, and bulging of the eardrum
- Clinical evidence of Eustachian, middle ear, or inner ear disease or pathology related to the tinnitus, based on the best clinical judgment of the examining physician;
- Clinical evidence of a vestibular disorder, vertigo, or dizziness related to the tinnitus;
- Presence of Meniere's disease as assessed by best clinical judgment;
- Presence of otosclerosis related to tinnitus;
- Presence of uncontrolled allergies creating fluid in sinus cavities contributing to the tinnitus;
- Clinical evidence of malocclusion or temporomandibular joint disease related to the tinnitus;

- Clinical evidence of a neurological condition related to the tinnitus, such as multiple sclerosis or an ear-related demyelinating or neurological disease;
- Clinical evidence of any immunological condition related to the tinnitus, such as Lyme disease or ear autoimmune disease;
- Uncontrolled hypertension, defined as a resting supine systolic blood pressure >160 mm Hg or a diastolic blood pressure >100 mm Hg despite adequate conventional oral anti-hypertensive therapy;
- Clinical evidence that the tinnitus is related to a vascular disorder, such as aberrant ear, head, or neck blood vasculature, or glomus tumors of the temporal bone;
- Uncontrolled diabetes, defined as a blood glucose level consistently over 200 mg/dl or a HBA1c above 8%, or best physician judgment;
- Evidence of a tumor contributing to the tinnitus, including an acoustic neuroma (or vestibular schwanomma), cerebellopontive angle tumor, skull base tumor, or any other type of tumor that the examining physician believes is responsible for the tinnitus, based on his or her best clinical judgment;
- Evidence from any laboratory study that suggests an etiology for the tinnitus that is treatable, including, but not limited to, abnormal thyroid stimulating hormone (TSH) or thyroid hormone (T3 or T4) levels, positive fluorescent treponomal antibody (FTA) test, or positive lyme titer;
- Evidence from an imaging study of abnormal vasculature or any other condition related to the tinnitus;
- Inability or unwillingness of patient to comply with study requirements;
- Unwillingness of audiologist to randomize the patient to treatment due to the presence of any condition, professional, physical, mental or social, which is likely to affect the patient returning for follow-up visits on schedule or which is likely to impair his or her performance on the functional tests, including a history of alcoholism or drug addiction, or systemic disease that might affect survival during the duration of the study or impair his or her ability to return for follow-up or to perform the tests.
- Unwilling or unable to provide informed consent allowing randomization.

## **Chapter 5**

### **Study Participant Entry and Baseline Eligibility Visits**

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#### **5.1 Introduction**

Study Participant entry to the Tinnitus Retraining Therapy Trial (TRTT) involves a series of examinations to determine whether an individual diagnosed with subjective, debilitating tinnitus

is eligible for TRTT. The participant flow through the entry process is shown in Tables 1 and 2 and Figure 1. For the success of the TRTT, it is important to follow the procedures outlined in this Manual when evaluating an individual for entry. This compliance ensures that systematic documentation is kept on all persons with tinnitus at each Clinical Center who are evaluated for TRTT and that informed consent is obtained on all Study Participants. This strict adherence to protocol also ensures that all Study Participants who enroll in the TRTT meet eligibility requirements. This determination will facilitate direct comparisons among groups randomized to the different treatment arms, thereby strengthening the results of the randomized trial.

## **5.2 Study Participant Entry**

### **5.2.1 Participant Screening**

Enrollment of every referred eligible individual with subjective annoying tinnitus into the TRTT is encouraged. Every person who is potentially eligible for TRTT should be screened for eligibility using the Eligibility Screening Form. To be potentially eligible, an individual must:

- be 18 or older;
- be able to speak English well enough to complete a series of questionnaires and benefit from counseling;
- have tinnitus that interferes with his or her daily activities;
- be willing to consider participating in a research study related to tinnitus;
- not wear hearing aids; and
- be eligible for medical care at a Department of Defense Clinical Center.

In addition, the interviewer should assess the ability of the individual to understand the screening questions or to give informed consent.

Study identifiers, used throughout the study, are assigned at screening. The Clinical Coordinator assigns a Study ID number (Patient ID) (using the next pre-printed ID label from the sheet of labels supplied by the Data Coordinating Center (DCC)) and name code to each individual screened for the TRTT using the Eligibility Screening Form. The ID label is affixed in the designated space in Section A of the Eligibility Screening Form. The Study ID number is

an alpha numeric code consisting of the letter “T” followed by a letter designating the clinical center, followed by three digits. Each ID is unique and cannot be reassigned to another participant, even if the participant is not randomized.

At this time the Clinical Coordinator also assigns a four-letter name code to the potential Study Participant. This identifier is assigned in addition to the permanent study identifier obtained from the next available pre-printed label, as described above. The name code may be generated by the clinic staff using the Study Participant’s name as follows: first letter of first name, first letter of middle name, and first two digits of last name. An “X” may be used if there is no middle name or is used to conceal the participant’s identity. If there is concern about the name code revealing the participant’s identity, then any four letter code may be chosen, but no four letter sequence may be used more than once in any Clinical Center. Together, this alpha-code and the ID number are used to identify the Study Participant throughout the trial, unless the participant transfers to another Clinical Center.

The Clinical Coordinator then records the four-letter name code (created by the Clinical Center), and date that the screening telephone call or in-person visit was completed in Section A. The eligibility criteria are assessed and the remaining form completed by entering the source of the individual, how the individual was screened (telephone or in-person), and basic demographics (gender, racial and ethnic status).

If, at the time of either referral or screening, the individual does not meet the eligibility criteria, no further contact is required, but the individual’s Eligibility Screening Form is data entered to “register” the individual and collect demographic information. No other forms are completed or entered for individuals who do not pass screening.

If the individual remains eligible after screening, however, the Clinical Coordinator explains the eligibility process to the potential Study Participant, along with the objectives, requirements for participation, including follow-up visits, and the risks and benefits of participation in TRTT. If the potential participant is willing to be considered for enrollment in the TRTT, then the Clinical Coordinator will schedule a Baseline Eligibility Visit. If, after having scheduled a Baseline Eligibility Visit, the participant does not come into the clinic for the visit, this is interpreted as *not providing informed consent*.

### **5.2.2 Informed Consent**

At the Baseline Eligibility Visit, **the informed consent process takes place when the Clinical Center Director or staff have established that the study candidate possibly is**

**eligible for entry into the study and is willing to undergo a medical examination to determine eligibility for the study.** The potential Study Participant is informed about the scope and aims of TRTT and the possible risks and benefits of TRT versus partial TRT, and/or the current standard of care (SC) treatment. The Clinical Center staff will give the potential Study Participant the Informed Consent Form (prepared by the Center Director and approved by the local Institutional Review Board and the Data and Safety Monitoring Board) to review. The detailed Informed Consent Form is read by the Clinical Center staff to the potential Study Participant in the presence of a family member or friend if possible.

All of the potential Study Participant's questions concerning the trial and proposed therapy should be discussed thoroughly. Sufficient time must be allotted for this discussion. All questions concerning the baseline examination, the trial and proposed therapy will be answered. The potential Study Participant is counseled that, in the absence of scientific proof regarding the value of full TRT or any of the components of TRT, the Clinical Center staff believes that a random process for assigning an individual to a given treatment is an ethical approach.

Under no circumstances should the potential Study Participant be "forced" or "pressured" to enter the trial. Moreover, no individual should be randomized if he or she does not understand completely the Study including that it involves at least 18 months of follow-up. Such an action would be unethical and would be damaging to the credibility and scientific integrity of the trial. In addition, an individual who does not clearly understand and willingly consent to the study may be likely to refuse treatment, withdraw from follow-up, or seek treatment elsewhere. Nonetheless, the Study participant should be informed that s/he has the right to withdraw from the study at any point in time. The potential Study Participant is also informed that s/he is not required to agree to be randomized to treatment, even if, after the baseline examination s/he is found to be eligible for participation.

A signed, dated, and witnessed Informed Consent Statement **must** be obtained before the potential Study Participant is examined and randomized to the TRTT. A copy of the completed (signed, dated and witnessed) informed consent form is given to the Study Participant, and the original form is filed at the Clinical Center (depending on local Institutional Review Board requirements) to allow evaluation for the TRTT. Local institutions most likely will also require that the participant sign a HIPAA (Health Insurance Portability and Accountability Act) authorization form to allow the baseline examination data to be sent to the Data Coordinating Center.

### **5.2.3 Baseline Eligibility Visit**

Each Baseline Eligibility Visit participant must have signed a consent form prior to the collection of any baseline data. At this time, the Clinical Coordinator will obtain contact information from the potential Study Participant. This information will be used to maintain contact with enrolled Study Participants and will be updated at each follow-up visit.

The purpose of the Baseline Eligibility Visit (or visits) is to evaluate the potential Study Participant's eligibility for the trial according to the inclusion and exclusion criteria (described in Chapter 4), to collect baseline data on each eligible Study Participant, and to review the TRTT with potential participants. The Baseline Eligibility Visit need not be completed within a single day. If, for reason of convenience, the Baseline Eligibility Visit occurs over two or more days, then all aspects of the visit must be completed within six weeks of initial contact.

Assessing eligibility for the TRTT during the Baseline Eligibility visit comprises at least the following forms (study abbreviations):

- Patient Locator Form (PL);
- Tinnitus Questionnaire (TQ);
- Beck Depression Inventory Fast Screen (BD);
- Tinnitus History Form (TH);
- Medical History Form (MH);
- Tinnitus Retraining Therapy Baseline Interview Form (BT);
- Baseline Audiological/Hyperacusis/Tinnitus Evaluation Form (BA);
- Physical Examination Form (PH); and
- Laboratory and Other Tests Form (LO).

The sequence of procedures followed at the Baseline Eligibility Visit is listed in Table 5.1.

If, at any time during the Baseline Eligibility Visit, the candidate participant is found not to be eligible for the TRTT, no forms need to be completed except for the Eligibility Screening Form and the Eligibility Checklist, which is used to record all known reasons that individual is not eligible for the study.

When the Baseline Eligibility Visit has been completed, the Clinical Coordinator checks all forms completed during the Baseline Eligibility Visit to make sure that all questions have been answered. All original forms are processed as described in Chapter 14, Forms and Instructions for Forms. Original forms are stored in the Clinical Center files.

#### **5.2.3.1 Patient Locator Form**

The Patient Locator Form is used to record contact information for the Study Participant and persons likely to know his or her whereabouts. This form is not submitted to the Data Coordinating Center, but is kept at the Clinical Center.

#### **5.2.3.2 Tinnitus Questionnaire**

The Tinnitus Questionnaire (TQ) measures five domains related to the impact of tinnitus on an individual, including psychological distress, intrusiveness, hearing difficulties, sleep disturbances, and somatic complaints. Change in TQ score is the primary outcome and will be used to evaluate the efficacy of each of the treatment arms in the TRTT. The potential Study Participant is asked to complete a Tinnitus Questionnaire (TQ) to assess the effect of his or her tinnitus. A score of 40 or greater on the TQ is required for an individual to enroll in the TRTT. A score of 40 or more indicates a level of intrusiveness of the person's tinnitus that may be helped by the treatment options in the TRTT.

#### **5.2.3.3 Beck Depression Inventory Fast Screen**

The potential Study Participant will be asked to complete the Beck Depression Inventory Fast Screen (BB), which is a measure of depressive symptoms and consists of 7 items. Since tinnitus may be associated with depression, the Beck Depression Inventory-Fast Screen will be used to identify potential Study Participants who have depression. The TRTT will define clinical depression as a score of 4 or greater on the Beck Depression Inventory-Fast Screen or endorsement of item # 7 (suicidal thoughts or wishes). Any potential Study Participant who fulfills these criteria should be referred for appropriate counseling and may not be eligible for the TRTT.

#### **5.2.3.4 Tinnitus History Form**

A tinnitus history may be taken by the Clinical Coordinator or Study Audiologist and responses recorded on the Tinnitus History Form (TH). This form is used to document the onset of the potential Study Participant's tinnitus and any treatment undertaken up to that point in time. The Tinnitus History also collects information on potential prognostic and confounding variables.

#### **5.2.3.5 Medical History Form**

A medical history may be taken by the Clinical Coordinator, Study Audiologist, or Study Otolaryngologist and responses recorded on the Medical History Form (MH). If the Study Otolaryngologist does not complete the form, it must be provided to him/her for review prior to the physical examination. Responses to some items (e.g., history of allergies, autoimmune disease, or head trauma) may indicate the need for further tests and the results of such tests are recorded on the Physical Examination Form (PH) or the Laboratory and Other Tests Form (LO).

#### **5.2.3.6 Baseline Tinnitus Retraining Therapy Interview Form**

The Baseline Tinnitus Retraining Therapy Interview Form, developed by Jastreboff and Jastreboff (Jastreboff *et al.*, 1999) and scripted by Henry (Henry *et al.*, 2003), is used to obtain information from participants about their tinnitus. This form collects information specific to the Study Participant's tinnitus and its etiology, and records his or her responses to questions related to hearing sensitivity. These questions are used to categorize tinnitus patients with respect to the presence of tinnitus, hyperacusis (or supra-threshold sound sensitivity), and hearing loss using the TRT scale. The form also contains questions that the Study Participant uses to characterize aspects of his or her tinnitus on a 10-point scale. These questions are used as a baseline for monitoring effects of treatment.

#### **5.2.3.7 Audiological/Tinnitus/Hyperacusis Evaluation Form**

An Audiological/Tinnitus/Hyperacusis examination will be conducted for both ears, including pure-tone thresholds, audiometric speech tests, tympanometry, acoustic reflex measures, and otoacoustic emission screening. These tests are conducted according to the procedures outlined in Chapter 7, Procedures for Audiological/Tinnitus/Hyperacusis Evaluation. Psychoacoustic measures, including tinnitus pitch and loudness match, and loudness discomfort levels also will be measured at this time according to the procedures outlined in Chapter 7. Audiometric pure tone thresholds measured  $\leq$  2 months before the Baseline Eligibility Visit may

be used if they were measured per study protocol, by a TRTT certified audiologist, and with the permission of the individual. Values obtained during the ATH examination are recorded on the Baseline Audiological/Hyperacusis/Tinnitus Evaluation Form (BA).

#### **5.2.3.8 Physical Examination Form**

A physical examination is performed following the procedures outlined in Chapter 8, Procedures for Physical Examinations, to determine whether there is any physical cause for the participant's tinnitus. Results of the physical examination are recorded on the Physical Examination Form (PH). It is not necessary for the Study Otolaryngologist to have performed the physical examination, but s/he must review the form and take responsibility for the examination.

#### **5.2.3.9 Laboratory and Other Tests Form**

If any laboratory, imaging, or other tests are required because the medical history or results from the physical examination suggest a medical etiology for the participant's tinnitus, results of such tests are recorded on the Laboratory and Other Tests Form (LO). The Study Otolaryngologist must review the results of any required laboratory and other tests.

#### **5.2.3.10 Baseline and Randomization Checklist**

The Baseline and Randomization Checklist is a worksheet and is not required to be completed or submitted to the DCC. The Baseline and Randomization Checklist provides a step-by-step checklist to ensure that all steps of the eligibility visit have been completed. This form also includes a list of all inclusion and exclusion criteria that the Clinical Coordinator may use to verify that all eligibility criteria have been fulfilled for the potential Study Participant.

### **5.3 Determination of Eligibility**

At the conclusion of the Baseline Eligibility Visit, the Clinical Center Director or Clinical Coordinator determines whether the potential Study Participant is eligible for the TRTT by evaluating the results of the TQ, medical history, tinnitus history, audiological/tinnitus/hyperacusis examination, physical examination, and laboratory and other tests as recorded on the baseline forms and completing an Eligibility Checklist. The Eligibility Checklist is completed for all potential Study Participants, even though the status may already be known. It is completed in its entirety for eligible Study Participants and will be used to verify eligibility at the time a randomized treatment assignment is requested. For ineligible or pending individuals, the

Sections of the Eligibility Checklist corresponding to the Baseline Eligibility Visit data collection forms that had been started or completed should be completed. At least one reason for ineligibility must be checked, but all known reasons for current ineligibility should be checked.

Eligibility status will be one of the following:

**Ineligible:** a participant ineligible for entry because one or more exclusion criteria apply.

**Pending eligibility:** an individual who is currently excluded from the TRTT because of criteria that may change over time. The presence of any one of the following provisional criteria may exclude a participant from being considered for randomization in the TRTT currently:

- Tinnitus of less than 12 months duration;
- Treatment for tinnitus within previous 12 months, including psychological or psychiatric, care, medications, tinnitus masker, bio-feedback, acupuncture, gingko biloba, or other treatments(s) designed to treat subjective tinnitus;
- Treatment for head or brain trauma (i.e., concussion, blunt trauma, blast injury, or skull fracture) 24 months before being screened or enrolled, or presence of head or brain trauma requiring treatment;
- Use of a cancer chemotherapeutic agent within the 12 months.

**Eligible:** an individual for whom none of the exclusion criteria apply.

### 5.3.1 Ineligible Study Participants

If it is determined that the potential Study Participant is ineligible for the TRTT based on one or more exclusion criteria, then he or she is referred back to his or her audiologist or physician for usual care. Only the Eligibility Screening Form and the Eligibility Checklist needs to be completed and data entered for these individuals.

### **5.3.2 Pending Study Participants**

A pending Study Participant is an individual who cannot yet be fully evaluated for eligibility in the TRTT because the reason for ineligibility is time-related. One or more of the following criteria is the only known reason for ineligibility:

- His or her tinnitus has not been present for at least 12 months;
- S/he has received treatment for the tinnitus within the 12 months;
- S/he has received treatment for a head or brain trauma within the past 24 months; or
- S/he has used a cancer chemotherapeutic agent within the 12 months.

Pending Study Participants may be evaluated for entry in the TRTT at such time as the eligibility criterion has been fulfilled. That is, the potential Study Participant has:

- Had tinnitus for at least 12 months;
- Has not received any treatment for his or her tinnitus within the past 12 months;
- Has had no treatment for head or brain trauma within the previous 24 months; and
- Had not required use of a cancer chemotherapeutic agent for at least 12 months.

At the Baseline Eligibility Visit, if one of the criteria listed above is the only known reason for ineligibility, the Clinical Coordinator must document the reason for current ineligibility on the Eligibility Checklist. The Clinical Coordinator will also complete a Pending Study Participant Status Form by entering the date when the Pending Study Participant might become eligible for TRTT. The Eligibility Screening Form, Eligibility Checklist and the Pending Study Participant Status Form are required to be entered online for pending study participants.

Eligibility for the TRTT of individuals with pending status should be monitored at the Clinical Center. The list of persons (by Patient ID and name code) who are potentially eligible for the TRTT and the dates when these Pending Study Participants could become eligible will also be kept on the TRTT website for each Clinical Center.

To aid the process of following those participants who are pending eligible for the TRTT, the Clinical Coordinator will be able to generate a Pending Study Participants Report from the TRTT web page that will list the Study ids of all pending study participants, together with the exclusion criteria and target dates for re-evaluation. For example, if the date of onset of tinnitus for a individual were February 15, 2011, then the date expected for potential entry to the TRTT would be February 15, 2012. The Data Coordinating Center will send monthly email reminders to the Clinical Coordinator to check the web page that lists pending participants who may become eligible for TRTT participation in the next month.

Upon receiving the reminder email, the Clinical Coordinator or the Clinical Center Director should contact those Pending Study Participants who may become eligible in the next month to determine eligibility. The Clinical Coordinator or Clinical Center Director should determine the Pending Study Participant's interest in being re-evaluated for entry in the TRTT. If the Pending Study Participant continues to express interest in participating in the TRTT, a Baseline Eligibility visit is scheduled, as shown in Table 5.2. The Pending Study Participant will be identified by the Patient ID and name code originally assigned to him or her. All Baseline Eligibility Forms, except the Eligibility Screening Form, are completed at this subsequent visit, even if one or more had been completed previously.

Following completion of the second Baseline Eligibility visit, a new Eligibility Checklist is completed. The Pending Study Participant's status may become ineligible, may remain pending, or may become eligible at this time. It is the responsibility of the Clinical Coordinator to determine and update the status of each Pending Study Participant listed on the Pending Participant Status Log and also to data enter the appropriate status code (ineligible, pending, or eligible) on the Pending Participant Status Log as posted on the TRTT website. The Clinical Coordinator also will enter the new Eligibility Checklist in the online database.

If any criteria have changed in the interim (e.g., the Pending Study Participant's tinnitus has improved to the extent it is no longer annoying, as indicated by a score of <40 on the TQ) and he or she is now ineligible for the TRTT, then the Clinical Coordinator refers the individual to his or her audiologist or physician for usual care. No further forms need to be completed for this person.

If the original exclusion criterion still applies (e.g., treatment for tinnitus within previous 12 months), then the Pending Study Participant's status is unchanged and remains pending. If the status remains pending, the Clinical Coordinator should fill out a new Pending Study Participant Status Form and enter a new date for when the Pending Study Participant should be re-contacted. The new form should be entered on the TRTT website. The updated information is entered into

the participant tracking system and a date to re-contact the Pending Study Participant can be generated by the Clinical Coordinator. A reminder to the Clinical Center Clinical Coordinator to re-contact the Pending Study Participants will also be sent as described above.

If the criterion no longer applies, and no new exclusion criteria apply, then the Pending Study Participant becomes eligible for the TRTT. The Clinical Coordinator should discuss with the individual his or her willingness to participate in the TRTT, as described in Section 5.3.3, Eligible Participants.

### **5.3.3 Eligible Participants**

A final meeting between the potential Study Participant and the Clinical Center Director should be held to discuss treatment options and enrollment into the TRTT. It is the responsibility of the Clinical Center Director or Clinical Coordinator to review the TRTT study design and procedures with eligible Study Participants and to discuss entry into the trial.

If an eligible participant has decided to participate in the TRTT (i.e. is willing and able to be randomized), then randomization may proceed immediately following the Baseline Eligibility Visit or the Clinical Coordinator may schedule an appointment for the Randomization Visit. During the Randomization visit, additional baseline forms are completed and a treatment assignment is obtained from the Coordinating Center via the randomization website as described in Section 5.6. Although the Baseline Eligibility Visit and the Randomization Visit may occur on the same day, it is advisable to give the potential Study Participant a few days to think about the study, to consult with friends and relatives, and to make sure that he or she has considered the pros and cons of randomization, the proposed treatments, and is comfortable with the decision to enter the trial. At the Randomization Visit, eligibility criteria are reviewed to ensure that the potential Study Participant meets all of the inclusion criteria and none of the exclusion criteria. This information is documented by completion of the Eligibility Checklist.

### **5.4 Completion of Baseline Tests**

After the Study Participant has verbally indicated his or her willingness to be randomized, but before the treatment assignment is requested from the Coordinating Center (i.e., randomization takes place), the following baseline forms are completed:

- Tinnitus Handicap Inventory (TI);
- Tinnitus Functional Index (TF);

- Digit Symbol Substitution Task (DS);
- Hearing Handicap Inventory (HH)
- State-Trait Anxiety Inventory (SA);
- Positive and Negative Affect Schedule (PA);
- Life Events Checklist (LE); and
- EuroQOL (EQ).

Almost all of these forms are self-report forms. The first two questionnaires, the Tinnitus Handicap Inventory, and Tinnitus Functional Index, are used to evaluate the effect of the participant's tinnitus on his or her well-being. The next instrument, the Digit Symbol Substitution Task, is not a self-report instrument, but must be administered by the Clinical Coordinator or the Study Audiologist. It is used to measure the participant's ability to concentrate. The Hearing Handicap Inventory is used to measure the impact of mild hearing loss, if any, on treatment efficacy. The next two instruments, the State-Trait Anxiety Inventory and Positive and Negative Affect Schedule, will be used to assess psychological factors that may have an impact on the efficacy of treatment. The Life Events Checklist will be used to assess personal factors which may have an impact on the efficacy of treatment, and the last instrument, the EuroQOL, is used to assess general health-related quality of life. Chapter 9, Procedures for Administration of Self-Report and Other Measures, describes each of these instruments in detail.

## **5.5 Participant Randomization Procedures**

Before Randomization takes place, the Clinical Coordinator reviews the current Eligibility Checklist to establish the potential Study Participant's eligibility. He or she confirms that the potential Study Participant has given informed consent as demonstrated by signing the Informed Consent Statement, and that he or she has completed all baseline forms. Finally, the Study staff again explains the study, ensures that the participant truly understands the study, and makes certain that no additional questions or concerns remain. Study staff also ensures that the Study Participant, even if eligible, is still willing to allow randomization to an assigned treatment.

The Clinical Coordinator then accesses the randomization page of the TRTT website to obtain a randomization assignment. Using the internet ensures that 24 hours per day, 7 days a

week central randomization for the TRTT will be available. The Clinical Coordinator first enters the study specific code and the site-specific password that has been provided to the Clinical Center for this purpose. After the system verifies that the investigator is eligible to use the system, he or she enters the Study Participant's ID number and name code. At this time the Clinical Coordinator will be required to enter the qualifying TQ and the Eligibility Checklist. In so doing, the TRTT inclusion and exclusion criteria will be reviewed to ensure that the person to be entered is actually eligible to participate and that informed consent has been obtained. At this time, the system will provide the randomized treatment assignment.

Participants are randomized to one of three treatment groups. The participant has an equal probability of assignment to full TRT (Directive Counseling (DC) and conventional sound generator (SG)); modified TRT (DC and placebo SG); or standard of care (SC) for tinnitus as provided in the military (See Chapter 23 for further details on the statistical design).

In the trial, randomization will be stratified by Clinical Center. The sequence of random treatment allocations is designed to occur in blocks within each Clinical Center. There are blocks of allocations equal in length to a multiple of the number of treatment groups, i.e. multiples of 3. The exact multiple varies, at random, from block to block to make any particular assignment impossible to predict even if the treatment becomes unblinded. If there is a block of size "n", then at the end of that block, " $n/3$  Study Participants will have been allocated to each of the treatment groups. For example, a block size of 12 assignments for a given clinic will result in exactly 4 Study Participants who are allocated to each of the three treatment groups in a random order. The random order of the allocations for each stratum (clinical center and hearing aid use) is generated using the Moses-Oakford algorithm for computer generation of random permutations.

After the treatment group has been assigned, the system will generate a printable Randomization Registration Report as confirmation of the treatment assignment. The Randomization Registration Report will provide a kit number. The kits are boxes which contain the randomization assignment, either "Directive Counseling and Sound Generator" or "Standard of Care." If assigned to "Directive Counseling and Sound Generator," the kit will also include the pair of sound generators assigned to that Study Participant.

The Study Participant is officially enrolled in the trial at the time the treatment assignment is generated online. Once randomized, the participant **must be included** in the primary analyses of the assigned treatment group regardless of any difficulties that may arise in the treatment or follow-up processes.

Treatment may begin at the Randomization Visit, if time and circumstances allow, or may be scheduled for a future date. The first Treatment Visit (T1) must occur within two months of the Randomization Visit, however. If it cannot be scheduled within two months, an application to the Steering Committee may be made to extend the allowable time window. Chapters 11, 12, and 13 of the TRTT Manual of Procedures describe the administration of the interventions in detail.

An appointment schedule will be generated following completion of T1. After entering the date T1 was completed, the TRTT online system will automatically generate a schedule for Study Participant treatment with time windows to allow flexibility in scheduling appointments. This schedule also will be available on the TRTT website immediately after following entry of forms associated with T1.

### **5.6 Failure to Randomize**

If the Study Participant chooses not to allow randomization, even though s/he is fully eligible, then no forms are entered on the TRTT website, except for the Eligibility Screening Form, and the Eligibility Checklist. The unwillingness of the individual to allow randomization is noted by checking the last criterion on the Eligibility Checklist, “unwillingness of individual to allow randomized treatment assignment”.

### **5.8 Entry into the Study**

During the Randomization Visit, ***official study entry into the TRTT occurs by request and receipt of the treatment assignment*** during the interactive internet randomization process, as indicated earlier in this chapter. At this Randomization Visit, informed consent is affirmed, and both the Study Participant and Clinical Center staff are officially committed to the TRTT protocol and procedures for this individual.

***After official study entry has occurred, at the time of treatment assignment, the Clinical Center staff are responsible for following the Study Participant until the study is officially closed.*** This responsibility continues even if, at the last minute, the Study Participant refuses to be treated or fails to return for one or more follow-up visits.

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**Table 5.1**  
**Participant Flow at Study Entry and Forms Completed**

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- **Screen Potential Study Participants using Eligibility Screening Form by asking if s/he:**
  - Is 18 or older;
  - Is able to speak English well enough to complete a series of questionnaires and benefit from counseling;
  - Has tinnitus that interferes with his or her daily activities;
  - Is willing to consider participating in a research study related to tinnitus;
  - Wears hearing aids; and
  - Is eligible for medical care at a Department of Defense Clinical Center.
- **Enter Eligibility Screening Form online for all individuals, whether eligible or not**
- **Conduct Baseline Eligibility Visit by completing:**
  - Informed consent
  - Patient Locator Form (PL)
  - Tinnitus Questionnaire (TQ)
  - Beck Depression Inventory Fast Screen (BD)
  - Tinnitus History Form (TH)
  - Medical History Form (MH)
  - Tinnitus Retraining Therapy Baseline Interview Form (BT)
  - Baseline Audiological/Tinnitus/Hyperacusis Evaluation Form (BA)
  - Physical Examination Form (PH)
  - Laboratory and Other Tests (LO)
- **Document eligibility by completing Eligibility Checklist (EC). Individual may be:**
  1. **Ineligible**
    - Enter reason(s) for ineligibility on EC
    - Enter EC online
  2. **Pending**
    - Enter reason(s) for current ineligibility on EC
    - Complete Pending Study Participant Status Form (PE) online with reason the individual is not yet eligible and the date when the participant may become eligible.
    - Complete EC, by entering reason(s) individual is not currently eligible
    - Enter EC and PS online

---

Table 5.1, Participant Flow at Study Entry and Forms Completed, cont'd

---

### 3. Eligible

- **Determine willingness to allow randomization**
  - If unwilling to allow randomization, complete EC by checking last criterion “unwilling to allow randomized treatment assignment” and enter EC online
  - If willing to allow randomization, ask Study Participant to complete:
    - Tinnitus Handicap Inventory (TI)
    - Tinnitus Functional Index (TF)
  - Administer:
    - Digital Symbol Substitution Task (DS)
  - Ask Study Participant to complete:
    - Hearing Handicap Inventory (HH)
    - State-Trait Anxiety Inventory (SA)
    - Positive and Negative Affect Schedule (PA)
    - Life Events Checklist (LE)
    - EuroQOL (EQ)
  - Enter TQ online
  - Enter Eligibility Checklist (EC) online showing eligibility on all items
  - Request and obtain randomized treatment assignment
  - Enter remaining forms online within one week of randomization

---

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**Table 5.2**  
**Pending Participant Flow at Subsequent Visits**

---

**Ask the Pending Participant to complete the Tinnitus Questionnaire (TQ). Score may be:**

- Less than 40, **STOP**, patient is ineligible
  - Enter as reason for ineligibility on a new Eligibility Checklist (EC)
- 40 or more, continue and complete
  - Beck Depression Inventory Fast Screen (BD)
  - Tinnitus History Form (TH)
  - Medical History Form (MH)
  - Tinnitus Retraining Therapy Baseline Interview Form (BT)
  - Baseline Audiological/Tinnitus/Hyperacusis Evaluation Form (BA)
  - Physical Examination Form (PH)
  - Laboratory and Other Tests (LO)

• **Document eligibility by completing Eligibility Checklist (EC). Individual may be:**

**1. Ineligible**

- Enter reason(s) for ineligibility on EC
- Enter EC online

**2. Pending**

- Enter reason(s) for current ineligibility on EC
- Complete Pending Study Participant Status Form (PE) online with reason the individual is not yet eligible and the date when the participant may become eligible.
- Complete EC, by entering reason(s) individual is not currently eligible
- Enter EC and PS online

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Table 5.2, Pending Participant Flow at Subsequent Visits, cont'd

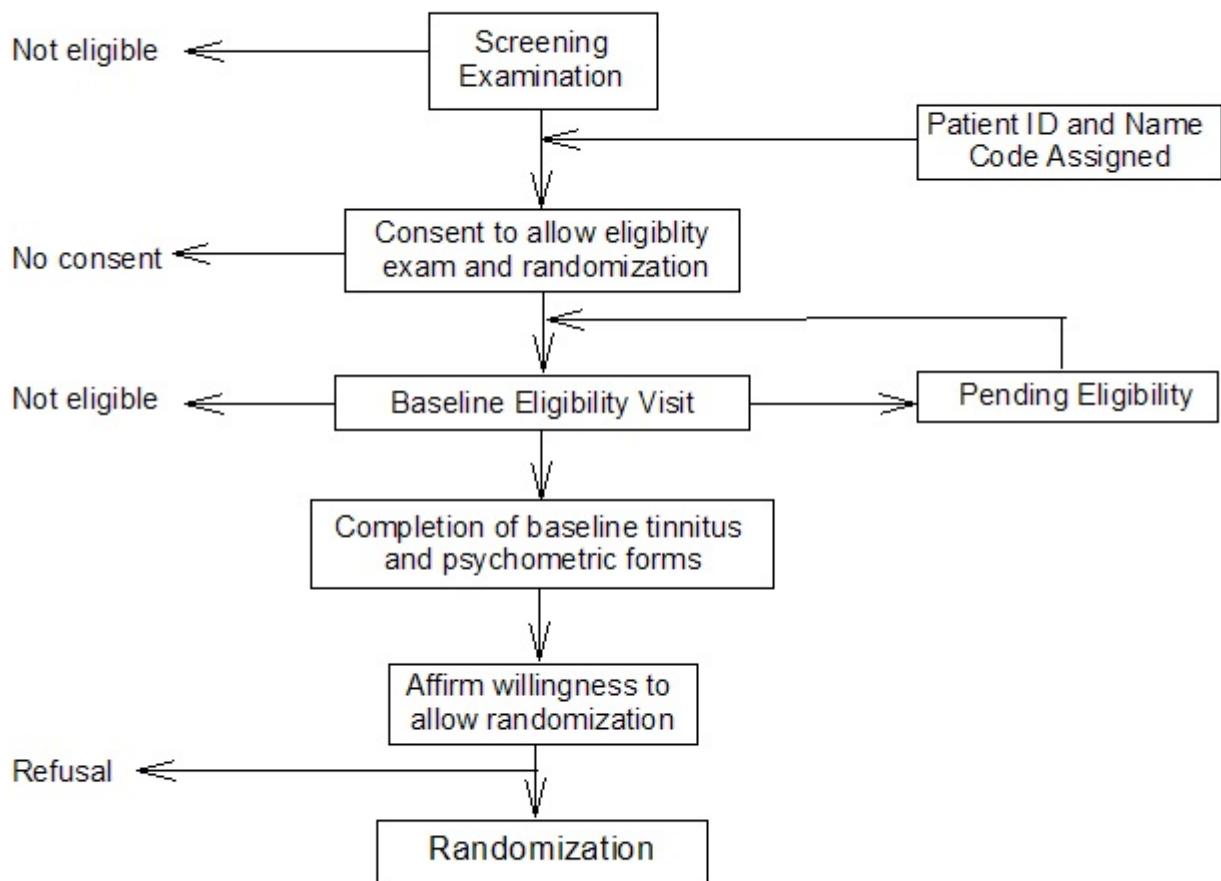
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### 3. Eligible

- **Determine willingness to allow randomization**
  - If unwilling to allow randomization, complete EC by checking last criterion “unwilling to allow randomized treatment assignment” and enter EC online
  - If willing to allow randomization, ask Study Participant to complete:
    - Tinnitus Handicap Inventory (TI)
    - Tinnitus Functional Index (TF)
  - Administer:
    - Digital Symbol Substitution Task (DS)
  - Ask Study Participant to complete:
    - Hearing Handicap Inventory (HH)
    - State-Trait Anxiety Inventory (SA)
    - Positive and Negative Affect Schedule (PA)
    - Life Events Checklist (LE)
    - EuroQOL (EQ)
  - Enter TQ online
  - Enter Eligibility Checklist (EC) online showing eligibility on all items
  - Request and obtain randomized treatment assignment
  - Enter remaining forms online within one week of randomization

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Figure 1

**Patient Entry to TRT Trial**

## References:

Henry, JA, Jastreboff MM, Jastreboff PJ, Schecter MA, Fausti SA. Guide to conducting tinnitus retraining therapy initial and follow-up interviews. *Journal of Rehabilitation Research and Development*. 2003. 40:1-21.

Jastreboff MM and Jastreboff RT. Questionnaires for assessment of the patients and their outcomes. In: Hazell, J, Ed. Proceedings of the VIth International Tinnitus Seminar, 1999. London. The Tinnitus and Hyperacusis Centre. p 487-91.

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**Chapter 6**  
**Procedures for Administering Baseline and Follow-up Tinnitus Retraining**  
**Therapy Interviews**

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## **6.1 Introduction**

During the baseline examination, each potential participant for the Tinnitus Retraining Therapy Trial (TRTT) will be asked a series of structured questions that are aimed at obtaining a description by the patient of his or her tinnitus, sound tolerance, and hearing status and the impact of each of these components on the patient. Responses to these questions are recorded on the Baseline Tinnitus Retraining Therapy (TRT) Interview Form. Results of the interview, along with the results of the audiological/tinnitus/hyperacusis (ATH) evaluation (See Chapter 7), form the basis to categorize each patient into one of the TRT categories (see Table 1). These categories, in turn, are used as the basis of individualized counseling for Study Participants assigned to directive counseling. Responses to questions of the baseline interview and data from the ATH evaluation then serve as a baseline reference for follow-up interviews and treatment outcomes for all patients.

## **6.2 General Guidelines for Interview and Testing**

A Study Audiologist will be responsible for the Baseline TRT Interview. The data collected must be accurate and complete. The directions on the interview form must be followed exactly as on the form and the patient's responses recorded exactly as the interviewer hears it. The Study

Audiologist must ask the questions exactly as they are written for the purpose of standardization. This adherence to protocol will ensure that each respondent is asked each question the same way no matter who is performing the interview. Ultimately, this standardization of the interview process is important for the scientific validity of the study. It is the role of the Study Audiologist to be familiar with the interview questions so that he or she can deliver the questions in a flowing manner, speaking clearly and accurately and recording the answers exactly as the respondent answers. Thus, the Study Audiologist should review and practice delivering the questions to feel comfortable during the interview process.

Confidentiality is an integral part of all survey research. It is the ethical responsibility of the Clinical Coordinator to maintain the confidentiality of the respondents interviewed. Interviews will be conducted in a private setting and the results of the interview are not discussed with anyone except for study personnel as necessary.

### **6.2.1 Interviewing Techniques**

The Study Audiologist, using his or her personality and voice, will establish and maintain rapport with the respondent at the initial meeting, and throughout the interview. Here are some suggestions of ways to establish rapport:

- Dress professionally;
- Be pleasant and friendly as you approach the respondent;
- Speak directly to the respondent. Use both body language and facial expression to develop a good first impression;
- Use only the low pitch of your voice;
- Do not consistently raise or elevate your voice. This results in a sing-song delivery and can be irritating to respondents or lead to refusal to complete the interview;
- Speak at a moderate rate of speech. Remember, the respondent does not have a copy of the questionnaire in front of him/her;
- Create a friendly atmosphere;
- Avoid saying "ok," "all right," "Yes, ma'am or Yes, sir," after every answer the respondent gives you. This is repetitious and sounds unprofessional;

- Have confidence in your voice, and speak distinctly with emphasis on key words;
- Above all, be pleasant and friendly. Always sound interested in what you are reading to the respondents. Remember, an uninterested respondent is usually the result of an interviewer communicating this atmosphere.

### **6.2.2 Maintaining Neutrality**

It is very important to maintain neutrality while conducting an interview. Maintaining neutrality means that the Study Audiologist should not imply criticism, surprise, approval or disapproval of anything that the respondent says or anything that is contained within the questionnaire. Non-neutral actions by the interviewer may influence how the respondent answers the questions.

### **6.2.3 Probing**

It may be necessary for the Study Audiologist to probe a respondent on a query to gain more information when the respondent's initial answer is unclear, irrelevant, or incomplete. Probing can be used to encourage a respondent to expand his or her response or to focus the respondent on the current question. The Study Audiologist must keep the probes neutral so as not to introduce bias and influence the way respondents might answer the questions. To probe properly the Study Audiologists must be familiar with the purpose of the question to know whether he or she is getting an appropriate response.

Probing in response to an open-ended question is slightly different than probing for a closed-ended question. If a respondent answers a closed-ended question with one of the given responses, then the interviewer does not need to probe; but if the respondent gives an answer that does not fit into the already designated categories, then probing is required. First try repeating the question and the response categories again. If the respondent feels he or she can not choose among the given categories, then say "In general . . .," or "In most cases . . .," or "Most of the time . . ."

In an open-ended question, one can probe an incomplete answer by saying, "Could you tell me more about that?" or "Could you give me an example." It is very important for the Study Audiologist to remain neutral and not let the respondent think that one answer is more appropriate than another.

An improper probe is one that makes interpretations or that puts words in the respondent's

mouth. The Study Audiologist should ask for a more specific response without making any assumptions about the respondent and his or her answer.

### **6.3 TRT Interview Forms**

The Baseline (sometimes called Initial) and Follow-up TRT Interview Forms will be used to define the tinnitus condition for each patient enrolled in the TRTT. These forms were originally developed and then refined by Jastreboff for use in TRT (Jastreboff and Jastreboff, 1999). The TRTT will use the scripted version of these forms that were developed and published by Henry for research purposes (Henry *et al.*, 2003).

#### **6.3.1 Baseline TRT Interview**

The goals of the baseline interview are to evaluate the role of the patient's tinnitus and the impact on his or her life. Specific goals are to:

- Identify complaints and any resulting problems related to the patient's tinnitus;
- Assess the emotional status and degree of distress caused by the tinnitus;
- Determine impact of the patient's tinnitus on his or her life;
- Evaluate the influence of sound exposure on the tinnitus problem;
- Assess the amount of time a patient is aware of the tinnitus;
- Estimate the extent of annoyance to a patient caused by the tinnitus;
- Form the basis for future assessment;
- Help in choosing the appropriate treatment protocol (i.e., with or without goals to address concomitant hyperacusis); and
- Choose the proper focus for counseling.

### **6.3.1.1 Instructions for Administration of Baseline TRT Interview**

The questionnaire is divided into four parts:

- Evaluation of tinnitus problem;
- Evaluation of sound tolerance problems;
- Evaluation of subjective hearing difficulties; and
- Ranking of reported complaints.

The following instructions for use are adapted from those published by Henry (Henry *et al.*, 2003).

#### **Instructions**

At the beginning of the Baseline TRT Interview Form are scripted instructions for the Study Audiologist to read to the Study Participant. These instructions emphasize to the participant the importance of understanding the functional differences between “tinnitus”, “sound tolerance”, and “hearing loss.”

#### **Questions 7 through 10, Section B**

Questions 7 through 10 obtain descriptive information concerning the tinnitus perception. Responses do not affect the patient’s TRT categorization. These questions define the patient’s tinnitus symptoms and provide a common reference for the remainder of the tinnitus-related questions.

#### **Question 12**

Question 12 seeks to determine the duration of the patient’s chronic tinnitus. This question is important for determining etiology. Also, tinnitus of recent onset may be more labile than longer-duration tinnitus and may resolve spontaneously. (All patients in the TRTT must have had tinnitus for at least one year to be eligible to participate in the randomized trial).

**Question 13**

Question 13 relates to identification of the most troubling, or bothersome, sound(s). In the TRTT, the psychoacoustic evaluation will be constrained to the most bothersome tinnitus sound to affect time and cost savings. In addition, the most bothersome sound(s) will be used to set the “mixing point” for the sound generators for those participants assigned to this arm of the trial.

**Question 14**

Most patients with tinnitus will have negative emotions associated with their tinnitus, with consequent affects on certain life activities. Question 14 seeks to determine if there are days when these tinnitus effects are noticeably worse than on other days. The patient is asked how often these “bad days” occur per week or month. This information provides one outcome variable to be assessed in the TRTT.

**Question 15**

Question 15 obtains the critical information for determining Category IV placement (See Table 1 for description of categories). Patients in Category IV commonly report that their tinnitus becomes louder as a result of exposure to certain sounds. This adverse effect typically lasts for minutes or for hours. If the tinnitus remains louder until the following day, however, the condition of “exacerbation” or “kindling” is indicated, and the patient is classified as Category IV.

**Question 16**

This item comprises a series of questions related to the patient’s use of hearing protection. The main purpose of Question 16 is to determine if the patient is overprotecting his or her hearing in the belief that earplug or earmuff use will prevent the tinnitus from becoming worse. The interviewer must use caution during the questioning so as not to give patients the new concern that sound might make their tinnitus worse.

**Question 17**

Question 17 asks if the patient is receiving any other tinnitus treatment. (Patients currently receiving other treatment for tinnitus are not immediately eligible for the TRTT, but may become eligible after 12 months of no treatment).

**Question 18**

Question 18 is open-ended to allow the Study Participant to identify the most bothersome aspect of his or her tinnitus, such as interference with sleep, and/or concentration and emotional consequences. This aspect will become the main objective of either directive or standard of care counseling.

**Question 19**

Question 19 identifies bothersome aspects of tinnitus from a closed set of different activities that can be adversely affected by tinnitus. Each of the activities must be discussed individually.

**Questions 20 and 21**

Questions 20 and 21 obtain an estimate of the percentage of waking hours that patients are consciously aware of, and annoyed by, their tinnitus. Patients are asked to average those percentages over the previous month. Question 20 determines the amount of time patients spend thinking about their tinnitus and Question 21 evaluates how much of the time they are annoyed by their tinnitus.

**Questions 22 through 24**

A visual analog scale of 0 to 10 is used for Questions 22 through 24. Patients are asked to rank their tinnitus with respect to loudness, annoyance, and life impact, respectively. Only the end points of the scale have labels; thus, patients must select a number on the continuum in relation to the two extremes. These rankings are particularly useful when assessing treatment outcome.

**Question 25**

Question 25 allows patients an opportunity to provide any additional information concerning their tinnitus. In most cases, the Baseline TRT Interview Form will have covered all the issues, and the patient will have nothing further to add.

**Question 26. Section C**

Question 26 starts the series of questions that are specific to supra-threshold sound tolerance problems (usually related to the loudness of sounds). It is important that patients clearly understand the intent of Question 26 because their response to it will determine whether they are

identified as having a problem with sound tolerance. The main consideration is to determine whether patients have trouble tolerating everyday sounds that are otherwise tolerated comfortably by most other persons. If the patient experiences sound tolerance problems, he or she can generally recall the types of everyday sounds that cause loudness discomfort. If the patient does not experience sound tolerance problems, then the remaining questions in Section C are skipped.

### **Question 26**

Decreased sound tolerance can involve different components, including hyperacusis, misophonia, and phonophobia. Hyperacusis is a physiological response to virtually all sounds above a certain intensity; thus, some physical discomfort is involved. Misophonia refers to “dislike of sound” and does not include physical discomfort. If the person dislikes and also fears sound, then phonophobia is indicated. Question 26 seeks to dissociate these problems and establish the primary complaint with respect to sound tolerance for initial treatment. Two or more of these problems may co-exist for some patients.

### **Questions 27 through 37**

Questions 27 through 37 relate to sound tolerance problems and are the same basic questions as questions 14 through 25 for assessing tinnitus complaints. Patients will often confuse functional effects of reduced sound tolerance with tinnitus effects. It is thus important to guide the patients to respond appropriately, keeping in mind the different components of reduced sound tolerance as described in Question 26.

Question 15 was the key tinnitus question for determining Category IV placement. There can also be Category IV placement specific to hyperacusis. In this case, certain sounds will exacerbate the hyperacusis for an extended period of time (at least until the next day).

### **Questions 38 through 40b, Section D**

Question 38 is the first of three questions that are specific to hearing loss. Some patients may reveal a significant reduction in hearing sensitivity and yet will not be bothered by their hearing loss. Other patients complain about considerable hearing difficulties that seem incongruous with the degree of hearing loss. The objective of these questions is to determine the patient's subjective feelings about his or her hearing status, regardless of hearing thresholds. The response will determine whether placement in Category II is appropriate, which would indicate the use of amplification.

### **Questions 41 through 43, Section E**

Visual analog scales of 0 to 10 are again used for questions 41 through 43. Over the course of the interview, patients will have learned to distinguish between the conditions of tinnitus, reduced sound tolerance, and hearing loss. Questions 41 through 43 now allow the patient to consider how much each condition is a problem in relation to the other. The responses should provide the final information to determine category placement.

#### **6.3.1.2 Assigning TRT Categories**

Patients are categorized based on information from the Baseline TRT Interview and the results of the ATH evaluation (see Chapter 7, Procedures for Audiological/Tinnitus/Hyperacusis Evaluation). Categories differ by the severity of tinnitus, the presence of hyperacusis, and evidence of the presence of kindling, (i.e., exacerbation of the tinnitus or hyperacusis problem upon exposure to a loud noise.) A detailed description of the categories is provided in Table 1.

### **6.3.2 Follow-up TRT interview**

The TRT Follow-up Interview is similar to the Baseline TRT Interview Form, but is shorter. Some questions are not repeated, while those that monitor treatment progress or measure treatment effects are repeated or modified. The main objective of the Tinnitus Follow-up Interview is to measure treatment progress and outcomes.

#### **6.3.2.1 Visits with Follow-up TRT Interview**

The Follow-up TRT Interview will be administered three times during follow-up and at the same study visits during which the ATH examinations are performed. These measures will be taken at the 6, 12, and 18 months follow-up visits.

#### **6.3.2.2 Instructions for Administering Follow-up TRT Interview**

The following instructions for use are adapted from those published by Henry (Henry *et al.*, 2003). Only questions that are different from the Baseline TRT Interview are described. Some questions are exactly the same as described previously (e.g., Baseline TRT Interview Questions 14, 15, 17, and 19 correspond to the Follow-up TRT Interview Questions 7, 8, 9, 10, and 11). Some questions do not apply at follow-up and are not asked (e.g., questions 18, 32, 39, and 40 on the Baseline TRT Interview Form).

**Question 7, Section B**

Question 7 contains a series of questions about whether patients experience some days that are more affected by their tinnitus than others. Additional questions have been added to determine if the patient feels that these “bad days” are fewer than before treatment started.

**Question 11**

Question 11 determines the impact of tinnitus on various activities (similar to Question 19 on the Baseline TRT Interview form).

**Questions 12 through 15**

Questions 12 through 15 are the key questions that assist in determining if patients are habituating to tinnitus perception (awareness) and reaction (annoyance), respectively. The patient is asked to report whether the amount of time he or she was aware of the tinnitus or annoyed by the tinnitus has changed during the previous month.

**Questions 16 through 18**

Questions 16 through 18 follow up on Questions 12 through 15 and ask the patient to estimate the tinnitus loudness, annoyance, and life impact using 0 to 10 point visual analog scales.

**Questions 20 through 30, Section C**

Questions 20 through 30 are specific to reduced sound tolerance. If reduced sound tolerance was not noted as a problem during the initial interview, these questions are skipped during the follow-up interview. If reduced sound tolerance was initially reported, then completing these questions will enable an evaluation of treatment efficacy.

**Question 31, Section D**

Question 31 is the only question about hearing difficulties, and requires only a yes or no response. The intent of the question is to evaluate whether the patient considers hearing loss a problem associated with his or her tinnitus.

**Questions 35**

Question 35 determines if the patient feels that his or her auditory condition, including tinnitus, sound tolerance, and hearing loss, has benefitted overall from the treatment administered in the TRTT.

The TRT Interview Forms provide for standardized collection of information from patients with tinnitus, hyperacusis, and hearing loss when administered using the instructions provided. Changes in the visual analog scales will be an important secondary outcome measure in the TRTT randomized trial.

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Table 1  
Classification of Tinnitus by Jastreboff Categories

### Category 0

<u>Component</u>	<u>Description</u>	<u>Information Source</u>
Hyperacusis	absent	Question 26
Noise exposure	no prolonged effect	Question 15a-f
Subjective hearing loss	irrelevant	Not applicable

Note: Tinnitus presents a small problem to the patient in category 0.

### Category I

<u>Component</u>	<u>Description</u>	<u>Information Source</u>
Hyperacusis	absent	Question 26
Noise exposure	no prolonged effect	Questions 15a-f
Subjective hearing loss	absent	Questions 38-40b

### Category II

<u>Component</u>	<u>Description</u>	<u>Information Source</u>
Hyperacusis	absent	Question 26
Noise exposure	no prolonged effect	Questions 15a-f
Subjective hearing loss	significant	Questions 38-40b

### Category III

<u>Component</u>	<u>Description</u>	<u>Information Source</u>
Hyperacusis	present	Question 26
Noise exposure	no prolonged effect	Questions 15a-f
Subjective hearing loss	irrelevant	Not applicable

### Category IV

<u>Component</u>	<u>Description</u>	<u>Information Source</u>
Hyperacusis	present	Question 26
Noise exposure	prolonged effect	Questions 15a-f
Subjective hearing loss	irrelevant	Not applicable

## References:

Jastreboff MM and Jastreboff RT. Questionnaires for assessment of the patients and their outcomes. In: Hazell, J, Ed. Proceedings of the VIth International Tinnitus Seminar, 1999. London. The Tinnitus and Hyperacusis Centre. p 487-91.

Henry, JA, Jastreboff MM, Jastreboff PJ, Schechter MA, Fausti SA. Guide to conducting tinnitus retraining therapy initial and follow-up interviews. Journal of Rehabilitation Research and Development. 2003. 40:1-21.

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## Chapter 7

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## 7.1 Introduction

As part of the eligibility examination, the Study Audiologist will conduct a comprehensive Audiological/Tinnitus/Hyperacusis (ATH) evaluation for each potential TRTT Study Participant. All Study Audiologists are experienced clinicians with graduate degrees in audiology and are fully credentialed (i.e., certified and/or licensed) to provide clinical services in the state in which they are practicing. Hearing status, tinnitus characteristics, and the presence of hyperacusis or sound tolerance problems will be evaluated to ensure that the individual is eligible for participation in the study. Interactions among the ATH variables will be identified and the contribution of each examined.

The Study Audiologist will use a TRTT data collection form to record the results of all ATH measures as they are collected. These data will be entered into the TRTT database at the TRTT website. In addition, an audiogram shell designed for the TRTT can be completed with audiometric data and used for subsequent counseling. This audiogram is consistent with the standard audiogram format and it is suggested that it be completed using standard symbols as recommended by the ASHA.

To ensure consistent evaluations across the Clinical Centers, clinicians will adhere to the evaluation protocol as delineated in this chapter and will record all results on the TRTT audiogram. Requirements for equipment maintenance and calibration, guidelines for test procedures, and the required order of evaluation procedures are described. Test procedures will be conducted in the following sequence:

- Pure-tone thresholds;
- Speech recognition thresholds;
- Tinnitus pitch match;
- Tinnitus loudness match;
- Loudness discomfort levels;
- Word recognition scores;
- Otoacoustic emissions; and
- Acoustic immittance.

## **7.2 Testing Equipment**

### **7.2.1 Equipment Requirements**

The Audiological/Tinnitus/Hyperacusis (ATH) evaluation will be performed using diagnostic audiometers that conform to the American National Standards Institute (ANSI) criteria for audiometer specifications (ANSI S3.6-R2004). The audiometers must allow for manual control of test frequency and sound presentation levels, air and bone conduction measures, pure-tone assessment at 250 through 12000 Hz, monitored live-voice and recorded speech testing, and ipsilateral and contralateral narrow- and broad-band masking.

All testing will be conducted in test booths that do not exceed the American National Standards Institute's maximum permissible ambient noise for audiometric test rooms (ANSI S3.1-R2003).

Immittance/Impedance audiometry equipment specifications must conform to ANSI S3.39 (R2002b).

### **7.2.2 Maintenance and Calibration of Equipment**

A record of all equipment calibration and maintenance will be kept by the Study Audiologist. The equipment will be calibrated to conform to the manufacturer's specifications. These procedures will be conducted on either the schedule recommended by the manufacturer's guidelines or per the Clinical Center's standard clinical protocol, depending on which one of the two is more stringent. Audiometers and immittance/impedance equipment will be calibrated in accordance with the standards noted above, ANSI S3.6-R2004 and ANSI S3.39-R2002, respectively. Sound level meters will be calibrated in accordance with ANSI S1.4-R1997. Coupler calibration of earphones should be conducted in accordance with ANSI S3.7-1995 (R1999). Reference equivalent levels for the calibration of pure-tones and earphones (supra-aural and insert), bone conduction vibrators, narrowband masking and extended high-frequency testing can be found in International Standards Organization (ISO) 389 1-5.

## **7.3 Otoscopic Examination of the Ear Canal and Tympanic Membrane**

Prior to the ATH evaluation, the Study Audiologist or Otolaryngologist will conduct an otoscopic examination of each potential Study Participant's ear canals and tympanic membranes. The purpose of this inspection is to rule out ear canal obstruction due to impacted cerumen or other debris, or the presence of any other visible condition that could contribute to the individual's tinnitus or affect his or her audiological test results. Cerumen removal or

management of a medical condition must be performed before audiological testing can proceed. If necessary, the individual's ATH evaluation can be rescheduled upon resolution of any treatable condition.

## **7.4 Audiological Evaluation**

Pure-tone and speech audiometry will be conducted to evaluate each potential participant's hearing sensitivity. These measures will be used to determine eligibility for the TRTT. The findings also will serve as a baseline regarding the individual's auditory function and as useful references for the tinnitus and hyperacusis evaluations. The administration of pure-tone threshold measurements and speech audiometry are basic to the practice of audiology. The tests are well-established, reliable measures that audiologists are trained to administer in standardized procedures. For further details please refer to the ASHA guidelines (1978, 1988a, 1988b).

### **7.4.1 Pure-Tone Testing**

Pure-tone thresholds for all potential Study Participants will be measured by air- and bone-conduction to establish their hearing sensitivity. Test frequencies will include 250 through 12,000 Hz, including inter-octave frequencies of 750, 1500, 3000, and 6000 Hz. Pure-tone testing will be conducted as prescribed by the ASHA Committee on Audiometric Evaluation (1978) using the modified Hughson-Westlake procedure (Carhart and Jerger, 1959).

The procedure is summarized below:

1. The tone is presented initially at a clearly audible level. A level of 30 dB HL is used for those with no apparent hearing impairment and a level of 70 dB HL is used for those who have obvious difficulty.
2. If no response is obtained, then the signal level is increased in 10-dB steps until the Study Participant responds. (Alternatively, it is permissible to start testing by presenting a "sweep up" continuous tone that is increased in intensity until a response is elicited.)
3. Once the Study Participant responds, the signal intensity is lowered in 10-dB increments until there is no response.
4. When the Study Participant fails to respond, the level is then raised in 5-dB steps until a response is obtained.
5. The signal level is then lowered in 10-dB steps and the adaptive process is repeated.

6. According to ANSI 3.21, threshold is determined as the “lowest hearing level at which responses occur in at least one-half of a series of ascending trials, with a minimum of two responses out of three required at a single level.”

Prior to conducting the pure-tone test, the Study Audiologist will familiarize the potential Study Participant with the procedure and provide instructions for responding to the pure-tone signals. The Audiologist will also ensure that the individual has no questions and that he or she is aware that it is possible to speak to the Audiologist at any time during the test.

The Audiologist will use contralateral masking during testing whenever there is a 40 dB or greater difference between the two ears. Appropriate masking also will be used during bone-conduction testing. Care will be taken to ensure that masking does not exceed the individual’s tolerance level. Individuals whose results are indicative of conductive and/or mixed hearing loss will be referred for medical intervention before eligibility can be determined.

Individuals with normal-hearing sensitivity or functionally normal hearing status who would not normally be considered hearing aid candidates are eligible for participation in the study if they meet other eligibility requirements. Individuals with aidable documented hearing loss are not eligible for the TRTT.

#### **7.4.2 Speech Recognition Threshold**

The speech recognition threshold (SRT) provides a validity check of the pure-tone air-conduction threshold results. Specifically, the SRT should be within  $\pm 7$  dB of the average of the pure-tone thresholds (PTA) obtained in the speech frequency range: 500, 1000, and 2000 Hz. In the event of a precipitously sloping hearing loss, it is permissible to calculate a two-frequency PTA to obtain better agreement with the SRT. The SRT also provides an index of hearing sensitivity for speech and serves as a baseline for determining the presentation levels for supra-threshold speech recognition testing. All Clinical Centers will use the following 20 spondees which, of the original 36-item PAL list, are considered to be the most homogeneous in terms of audibility (Olsen and Matkin, 1991):

Airplane	Iceberg	Railroad	Woodwork
Birthday	Mousetrap	Sidewalk	Workshop
Cowboy	Mushroom	Stairway	
Farewell	Northwest	Sunset	
Greyhound	Oatmeal	Toothbrush	
Hardware	Playground	Whitewash	

Each prospective participant will be informed that this test determines the presentation level required for him or her to recognize speech. The Study Audiologist will familiarize him or her with the spondee word list prior to beginning the test. Research has shown that there is no significant difference in the SRT level obtained for monitored live voice (MLV) vs. recorded spondees provided the speaker presents the words with equal emphasis on each syllable. Hence, Study Audiologists may use MLV to obtain the SRT provided that care is taken to ensure that each syllable is presented at 0 VU ( $\pm 3$  dB). Although there are several published recommended procedures for obtaining the SRT, no standard exists for the procedure. Hence, either the established ascending or descending procedure is acceptable. The SRT represents the lowest dB level at which an individual can correctly repeat 50% of the spondaic words that are presented (Carhart, 1946).

## **7.5 Tinnitus Evaluation**

Upon completing the pure-tone and SRT tests, the Study Audiologist will conduct an evaluation of the prospective participant's tinnitus. The results from these measures will be recorded and displayed on the TRTT audiogram.

### **7.5.1 Tinnitus Pitch Match**

The objective of the tinnitus pitch match is to identify the frequency or frequency range that most closely matches the pitch of the potential participants' most troublesome tinnitus (MTT) component. The test is conducted separately for each ear if tinnitus is present in both ears or is in -the- head. If tinnitus is present in only one ear, then only that ear is tested. The Study Audiologist may use pure tones, narrow-band noise, and/or white noise. The choice of stimulus will depend on the characteristics of the participant's tinnitus in that ear.

If the tinnitus is intermittent and is not present on the day of the study visit, then it may not be possible to obtain the tinnitus pitch and loudness on that day. This measure must be obtained at all visits when it is possible to do so, however.

#### **7.5.1.1 Instructions to the Participant**

The Study Audiologist will instruct the participant as follows:

“We are trying to match your most troublesome tinnitus sound. I will present brief sounds beginning with low-pitched sounds and then present sounds that become higher in pitch. Please, tell me when you hear the sound that is closest to your tinnitus. Do not worry about how loud the sound is. We will match the loudness of the tinnitus later.

We are trying to capture a quick “snap shot” of your tinnitus at this time. The sound you select does not have any special meaning related to what will happen with your hearing or your tinnitus.”

#### **7.5.1.2 Procedures for Conducting the Test**

The Study Audiologist will initially present pure tones at octave and inter-octave frequencies between 250 and 12,000 Hz. Tones should be presented at approximately 10 to 15 dB SL at each frequency (10 to 15 dB above the detection threshold). All tones will be presented during testing, because there is frequently octave confusion when matching the pitch. If during testing the Study Participant reports that a certain tone is closest to his or her tinnitus, the Study Audiologist will make note of that frequency and continue testing, but reassure the Study Participant that he or she will return to the noted frequency if no other frequencies seem closer. If the Study Participant cannot match the exact pitch of his or her tinnitus, he or she will be asked to identify the frequency closest to the tinnitus signal. The MTT is usually one sound in each ear, but if more than one tone is identified by the Study participant as bothersome, then the Study Audiologist will encourage the Study Participant to choose one sound and record the frequency of that tone. The Frequency Match is recorded and noted as “pure tone.” The Study Audiologist will then obtain and record a detection threshold in 1 dB steps for the tone(s) to be used in the loudness matching task described below.

If the perceived pitch is judged by the participant to be diffuse rather than tonal, then the Study Audiologist will present narrow-band stimuli to approximate the sound of the individual’s perceived tinnitus. If he or she reports that narrowband noise matches his or her tinnitus pitch more closely than a single tone, then the center frequency of this noise stimulus is recorded and noted as “narrow-band.” The detection threshold for this narrow-band noise is obtained in 1 dB steps and recorded.

If the Study Participant does not identify either a pure tone or a narrow-band noise as most similar to his or his tinnitus, then white noise is presented for a comparison judgment. A detection threshold is obtained in 1 dB steps and recorded. There will be no Frequency Match if “white noise” is noted and recorded.

#### **7.5.2 Tinnitus Loudness Match**

The objective of the tinnitus loudness match is to identify the intensity of the Study Participant’s most troublesome tinnitus component. The Study Audiologist will use the tone or noise stimulus that was identified in the tinnitus pitch match as most closely approximating the sound of the participant’s tinnitus, either pure tone, narrow-band, or white noise. If the tinnitus is

perceived as binaural, then the loudness match is evaluated for each ear separately. If the tinnitus is perceived as in-the-head, then the loudness match is performed using a binaural presentation of the test stimuli, with loudness match for each ear determined using appropriate adjustments to achieve the loudness match.

#### **7.5.2.1 Instructions to the Participant**

The Study Audiologist will instruct the participant by saying:

“We would now like to determine the loudness of your most troublesome tinnitus sound. I will present some brief sounds beginning with soft sounds and then go to louder sounds. Please tell me when you hear the sound that is closest to the loudness of your tinnitus.”

#### **7.5.2.2 Procedures for Conducting the Test**

The Study Audiologist begins the loudness matching test by presenting the level of the individual’s pitch-match stimulus slightly below the recorded detection threshold. The stimulus level will then be increased in 1-dB steps until the participant reports that the loudness of the stimulus matches the loudness of his or her tinnitus. This presentation level then is recorded for the loudness match.

Most individuals report their tinnitus loudness match at 0 to 10 dB SL above their audiometric threshold for the pitch match stimulus. If the loudness match exceeds 15 dB SL, then the pitch and loudness matches should both be rechecked. The detection threshold also should be reestablished so that the loudness match can be reported accurately in dB SL.

### **7.6 Hyperacusis Evaluation**

Upon completion of the Tinnitus Evaluation, the Study Audiologist will evaluate each potential Study Participant to identify the presence of hyperacusis or sound tolerance problems. This is achieved by testing the loudness discomfort level. The loudness discomfort level (LDL) is the level at which an individual first subjectively judges the loudness of a sound to cause discomfort. This sound level corresponds to the individual’s sound tolerance for a given auditory stimulus. The LDL sets the functional upper limit of the listener’s dynamic range (i.e., the range of sound levels between the audiometric threshold and the LDL).

The Study Audiologist will obtain an LDL for speech via monitored live voice prior to familiarizing the participant with the LDL task. Estimates of LDL are used to establish hyperacusis, phonophobia, and related supra-threshold sound tolerance problems.

### **7.6.1 Instructions to the Participant**

The Study Audiologist will instruct the Study Participant as follows:

“We have identified the softest sounds you can hear. Now, I will be assessing your tolerance for loud sounds. First, I want to assure you that I will not present sounds so loud that they will harm your hearing. I will test your tolerance for my voice first and then I will test pure tones.

“You will hear my voice become louder and louder. We want to get past the point at which you report a sound is “too loud” and to the point where the sound is actually uncomfortable. Push the button if the sound becomes uncomfortable and you cannot tolerate it for more than a few seconds. Try to hold off as long as possible, but don’t be heroic. I will stop the test immediately upon request. We will test one ear and then the other ear.”

### **7.6.2 Procedures for Conducting the LDL Test**

The Study Audiologist will begin the LDL measurements at a comfortable listening level and increase the presentation level in 5-dB steps (in 2.5-dB steps if hyperacusis is already a concern) until the participant pushes the button to indicate discomfort or to a maximum of 110 dB HL.

The LDL measurements will begin with a 500-Hz tone presented at a presentation level approximately 20 dB below the LDL obtained for live voice. The Audiologist will increase the sound level in 5-dB steps until the Study Participant pushes the button or to a maximum of 110 dB HL. The test is repeated at 1000, 2000, 4000, 6000, and 8000 Hz, and, if possible, at the participant’s tinnitus pitch-match frequency. For reliability purposes, the Study Audiologist will then repeat the measure at all frequencies prior to testing the second ear. The LDL obtained for the second measurement is the value that is recorded as the LDL.

## **7.7 Word Recognition Scores**

Word recognition or speech discrimination scores will be obtained for all potential Study Participants as a baseline measure of speech comprehension. Scores will be obtained for each ear. The percentage score represents the number of phonetically balanced monosyllabic words presented at a normal conversation level that the Study Participant repeats correctly. This measure is conducted after the LDL test to ensure that the speech level does not exceed the participant’s tolerance level.

The Study Audiologist will inform the Study Participant that the test is a measure of his or her ability to understand general speech. CDs or other standardized recordings of NU6 word lists will be used in the TRTT. Presentation levels for the word lists are controlled through the audiometer and are presented via headphones. The word lists will be presented at 40 dB SL re: the individual's SRT for the test ear. If this level exceeds the individual's LDL, then the Audiologist will attempt to present the words at a comfortable and acceptable level below the LDL. For the purpose of the TRTT, 25-word lists will be used.

## **7.8 Otoacoustic Emissions**

Otoacoustic emissions (OAE's) reflect measurable acoustic activity in the external auditory ear canal. This activity arises from either spontaneous or evoked mechanical oscillations emanating from the outer hair cells of the cochlea. This mechanical activity is projected outward through the middle ear system and can be detected by means of a miniature microphone placed within the external ear canal near the tympanic membrane. Spontaneous otoacoustic emissions (SOAE), when measurable, arise without any physical stimulation from an associated external sound stimulus. In contrast, distortion product otoacoustic emissions (DPOAE) are evoked in response to the simultaneous presentation of two specifically selected sinusoids. The measurement of OAEs from Study Participants will be used to rule out OAE activity that might explain the tinnitus and for counseling purposes only.

### **7.8.1 Spontaneous Otoacoustic Emissions (SOAE)**

Measurement for SOAEs will be performed to rule out an objective localized source that might explain an individual's tinnitus. Evidence of an objective source of tinnitus would disqualify the individual from participation in the TRTT. The Study Audiologist should follow the manufacturer's instructions for operation of the OAE test equipment in his or her clinic and use whatever protocol he or she would normally use to measure SOAE activity.

The results of the SOAE test are examined for evidence of spontaneous emissions that could account for the prospective participant's tinnitus. The Study Audiologist should use his or her best judgment in estimating whether a spontaneous emission is present. For the TRTT, any emission that is 3 or more times larger than the measured amplitude variation in the response activity across all frequencies and is also at the frequency of the individual's tinnitus pitch match is suggestive of cochlear involvement as a contributing factor or cause of the tinnitus. An individual with a characteristic spontaneous emission with these properties should be further evaluated by the Study Otolaryngologist.

### **7.8.2 Distortion Product Otoacoustic Emissions (DPOAE)**

DPOAEs also will be measured to assess function and integrity of outer hair cell (OHC) activity. This test should be performed after determination of LDLs so that the presentation levels used do not exceed a participant's LDLs. The  $2F_1 - F_2$  DPOAE data will be measured using standard clinical protocol for each Study Audiologist's facility and will be used primarily for guidance in directive counseling.

The DPOAE test results will be examined by the Study Audiologist. DPOAE activity that is not consistent with the measured audiometric thresholds may suggest retrocochlear pathology or a nonorganic contribution to an individual's tinnitus condition. If an individual's DPOAE is inconsistent with other audiometric test results, then further evaluation by the Study Otolaryngologist is warranted.

## **7.9 Acoustic Immittance**

The Study Audiologist will administer acoustic immittance tests to evaluate middle ear function and the integrity of the acoustic reflex system. Tympanometry will be conducted to assess bilateral middle ear function. Ipsilateral and contralateral acoustic reflex thresholds will be obtained, and reflex decay will be assessed if deemed necessary by the Study Audiologist to rule out auditory disease, in which case the participant would be excluded from the study.

It is essential that an otoscopic exam be conducted prior to immittance testing. If one was not performed prior to the ATH evaluation, then the Study Audiologist must perform the otoscopic examination at this point. While administering these measures, the Study Audiologist will ensure that presentation levels do not exceed the individual's LDL. If the probe tone levels or acoustic reflex threshold levels (if measured) exceed the Study Participant's LDL, then these tests will not be performed. In addition to tolerance problems, other contraindications for immittance testing include otorrhea, stapedectomy or ossicular reconstruction, mastoidectomy, or a recent (within the past two months) tympanoplasty.

Equipment for immittance tests may vary across the Clinical Centers, hence, Study Audiologists will adhere to instructions for the equipment in use at their centers.

### **7.9.1 Tympanometry**

Tympanometry is conducted in the TRTT to rule out any middle ear pathology that could be causing or contributing to an individual's tinnitus. The Study Audiologist will select an appropriately sized probe tip and ensure that a hermetic seal has been achieved. If the

tympanometer does not feature automated graphic display of the tympanogram, then the Study Audiologist will document the results of tympanometry including the participant's ear-canal volume, peak- pressure point, and tympanogram type. Individuals whose results reveal negative pressure below -200 daPa, ear-canal volume greater than 1.5 mm, absence of a peak pressure point, markedly reduced mobility, or hypermobility of the middle ear mechanism will be referred for medical evaluation and possible treatment. Based on the medical outcome, those individuals whose tympanometry results were not within normal limits, may be reconsidered for eligibility in the TRTT at a subsequent date after normal function returns. For additional information on evaluation of the tympanogram, please see ANSI S3.39- R2002.

### **7.9.2 Acoustic Reflex Threshold and Decay**

If the Study Audiologist believes acoustic reflex testing is necessary to rule out medically manageable auditory disease as a contributing factor to the tinnitus condition, then such testing should be conducted following a standard clinical protocol of the kind described below.

The acoustic reflex threshold and decay measurements assess a reflex arc involving the ascending and descending neural tracts, including the auditory and facial nerves and associated brainstem pathways. Elevated thresholds, absent reflex and/or abnormal decay in response to pure-tone stimulation may indicate middle ear pathology, cochlear, or retro-cochlear pathology. Such abnormalities warrant a medical referral. The individual may be ineligible for the TRTT or may be scheduled for reconsideration upon resolution of the medical condition.

The Study Audiologist will obtain acoustic reflex thresholds with contralateral stimulation at 500, 1000, 2000, and 4000 Hz. The Audiologist will begin stimulus presentation in the 70-80 dB range, increasing the presentation level in 10-dB steps until the reflex is detected. Presentation levels should not exceed 110 dB HL. The threshold will be targeted using descending and ascending 5-dB steps. The level at which there is an admittance change of 0.02 mm or greater is recorded as the reflex threshold. Reflexes will be obtained for both ears. Ipsilateral acoustic reflex thresholds will be obtained at 500, 1000, and 2000 Hz if contralateral reflexes are abnormal.

To rule out acoustic reflex decay, which may be indicative of retrocochlear pathology, a 1000-Hz tone will be presented contralaterally at 10 dB SL (re: the acoustic reflex threshold) for 10 seconds. If the response decays to  $\geq 50\%$  of its initial amplitude within the 10 seconds of stimulation, then the Audiologist will recheck the probe tip seal and repeat the measure at 15 dB SL. If the test is again positive, then the positive findings will be more pronounced at the increased SL, suggestive of retrocochlear pathology.

If the prospective participant has complaints of pulsatile tinnitus, then the Audiologist will reset the equipment to monitor and record the spontaneous pulsations within the ear. If present, then these pulsations will likely be synchronized with the participant's heartbeat.

Upon conclusion of the immittance test measures, the Study Audiologist will print out or record the acoustic reflex decay results. Elevated or absent reflex thresholds or positive reflex decay may be indicative of retrocochlear pathology. Individuals with these findings should be evaluated further by the Study Otolaryngologist.

#### **7.10 Follow-up ATH Evaluation**

At the 6, 12, and 18 month Follow-up Visits, an ATH evaluation will also be conducted. At each evaluation the tests will be administered in the same order. Only LDLs will be measured at the one month Treatment Visit and the 3 month Follow-up Visit.

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## References:

American National Standards Institute. (R1999) Coupler calibration of earphones (ANSI S3.7-R1999).

American National Standards Institute. (R2002a) Mechanical coupler for measurement of bone vibration (ANSI S3.13-R2002) New York: Acoustical Society of America.

American National Standards Institute. (R2002b). Specifications for instruments to measure aural acoustic impedance and admittance (aural acoustic immittance) (ANSI S3.39- R2002). New York: Acoustical Society of America.

American National Standards Institute. (R2003). Maximum permissible ambient noise levels for audiometric test rooms (ANSI S3.1-R2003). New York: Acoustical Society of America.

American National Standards Institute. (R2004a). Method for manual pure-tone threshold audiometry (ANSI S3.21 R2004). New York: Acoustical Society of America.

American National Standards Institute. (R2004b). Specifications for audiometers (ANSI S3.6 R2004) . New York: Acoustical Society of America.

American Speech-Language-Hearing Association. (1978). Manual pure-tone threshold audiometry. *Asha*, 20(4), 297-301.

American Speech-Language-Hearing Association. (1988). Guidelines for determining threshold level for speech. *Asha*, 30(3), 85-89.

Carhart, R. (1946). Monitored live-voice as a test of auditory acuity. *Journal of the Acoustical Society of America*. 17. 339-349.

Carhart, R., & Jerger, J.F. (1959). Preferred method for clinical determination of pure-tone thresholds. *Journal of Speech and Hearing Disorders*, 24, 330-345.

Olsen, W. O., & Matkin, N. D. (1991). Speech audiometry. Hearing assessment. Baltimore: University Park Press. pp. 39-135.

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## **Chapter 8** **Procedures for Physical Examinations**

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### **8.1 Introduction**

The medical and audiological history and physical examination are performed to evaluate the eligibility of an individual for the Tinnitus Retraining Therapy Trial (TRTT). A complete medical evaluation of the potential Study Participant includes a detailed, focused history and physical examination aimed at excluding treatable conditions or diseases that can cause tinnitus or threaten his or her health. Such disorders include cerumen impaction, Meniere's disease, acoustic neuroma, thyroid diseases, otosclerosis, glomus tumors of the temporal bone, syphilis, and diabetes. If found, these disorders are treated separately using the appropriate medical approach.

The Study Otolaryngologist, Study Audiologist, or Clinical Coordinator will take a detailed tinnitus and medical history and the Study Otolaryngologist will perform the physical examination to confirm a diagnosis of subjective tinnitus and to rule out any treatable condition

that may be manifested as tinnitus. The second goal of the physical examination is to evaluate the overall well being of the individual. Procedures and guidelines for the examinations are presented below in the order used in the Physical Examination Form.

### **8.2 Tinnitus History**

The Study Audiologist or Clinical Coordinator will collect a detailed description of each individual's tinnitus condition. Potential study participants are asked to describe the following:

- Type of sounds heard, e.g., buzzing, ringing etc.;
- Location of the tinnitus, i.e., right ear, left ear, or within the head;
- Date of onset of tinnitus;
- Time course over which tinnitus developed;
- Changes and fluctuations in tinnitus sound and whether it is ever absent;
- Percentage of the time the participant is aware of the tinnitus;
- Perception of severity;
- Events thought to precipitate onset; and
- Factors exacerbating the tinnitus.

### **8.3 Medical History**

A complete medical history is essential for each TRTT participant. Each potential Study Participant will be asked about the presence of current and past diseases or co-morbidities and any medications used to treat or control these diseases, especially ototoxic medications that may directly link to the tinnitus condition. The presence of symptoms related to diabetes, heart disease, atherosclerosis, and other serious medical conditions will be assessed.

The Study Audiologist, Study Otolaryngologist, or Clinical Coordinator will question potential Study Participants about previous diagnoses and treatments of diseases known to be associated with tinnitus (e.g., Meniere's disease, otosclerosis, facial nerve disorders, etc.), as well

as any history of ear injuries, recurrent ear infections, sensation of ear fullness or pain related to sound tolerance problems, and dizziness and medications used to treat these conditions.

Potential participants will also be asked about a history of chronic allergies, headaches, head injuries, jaw disorders, and recent visual changes. Lastly, the candidate will be asked about his or her social history as it relates to the use of tobacco, caffeine, and alcohol. Occupational exposures to loud noises or to toxic or hazardous noises will also be noted. Note that if the form is not completed by the Study Otolaryngologist, it must be provided to him/her for review before submission.

## **8.4 Physical Examination**

### **8.4.1 Introduction**

The Study Otolaryngologist will perform a thorough neurologic and otologic physical examination as part of the diagnosis of subjective tinnitus. This examination is important in distinguishing between those causes of tinnitus that are medically or surgically treatable and those that are not. Medically or surgically treatable tinnitus may arise from otologic, neurologic, infectious, and drug-related causes.

Medical conditions resulting in objective tinnitus may include:

- Pulsatile events, including carotid stenosis, abnormal vascular findings (e.g., glomus tumor, arteriovenous malformations) or conditions with altered cardiac output (e.g., uncontrolled blood pressure, aortic stenosis, etc.); or
- Middle ear or Eustachian tube disorders.

The physical examination will usually follow a standard order. The Study Otolaryngologist will focus on examination of the head and neck and include evaluation of the outer ear, tympanic membrane, and oral cavity, with attention to the temporomandibular joint and oral palate. The relevant cranial nerves will also be evaluated along with auscultation of the carotid arteries. Laboratory or imaging tests may be required to rule out some causes of treatable tinnitus. These laboratory tests will not be required of all individuals and will be ordered at the discretion of the Study Otolaryngologist.

### **8.4.2 Outer Ear and Tympanic Membrane**

The tympanic membrane should be evaluated with otoscopy, carefully monitoring movements during respiration or myoclonic activity. The middle ear should also be evaluated for

carotid artery or jugular vein abnormalities, vascular tumors, and evidence of glomus tumors. Tuning forks may be used to assess sensorineural or conductive hearing loss.

#### **8.4.3 Nose and Nasopharynx**

An examination of the potential study participant's external nose and septum will be completed to rule out trauma, deformity, evidence of masses, polyps, or exudate. Inspection of the nasopharynx and Eustachian tube for normal appearance and absence of obstructing growths, adenoid hypertrophy, inflammation or post-nasal drainage will be documented.

#### **8.4.4 Oral Cavity and Oropharynx**

The oral cavity should be examined including palpation of the temporomandibular joint for TMJ syndrome, inspection of dentition for malocclusion, and observation of the palate for evidence of palatal myoclonus. The tongue, throat, and tonsils should be examined for signs of inflammatory conditions, abnormal masses, aberrant blood vessels, and conditions that might be associated with tinnitus or hearing loss.

#### **8.4.5 Larynx, Hypopharynx, and Neck**

The larynx, hypopharynx, and neck will be examined for normal laryngeal and hypopharynx function and appearance, including normal gag reflex. The examination will also be performed to rule out evidence of enlarged glands or nodes of the neck and any masses, growths, or bruits present upon auscultation.

#### **8.4.6 Cranial nerves**

Careful testing of each of the cranial nerves is necessary to assess the presence of neurological abnormalities. This examination includes evaluation for neuromas, meningiomas, or multiple sclerosis which might contribute to the tinnitus condition.

#### **8.4.7 Visual Screening and Vestibulo-ocular System and Reflex**

The Study Otolaryngologist will use his or her best clinical judgment as to whether a complete visual examination is required. However, a fundoscopic examination should be performed to rule out the presence of benign intracranial hypertension. An evaluation of spontaneous or gaze evoked nystagmus or related signs consistent with abnormal vestibulo-ocular function should also be performed.

#### **8.4.8 Cardiovascular system**

Auscultation of the heart, carotid arteries, and periaural region must be performed to determine whether carotid bruits, jugular hum, or arterio-venous malformation thrill are present and may contribute to the tinnitus. Blood pressure should be measured to evaluate hypertension as a causative agent for tinnitus. Auscultation of the carotid arteries and the region of the ear is performed to detect somatosounds. Occlusion of the ipsilateral jugular vein may reduce or abolish the tinnitus produced by venous flow disturbances.

Because high cardiac output states (anemia, hyperthyroidism) can cause pulsatile tinnitus, patients suspected of having these conditions should have the circulating level of thyroid and thyroid stimulating hormone measured and a hematocrit taken.

#### **8.5 Imaging and Laboratory Tests**

No specific imaging or laboratory tests are required for entry into the TRTT. The physician should use his or her best clinical judgment in determining whether additional tests (e.g., imaging or laboratory tests) are needed to verify a diagnosis of subjective tinnitus that is not treatable by medical or surgical means.

#### **8.6 Other Tests**

No cognitive nor psychological tests are required for entry into the TRTT. The physician should use his or her best clinical judgment in determining whether a referral for cognitive or psychological testing is required to determine a diagnosis of traumatic brain injury or an emotional, psychological, or psychiatric condition requiring treatment.

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## Chapter 9

### Procedures for Administration of Self-Report and Other Measures

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#### **9.1 Introduction**

Self-report instruments will be administered to all Study Participants in the TRTT. Three categories of self -report measures will be used: tinnitus, psychological, and health/well-being. One cognitive measure will also be administered. Results from these instruments will be used to determine eligibility for participation in the TRTT, to assess outcome, and to identify prognostic indicators of treatment benefits and outcome. The self-report measures are standardized instruments with well-documented psychometric properties. The usual and preferred method for completion will be using paper format per their standardization. Clinical Coordinators will enter the data recorded on the forms into the TRTT database via the TRTT website.

Measures of tinnitus distress that will be used in the TRTT were selected on the basis of their psychometric qualities and their use in other tinnitus investigations to which the TRTT results are likely to be compared. The tinnitus measures will serve as the primary and secondary outcome measures. TRT and cognitive approaches to tinnitus management are both based on the premise that tinnitus distress is related to the individual's awareness of and reactions to tinnitus. To establish a baseline for intervention and to assess change as a function of intervention, the individual's subjective, self-reported perceptions of tinnitus distress are focal. Consequently,

self-report data will be used to document treatment benefits and outcome. Differential treatment effects will be determined by assessing change within each arm of the study.

Personality and psychological variables can affect adjustment to chronic illness and disability. They also figure prominently in compliance with and benefit from treatment recommendations. Although many people are profoundly affected by their disabilities, type and degree of disabilities, in general, are not associated with type or degree of personality traits, or with adjustment (Cook, 1987; English, 1977, Shontz, 1977; Wright, 1983). If correlations are interpreted as causative or if the study population is inadequately defined, then the relationship between physical conditions and psychological variables can be overstated or misinterpreted. The relation between depression and tinnitus is one such example. Claims suggesting that tinnitus can lead to depression remain equivocal in research studies. It is equally, if not more, likely that individuals who are depressed may have more severe tinnitus complaints. Publications in which the conclusions emphasize the endorsement of depressive symptoms despite mean scores well within the normative range, often fail to make the distinction between diagnosed depression and the experience of specific depressive symptoms. Undoubtedly, tinnitus can be depressing. This does not mean, however, that an individual with tinnitus has depression, or that he or she will develop depression. It is entirely possible that depression, or a predisposition to depression, portends greater tinnitus distress. Or, it may be that generalized negative affectivity simply leads to more frequent reports of depressive symptomatology and of tinnitus distress. Tinnitus research is frequently conducted with clinical populations which, by definition, consist of complainers rather than non-complainers who have vastly different reactions to tinnitus (Hallberg and Erlandsson, 1993). In the TRTT, as in many investigations of tinnitus, marked tinnitus distress is an eligibility criterion. This minimizes the possibility of ceiling effects confounding outcome assessments. The study population will not be representative of a general population of people who have tinnitus; rather, it will be representative of those who are likely to be seeking relief from their tinnitus. Hence, care will be taken in interpreting relations among these measures. Mean data will be contrasted with normative data for the psychological measures to determine the extent to which the study population differs from other populations. Correlations between the psychological variables and reports of tinnitus distress will be explored to identify possible prognostic indicators.

The psychological measures will also serve as secondary outcome measures; change in scores will be monitored at specific time intervals during the TRTT. The measures included in the TRTT are brief instruments that focus on variables previously identified as being correlated with subjective tinnitus complaints (e.g., depression, anxiety) and variables that may predict tinnitus distress and benefit from treatment (e.g., positive/negative affectivity).

To assess other factors that may contribute to tinnitus distress and to overall well-being, a life-events questionnaire (Kricos, Erdman, Bratt, and Williams, 2005) will also be completed.

## **9.2 General Guidelines for Administration of Self-report Measures**

By definition, the self-report measures will be completed by the Study Participants. Each participant will be provided access to a quiet, private, and comfortable setting in which the self-report measures can be completed. Instructions, which are included on each instrument, will be reviewed with the Study Participant to ensure that the instructions are understood. Upon completion, the Study Audiologist will verify that all pages of each instrument have been completed. The questionnaires will be administered in paper format per their standardization. The sequence for administration of these measures is described in Table 1.

## **9.3 Self-report Measures**

### **9.3.1 Tinnitus Outcome Measures**

In the TRTT, assessment of the impact tinnitus has on an individual's well-being and daily living is conducted through the use of self-report measures. A number of self-report instruments have been developed to measure tinnitus distress and to document change in the level of distress as a function of treatment. The content area, the reliability and validity, and the specificity and sensitivity of existing tinnitus measures vary considerably. Each Study Participant will complete three tinnitus self-report measures to capture a broad view of the impact that tinnitus has had on his or her well-being and daily living. These three self report measures are largely independent of one another in terms of the type of information obtained from the responses (Newman *et al.* 2004). The measures include the following:

- Tinnitus Questionnaire (Hallam, Jakes, and Hinchcliffe, 1988);
- Tinnitus Functional Index (M. Meikle, personal communication); and
- Tinnitus Handicap Inventory (Newman, Jacobson, and Spitzer, 1996).

#### **9.3.1.1 Tinnitus Questionnaire**

The primary outcome measure selected for the TRTT is the Tinnitus Questionnaire (TQ). The TQ, which is popular in Europe, is a broad-spectrum assessment tool with a total of 52 items. It features a 3-point response scale and can be completed easily in 20 minutes. The instrument has been widely used for clinical and research purposes and is respected for its robust psychometric characteristics (Goebel and Hiller, 1999; Nobel, 1998, 2000). Validated German and Spanish translations of the TQ are available, as is a test manual (Hallam, 1996). The instrument's five-

factor structure has been replicated in several studies attesting to its validity and generalizability. Quartile analyses have been completed for total and for all five factors, or sub-scales. The factors include:

- Psychological distress;
- Intrusiveness;
- Hearing difficulties;
- Sleep disturbances; and
- Somatic complaints

Several aspects of the TQ contribute to its appropriateness to serve as the primary outcome measure for the TRTT. The scope of the instrument and its five-factor structure are well suited to the target areas addressed in TRT and in the standard of care (SC) treatment that will be evaluated in the TRTT. Other instruments include some but not all of these focal areas. The TQ also provides a comprehensive assessment of sleep disturbances experienced secondary to tinnitus, perhaps the most vexing tinnitus problem for many sufferers (Hallam, 1996a). Sleep deprivation impacts psychological well-being, physical health, and daily functioning. Thus, evidence that treatment can improve the quality and amount of sleep for individuals who have tinnitus would have significant public health implications beyond the amelioration of tinnitus *per se*. The TQ's specificity and sensitivity make it an excellent choice for identifying treatment effects and exploring mechanisms of change.

The baseline administration of the TQ will be used to determine eligibility (score  $\geq 40$ ) for the TRTT and to provide a baseline value for comparison at follow-up. The TQ will also be administered at the 3, 6, 12 and 18 month Follow-up Visits, and annually thereafter until study close-out. The primary outcome is a repeated measures analysis of the difference between TQ score at Baseline and Follow-up visits. The difference in TQ score between Baseline and the 18 month Follow-up visit is an additional primary outcome measure. TQ factor (sub-scale) scores at the various follow-up time points will be used as secondary outcome measures.

### **9.3.1.2 Tinnitus Functional Index**

Instruments selected as secondary outcome measures for the TRTT include the Tinnitus Functional Index and the Tinnitus Handicap Inventory. The Tinnitus Functional Index is a newly developed instrument by a group of experienced tinnitus investigators and funded by the Tinnitus Research Consortium. It has 25 items and an eight-factor structure including:

- Intrusiveness;
- Reduced sense of control;
- Cognitive interference;
- Sleep disturbance;
- Auditory difficulties (related to tinnitus);
- Relaxation interference;
- Reduced quality of life; and
- Emotional distress.

Each question on the instrument has a 10-point response scale (ranging from no effect to extreme effect). The Tinnitus Functional Index, particularly designed to assess change, will be especially valuable as an outcome measure for the TRTT. It will be administered at Baseline in the TRTT and at the 3, 6, 12 and 18 month Follow-up Visits, and annually thereafter until study close-out.

### **9.3.1.3 Tinnitus Handicap Inventory**

The Tinnitus Handicap Inventory was developed by Newman *et al.* (1996). It consists of 25 items and is purported to have three factors:

- Functional;
- Emotional; and
- Catastrophic.

The 3-point response scale for the Tinnitus Handicap Inventory consists of “No, Sometimes, and Yes.” The Tinnitus Handicap Inventory has been widely used in the U.S., including by the University of Maryland Tinnitus and Hyperacusis Center (Berry, *et al.*, 2002), but significant questions have been raised regarding item selection, interpretation, and reliability, as well as the validity of the quartile analysis (Goebel and Hiller, 1999; Baguley *et al.*, 2001). In addition, Zachariae *et al.* (2000) report that a factor analysis of a Danish version of the Tinnitus Handicap Inventory did not confirm the structure reported initially. Consequently, only a total score will be used as an outcome measure.

We will use the Tinnitus Handicap Inventory as a secondary outcome measure in the TRTT to permit comparison to other outcome studies in which it has been used. It will be administered at the Randomization Visit and at the 3, 6, 12 and 18 month Follow-up Visits, and annually thereafter until study close-out.

### **9.3.2 Psychological Measures**

The psychological measures included in the TRTT represent a set of variables that are often associated with adjustment to tinnitus and other chronic health conditions. Tinnitus can be a depressing and anxiety-provoking condition. An individual’s general affect, whether positive or negative, influences the ways in which he or she copes with stress. Dispositional optimism is also related to effective management of stress. These measures will be completed by the Study Participants at the Randomization visit and at specific Follow-up Visits, as indicated in Table 1.

#### **9.3.2.1 Beck Depression Inventory Fast Screen**

The Beck Depression Inventory (Beck, Brown, and Steer, 1996) is the most widely used measure of depressive symptoms. The original inventory had 21 items, employed a 4-point Likert scale of 0-3 for each response item, and could be completed in approximately 10 minutes. The areas of assessment relate to cognitive, affective, and somatic symptoms. The Beck Depression Inventory has been used in scores of outcome studies examining treatment effectiveness with both clinical and non-clinical populations. A more recent version, the Beck Depression Inventory II, was revised specifically to conform with two-week criterion for symptom duration described in the Diagnostic and Statistical Manual, 4th Edition (DSM-IV). In addition, a 7 item version, the Beck Depression Inventory Fast Screen (or Quick Screen) was introduced with comparable psychometrics to the original version ( Benedict, *et al.*, 2003). We will use the Beck Depression Inventory Fast Screen in the TRTT.

The Beck Depression Inventory Fast Screen will be completed during the Baseline Eligibility Visit to determine whether the individual should be further evaluated for depression. The threshold score on the Beck Depression Inventory Fast Screen for determining the need for

further evaluation is a score  $\geq 4$  or endorsement (a response of 2 or 3) on item # 7 (suicidal thoughts or wishes). The Clinical Center Director must take appropriate steps with respect to requesting or scheduling an appropriate consultation for individual failing the screen. Following professional evaluation, individuals who have not passed the screen may be evaluated for eligibility for participation in the TRTT. Repeated measures of the Beck Depression Inventory Fast Screen over the course of the TRTT will permit Study Participants to be monitored for onset of serious depression as a possible consequence of treatment or other contributing factors. The TRTT will define the same threshold - a score of 4 or greater on the Beck Depression Inventory Fast Screen or endorsement of item # 7 (suicidal thoughts or wishes) - as an adverse event. The Clinical Center Director is responsible for referring the Study Participant to an appropriate health care provider in this circumstance.

### **9.3.2.2 State-Trait Anxiety Inventory**

The State-Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, Vagg and Jacobs, 1983) has been used extensively in research and clinical practice as a self-report measure of trait anxiety (or anxiety "proneness") and state anxiety (i.e., transitory anxiety experienced under specific conditions). The State-Trait Anxiety Inventory consists of 20 items for each subscale. The entire State-Trait Anxiety Inventory can be completed in approximately 10 minutes; a single subscale can be completed in about 6 minutes. It should be noted that the instrument is always referred to as the "Self-Evaluation Questionnaire" when speaking to respondents; the term anxiety is never used to describe the focus of the instrument. The State (i.e., how an individual feels at this moment) subscale's four-point response scale options are "Not At All, Somewhat, Moderately So, and Very Much So." The Trait (i.e., how one generally feels) subscale's response options include "Almost Never, Sometimes, Often, and Almost Always."

Prior to participation in the TRTT patients will complete both subscales of the State-Trait Anxiety Inventory ; only the State subscale, in which change is typically evidenced as conditions change, will be administered at the 6- and 18-month Follow-up Visits. Trait anxiety will be evaluated only to explore its possible role as a prognostic indicator.

### **9.3.2.3 Positive and Negative Affect Schedule**

The Positive and Negative Affect Schedule (Watson, Clark and Tellegen, 1988) consists of 20 adjectives describing feelings or emotions (e.g., excited, scared, irritable, nervous). Respondents rate the extent to which they feel each of the 20 adjectives. A 5-point scale includes options ranging from "Very Slightly or Not at All, to Extremely." The 20 adjectives can be rated in approximately 10 minutes. The instrument can be administered using a variety of different temporal options ranging from *right now* to *generally*, permitting the feelings and emotions to be assessed as a characteristic *trait*, or a current *state* of mind. Treatment benefits are likely to

effect changes in an individual's state. Trait findings, however, are not typically sensitive to treatment effects. To elucidate further the relation between reports of tinnitus distress and reports of depressive symptoms, it is helpful to determine whether negative affect is characteristic of the individual in general, or if the negativity is a current state related to events that are impacting him or her now.

In the TRTT, the Positive and Negative Affect Schedule will be used to rate how much each Study Participants generally believes each of the adjectives apply to him or herself, and will be administered at baseline, and at the 6 and 18 months Follow-up Visits.

#### **9.3.2.4 Life Events Checklist**

The instrument used to assess well-being in the TRTT is the Life Events Checklist. Life events can result in stress and anxiety that impact well-being in a number of ways that can ultimately affect or confound treatment efficacy and success. In the TRTT we will use the Life Events Checklist (LEC, Kricos, Erdman, Bratt, and Williams, 2005). The LEC is based on the content of the 43-item Social Readjustment Rating Scale (Holmes and Rahe, 1967; Miller and Rahe, 1997) and the 90-item Life Events Inventory (Cochrane and Robertson, 1973). It was originally developed for use in the National Institute of Deafness, and Other Communication Disorders/Veterans Administration Hearing Aid Clinical Trial to identify life events that could interfere with adjustment to hearing problems and/or hearing aid use. The content of the parent instruments were reviewed by a panel of VA and consulting audiologists and consolidated into 13 items by combining related content areas. The Life Events Checklist can be completed in 5-20 minutes depending on the extent to which a patient chooses to describe the impact of the intervening life event on his or her tinnitus.

The Life Events Checklist will be administered at entry into the TRTT and again at the 6 and 18 month Follow-up Visits to monitor significant changes in an individual's life that could contribute to or confound tinnitus distress or benefit from treatment.

#### **9.3.4 Digit Symbol Substitution Task**

The Digit Symbol Substitution Task is a test of cognitive function that assess the ability of an individual to focus attention to a task and recall. It consists of digit-symbols pairs followed by a series of digits with blanks below. The respondents are required to write in the symbol that is paired with the digit in the blank space as quickly as possible within the allocated time, usually 90 seconds. In the TRTT, we will use the Digit Symbol Substitution Task to assess the ability of the Study Participant to concentrate. Indirectly, this measure will assess the ability of the Study Participant to ignore the tinnitus signal to complete a task requiring attention and psychomotor

skill. Strictly speaking, the Digit Symbol Substitution Task is not a self-report instrument, but will be administered by the Clinical Coordinator or Study Audiologist at baseline, and at the 6 and 18 month visits.

### **9.3.5 Other Quality of Life Measures**

#### **9.3.5.1 Hearing Handicap Inventory**

The Hearing Handicap Inventory for Adults (Newman, Weinstein, Jacobsen, and Hug, 1990) is a 25-item self-assessment scale that measures the impact of hearing impairment on communication ability in daily life and assesses two subscales (emotional and social/situational). A screening version was derived from the original Hearing Handicap Inventory for Adults with only 10 items and similar psychometric properties and with 5 items contributing to each subscale (Newman, Weinstein, Jacobsen and Hug, 1991).

In the TRTT, the Hearing Handicap Inventory for Adults screen will be used to assess how much the impact of hearing loss will affect the overall and tinnitus related quality of life for Study Participants with mild hearing impairment. The Hearing Handicap Inventory for Adult Screening version will be administered at Baseline and then again at the 6- and 18-month Follow-up Visits.

#### **9.3.5.2 EuroQOL**

The EuroQOL is an instrument used to assess general health-related quality of life. It consists of 5 items assessing difficulty in performing activities of daily living using a three part Likert scale assessing degree of ability to perform the task (none, some, or cannot perform). The EuroQOL also has a visual analogue scale, which is a 20 cm scale with an endpoint at the top labeled as best imaginable health state and a score of 100 and an endpoint at the bottom labeled worst imaginable health with a score of 0. The EuroQOL is widely used as a measure to assess overall health benefit of an intervention for determination of cost-benefit analyses. In this setting, the instrument is used to compare the effectiveness of an intervention compared with other health conditions.

The EuroQOL will be administered at entry into the TRTT and again at the 6 and 18 months Follow-up Visits to assess change in general health related quality of life.

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**Table 1**  
**Sequence of Administration of Self-Report Instruments**

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The self-report and cognitive instruments will be administered in the same sequence for all Study Participants. The test order for baseline and follow-up visits is as follows:

**Baseline Visit: during baseline visit to assess eligibility**

1. Tinnitus Questionnaire
2. Beck Depression Inventory Fast Screen

**Randomization Visit: after patient has signed informed consent, but before randomization takes place (in this order)**

1. Tinnitus Functional Index
2. Tinnitus Handicap Inventory
3. Digit-Symbol Substitution Task
4. Hearing Handicap Inventory
5. State-Trait Anxiety Inventory
6. Positive and Negative Affect Schedule
7. Life Events Checklist
8. EuroQOL

**3 and 12 month Follow-up Visits**

1. Tinnitus Questionnaire
2. Tinnitus Functional Index
3. Tinnitus Handicap Inventory
4. Beck Depression Inventory Fast Screen

**6 and 18 month Follow-up Visits**

1. Tinnitus Questionnaire
2. Tinnitus Functional Index
3. Tinnitus Handicap Inventory
4. Beck Depression Inventory Fast Screen
5. Digit-Symbol Substitution Task
6. Hearing Handicap Inventory
7. State-Trait Anxiety Inventory
8. Positive and Negative Affect Schedule
9. Life Events Checklist
10. EuroQOL

**30, 42, and 54 month Follow-up Visits (annual visits until study close-out)**

1. Tinnitus Questionnaire
2. Tinnitus Functional Index
3. Tinnitus Handicap Inventory

## References:

Baguley, DM, & Andersson, G. Factor Analysis of the Tinnitus Handicap Inventory. *American Journal of Audiology, American Journal of Audiology*, 2003; 12: 31-34.

Beck AT, Steer RA, and Brown GK. (1996). *Beck Depression Inventory II (BDI-II) Manual*. New York: Harcourt Brace Jovanovich.

Benedict RH, Fishman I, McClellan MM, Bakshi R, Weinstock-Guttman B. Validity of the Beck Depression Inventory-Fast Screen in multiple sclerosis. *Mult Scler*. 2003 Aug;9(4):393-6.

Berry, JA, Gold SL, Frederick EA, Gray, WC, Staeker, H. Patient-based outcomes in patients with primary tinnitus undergoing tinnitus retraining therapy. *Archives of Otolaryngology Head and Neck Surgery*, 2002, 128(10), 1153-7.

Budd RJ, Pugh R. (1995). The relationship between locus of control, tinnitus severity, and emotional distress in a group of tinnitus sufferers. *Journal of Psychosomatic Research*, 39(8): 1015-1018.

Budd RJ, Pugh R. (1996). Tinnitus coping style and its relationship to tinnitus severity and emotional distress. *Journal of Psychosomatic Research*, 41(4): 327-335.

Cochrane, R and Robertson, A. The life events inventory: a measure of the relative severity of psycho-social stressors. *Journal of Psychosomatic Research*. 1973;17:135-40.

Cook, D., Psychosocial impact of disability. In R.M. Parker (Ed.), *Rehabilitation Counseling: Basics and Beyond*. Austin, TX: Pro-Ed. 1987.

English, R.W., The application of personality theory to explain psychological reactions to physical disability. In R.P. Marinelli, and A.E. Dell Orto (Eds.), *The Psychological and Social Impact of Physical Disability*. New York: Springer Publishing Company. 1977.

Hallam, R.S. Manual of the Tinnitus Questionnaire (TQ). London: Psychological Corporation. 1996a.

Hallam, R.S. Correlates of sleep disturbances in chronic distressing tinnitus. *Scandinavian Audiology*, 1996b; 25, 263-266.

Hallam, R.S., Jakes. S.C. & Hinchliffe, R. Cognitive variables in tinnitus annoyance. *British Journal of Clinical Psychology*, 1988; 27, 213-222.

Holmes TH and Rahe RH. The social readjustment rating scale. *Journal of Psychosomatic Research*, 1967; 11:213-8.

Kricos, P.B, Erdman S.A., Bratt, G., and Williams, D. (2005). Psychological correlates of hearing aid adjustment. *J Am Acad Audiol* 2007 18:304-22.

Miller MA and Rahe RH. Life changes scaling for the 1990s. *Journal of Psychosomatic Research*, 1997; 43:279-92.

Newman C.W., Weinstein B.E., Jacobson G.P., Hug G.A. The Hearing Handicap Inventory for Adults: psychometric adequacy and audiometric correlates. *Ear Hear*. 1990 11:430-3.

Newman C.W., Weinstein B.E., Jacobson G.P., Hug G.A. Test-retest reliability of the Hearing Handicap Inventory for Adults. *Ear Hear*. 1991 12:355-7.

Newman, C. W. & Sandridge, S. A. "Tinnitus questionnaires", in Snow, J.B.(ed.), *Tinnitus: Theory and Management*, B.C. Decker: Hamilton, Ontario Canada, pp. 237-254 (2004).

Scheier MF, and Carver CS. Optimism, coping, and health: assessment and implications of generalized outcome expectancies. *Health Psychology*, 1985; 4: 219-47.

Scheier MF, Carver CS, and Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): A reevaluation of the Life Orientation Test. *Journal of Personality and Social Psychology*, 1994; 67:1063-78.

Shontz, F.C., Physical disability and personality: Theory and recent research. In R.P. Marinelli, and A.E. Dell Orto (Eds.), *The Psychological and Social Impact of Physical Disability*. 1977. New York: Springer Publishing Company.

Spielberger CD, Gorsuch RL, Lushene RE, Vagg PR, and Jacobs GA. Manual for the State-Trait Anxiety Inventory (Form Y). 1983. Palo Alto, CA: Consulting Psychologists Press.

Watson D, Clark LA, and Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS Scales. *Journal of Personality and Social Psychology*, 1988; 54:1063-70.

Wright, B.E., *Physical Disability: A Psychosocial Approach*. 1983. New York: Harper and Row.

Zachariae, R., Mirz, F., Johansen, L.V., Andersen, SE, Bjerring, P, & Pedersen, CE. Reliability and validity of a Danish adaptation of the Tinnitus Handicap Inventory. Scandinavian Audiology, 2000; 29; 198-210.

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## Chapter 10

### Study Participant Visits and Examinations

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#### **10.1 Introduction**

Each randomized participant enrolled into the Tinnitus Retraining Treatment Trial (TRTT) is seen for the following visits: Baseline Eligibility Visit, Randomization Visit, two Treatment Visits, and Follow-up Visits at 3 months, 6 months, 12 months, and 18 months after the first Treatment Visits, and annually thereafter until study close-out. Additional clinic visits to provide patient care may be scheduled as needed, but such visits are at the discretion of the Study Audiologist or request by the Study Participant. Any pertinent information collected at these additional visits is recorded on an Unscheduled Contact Form. The regularly scheduled study visits are listed in Table 10.1.

Information for the specific study visits is provided in the following sections: Baseline Eligibility Visit and Randomization Visit (Chapter 5), Treatment Administration, Sections 10.2; Follow-up Visits, Section 10.3 and 10.4. Procedures for handling missed visits, inactive Study Participants, transfer Study Participants, deceased Study Participants, and other special problems in follow-up are found in Sections 10.4 through 10.8.

## **10.2 Treatment Administration**

The Initial Treatment Visit (T1) may take place immediately following the Randomization Visit, but must take place within two months following the Randomization Visit. If, for any reason, T1 cannot take place within two months, then an application may be made to the Steering Committee to extend the time window.

T1 will include directive counseling (DC) or the standard of care (SC) clinical consultation usually provided in the military, according to the treatment assignment. For Study Participants assigned to sound generators (SGs), T1 will also include fitting and activation of these devices. Procedures used to administer these treatments are described in Chapters 11 and 12.

When T1 has been completed and the date of the visit recorded on the TRTT website, an appointment schedule for the Study Participant will be automatically re-generated. The dates specified on this schedule are based on the date of T1. This schedule lists the ideal dates for all succeeding follow-up study visits, with the permissible time window within which each visit must be completed. There will be a data entry slot on the schedule for the Clinical Coordinator to record the actual date of completion of each follow-up visit.

At one month following T1, Study Participants assigned to DC will complete reinforcement counseling. At this time, the proper use, and maintenance of SGs will also be reviewed. This one month follow-up visit is considered part of the Treatment Visit, and is called Treatment Visit 2 (T2). Study Participants assigned to SC will also be seen at T2 to monitor progress and to maintain the same amount of personal contact.

Measurement of loudness discomfort level (LDL) is an important piece of the treatment protocol for all patients and especially for hyperacusis patients. LDL is tested by measuring pure tone thresholds at the frequencies that the LDL is measured, and then by measuring LDL thresholds. The blinded Study Audiologist will measure LDLs at T2 and at the 3 month Follow-Up Visit using the LDL Assessment for Treatment Form. It is also collected during the Baseline and Follow-up ATH exams. The counseling Audiologist is permitted to view this information to use during counseling.

## **10.3 Follow-up Visits**

Follow-up Visits will take place at 3, 6, 12, and 18 months after T1, and then annually until study close-out. Study Participants in all groups are seen at all Follow-up Visits. All Follow-up Visits involve reinforcement counseling as needed.

The Clinical Coordinator or the blinded Study Audiologists (i.e., the Clinical Center Study Audiologist who is not involved in counseling the Study Participant) will complete the Follow-up Medical History Form at each follow-up visit, and ask each participant to complete the following data collection instruments: the Tinnitus Questionnaire, Tinnitus Handicap Inventory, Tinnitus Functional Index, and the Beck Depression Inventory Fast Screen at each Follow-up Visit.

The Follow-up TRT Interview and a full audiological/tinnitus/hyperacusis evaluation, consisting of audiometric pure tone, speech recognition threshold, tinnitus pitch and loudness match, loudness discomfort level (LDL), and word recognition testing will be completed at the 6, 12 and 18 months visit. In addition, the following forms will also be completed at the 6 and 18 month study visits: the Digit Symbol Substitution Test, Hearing Handicap Inventory, State Trait Anxiety Inventory, Positive and Negative Affect Schedule Life Events Checklist, and EuroQOL. It is important that the Study Audiologist who is **not counseling the Study Participant** perform these activities to preserve blinding when measuring these outcomes (see Table 10.2 ).

Note that LDL is checked at all follow up visits. At T2 and the 3 month follow-up visit (F1), the LDL is recorded on the LDL Assessment for Treatment Form for each participant, and at the 6, 12, and 18 months visits, it is recorded on the Audiological/Tinnitus/Hyperacusis (ATH) Examination. LDL testing at these visits is completed by the blinded study Audiologist who is not involved in the treatment of the Study Participant, but the counseling Audiologist may use the LDL results for treatment.

All follow-up visits past 18 months follow-up include only the tinnitus specific health-related quality of life instruments are collected (i.e, the Tinnitus Questionnaire, Tinnitus Functional Index, and Tinnitus Handicap Inventory). These forms may either be completed in person or mailed and returned by post. An in-person visit is not required.

#### **10.4 Time Windows for Completing Study Visits**

The time windows within which study visits must occur are shown in Table 10.1. Time is measured from the date of the T1 for Follow-up Study Visits. All visits should be completed as close as possible to the expected date of the visit per the appointment schedule. In monitoring adherence to the protocol, the proportion of visits from each clinic that fall within 2 weeks of the ideal date is reported.

#### **10.4.1 Missed Visits**

If any Follow-up Visit is missed and, for whatever reason, cannot be rescheduled within the permissible time limits for the visit, a notation that a visit has been missed should be noted on the TRTT website and a Missed Visit/Forms Form completed.

Whenever a Study Participant misses a scheduled study appointment, the Clinical Coordinator should contact him or her immediately and arrange another appointment so that the follow-up visit occurs within the permissible time window. If, at any time, the Study Participant cannot be located (which is unlikely for military personnel), an intensive search should be instituted by the Clinical Center immediately, even if the Study Participant has not missed a visit. The Clinical Center should use all available resources to locate the Study Participant, including writing or telephoning each of the contacts listed on the Patient Locator Form. Because this search may be long and time-consuming, it is important that this search be started as soon as any member of the Clinical Center staff is aware that there is a problem. The steps taken to locate the Study Participant should be documented. Experience has shown that with sufficient ingenuity and effort it is almost always possible to find missing Study Participants. When all avenues have been exhausted by the Clinical Center staff and the Study Participant has not been located, the Study Chair should be notified and the procedures outlined in Section 10.4.2 (Inactive Study Participants) followed.

#### **10.4.2 Inactive Study Participants**

Any Study Participant who has missed two consecutive visits is considered to be inactive, or lost to follow-up until she or he is seen by a study staff member for a complete study visit and is reinstated. The Clinical Center staff is not relieved of responsibility for "inactive" Study Participants. On the contrary, such Study Participants generally require much more staff time than those following the regular schedule. The requirements for managing inactive Study Participants are:

- The Study Participant should be contacted at least every three months. At this time, his or her situation should be reviewed, and if possible, arrangements should be made for him or her to return to the Clinical Center;
- If possible, the Study Participant will be requested to complete the self-test instruments using paper forms that can be mailed to him or her.
- If a Study Participant cannot be located, it is the responsibility of the Clinical Center Director to notify the Study Chair in writing, reviewing in detail the Study Participant's situation and the measures that have been taken to assure adequate

follow-up. The Steering Committee reviews the Study Participant's record and formulates recommendations for action to be taken.

- It is the responsibility of the Clinical Center Director to send written notification to the Study Chair (and a copy to the Director of the Data Coordinating Center (DCC)) outlining the steps taken to locate the Study Participant.

Every effort should be made to encourage an inactive Study Participant to return. If an inactive Study Participant is persuaded to resume clinic visits, the follow-up visit indicated on the Appointment Schedule (as appropriate for that time period) should be completed for this Study Participant. Receipt by the DCC of a Follow-up Visit form completed by Clinical Center staff automatically removes the Study Participant from the inactive category.

All pertinent facts concerning the interim history since the participant's last completed Follow-up Visit should be summarized under the appropriate items on the first Follow-up Visit form which is completed following reinstatement.

## **10.5 Other Contact with Study Participants**

### **10.5.1 Unscheduled Visits to the Clinical Center**

In certain cases, the Study Audiologist or Clinical Director may decide that it is in the Study Participant's best interest to return for additional visits beyond the follow-up visits required by the study protocol. Study Participants who experience difficulties also may call and request such visits. The Study Participant may be scheduled for a non-study visit at any time at the discretion of the Study Audiologist. The information obtained at non-study visits should be collected and submitted to the DCC as an Unscheduled Visit., recorded either on the usual data collection forms, or on an Unscheduled Contact Form.

### **10.5.2 Telephone Contacts between Visits**

Maintaining contact with the Study Participant between visits to the clinic has been demonstrated to be an important aspect of continued Study Participant interest and satisfaction. All Study Participants are to be called by the Clinical Coordinator at the midpoint between each follow-up visit or as deemed necessary for effective counseling by the Study Audiologist.

Clinical Coordinators should call any Study Participant more frequently if deemed necessary to maintain this Study Participant's cooperation.

## **10.6 Transfer Study Participants**

If any Study Participant expects to move from the area served by the Clinical Center in which he or she is enrolled, the Study Audiologist caring for the Study Participant should determine whether it is feasible for the Study Participant to travel to any other TRTT Clinical Center for follow-up care. If the Study Participant's new location is expected to be within a reasonable distance of another Clinical Center, the Study Participant should be given the name and telephone number of the Center Director and Clinical Coordinator of that Clinical Center, and the original Clinical Coordinator should schedule an appointment for transferring the Study Participant at the new Clinical Center. Before the Study Participant moves, the Clinical Coordinator should update the Patient Locator Form. After contact with the new Clinical Center has been made, and an appointment has been scheduled, the original Clinical Center should forward copies of all the Study Participant's records to the new Clinical Center. When the Study Participant has been seen once in the new Clinical Center, the DCC transfers the Study Participant officially to that Clinical Center. At that time, the new Clinical Center becomes responsible for following the Study Participant. The Study Participant's I.D. number will change at the time of transfer to reflect that the second Clinical Center is responsible for treating and seeing the transferred Study Participant.

If a Study Participant will be away from their primary Clinical Center during the allowable time window for the next scheduled visit and if they are in the vicinity of another Clinical Center, then such participants may be temporarily transferred to the second Clinical Center. In this case, the primary Study Audiologist should write a letter summarizing the Study Participant's history and present status to the Study Audiologist of the second Clinical Center where the Study Participant is to be seen. Audiological data may be sent with this letter if indicated for the Study Participant's care. The Clinical Coordinator should call ahead and schedule an appointment for the Study Participant. In the case of a temporary transfer, the Study Participant's entire record does not need to be sent; a letter will suffice.

A copy of the correspondence between the Clinical Centers regarding all transfer Study Participants should be sent to the DCC after removing all identifying information.

## **10.7 Death of a Study Participant**

As soon as Clinic personnel become aware that a Study Participant has died, a Study Termination Form must be completed and forwarded to the DCC.

## **10.8 Special Problems in Follow-up**

Every effort should be made to maintain the follow-up visit schedule outlined in Table 10.1 for each Study Participant. However, during the course of the trial particular Study Participants may develop special problems that require some individualization of the procedures. Problem participants include those who move from the area of the Clinical Center, participants who are called to active duty and deployed, or those who become debilitated and cannot return to the Clinical Center. One important principle should be kept in mind in determining the management of these Study Participants. Even if a Study Participant should become inactive, every effort should be continued to reinstate him or her to active status. Maximum possible contact between Study personnel and the Study Participant should be maintained until the Study Participant dies or the study is terminated.

If, for any of the reasons discussed above, a Study Participant cannot reasonably be expected to return for every scheduled study visit, then the Clinical Center Director should review the participant's situation and make an alternative plan for completing each follow-up visit. It may be possible to transfer the Study Participant to another Clinical Center, arrange special transportation for the Study Participant, or conduct a Study Visit at another location. At the very least, Study Participants should be requested to complete the questionnaires evaluating tinnitus intrusiveness and annoyance (Tinnitus Questionnaire, Tinnitus Functional Index, and Tinnitus Handicap Inventory) by sending a paper copy of the form to the Study Participant along with a pre-posted return envelope.

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**Table 10.1 Study Visit Schedule****A. Treatment Visits**

<b>Visit Number *</b>	<b>Visit Acronym</b>	<b>Permissible time window</b>
Initial Treatment Visit	(T1)	0 to 2 months after randomization
Second Treatment Visit	(T2)	3 to 5 weeks after T1

**B. Follow-up Visits**

<b>Visit Number *</b>	<b>Visit Acronym</b>	<b>Target time from T1</b>	<b>Permissible time window</b>
Follow-up Visit 1	(F1)	3 months	>10 weeks to 4½ months
Follow-up Visit 2	(F2)	6 months	>4½ months to 9 months
Follow-up Visit 3	(F3)	12 months	>9 months to 15 months
Follow-up Visit 4	(F4)	18 months	>15 months to 21 months
Follow-up Visit 5	(F5)	30 months	>24 months to 36 months
Follow-up Visit 6	(F6)	42 months	>36 months to 48 months
Follow-up Visit 7	(F7)	54 months	>48 months to 60 months

**Table 10.2 Study Visit Schedule**  
Data Collected at Follow-up Visits

**A. Questionnaires and Forms**

Visit	Questionnaires and Forms											
	FM	TQ	TF	TI	BD	FT	DS	HH	FS	PA	LE	EQ
3 mo	✓	✓	✓	✓	✓							
6 mo	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12 mo	✓	✓	✓	✓	✓	✓						
18 mo	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
30 mo		✓	✓	✓								
42 mo		✓	✓	✓								
54 m		✓	✓	✓								

FM Follow-up Medical History Form

DS Digit Symbol Substitution Task

TQ Tinnitus Questionnaire

HH Hearing Handicap Inventory

TF Tinnitus Functional Index

FS State-Trait Anxiety Inventory

TI Tinnitus Handicap Inventory

PA Positive &amp; Negative Affect Schedule

BD Beck Depression Inventory

LE Life Events Checklist

FT Follow-up TRT Interview

EQ EuroQOL

**B. Audiological/tinnitus/hyperacusis (ATH) Measures**

Visit	ATH Evaluation Measures						
	audiometric pure tone	speech recognition threshold	tinnitus pitch match	tinnitus loudness match	loudness discomfort level	word recognition scores	
1 mo (T2)	✓				✓		
3 mo	✓				✓		
6 mo	✓	✓	✓	✓	✓	✓	
12 mo	✓	✓	✓	✓	✓	✓	
18 mo	✓	✓	✓	✓	✓	✓	

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## Chapter 11

### Directive Counseling

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#### 11.1 Introduction

Directive Counseling (DC) is one of the two essential components of Tinnitus Retraining Therapy (TRT). The other essential component is low-level sound or sound therapy (ST). The overall goal of DC is to educate the participant about his or her condition, facilitating the “demystification” of the participant’s tinnitus problem and neutralization of the participant’s negative emotional associations with his or her tinnitus. The Study Audiologist also uses DC to help the Study Participant separate problems related to his or her supra-threshold sound sensitivity (hyperacusis or phonophobia) from the tinnitus condition. The way in which these goals are achieved is through education. Both are considered crucial for the successful management of tinnitus and/or hyperacusis.

In this chapter the components of the initial DC appointment are described, including key points that direct the participant toward habituation of his or her tinnitus. Visual aids include a flip-chart presentation specifically designed for the TRTT and a three-dimensional model of the ear. The visual aids required for the DC session are identified at the point in the counseling session where they are used. These materials serve to pace and guide the counselor through the DC session, insuring that the DC rigor, intensity, and length are equivalent across Study Participants and Clinical Centers.

This chapter also describes the strategies used during follow-up DC sessions.

## **11.2 Initial DC Appointment**

The Study Audiologist must prepare and review all materials needed for counseling before the initial DC session. These materials include the Baseline TRT Interview Form (which is completed at baseline by the Study Participant), the TRT category assigned to the Study Participant at baseline by the Study Audiologist, all audiological/tinnitus/ hyperacusis (ATH) evaluation test data, and the visual aids used during the counseling session. The Study Audiologist is also responsible for ensuring that the visual aids, including the three-dimensional model of the ear and the flip-chart, are ready in advance. The Study Audiologist should also bring a copy of the TRT checklist for the imminent counseling session. S/he should complete Sections A and B before counseling begins and complete the remaining sections during and after the counseling session. Appendix A includes a script and copies of the visual aids, and Appendix B some additional examples that can be used during Directive Counseling.

The voice recorder which is used to monitor the counseling session for quality control should be set up and checked prior to the counseling session to ensure that there are no difficulties or delays associated with this aspect of the study.

During the initial DC session, the Study Audiologist:

- Explains the results of the ATH evaluation;
- Educates the Study Participant about the anatomy and physiology of the normal auditory system;
- Describes how the central auditory system and higher cortical processes may interpret an auditory signal and how this processing relates to the participant's tinnitus perception;
- Describes the Jastreboff model of tinnitus; and
- Sets goals with and for the individual participant.

Each participant is counseled individually, along with any family members who may be present during the session. At the Initial Treatment Visit (T1), which lasts approximately 2 hours, the Study Audiologist systematically presents information designed to help the Study Participant change the way that he or she views his or her tinnitus and/or hyperacusis, addresses the individual participant's concerns, and recommends strategies to help the participant achieve the long-term goal of habituating the awareness of, and annoyance to, his or her tinnitus. Sufficient time is allowed to answer the participant's questions and to ensure that he or she understands all information presented and the treatment goal of reducing the impact of tinnitus in the participant's life.

### **11.2.1 ATH Evaluation**

The first step in a DC session is to review and explain to the participant the results of his or her ATH evaluation. One objective of this review is to help the participant begin to understand and separate his or her hearing status and/or sound tolerance problem from the tinnitus condition. It is necessary to have a copy of the audiogram and other materials generated at the participant's ATH evaluation. These materials may be enlarged using a photocopier for easier viewing and explanation.

During the review of the participant's audiometric results, the Study Audiologist will show the participant the audiogram for each ear separately and explain to the participant how to interpret the pure-tone results and speech-test data. The Study Audiologist then will compare the participant's results to those expected for a normal-hearing person, noting any differences between ears and the relation between the participant's audiometric configuration and history of associated noise trauma or ototoxicity.

The concept and measurement of Loudness Discomfort Level (LDL) are reviewed next. The Study Audiologist describes the test and shows the participant his or her results. These results are then compared with those for someone with normal supra-threshold sensitivity to sound, and also to those for someone with reduced sound tolerance. The Study Audiologist will use the results from the Baseline TRT Interview Form to discuss with the participant how the LDL provides evidence of hyperacusis, phonophobia (i.e., fear of specific sounds), misophonia (i.e., dislike of specific sounds), or normal sound tolerance.

The Study Audiologist next describes the results of the Tinnitus Pitch Match, emphasizing that the pitch obtained may not be an exact match, but rather a "snapshot" of the sound closest in frequency and sound quality to the pitch of the participant's most troublesome tinnitus signal. The Study Audiologist explains that the frequency of the pitch match will vary from participant to participant (and even from day-to-day for a given participant), and that each participant will

describe his or her tinnitus quality differently (e.g., hissing, ringing, buzzing, chirping, etc). The Study Audiologist will emphasize that the pitch match or qualitative type of sound has little or no predictive value for the process of habituation. The Study Audiologist specifically should reinforce the idea that the type of noise or the pitch of tinnitus is meaningless with respect to whether the treatment will be effective, but changes in the qualitative aspects of the tinnitus signal may make it more or less annoying from one day to the next.

Immediately following discussion of the Tinnitus Pitch Match, the Study Audiologist will review the results for the Tinnitus Loudness Match. The loudness of the tinnitus signal is matched to the loudness of the Tinnitus Pitch Match stimulus, which usually is judged by participants to be within 2 to 10 dB of the audiometric threshold of the Tinnitus Pitch Match frequency. The Study Audiologist presents the tinnitus loudness in terms of sensation level (i.e., the number of decibels above the audiometric threshold for the Tinnitus Pitch Match frequency). The Study Audiologist should emphasize that tinnitus is a weak signal in terms of sensation level, despite the fact that it may be annoying or intrusive to the participant. In particular, the Study Audiologist should use care not to minimize the importance of annoyance or intrusiveness of the tinnitus signal to the participant. A neutral statement to use is that, "The physical properties of the tinnitus signal indicate that it is an extremely weak signal in relation to your hearing thresholds; however, this does not mean that the tinnitus is not annoying or intrusive for you." The concept that the tinnitus is a weak signal will be reinforced later in the DC.

Finally, the Study Audiologist reviews the speech tests, explaining that these tests are designed to demonstrate the ability of the participant to detect and understand normal conversational speech. The Study Audiologist explains the speech-tests results, beginning with the speech reception threshold (SRT). The SRT measures the participant's ability to detect two syllable words having equal stress on each syllable (e.g., baseball, hotdog). The SRT result (reported in dB HL) for each ear should agree closely with the pure-tone average (also reported in dB HL) for the audiometric speech frequencies (i.e., 500, 1000, and 2000 Hz).

The word recognition or speech discrimination score (% correct), represents the participant's ability to understand familiar single-syllable words delivered to each ear at an optimum presentation level. The 25-word lists used in measuring word recognition are phonetically balanced and represent the range of speech sounds heard in normal conversation.

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### **11.2.2 Anatomy and Physiology of the Auditory System**

The next portion of DC is comprised of a review and explanation of the anatomy and physiology of the auditory system. The Study Audiologist will use the presentation materials designed for the TRTT during this part of the counseling session to illustrate the points being discussed. The three-dimensional model of the ear will also be used for this part of the DC session.

The visual aid presentation starts with a diagram of the ear, including the gross anatomy of the components of the ear. The Study Audiologist will simultaneously use both the first slides in the visual aid material and the three-dimensional model of the ear to describe the anatomy and physiology of the outer, middle, and inner ear and to discuss their relations to possible origins of tinnitus and the site of an associated hearing loss. The Study Audiologist should spend the majority of time in this section educating the participant about the inner ear.

Points to cover about the outer ear are:

- The pinnae direct sound waves to the eardrums
- Sound waves cause mechanical vibration of the eardrum

Points to cover about the middle ear are:

- The middle ear is air-filled
- Transmission of sound takes place via three small bones in the middle ear (malleus, incus, and stapes)
- Mechanical transmission of sound through the middle ear (from the eardrum to the inner ear) occurs by vibration of these three bones

The Study Audiologist uses the three-dimensional model of the ear to describe the anatomy of the inner ear, including the cochlea and semicircular canals. The Study Audiologists will point out these structures and explain that the semicircular canals are important for maintaining balance, while the cochlea is the important organ for hearing. The Study Audiologist will focus primarily on the cochlea, and demonstrate the relation between the bones of the middle ear, the semicircular canals, and the cochlea. The outer and middle ear structures facilitate the sound transmission to the cochlea, which is best described as a hollow spiral tube filled with fluid that bathes sensory cells called inner and outer hair cells. The Study Audiologist should stress that the

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transmission of a sound signal within the cochlea is due to the wave motion of the fluid within the cochlea.

The Study Audiologist uses the next set of diagrams in the presentation to show the inner and outer hair cells and the neural fibers that extend from the bottom of the hair cells to become the auditory nerve bundle. This neural bundle conveys the sound signal to the brain via a series of electrical impulses. The Study Audiologist will point out the hair cell bodies, cilia, and nerve fibers that form the auditory nerve and explain that the inner and outer hair cells are key sensory structures that transduce and amplify the mechanical sound signal from the eardrum. These ear structures act as a transformer changing mechanical energy into an electrochemical signal. It is at the inner and outer hair cells that the sound signal is converted to a signal that is recognized by the brain as sound. The Study Audiologist will emphasize that we “hear” when higher centers within the brain are activated. The ear is the primary peripheral processor of sound stimulation.

The Study Audiologist will then go on to describe the separate functions of the inner and outer hair cells. (The visual aid material will have electron microscopy images of the basilar membrane and hair cells.) Inner hair cells (IHCs) are the primary sensory transducers of sound. The signal from the movement of fluid is detected by the inner hair cells when the fluid deflects their stereocilia. The IHCs, in turn, send information to central auditory pathways and the auditory cortex via nerve fibers. The neural activity is in the form of a series of impulses and goes in only one direction, i.e. sending information from the IHC to the brain. The IHCs receive little or no input back from the brain. Thus, the IHCs are the sensory cells that primarily convey sound information to the brain.

In contrast, outer hair cells (OHCs) “boost” the signal provided to the inner hair cells and “fine tune” the auditory system. The brain constantly monitors environmental sound and, somehow through processes that we do not now understand, amplifies weak sounds and attenuates or compresses moderately intense sounds. Thus, OHCs are important in the overall “gain” adjustment to sound. OHCs synapse with nerve fibers going up to the brain (afferent fibers), but, unlike the IHCs, they also have large numbers of nerve fibers coming from the brain back to the OHCs (efferent fibers). This unique innervation characteristic suggests that the OHCs may be important in regulating auditory system gain and amplifying or changing the signal-to-noise levels reaching the brain.

Finally, the Study Audiologist will return to the discussion of the cochlea and explain that there are two aspects of the cochlear structure that are important for understanding tinnitus. The first aspect is that the cochlea is a coiled structure that is frequency specific. This frequency specificity means that the cochlea vibrates at different frequencies, with high-frequency sounds stimulating mechanical activity at the entrance to the cochlea and low-frequency sounds activating the far end. To illustrate this point, the Study Audiologist will show the Study

Participant a visual aid with familiar sounds represented schematically on an audiogram. The Study Audiologist also will relate and explain high-frequency hearing loss typical of age-related deficits, acoustic trauma, and ototoxicity within the context of the cochlear anatomy and its frequency specificity.

The second aspect of the cochlea that the Study Audiologist will emphasize is that there is constant low-level electrical (auditory) activity arising from the cochlea, the hair cells, and the auditory nerve fibers. This spontaneous auditory activity is independent of external sound input. This weak auditory activity is present at all times and is being relayed to the brain. When detected, the brain will always interpret this low-level activity as sound.

### **11.2.3 Processing at the Level of the Brain**

The Study Audiologist uses the next series of visual aids to address how the brain and central auditory pathways process the input from the peripheral auditory system. The Study Audiologist will point out the auditory fibers as they go from the cochlea to the auditory cortex. Points to make:

- The nerve fibers cross over, so that fibers from one ear stimulate both sides of the brain. This crossover facilitates localization of sound. The neural pathways that lead from the cochlea to the cortex consist of a series of complex interconnected nerve cells called neural networks. Auditory signals are recognized as neural patterns.
- The auditory nerve has both afferent and efferent fibers, meaning that signals go from the inner hair cells to the brain and from the brain to the outer hair cells.

The Study Audiologist will explain that these signals are interpreted within higher cortical areas of the brain, which are responsible for cognition, (i.e., our thoughts, perceptions, and understanding).

The Study Audiologist will then explain that the brain has other sub-cortical (lower) areas that operate at a subconscious level. There are at least five different lower, subconscious levels that are responsible for filtering and enhancing information from the peripheral auditory inputs to the brain. Each individual will weight and process this information differently at these lower levels. Auditory signals are recognized as neural patterns and classified as important (good or bad) or unimportant. Important signals can be reinforced and become conditioned reflexes. The classification of the importance of a signal can vary from person to person and in different situations for the same person. The classification of signal importance for each individual is “programmed” by years of experiences, learning, genetic makeup, and personality. These factors will influence the emphasis that he or she places on the sound information that is available to him

or her. Thus, information that one person thinks is important, may be ignored by another person. This important concept also relates to tinnitus. The processes involved in determining what is important to a given listener include selective perception, sensory contrast, and prioritization

**Selective Perception:** The subconscious areas of the brain are constantly monitoring and filtering signals prior to auditory perceptual processing by higher cortical centers. The objective of this lower-level processing is to filter out neutral information and to enhance information that is different, dangerous, new, or important. One example of this filtering is refrigerator noise. A listener does not pay attention to the noise of a properly working refrigerator, but usually “tunes it out”. If the refrigerator starts making a new noise, or if the listener decides to focus on the refrigerator noise, then the listener can readily hear that noise. Otherwise, the sub-cortical areas of the brain filter out the refrigerator noise and the listener is unaware of it. Another example is clothing. A few minutes after dressing, one does not typically pay attention to the sensation of the clothing on the skin. If it is brought to the wearer’s attention, then he or she will become aware of the clothing. A third example is driving your car on a familiar route (home to work/work to home). Periodically, one does not remember performing the repetitive activity which has become automated. Habituation occurs when the brain considers these activities non-significant and the perception of that activity disappears.

**Sensory Contrast:** The subconscious areas of the brain interpret a signal against the background of the signal. Perception of a signal is not only based on absolute physical intensity, but its relative strength compared to the surrounding signals. For example, a birthday candle in a dark room is very visible due to the great contrast between the light of the candle and the darkness in the room. The same candle in a sunny window produces much less contrast against the bright background, even though the candle is putting out the same amount of light. This process applies to tinnitus. The perception is stronger or louder when one is in a quiet setting.

A classic study performed by Heller and Bergman (1953) demonstrates the implications of sensory contrast as it relates to tinnitus. Eighty individuals without tinnitus were placed one by one in a sound proofed room and asked to report “any sounds they might hear”. Within 5 minutes, 94% heard sounds identical to those described by tinnitus sufferers (hissing, ringing, buzzing, whistling, etc.) which disappeared after they left the sound proofed room. When there is a less than normal level of sound in our environment, the gain or amplification is increased at all levels within the auditory system and small variations of spontaneous activity in the auditory pathways become apparent and are perceived as sound.

**Prioritization:** Most persons can only perform one important task well at a time. For example, we cannot read a book and write a letter at the same time. We can decide to read a

book, but, if the subconscious areas remind or alert us about something (say a baby crying), then the subconscious thought can override our consciousness. The new priority message is conveyed upward to our cortex, and our reading is interrupted. The point here is that our thoughts are ultimately prioritized based upon some internal scheme reflecting their significance in our lives.

We are unable to ignore a threatening signal. Example: Suppose that as we are sitting and talking while there is a tiger sitting on the other side of the room. Even if I tell you that the tiger will not hurt you, your subconscious knows this is a real and present danger, and you will probably leave the room. An important job of the sub-cortical areas is to protect you, and enhance any signal or activity that is determined to be a threat. This information may be misperceived or misinterpreted, but ultimately, the subconscious processing serves to protect and alert you.

The perceived meaning, rather than the magnitude of the threatening signal, right or wrong, real or imagined, determines whether the subconscious alerts us or not. For example, if someone were lying in bed and heard a tiny crack in the floor, then he might think that an intruder is in the house. Such a small sound can be very powerful and stimulating. By contrast, he could probably sleep through a big, booming thunderstorm because he knows that it will not likely be harmful.

It is important to note that these classifications and connections can be altered or relearned. It takes longer to “relearn” a conscious or sub-conscious connection, but the brain is very plastic and under constant reconstruction and can be “retrained” to filter out a signal.

#### **11.2.4 Relation to Tinnitus**

At this point, after having discussed higher-level processing of the auditory system with the participant, the Study Audiologist relates this processing to the Study Participant’s tinnitus. In the next visual aid, the Study Audiologist will show an electron microscopy photograph that demonstrates the irregular pattern of OHCs. Although the IHCs are very sheltered and protected, the OHCs are not. They are vulnerable to damage from noise, ototoxic drugs, and normal wear and tear associated with aging. The Study Audiologist will explain that most individuals normally lose about 0.5 % of their OHCs per year beginning from the time we are very young. Fortunately we have many more OHCs than we need. We could lose about 30% of the OHCs spread across the basilar membrane and still have audiometrically normal-hearing sensitivity.

The Study Audiologist will then remind the Study Participant of two key concepts previously described. First, it is important for the Study Audiologist to re-emphasize that there is constant low-level activity at the cochlear level. Second, the Study Audiologist should reinforce the idea

that subconscious structures within the brain constantly monitor the patterns of signals coming from the cochlea and interconnected cells called neural networks. The brain learns the “usual and customary” patterns of activity that it has classified as neutral. Everyone has patterns of irregularities and it can be a change in that pattern, large or small, that may alert the sub-cortical areas to pay attention. Tinnitus can be a small variation of spontaneous activity in the auditory pathways which is perceived as sound. New neural patterns along the auditory pathways are classified as either important or unimportant. Important signals require some action and an unimportant signal will not. An auditory signal that has been labeled as important or negative can become a conditioned reflex. Individuals frequently associate an event, an activity, a medication, or an illness with the onset of their intrusive tinnitus. It is important to discuss that a viral infection, sudden sensory-neural hearing loss, a medication, or exposure to loud sound, for example, may change the signal patterns in the neural network, but that the change may or may not be labeled as negative or important. If it is labeled as negative or important, the subconscious processing of this changed activity will alert the higher centers. This altered neuronal activity will be perceived as some form of sound that the participant may recognize as “tinnitus.” The Study Audiologist should emphasize that the tinnitus arises as a consequence of the increased recognition at the subconscious level of a novel change pattern. The enhanced recognition of this novel auditory activity alerts the higher cortical centers of this new signal.

One theory related to the emergence of tinnitus is called the discordant damage/dysfunction theory. When there are areas of the cochlea that have intact IHC but no OHC, there are excitatory signals coming from the IHC to the brain, but no corresponding inhibitory signals coming from the OHCs. The imbalance can cause bursting activity that can be perceived as tinnitus.

### **11.2.5 Neurophysiological Model of Tinnitus (Jastreboff Model)**

At this point in the counseling session, the Study Audiologist will introduce the next visual aid, which shows the Jastreboff model. The remainder of the session is devoted to concepts unique to DC as used for TRT.

The Study Audiologist goes through the block diagram, identifying the various components of the model and discussing the contribution of each of these areas to the participant’s tinnitus. The order of presentation is:

- Source (cochlea);
- Detection mechanisms (sub-cortical areas)
- Emotional associations (limbic system);
- Annoyance (autonomic nervous system); and

- Perception and evaluation (auditory and other cortical areas).

The essential points the Study Audiologist will cover are covered below:

#### **11.2.5.1 Source**

The cochlea is typically the source of the tinnitus signal. This signal arises from a change in (or possibly the absence of) low-level random neural activity. The random neural pattern of activity may be altered as a result of an insult, such as acoustic trauma or use of ototoxic drugs.

Sensory contrast enhances the tinnitus signal. For example, people in an inordinately quiet room such as an anechoic chamber hear self-generated noises (e.g., breathing, heart beating, etc.). They also often hear tinnitus, which they otherwise would not hear in a normal sound environment.

#### **11.2.5.2 Detection**

The sub-cortical or subconscious structures filter random neural activity (coming from the peripheral source) and otherwise unimportant sound-induced neuronal activity, preventing detection of this activity at a higher-level site. A signal can be filtered out here at the sub-cortical level if it has no meaning or significance, if it does not have emotional association, or if it has lost its novelty. This means the tinnitus signal may never reach the consciousness, in which case it will not be perceived by the participant.

#### **11.2.5.3 Emotional Associations**

If a tinnitus signal is detected and labeled as having negative associations at the sub-cortical levels, there is increased activation of the limbic system (emotions) and detection of the tinnitus signal is enhanced. The neural networks become highly tuned to monitor the signals resulting in annoyance and anxiety. The limbic system plays an important role in controlling our emotions and there are direct connections between the limbic and auditory systems. If a sound does not activate the limbic system, then the sound will have no emotional meaning and will automatically be habituated.

### **11.2.5.4 Annoyance**

The crucial difference between someone who barely notices tinnitus versus someone who is profoundly affected by it is the relative strength of the negative emotional associations and reactions to the tinnitus signal. It is this emotional association with the tinnitus signal that results in what we call annoyance. Persistence of the tinnitus signal can result in activation of the autonomic nervous system. Activation of the autonomic nervous system (ANS), in turn, can result in muscle tension, anxiety, high levels of stress hormones, increased blood flow, fight or flight reactions, or panic attacks. If over activation of the ANS is prolonged by the tinnitus, then an unhealthy stress response may arise as evidenced by insomnia or exhaustion. The ANS becomes negatively conditioned to the signal, reacts strongly to its presence, and puts the tinnitus signal at the top of the list of things that the brain needs to monitor and consider (prioritization). This annoyance results in even greater awareness of the tinnitus signal, which would otherwise be filtered out.

The Study Audiologist should stress in this portion of the discussion that this annoyance is not the consequence of a system that is working poorly. Rather, it is an indication of a system that is over-compensating to a small irregularity in the normal pattern of low-level auditory activity.

Large activation can take place at a sub-conscious level (sub-conscious loop) without any involvement of conscious thoughts. There can also be a conscious loop present involving the cortex and the limbic system with conscious worries such as a brain tumor, physical disease, impending deafness or stroke, job considerations, no available treatment, or mental illness. These thoughts can activate the conscious loop increasing activation and monitoring of the tinnitus.

### **11.2.5.5 Perception and Evaluation**

The Study Audiologist will explain the following points to the participant:

- Tinnitus annoyance and its enhancement by the limbic system probably depend relatively little on characteristics of the tinnitus such as pitch, perceived loudness, or other qualities of sound. Likewise, the annoyance does not appear to be dependent on whether the tinnitus is heard in one or both ears or in which ear it is perceived. The tinnitus signal and its enhancement also do not depend on a specific event that the participant may associate with the onset of the tinnitus, the length of time the participant has had tinnitus, nor his or her conscious beliefs about the tinnitus. Rather, the annoyance depends on the strength of the negative activation of the limbic system. The perception of tinnitus is benign. It only becomes a problem when inappropriate conditioned reflexes are created

that link it to the limbic and ANS. The level of activity of the ANS relates closely to the severity perceived by the individual..

- Tinnitus is a separate issue from hearing loss, which is not a factor in the TRTT.
- Tinnitus does not cause hearing loss; however tinnitus is more common among people with hearing loss, perhaps because of the diminished audibility of the environmental sound background. Because of the diminished background, the tinnitus signal appears to be augmented against the reduced auditory input.
- Because a person has tinnitus does not mean that the individual will likely lose his or her hearing sensitivity more than an individual without tinnitus.
- The tinnitus sound is not usually a large signal. The Study Audiologist will refer to the audiogram, and demonstrate the sensation level difference between the tinnitus signal and the associated hearing threshold.
- Tinnitus is a weak signal and a neutral signal. The impact is coming from the way the participant perceives that signal, sometimes filtering it out, and sometimes enhancing it. If we match the loudness of the tinnitus on a day when the participant can hardly hear it, and again on a day when it seems loud, the loudness match is usually similar. Thus, the tinnitus does not change greatly despite one's day-to-day perception of fluctuation.
- The only way the brain can interpret activity from the cochlea is as sound. It is not an "outside sound," rather, it is an "inside sound." When it is an inside sound, one cannot control it. In response to this uncontrollable internal sound, the autonomic nervous system may be activated. This activation is manifested by a host of adverse reactions (e.g., greater muscle tension, adrenaline and hormonal levels, increased anxiety, panic attacks) in response to the annoyance to the tinnitus.
- We have no way currently to repair the anatomical and resulting response irregularities in the cochlea, but we can change (retrain) the way the brain views the irregular activity pattern associated with the tinnitus.

#### **11.2.6 Treatment Goals**

The overall goal of DC is to help the participant habituate to the tinnitus signal. The signal will remain, but the participant will not notice it unless he or she is listening specifically for the tinnitus signal. It is essential that the Study Audiologist clearly explain that habituation of the tinnitus is the goal of the TRT. It is not that the tinnitus is "not there", but individuals can go for

long periods of time without being aware of the tinnitus. Even when it is noticed, there is no negative reaction. This habituation is achieved by two sub-goals, habituation of the reaction (annoyance to the tinnitus) and habituation of the perception (awareness of the tinnitus).

#### **11.2.6.1 Habituation of Reaction**

The main goal of TRT is habituation of the participant's reaction to the tinnitus. The tinnitus stops impacting the patient's life even though there is still awareness of the tinnitus. The limbic and ANS stop reacting to the tinnitus signal as the negative emotional associations are neutralized. The tinnitus is classified as more neutral. The DC sessions serve to educate the patient. Ultimately, a known danger causes a weaker reaction in the ANS than an unknown danger. As the DC information is internalized and digested, the brain becomes less concerned with the tinnitus signal and pays less attention to it at a conscious level. This is the first step in the habituation process. The goal is to reduce and, ultimately, eliminate the negative reactions of the limbic and autonomic nervous systems to the tinnitus signal. This goal, which is achieved by neutralizing negative emotional associations, can occur only when the fear induced by the tinnitus is removed.

The DC session serves to educate the participant. The intent is to provide the information to help alleviate the participant's undue fears and concerns about the tinnitus condition, thereby neutralizing the negative reaction to the tinnitus. Habituation can occur only after the participant has reclassified tinnitus as a neutral stimulus. Gradually, the subconscious levels of the brain are trained to eliminate the reactionary response contributions from the limbic and autonomic nervous systems. This process is key to the habituation of the reaction to the tinnitus.

The habituation process occurs in the auditory nervous system above the source of the tinnitus. The tinnitus signal is unaffected. This also means that the cause of the tinnitus is irrelevant and habituation can occur regardless of the cause.

Any questions the participant has at this point should be answered fully. It is important to ascertain that the participant has assimilated the information, understands it, and believes it to be true. Any problems or issues unique to the participant not previously discussed should be covered at this point. This information should be repeated and reinforced during follow-up appointments.

#### **11.2.6.2 Habituation of Perception**

The secondary goal of TRT is habituation of tinnitus perception. The tinnitus signal remains active in the auditory nervous system, but it is blocked from reaching the cortex where it would be perceived. This occurs automatically once a sufficient level of habituation of reaction is achieved. It is generally a slow and incremental process that takes about 1 to 1 ½ years.

Habituation of the perception is facilitated by reducing the contrast between the tinnitus and the sound background so tinnitus is more difficult to perceive. The reduced sensory contrast facilitates the habituation process as the participant becomes less aware of the intrusive signal. This process of habituation of the awareness of the tinnitus is promoted and expedited with the aid of low-level sound. In the TRTT, complete instructions will be given to each Study Participants, individually, regarding sound therapy. Low-level sound therapy will be achieved using sound generators (SGs). In addition, various environmental means may be offered to participants. These alternatives include the following:

- Fans;
- Low-volume radios;
- Sound tapes; and
- Sound pillows.

The purpose of low-level sound in the habituation of the tinnitus is to:

- Reduce the contrast between the tinnitus signal and the random background activity, thereby making it harder for the participant to monitor the tinnitus signal;
- Facilitate filtering of the tinnitus signal at the subcortical levels so that it never reaches the level of cortical awareness. The expected treatment effect is that gradually the participant will lose awareness of his or her tinnitus; and
- Turn down the “gain” within the auditory system.

This last point has particular importance in the area of hyperacusis, if present. With successful treatment, the LDL responses will shift to higher sound levels and sound tolerance will improve. Ultimately, the goal of TRT is for the participant to become comfortable in daily activities that were previously uncomfortable because of the tinnitus. (See Section 11.2.7 for instructions related to reduced sound tolerance).

It is important in DC to emphasize that both habituation of the reaction and habituation of the perception are important to the total habituation process.

It is also critical for the Study Audiologist to inform the participant that he or she may not notice any change in the first few weeks of treatment. The changes may be slow, incremental,

and subtle, and may take many months before a benefit is realized. For example, the Study Audiologist may say:

“Our goal is for you to get to the point where tinnitus is a ‘non-issue’ in your life. That is, we want you no longer to think about it, and even if you do notice the tinnitus, it does not trigger negative emotional reactions. This does not mean the tinnitus is not there. For example, it is like the refrigerator noise. If you stop to listen for it, then you can hear it, but you usually ‘tune it out.’ There will be periods of time when you are more aware and less aware of the tinnitus. It is important for you to know that ‘rough patches’ will occur, and that this is normal. The tinnitus is not getting worse. We are trying to ‘grow’ the better periods when you are less aware of the tinnitus. Do not worry if the tinnitus gets ‘worse’ after a few weeks. It is a very common and temporary stage in the habituation process. You are adjusting to the new signal.”

The Study Audiologist also must emphasize that tinnitus is related to a set of dynamic interactions involving the ear, the brain, the emotions, the stresses the participant is under, etc. Habituation of a response to a neutral stimulus is a natural process. Habituation will occur as the result of neutralizing negative emotional associations with the tinnitus through counseling and the use of low-level sound to reduce the contrast between the tinnitus and the background sound, thereby making it harder to detect the tinnitus. The neuronal processes and networks that are involved in tinnitus are very plastic and are under constant reconstruction that can be modified to improve the tinnitus condition.

We cannot cure or eliminate tinnitus completely, but your treatment will help you go through a natural habituation process.

#### **11.2.7 DC for Decreased Sound Tolerance**

Not all Study Participants will have decreased sound tolerance, but if present, the sound tolerance must be addressed. If both tinnitus and decreased sound tolerance are present, DC remains substantially unchanged. Reduced LDL/UCLs are noted and explained while discussing the ATH. Study Participants with decreased sound tolerance are told that the sound tolerance issue will be addressed before the tinnitus. The protocol for sound therapy is similar, but more gentle. Frequently, improvements in decreased sound tolerance occur quickly within the first several months and for some Study Participants, once the sound tolerance problems improve, the tinnitus is not as much of an issue. The goal for this treatment is for Study Participants to live comfortably in a busy, noisy world without fear of physical discomfort, damaged hearing, or overprotecting the ears. The Study Audiologists will use the same visual aids, but add the Jastreboff Model with external sound as the source. If decreased sound tolerance occurs without

tinnitus, the discussion will include the section on how the brain handles the input, stressing the control of the gain of the auditory mechanism.

Reduced sound tolerance may present as the following:

**Hyperacusis:** a hypersensitivity to sound caused by abnormally strong reactions (over amplification) confined mainly to the auditory pathways. There is physical discomfort when exposed to sounds that are generally comfortable for other people.

**Misophonia:** an aversion to certain sounds due to conditioned emotional responses at the limbic and autonomic levels.

**Phonophobia:** a specific form of misophonia when fear is involved.

A sound tolerance problem usually consists of a combination of hyperacusis and misophonia. If a Study Participant has physical discomfort when exposed to certain sounds or sounds above a certain loudness, aversion and emotional responses will become involved. The brain is constantly monitoring surrounding sounds with an automatic gain control, and can modify the gain or sensitivity to sound at the cochlear (OHC) level and along the auditory pathways. Soft sounds can be amplified. Sometimes the gain mechanism amplifies too much and sounds become uncomfortable or even painful, even though they are comfortable for other people. To treat hyperacusis, the systematic and controlled use of sound is introduced, initially at very soft levels slightly above the hearing threshold. This is usually best done with SGs. Improvements can generally be seen in a few weeks. LDL/UCLs are tested at follow-up visits to monitor progress and adjust volume slightly. If both tinnitus and hyperacusis are present, the hyperacusis is treated first. The goal of the sound therapy is to reduce the gain of the auditory system allowing the individual to be comfortable in a busy, noisy world. Study Participants with decreased sound tolerance will be given specific instructions for sound therapy.

To treat misophonia, brief periods of active listening to pleasant sounds will be implemented several times a day. Specific instructions will be given for this activity which addresses the connection between the auditory, limbic and ANS (See Appendix C, Handout 2 for specific instructions for Treatment of Misophonia, Active Extinction). Study Participants with misophonia only and no hyperacusis will most likely not benefit from sound generating instruments.

Phonophobia can involve the fear that sound will damage the auditory system, fear of discomfort, or fear of exacerbating hyperacusis or tinnitus. There can be a tendency to overprotect the ears which can make the auditory system even more sensitive. Appropriate noise protection is important, but wearing plugs or muffs inappropriately will give the brain incorrect

information regarding sound in the environment and it will not be able to adjust the gain properly. Detailed instructions for sound therapy will be given to the Study Participants with hyperacusis and phonophobia .

### **11.2.8 Summary**

Study Participants will receive a copy of the summary (Appendix C, Handout 1).

- The tinnitus must be reclassified as unimportant (neutral/semi-neutral) for habituation of the reaction to occur. We cannot force that to happen, but we can introduce this information and reduce the ANS activity.
- Tinnitus is a separate issue from hearing loss. Tinnitus does not cause hearing loss. Although it is more common for people with hearing loss to have tinnitus, that is more related to the decrease in ambient sound so that they are more aware of the internally produced sounds (tinnitus). Not everyone with hearing loss has tinnitus. Not everyone with tinnitus has hearing loss.
- Tinnitus is not a red flag that you will lose hearing.
- The annoyance factor of the tinnitus is determined by the strength of the negative emotional association given to otherwise normal neural activity.
- We cannot repair any damage or irregularities in the cochlea, but we can change the way the brain views the neural activity that is labeled as negative.
- Factors such as pitch of tinnitus, loudness, one ear or both ears, which ear it is in, maskability, what the Study Participant associates the onset with have no predictability for improvement or no improvement.
- Tinnitus is a weak, neutral signal. If we match the loudness on a day it is perceived as strong or loud, it will be virtually the same as on a day it is perceived as soft.
- The only way the brain can interpret activity from the cochlea and auditory pathways is as sound. If I punch you in the eye, the only way the brain can interpret that activity is as light.
- Tinnitus is not an external sound. It is a perception of neural activity perceived as an “inside sound”. Therefore, we cannot control it and when we cannot control something, the limbic and ANS can become highly activated, especially if the Study Participant is one who likes to control or is a perfectionist.

- Tinnitus annoyance is not because the system is not working well enough. Rather, it is an indication of a system overcompensating and working too well.
- The brain is very plastic and under constant reconstruction. It can be retrained to filter out this signal. Much like a floater in the eye, once we know that it is not related to retinal damage, we begin to look past it without noticing it even though we can see it if we look for it. Tinnitus is much like a floater in the ear.
- We can't force habituation, but understanding the mechanism, the goals and the use of sound therapy to reduce the contrast between the tinnitus signal and the background sound will lay the groundwork for habituation of the reaction to and perception of the tinnitus signal (passive extinction)

At the end of the DC session, the Study Audiologist will ascertain that the participant is comfortable with the treatment goals and has no further questions.

At the conclusion of the first treatment study visit, the Study Audiologist will provide a summary of the information that was provided to the participant during the DC session (a printed copy of the visual aid presentation) and a copy of the participant's ATH test results. The Study Audiologist will schedule the second treatment visit (T2), advising the Study Participant that this visit will be used to monitor his or her status and treatment progress, but that the participant may elect to contact the Study Audiologist before then if so desired.

### **11.3 Follow-up DC Sessions**

Follow-up DC contacts in the TRTT are held at the second treatment visit (T2) held at one month and at 3, 6, 12, and 18 months at the Clinical Center. The T2 session may be as short as 15 minutes or as long as one hour, depending on the individual participant's needs. Follow-up contact is necessary to reinforce the goals, i.e, to reinforce the information presented in the initial DC session as the participant goes through the habituation process and to address specific concerns of the individual participant. Treatment progress is monitored and the Study Participant's questions and concerns are addressed. Appendix D contains a script for the follow-up counseling.

Elements of the initial DC counseling are reviewed, depending on the individual Study Participant's questions, concerns, and progress. Concepts that might be covered include:

- Auditory gain
- Heller Bergman experiment
- Neurophysiological model of tinnitus
- Conscious loop
- Subconscious loop
- Classification of new sound as “important” or “unimportant”
- Reclassification of sound
- Habituation of reaction
- Habituation of perception
- Reducing contrast = reducing strength
- Sound therapy
- Habituation takes time

In addition to reinforcement counseling, the compliance of the Study Participant will be checked with regard to the protocol for recommended sound therapy at each Follow-up Study Visit. In addition, change in the Study Participant's progress will be assessed by completing the follow-up data collection forms.

## **11.4 Determining End of Treatment**

With TRT, there is no precise way to identify the end-point of treatment, decide when a significant therapeutic effect has been achieved, or identify any specific value or sufficient change. This point in time is very individual and depends on different expectations and goals of what the individual with tinnitus expects to achieve. The time to end treatment must be agreed upon with the Study Participant and the Study Audiologist. Because this point can occur after about one year of treatment or occasionally sooner, ending treatment sooner must be considered. For the purposes of TRTT, if the Study Participant reaches the point where the tinnitus and/or hyperacusis is no longer an issue in his or her life, s/he may be instructed in how to reduce the use of the SGs and enriched environmental sound. Study Participants will, however, be required to continue to complete all TRTT Follow-up Visits and required ATH evaluations and psychometric measures.

### **11.4.1 Determining the end-point**

The following guidelines should be considered when determining the end of treatment.

- The Study Participant may report that he/she goes for long periods of time without thinking about the tinnitus and even when noticed, it does not bother/annoy him or her (habituation of perception and habituation of reaction are involved).
- The Study Participant reports that wearing instruments is more of a problem than the tinnitus itself (habituation of reaction, tinnitus is less annoying).
- The Study Participant reports that they have forgotten to wear the instruments for three weeks or more. This suggests that the Study Participant is forgetting about the tinnitus and is probably ready to stop sound generator use. Forgetting about the instruments implies they have "forgotten" about the tinnitus (habituation of perception).
- Occasionally, a Study Participant may not be able to hear tinnitus, even with hard listening. This is not a goal of TRT, but happens to some people.

In addition, the Study Audiologist should assess the responses of the Study Participant on the TRT Follow-up Interview form.

- The Study Participant reports that s/he has no "bad days" or if there are occasional "bad days", they are not as bad as before.
- There is no effect of loud sound on the tinnitus.
- There are no activities that are affected or prevented by the tinnitus and/or hyperacusis, or only one activity is affected and that only occasionally.
- The Study Participant reports being aware of tinnitus only about 5 to 10% of total awake time over the past 1 to 2 months (habituation of perception).
- The Study Participant reports being annoyed/distressed/irritated by tinnitus and/or hyperacusis as close to zero as possible over the past 1 to 2 months (habituation of reaction).
- The Study Participant reports that the "effect on life" of tinnitus and/or hyperacusis is as close to zero as possible.

#### **11.4.1 Reducing sound therapy**

The end of treatment, in this case, will mean reducing the use of SGs and enriched environmental sound. Study Participants will, however, be required to continue to complete all

TRTT Follow-up Visits and required ATH evaluations and psychometric measures. This also allows the Study Audiologist to monitor the stability of the treatment effects.

To terminate treatment, it is important not to make rapid changes. In stopping the use of instruments, it is important to let the Study Participants know not to wear them for several shorter periods of the day (on/off), because wearing the SGs intermittently draws attention to the symptoms. Rather, Study Participants should stop wearing the devices certain days of the week (e.g., weekends) and then gradually stop the use of sound enrichment in the same way.

Finally, Study Participants can stop the use of enriched sound at night, although many like to keep it on at night as it helps sleep. They can continue to use the instruments periodically if they feel it is necessary.

For Study Participants with tinnitus and hyperacusis, the hyperacusis is treated first with generally good results within the first 6 months. For some Study Participants with tinnitus and hyperacusis, when the hyperacusis is no longer an issue, the tinnitus is significantly improved. If Study Participants reach this point before nine months of full TRT treatment, they should be required to wear the SGs and use enriched environmental sound for at least nine months.)

Occasionally, although it is uncommon, troublesome tinnitus can re-emerge after a full TRT program. Study Participants should be reassured that once they have habituated to their troublesome tinnitus, it is easy to treat with a short term use of sound therapy and renewed contact with professional support. Subjects should be informed of this possibility at the time their treatment is concluded.

More commonly, as subjects go through the habituation process, they internalize the concept that there will be “rough patches”, but these are typically temporary and if they wait for a short period of time the situation is improved again. This tends to carry over to post treatment so that these episodes do not evoke alarm and, after a while, are not even noticed.

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## Appendix A Steps for Directive Counseling

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**To the Audiologist:** There are **six key areas** to be covered in directive counseling:

1. Results of the ATH examination
2. Anatomy and physiology of the auditory system
3. How the brain handle auditory input
4. How this relates to the tinnitus
5. Jastreboff model of tinnitus
6. Goals of treatment

### **Script used during Directive Counseling**

#### **1. General Overview of Directive counseling as implemented in TRTT**

During this session we will discuss your tinnitus and what it is and what it is not. Our goal for you is habituation which means that you can go for long periods of time when you are not aware of the tinnitus. Not that the tinnitus is not there, but your brain will view it as a neutral signal rather than a negative one and no longer pay attention to it. To achieve the goal of habituation, the first step is to review your audiometric test results and teach you how the brain and the emotional system handle the input from the auditory system. We will talk about our options for implementing this treatment. This is the first step in the TRT process. Please feel free to ask any questions at any time.

#### **2. Review of audiometric test results**

*(Use enlargement of subjects own audiogram with right and left ear separate).*

- *Review of audiometric test results* including explanation of pure tone thresholds, speech testing, relationship of normal hearing versus hearing loss across the frequency spectrum, noting any differences between ears and relationship of audiometric patterns to history of noise trauma
- *Review of Loudness Discomfort Levels* (LDL/UCL) tests including whether results indicate presence of normal sound sensitivity, hyperacusis, misophonia, or phonophobia. *(Relate test results to information recorded on Baseline TRT Interview Form.) Note: If hyperacusis is present, incorporate information from script for decreased sound tolerance found at the end of this section (Appendix A). If there are no reduced LDL/UCLs and no complaints*

**of sound sensitivity, it is not necessary to discuss hyperacusis, misophonia, or phonophobia.**

- *Review of tinnitus pitch match* including discussion that it will vary from person to person and has no predictive value for the process of habituation.
- *Review of tinnitus loudness match* which is measured in decibels as a value relative to the audiometric threshold at the pitch match frequency. Usually the physical properties indicate that even though it may be an intrusive signal, it is a **weak** signal. (We will return to this issue at a later point in the counseling.)

### **3. Overview of the auditory system**

*(Use anatomy illustration and model of a human ear.)*

Explain the anatomy and physiology of the auditory system using illustrations and a model of the human ear.

- Explain the **structures of the outer, middle, and inner ear** and associate any audiometric test results indicating conductive or sensorineural components to anatomical structures.

*(Use electron microscope illustration of basilar membrane with IHC, OHC, and nerve fibers, and close-up of cilia.)*

Explain structure and function of the inner ear, cochlea, Organ of Corti, and nerve fibers which take the message to the brain. We do not hear at the ear. We hear at the brain. **The ear structure acts as a transformer changing mechanical energy into electrochemical energy that the brain can process.** The only way the brain can interpret the activity in the cochlea is as sound, just as the only way the brain can interpret activity in the eye is as light.

- **IHC** are responsible for 95% of our hearing. They are transducers which convert vibrations on the basilar membrane into nerve impulses. Most of the nerve fibers are afferent, taking information to the brain.
- **OHC** are responsible for the “fine tuning” of the system, giving a “boost” to the IHC of up to 50 dB. They have all the properties of a muscle. They are mechanical amplifiers enhancing vibrations for low level sound. The brain is constantly monitoring the sound in our environment and has the ability to make adjustments in the “gain” of the system. This action is similar to the pupils of the eye opening and closing to let in more or less light.

*(Use photo of cochlea.)*

- Explain the **two aspects of cochlear structure** that are important as they relate to tinnitus.
  - First, the **structure is frequency specific** and designed like a piano keyboard. The high frequencies stimulate activity at the entrance to the cochlea which is why we all tend to lose higher frequencies as we age and as we are exposed to noise. Like the carpet at the front door, they get all the wear and tear. Relate this information to the audiogram if there is a high frequency hearing loss.
  - Second, we used to think that when there was silence, the structures in the cochlea were dormant. We now know that there is **constant low level mechanical-electrical activity** at all times at the OHCs. There are extremely weak emissions present at all times.

#### 4. How does the brain handle input from the auditory system? *(Use illustration of Afferent Auditory Pathways)*

- Point out the nerve fibers that go to the brain from the IHC and OHC (afferent fibers). There are dedicated areas of the brainstem and brain that process auditory signals.
- The **cortical structure** is responsible for our cognitive awareness of what is happening for all of our senses.
- There are at least five lower levels that work at **a pre-cortical or subconscious level and are responsible for monitoring, filtering and enhancing** information from all of our systems. We can't possibly pay attention to everything going on around us, so the brain must have some way to filter out the "junk" and enhance the things that are different, new, important, dangerous, familiar, pleasurable, etc.
- **Auditory signals are recognized as neural patterns and classified as important (good or bad) or unimportant.** The way a signal is classified in importance can vary from person to person and in different situations for the same person. This classification is programmed by our years of experience, our learning, our genetics, and our personality. What one person thinks is important, another person does not care about. As this relates to tinnitus, it works in several different ways:

**Selective Perception:** the subconscious areas of the brain are constantly monitoring and filtering. They have the ability to filter out (block) neutral information and enhance information that is different, dangerous, new, or important. We can't possibly pay attention to everything going on around us. An example is the refrigerator noise. If you know the

refrigerator is working properly, your brain does not pay attention to it. If you listen for it, you can hear it, but usually your brain will “tune it out”. A second example is your clothing. When you first put on your clothes, you can feel them, but after a few minutes your brain does not pay attention to the sensation of clothing on your skin unless I say something about it. The third example is driving in your car on a familiar route. Repetitive activity becomes automated. These are examples of habituation – if the brain does not care about something, it will not pay attention.

**Sensory contrast:** when the sub-cortical area looks at a signal, it looks at it as it relates to its background. Perception of a signal is not based only on absolute physical intensity, but its relative strength compared to surrounding signals. Example: a birthday candle in a dark room which appears bright. The same candle in a sunny window is not as noticeable. This applies to the tinnitus. The perception is stronger or louder when you are in quiet.

*(At this point, discuss the Heller and Bergman (1953) paper)* Eighty individuals without tinnitus were placed in an anechoic chamber and asked to report “any sounds they might hear”. Within 5 minutes, 94% reported buzzing, pulsing, whistling, ringing sounds identical to sounds reported by tinnitus sufferers. This demonstrates that the auditory system is a busy, noisy place and when it is sufficiently quiet almost everyone has tinnitus, especially if they are listening for it. Tinnitus does not necessarily indicate that there is something wrong in the system.

**Prioritization (ranking):**

**(1) we can only perform one important task at a time.** We can't read a book and write a letter at the same time. We can make a conscious decision about what we would like to concentrate on, but if the sub-cortical areas think they need to remind us or alert us about something, they can override everything else and send that message up to the cortex. Example: you are trying to complete a certain task, read a book, write a report, etc. and the subconscious says “don't forget to go to the bank, don't forget go to the post office, or don't forget to pick up the prescription” (important).

**(2) We have an inability to ignore a threatening signal.** Example: if we are sitting here talking and there is a tiger sitting across the room. Even if I assure you that he is very friendly, your sub-cortical areas know better. The tiger will be given great importance, you will have difficulty concentrating on what I am saying, and you just may leave. The job of the sub cortical areas is to protect you and enhance any signal that it determines is a threat. It may be working on wrong information, but its job is to protect and alert you. Your tinnitus has been labeled as a threat to you in some way and even if I tell you it is not, your subconscious continues to give it a high priority as a threat.

**(3) It does not depend on the size of the signal but rather the perceived meaning of that signal**, right or wrong, as to whether the subconscious alerts us or not. Examples include the following:

- You are lying in bed and hear a tiny crack in the floor. You think someone is in the house and it may awaken you as you are dozing off, but we can sleep through a big booming thunderstorm.
- If you have raised a family, you are familiar with the experience of the mother who wakes up immediately when the baby cries. The quiet sound made by the baby has a high level of significance to the mother.
- We are distracted by the sound of our name being mentioned in a nearby conversation or noisy meeting.

It is important to note that **these classifications and connections can be altered or relearned**. It takes longer to “relearn” a conscious or subconscious connection, but the brain is very plastic and under constant reconstruction and can be “retrained” to filter out this signal (tinnitus).

**5. How does this relate to your tinnitus? (Use repeat photo of enlarged basilar membrane with perfect IHC and OHC. )**

- Using electron microscopy photo of basilar membrane with “perfect” inner and outer hair cells, review that the IHC do 95% of the work for hearing. They are very sheltered and protected. The OHC act as amplifiers and give a “boost” to the IHC. The OHC are very vulnerable to damage from noise, ototoxic drugs, viral infections, normal wear and tear, aging, genetics, autoimmune disorders, and other factors. We lose about  $\frac{1}{2}\%$  a year from the time we are very young. But, we have many more than we need and we have built in redundancy. We could lose about 30% of the OHC (spread across the basilar membrane) and still have normal hearing. We could lose all of the OHC and have about 50 dB of hearing loss. In contrast, if we lost all of the IHC, we would lose all of our hearing. We are now looking at the hair cells of a nice young guinea pig. No one gets to adulthood looking like this.

*(Introduce electron microscope photo of basilar membrane with damaged OHC.)*

- Most of us look more like this. Remember that we said two things:

- 1) There is **constant low level electrical and mechanical activity in the cochlea** at the hair cell level.
- 2) The **sub-cortical areas of the brain are constantly scanning and monitoring that activity** just as it is monitoring the activity of the rest of our systems – our heart, eyes, nose, toes, skin, etc.

- Therefore, as it scans the pattern of activity in the cochlea and interconnected cells, it will pick up an irregular pattern. This is not perceived as sound. It does not reach the cortex. But the brain learns the “usual and customary” patterns that it has classified as neutral. It does not have to look perfect in order for the brain to think everything is “OK”. It is important to note everyone has a pattern of irregularities, and it can be a change in that pattern, large or small, that may alert the sub-cortical areas of the brain to pay attention. Tinnitus can be a small variation of spontaneous activity in the auditory pathways which are perceived as sound. The brain is trying to keep the “status quo”. **New patterns along the auditory pathways are classified as either important (good or bad) or unimportant. Important signals require some action or attention and unimportant signals do not.**

Example: You go to a concert and for 2 hours are exposed to very loud sound. You may have some damage to the OHC, maybe temporary or maybe permanent. After the concert the subconscious checks the signal pattern of hair cells and neural networks. It may say, “it’s a new pattern, but it’s OK” or it may say, “uh oh, what has s/he done to me now?” If it labels something as different, dangerous, new or a threat, it can keep reinforcing the negative label. So, it’s not that you went to the concert or took a medication, or contracted a virus, but rather how the subconscious labels the change in the neural pattern at that particular instant and if the new signal becomes conditioned and reinforced as negative.

## 6. Neurophysiological model of tinnitus (*Use diagram 1 of Jastreboff model*)

- Using the diagram of the model, **explain the components** beginning with **the random neural activity in the cochlea (source)**. This **information is constantly assessed and classified at the subcortical level as important or not important**. Once it is classified as neutral, not important, no threat, or loses its novelty, it has no meaning, significance, or emotional association, it is filtered out at a sub-cortical level and we are not aware of its presence.
- If this signal is labeled as negative or a threat, right or wrong, **the limbic system** (emotions) becomes involved and becomes highly tuned to monitor the signals resulting in **annoyance and anxiety**. We know that the limbic system plays an important role in controlling our

emotions and that there are direct connections between the limbic and auditory systems. If a sound does not activate the limbic system, then the sound will have no emotional meaning and will be automatically habituated.

- The **autonomic nervous system** can become activated resulting in increased muscle tension, adrenaline, heart rate, hormones, fight or flight, and panic attacks. If over-activation of the Autonomic nervous system is prolonged by the tinnitus then an unhealthy stress response may arise as evidenced by insomnia, exhaustion, etc. The autonomic nervous system becomes **negatively conditioned to the signal, reacts strongly to its presence, and the signal is put at the top of things the brain needs to pay attention to (prioritization)**. This results in increased awareness of a signal that would otherwise be filtered out. The annoyance is not because the system is not working well enough. Rather, it is an indication of a system working too well. Example: Imagine that the son of a neighbor you don't particularly like played a song again and again through the day. Even though the song is not harmful and you are not afraid of it, it evokes a very strong reaction and "drives you up the wall".
- Large activation can take place at a subconscious level (**subconscious loop**) without any involvement of conscious thoughts.
- There can also be a **conscious loop** present involving the cortex and the limbic system with conscious worries such as brain tumor, impending deafness, or mental disorder. These (usually unfounded) thoughts can activate the conscious loop increasing activation and monitoring of the tinnitus.
- The crucial difference between someone who experiences, or just notices tinnitus, and someone who suffers from it is the negative associations and reactions of the limbic and autonomic nervous systems to the tinnitus signal. Tinnitus activity labeled as unimportant is blocked from activating the limbic and autonomic nervous system.
- The **annoyance or distress of the tinnitus depends on the strength of the negative activation of the limbic system, not on the qualities of tinnitus (loudness, pitch, etc.), or conscious beliefs**. The level of activity of the autonomic nervous system relates closely to the severity perceived by the individual.

**7. Goals** (*Use diagram 2 of the Jastreboff model showing Habituation of Reaction and Habituation of Emotions from limbic and autonomic nervous systems.*)

- **Main Goal of TRT Treatment**

**Habituation of Reaction:** the tinnitus stops impacting the patient's life even though there is still awareness of the tinnitus. The limbic and Autonomic nervous system stop reacting to the tinnitus signal as the negative emotional associations are neutralized. The tinnitus is reclassified as more neutral. The directive counseling sessions serve to educate the patient. A known danger causes a weaker reaction in the Autonomic nervous system than an unknown danger. As the information is internalized and digested, the brain becomes less concerned with the tinnitus signal and pays less attention to it at a conscious level. This is the first step in the habituation process.

- **Secondary Goal of TRT Treatment** (*Use diagram 3 of the Jastreboff model showing additional Habituation of Perception.*)

**Habituation of Perception:** the tinnitus signal remains active in the auditory nervous system, but it is blocked from reaching the cortex where it would be perceived. This occurs automatically once a sufficient level of habituation of reaction is achieved. It is a slow and incremental process usually taking about (9 to 18 months).

- The **habituation process occurs in the auditory nervous system above the source of the tinnitus. The tinnitus signal is unaffected. This also means that the cause of the tinnitus is irrelevant and habituation can occur regardless of the cause.**

**8. Summary** (*Give participant handout*)

- The **tinnitus must be reclassified as unimportant by the brain** for habituation of reaction to occur. This is a passive process. We can't force it to happen, but we can introduce this information at the conscious level and reduce the autonomic nervous system activity.
- **Tinnitus is a separate issue from hearing loss.** Tinnitus does not cause hearing loss. Although it is more common for people with hearing loss to have tinnitus, that is more related to the decrease in ambient sound so that they are more aware of the internally produced sounds (tinnitus). Not everyone with hearing loss has tinnitus. Not everyone with tinnitus has hearing loss.
- **Tinnitus is not a red flag that you will lose hearing.**

- The **annoyance factor is determined by the strength of the negative emotional association** given to otherwise normal neural activity.
- We can't repair any damage or irregularities in the cochlea, but we can change the way the brain views neural patterns that have been labeled as negative.
- Factors such as pitch of tinnitus, loudness, one ear or both ears, which ear it is in, maskability or what you associate the onset with have no predictability of improvement or no improvement.
- Tinnitus is a **weak, neutral signal**. If we match the loudness on a day it is perceived as loud, it will be virtually the same as on a day it is perceived as soft.
- The only way the brain can interpret activity from the cochlea and auditory pathways is as sound. If I punch you in the eye, the only way the brain can interpret that activity is as light.
- Tinnitus is not an external sound. It is a **perception of neural activity** perceived as an “inside sound” not an outside sound. Therefore, we cannot control it and when we can't control something, the limbic and autonomic nervous system can become highly activated (especially if the patient likes to be “in control” or is a perfectionist). Example: neighbor's dog barking versus your own dog barking.
- Tinnitus annoyance is not due to the system not working well enough. Rather, it is a system that is overcompensating and working too well.
- The **brain is very plastic and under constant reconstruction. It can be retrained to filter out this signal**. Much like a floater in the eye, once we know it is not a threat or related to retinal damage, we begin to look right past it even though we can see it if we look for it. The tinnitus is much like a floater in the ear.
- We can't force habituation, but understanding the mechanism, the goals, and the use of sound therapy to reduce the contrast and the strength of the tinnitus signal will lay the groundwork for reaction to and perception of the tinnitus signal (passive extinction).

**9. Directive counseling for decreased sound tolerance, if indicated.** Directive counseling for Study Participants with hyperacusis initially consists of many of the same components as for tinnitus, but the emphasis to start is on “auditory gain.” This can be incorporated into the

directive counseling for tinnitus if there is a decreased sound tolerance component. (*Use Jastreboff model with external sound as source.*)

- **Hyperacusis** is a hypersensitivity to sound caused by abnormally strong reactions confined mainly to the auditory pathways.
- **Misophonia** is an aversion to certain sounds due to conditioned emotional responses.
- **Phonophobia** is a specific form of misophonia when **fear of damage to the ear of physical discomfort from sound** is involved.
- A sound tolerance problem usually consists of a combination of hyperacusis and misophonia. Tinnitus may or may not be present. If someone has physical discomfort when exposed to certain sounds or sounds above a certain loudness, aversion and emotional responses will frequently become present.
- (*Use enlargement of Study Participant's audiogram.*) Review audiometric tests with emphasis on the LDL/UCLs and their relationship to the problems the subject is having.
- (*Use anatomy illustration and model of a human ear.*) Anatomy and physiology of the auditory system is described with emphasis on the function of the inner and outer hair cells, frequency specificity of the cochlear structure, and how the brain controls the "gain" of the auditory system.
- The brain is constantly monitoring the sound around us with an automatic gain control. It has the ability to modify the gain or sensitivity to sound. Soft sounds can be amplified and amplification can be decreased.
- Sometimes the gain mechanism amplifies too much and sounds become uncomfortable or even painful, even though they are comfortable for other people.
- It is essential for subjects with hyperacusis to know that this problem can be treated and, in most cases, be reversed. Our goal is for them to live comfortably in a busy, noisy world and to resume any activities that hyperacusis has kept them from doing.
- Using the Jastreboff model for hyperacusis, describe how the subcortical areas of the brain monitor the external sounds and amplify them and **only the auditory pathways are involved. If misophonia is present, describe the somewhat increased activation of the**

**limbic and autonomic nervous systems.** Describe our goal which is to reverse the way the subcortical areas of the brain are increasing the gain.

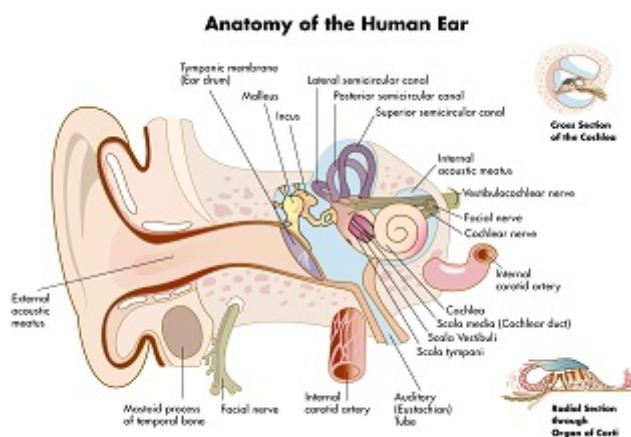
- **To treat hyperacusis, systematic and controlled use of sound is used at very soft levels.** Improvements can be seen in a few weeks. LDLs will be tested to monitor progress. If both tinnitus and hyperacusis are present, the hyperacusis is treated first.
- To treat **misophonia**, we will implement brief periods of active listening to pleasant sounds several times during the day.
- **Phonophobia** can involve fear that sound will damage the auditory system, fear of discomfort, or fear of exacerbating hyperacusis or tinnitus. There can be a tendency to overprotect the ears which can make the auditory system even more sensitive. **Appropriate noise protection** is important, but wearing plugs or muffs inappropriately will give the brain incorrect information regarding sound in the environment and it will not be able to adjust the gain properly.

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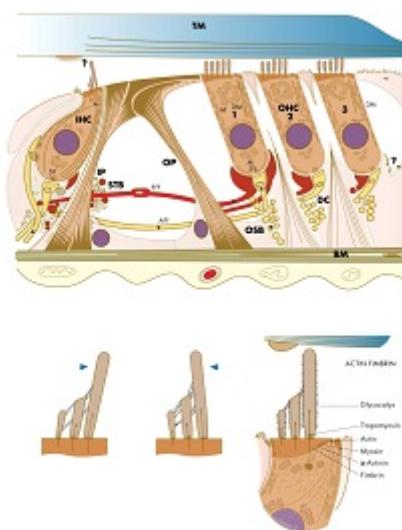
### Illustrations used during directive counseling

Illustrations have been modified from those developed by Jastreboff or Henry, or provided for the TRTT trial by Widex. Additional illustrations are modifications of Netter diagrams.

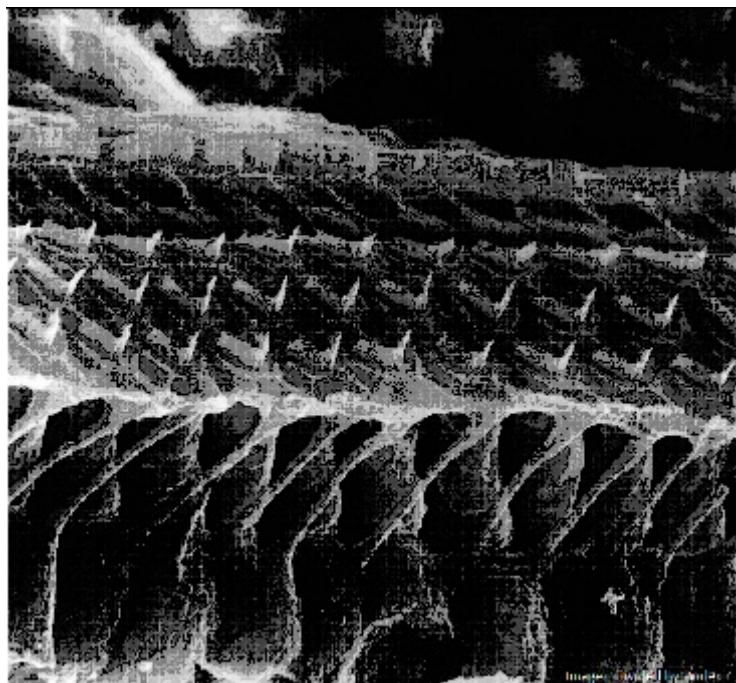
Picture 1. Anatomy of the human ear



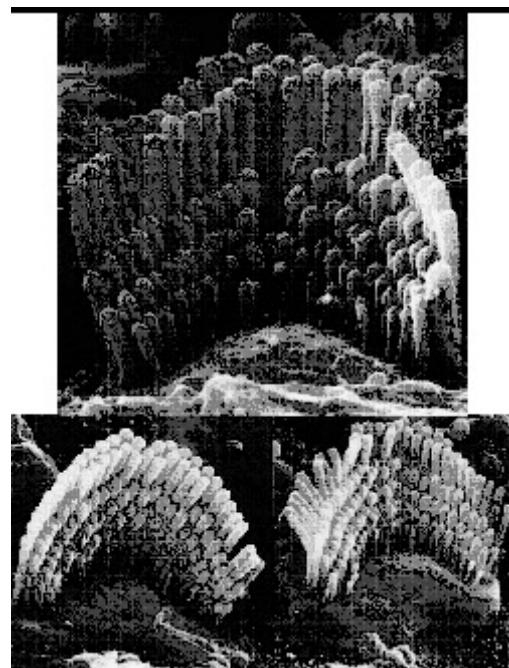
Picture 2. Drawing of IHC and OHC



Picture 3. Electron micrograph of basilar membrane with nerve fibers



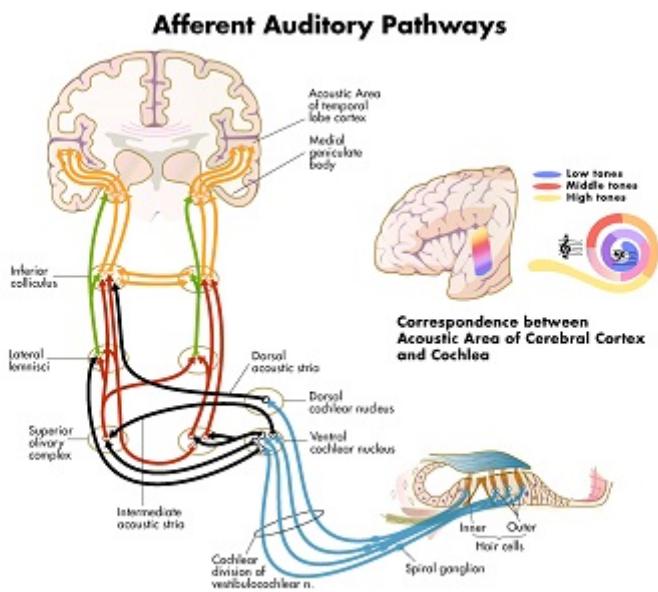
Picture 4. Close-up of cilia



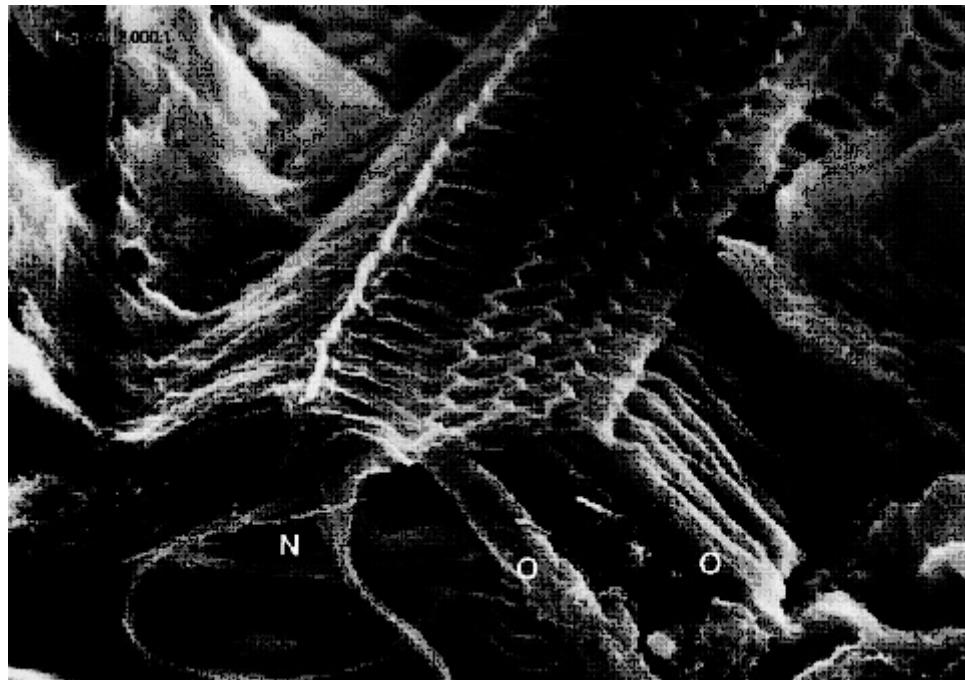
Picture 5. Cochlea



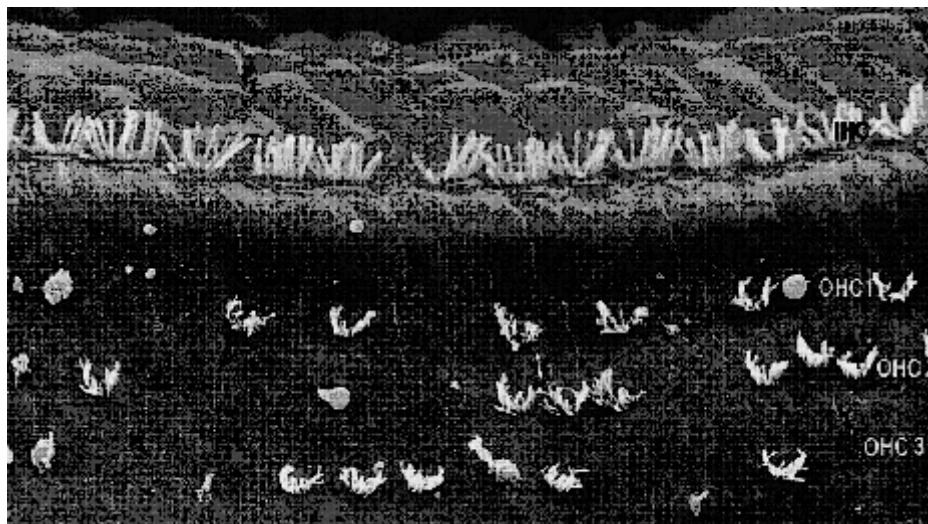
Picture 6. Afferent auditory pathways



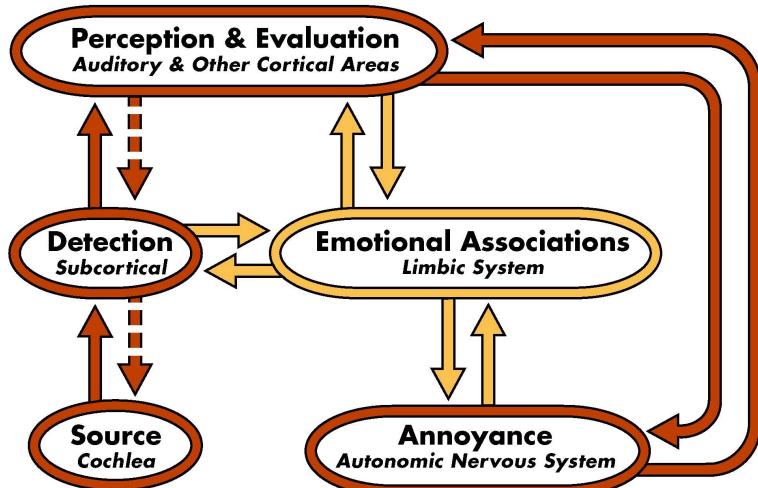
Picture 7. Enlarged basilar membrane with perfect IHC and OHC



Picture 8. Basilar membrane with damaged OHC

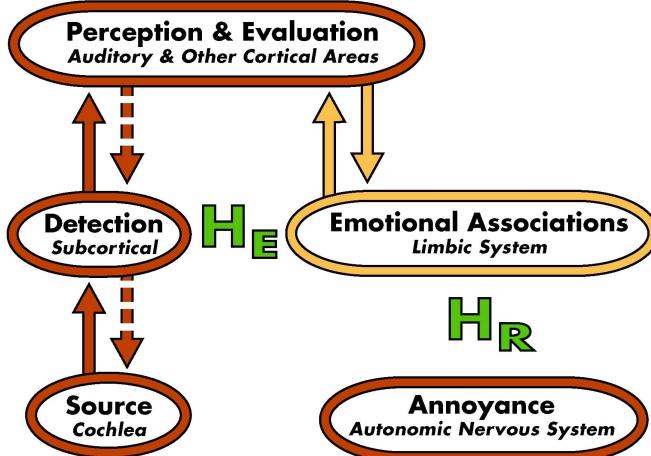


Picture 9. Diagram 1 of Jastreboff model



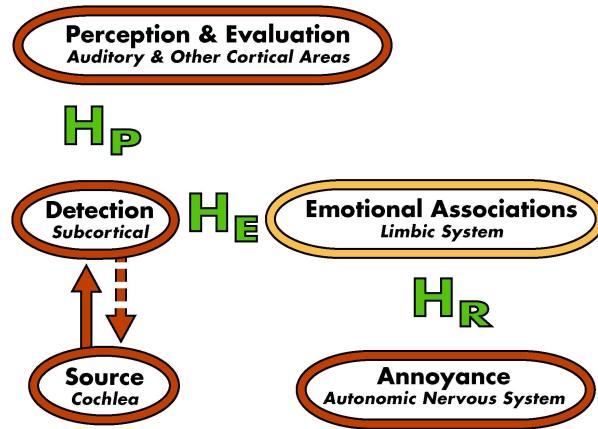
(after Jastreboff, 1995)

Picture 10. Diagram 2 of the Jastreboff model showing Habituation of Reaction and Habituation of Emotions



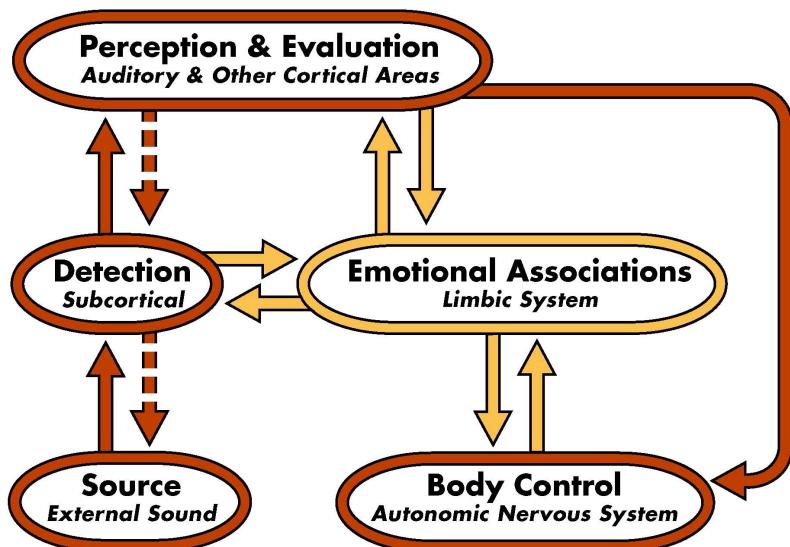
(after Jastreboff, 1995)

Picture 11. Diagram 3 of the Jastreboff model showing additional Habituation of Perception



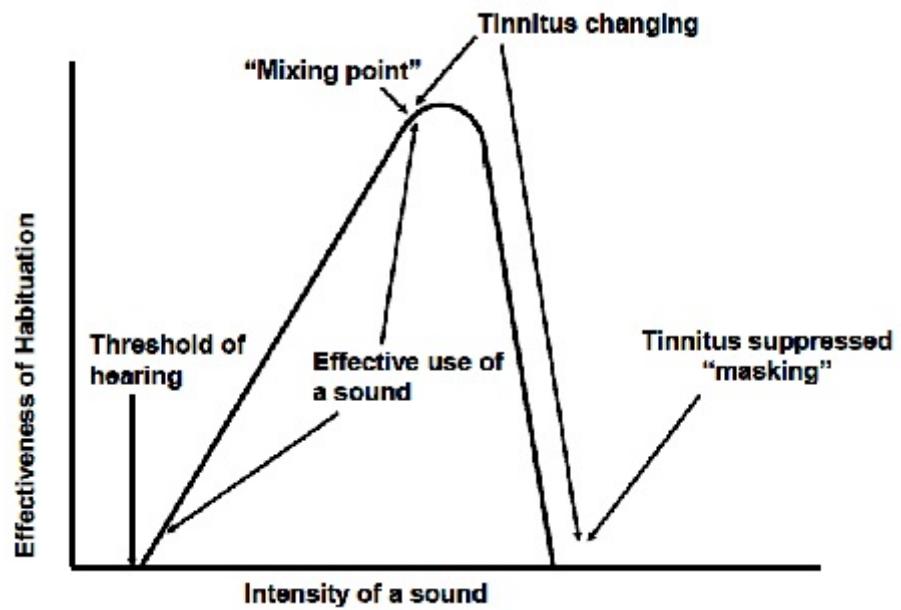
(after Jastreboff, 1995)

Picture 12. Diagram 4 of the Jastreboff model to be used for hyperacusis



(after Jastreboff, 1995)

Picture 13. Mixing point



## Appendix B

### Examples and Illustrations Used During Directive Counseling

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*The following are modified from Tinnitus Retraining Therapy Courses presented by Margaret & Pawel Jastreboff, 1996 to the present. Using some of the following examples during directive counseling and follow-up counseling may help the subjects understand, remember and/or internalize some of the complex concepts presented. You are encouraged to add your own examples.*

**1. New signals are always monitored.** As these signals become neutralized, habituation of stimuli occurs to a specific stimulus in a pattern matching way and the brain no longer monitors and pays attention to them. Some time is often needed to re-tune the neural networks within the auditory system to adjust and habituate to the new signal. Some examples are:

- *A new refrigerator or living near the train tracks or airport:* When you have a new refrigerator or move in to a house with a train running nearby or planes flying overhead typically you monitor the loudness of the new sounds. As you learn that these are the normal working noises, after a few weeks you are not aware of the sound of them. Furthermore, it demonstrates how deceiving our perception of sound loudness is, and how strongly it depends on the expectation and the emotional context. Note that you can learn to habituate to very loud and/or intermittent sounds.
- *Grandfather clock chiming every 15 minutes in your house:* After a while you don't even hear it (habituation). You have to check to see if it is still running. When a guest sleeps over, they may be awake all night because of the clock chiming.
- *Clothing:* When you first put your clothing on, you can feel them on your skin. After a short time you do not perceive their touch even though your skin receptors are sending signals to the brain. If you are reminded, you can instantly feel the clothes.
- *Floater in the eye:* If you notice a floater in your eye and go to the eye doctor, a careful examination will typically rule out any medical problem or disease process. The doctor will tell you not to pay attention to it and, in this case, you stop being concerned. After a while you do not notice it and have to actually look for it to see it. Tinnitus is sometimes described as a "floater in the ear" and once any medical problems or disease process in the ear has been ruled out, for some people, the signal becomes neutralized and habituation can occur.

**2. Importance of meaning versus the loudness of the signal**

- *Baby crying at night.* All those who have raised a family are familiar with the experience of the mother who wakes immediately in the night when her baby makes a sound just before beginning to cry. It is not uncommon for the husband or rest of the family to sleep right through the crying. The quiet sound made by the baby has a high level of significance to the mother relating to its protection and basic needs. These patterns of sound are selectively detected in the central auditory pathways, and their enhancement is such that the baby's mother is awakened from sleep. Interestingly, if the mother is away, the husband will start to awaken immediately when the baby starts to cry and then stop doing so after a short period of time after the mother returns.
- *Sound of your first name.* Similarly, we are all familiar with noticing the sound of our first name being mentioned in a nearby conversation at a party or noisy meeting. We are unable to avoid being distracted by this which has no effect on our nearby neighbors who have different names. The constant repetition of our first name during an early stage of life results in strong programming of neuronal networks and central auditory pathways resulting in the immediate, unconscious reflex reaction to our first name.

**3. Overprotection yields oversensitivity** - typically used during counseling for hyperacusis, misophonia, or phonophobia

- *Light levels.* Imagine going to a movie theater in the middle of the day. When you walk outside and are exposed to bright sunshine after spending a couple of hours in the semi-dark, the daylight will be very unpleasant, even painful. There are two methods to prevent this: put on very dark sunglasses before walking outside (in which case the eyes do not ever adjust to full daylight), or walk out very slowly – allowing time to gradually decrease the sensitivity to light. Overprotection by extensively wearing earplugs is like putting on those dark sunglasses – the ear (eye) becomes more and more sensitive and finally you would not be able to be exposed to normal everyday sounds (lights).

**4. Repeated neutral sounds can produce high levels of anxiety if these sounds are given an initial negative association and are also outside of the participant's control.**

- *Neighbor's son playing the same song repeatedly:* Imagine that the son of a neighbor, whom you don't particularly like, became very fond of a song and plays it over and over again through the day. Even though you know that this song is not harmful in any way, it evokes a very strong reaction and "drives you up the wall". (Note that if you own son was doing this in your own house, the reaction might be different because you are in "control" of the situation.)

This illustrates that a sound can evoke a very strong reaction from the brain and the body, without fear, avoidance of danger, survival reflexes, beliefs, etc. being involved. Similarly, tinnitus can be just plain annoying.

### **5. Strength of perception depends on contrast.**

- *Birthday candle:* Imagine entering a totally dark room in which there is just a single birthday candle lit in one corner. The candle appears to have a great brilliance in the otherwise dark room. However, once the curtains covering the window are opened and the sunlight illuminates the room, the candle (same amount of light) becomes virtually invisible.

### **6. Suppression of enjoying pleasant moments by the presence of stimuli representing negative events**

- *Waiting for dental surgery:* Let's imagine you are sitting in a dentist's waiting room expecting a root canal or extraction. Even if you are offered a delicious snack to eat while you are waiting, you will have great difficulty eating or enjoying it.

In this case, the fear induced by the anticipation of unpleasant treatment and pain suppresses the appetite, and any other pleasant emotions which would normally be evoked by such an offer. Similarly, the presence of tinnitus, which induces fear and has strong negative associations, suppresses the enjoyment of life, and through this mechanism has an enormously powerful impact on the quality of life. The presence of tinnitus can "color" everything you do.

### **7. Impact of elevated autonomic nervous system activity on sleep patterns**

- *Catching a plane early in the morning:* Imagine that you have to fly to a meeting in the morning and you must leave the house by 5:00 AM. Several alarm clocks are set to ensure that you wake up in time, your spouse is primed to wake you, and your colleague will telephone you at the same time. Despite all these precautions, your sleep will probably be very shallow and fitful during the night and you will probably become wide awake before the alarm clock goes off.

This reflects an elevated level of activity in the autonomic nervous system , preparing you to wake up on time and be ready for immediate action in order not to miss the plane. Imagine having to repeat this scenario on a daily basis moving from one city to another catching early morning planes. Going to bed early does not result in improving the quality of your sleep which will still be fitful and disturbed. Similarly tinnitus inducing even mild activation of

the autonomic nervous system promotes a prolonged “catch the morning plane” situation and might profoundly affect your sleep patterns.

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**Appendix C**  
**Tinnitus Retraining Therapy Trial**  
**Handouts**

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**HANDOUT 1: Summary of Directive Counseling**

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- ◆ **The tinnitus must be reclassified by the brain as unimportant (neutral/semi-neutral) for habituation of reaction to occur.** This is a passive process. We can't force that to happen, but we can introduce this information at the cognitive level and reduce the autonomic nervous system activity.
- ◆ **Tinnitus is a separate issue from hearing loss. Tinnitus does not cause hearing loss.** Although it is more common for people with hearing loss to have tinnitus, that is more related to the decrease in ambient sound so that they are more aware of the internally produced sounds (tinnitus). Not everyone with hearing loss has tinnitus. Not everyone with tinnitus has hearing loss.
- ◆ **Tinnitus is not a red flag that you will lose hearing.**
- ◆ **The annoyance factor is determined by the strength of the negative emotional association** given to otherwise normal neural activity.
- ◆ We can't repair any damage or irregularities in the cochlea, but we can change the way the brain views neural patterns that have been labeled as negative.
- ◆ Factors such as pitch of tinnitus, loudness, one ear or both ears, which ear it is in, maskability or what you associate the onset with have no predictability of improvement or no improvement.
- ◆ **Tinnitus is a weak, neutral signal.** If we match the loudness on a day it is perceived as loud, it will be virtually the same as on a day it is perceived as soft.
- ◆ The only way the brain can interpret activity from the cochlea and auditory pathways is as sound. If I punch you in the eye, the only way the brain can interpret it is as light.
- ◆ **Tinnitus is not an external sound.** It is a perception of neural activity interpreted as an "inside sound" not an outside sound. We cannot control it and when we can't control something, the limbic and autonomic nervous system can become highly activated, especially

if a person likes to be “in control” or is a perfectionist.

- ◆ The annoyance is not due to the system not working well enough. Rather, it is a system that is working too well.
- ◆ **The brain is very plastic and under constant reconstruction. It can be retrained to filter out this signal.** Much like a floater in the eye, once we know it is not a threat or related to retinal damage, we begin to look right past it even though we can see it if we look for it. The tinnitus is much like a floater in the ear.
- ◆ We can’t force habituation, but understanding the mechanism, the goals, and the use of sound therapy to reduce the contrast and the strength of the tinnitus signal will lay the groundwork for reaction to and perception of the tinnitus signal (passive extinction).

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## **HANDOUT 2: Treatment of Misophonia**

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**Note: Use only if misophonia is present.**

Misophonia (dislike of sound) is treated by involved engagement in activities which you enjoy and which has sound as an inevitable component.

The main concept is to create association of sound with a pleasant situation. This can be achieved by engaging in activities which you like, and in which sound is an indispensable part, such as listening to music, shopping in a mall, going to parties, restaurants, etc. You should always have full control over the situation and be able to discontinue sound exposure at any time (for example, listening to music at home, but not going to a concert.)

The most common method is to listen to music at home. Select your favorite type of music and listen to it attentively once or twice every single day for 20 – 40 minutes. The music should have a reasonably stable volume level without going from very quiet to very loud.

The treatment consists of 3 week cycles repeated as many times as it is needed.

- For the first week, the sound volume should be set every day at the most comfortable volume level.
- For the second week you should increase the volume level by one “just noticeable step” louder than the most comfortable volume level for a given day.
- For the third week, the sound volume should be increased by another step, that is, sound is initially set at the most comfortable volume level and then increased by two “just noticeable steps” louder.
- Repeat this three week cycle. Generally, the most comfortable volume level increases in a gentle manner.

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## Appendix D

### Script for Follow-up Counseling

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#### **1. General Overview of follow-up counseling**

Follow-up DC contacts in the TRTT are held at the one month treatment visit (T2) and at 3, 6, 12, and 18 month follow-up visits at the Clinical Center. The first follow-up treatment session may be as short as 15 minutes or as long as one hour, depending on the individual participant's needs. Follow-up contact is necessary to reinforce the attempted goals. Treatment progress is monitored and patient's questions and concerns are addressed.

#### **Part 1: For the one month treatment visit (T2)**

Review the results of testing for pure tones and LDL/UCLs with the Study Participant. (*Note that improvements in LDL/UCLs indicate the changes in auditory gain are taking place even if there is no noticeable subjective improvement by the Study Participant.*)

The Study Audiologist asks the following questions at each follow-up appointment, beginning at T2. These questions are included in the Sound Generator Use Form, to be completed at T2

**The compliance of the patient is checked** with regard to the protocol for recommended sound therapy by asking:

- Are you wearing the sound generators?
- At what volume level? (*Review with the subject, if necessary.*)

It is important that the volume is set at or just below the “mixing point” where the sound of the instrument **starts** to mix or blend with the tinnitus. The two sounds do not have to be equal. You should be able to separate the tinnitus from the sound of the instrument.

Key factors should be:

- The sound of the instrument should not change the characteristics of the tinnitus signal
- The sound of the instrument should not be above the “mixing point”.

The tinnitus should not be masked because the brain cannot learn to ignore something it cannot detect and habituation will not occur.

- The loudness or quality of the instruments should not induce any negative reaction or annoyance. This would enhance activation of the limbic and autonomic nervous system and hinder habituation
- If there is any question concerning the correct volume setting, it is better to be just below the level that will induce annoyance or change the characteristics of the tinnitus.

Once the volume has been set in the “worse” ear, match the volume in the second ear. If when the volume in both ears has been set and the sound seems too loud, the characteristics of the tinnitus have changed, the tinnitus is masked, or the sound induces any kind of annoyance, it is better to reduce the volume in both ears **slightly** so that none of these problems occur. (*It is acceptable if any less bothersome tinnitus is covered*).

- What is the general wearing schedule? (Should be at least 8 hours per day. It is not necessary for the instruments to be worn continually for 8 hours, but they can be worn intermittently. They can be worn all day, if comfortable.)
  - Are the instruments comfortable on your ears?
  - Are you using enriched background sound throughout the day and at night during sleep? (*Review what types. They should be neutral and soft.*) **When you are surrounded by normal environmental sound, you may not be aware of the sound from the instruments.**
  - Are you wearing noise protection? (*Overprotection? See below, under hyperacusis for suggestions related to ear protection.*)
  - Do you forget about the instruments for short periods of time while they are on? (*If so, point out that they are beginning to habituate to the sound of the instrument. This will carry over to the tinnitus itself.*)

Repeat these concepts that were introduced at the instrument fitting appointment, if necessary:

*Rough patches:* It is important to know that there will be periods of time when you are more aware or less aware of the tinnitus. The rough patches will occur, but they are temporary. We are trying to grow those periods when you are less aware of the tinnitus. Tinnitus awareness is related to a dynamic relationship between the ear, the brain, the emotions, the biochemistry, what you ate, what you drank, how much sleep you got, the stresses you are under, etc. You can't control these issues but you can know that the rough patches are typically temporary.

*Keep the focus off the tinnitus.* Don't keep diaries or journals. Do not worry about normal fluctuations from caffeine, wine, alcohol, chocolate, exercise, naps, etc. These can cause normal fluctuations in the biochemistry. **The tinnitus can get better or worse, but either way the changes are temporary.** Live your life without worrying about these fluctuations.

End the T2 and the 3 month follow-up visits by asking if there are any questions or concerns and discussing any issues that arise. (*See following sections for repeating specific topics of directive counseling.*)

### **Part 2: Beginning at the 6 month follow-up appointment (in addition to Part 1)**

**Change in patient's status is assessed by reviewing the TRT Follow-up Interview** (*completed by the blinded Audiologist*) beginning at the 6 month follow-up visit, and comparing answers to the Baseline TRT Interview. Questions about the number of "bad days" and percentage of time the patient was aware of the tinnitus over the past month relate to habituation of perception.

Questions about how strong or loud your tinnitus has been over the past month is related to habituation of perception. Annoyance levels are related to habituation of reaction. Ranking of different issues (i.e. tinnitus, sound tolerance, and hearing) can change as progress occurs.

Discuss any questions, concerns or issues the Study Participant has. (*See Part 4, below, on discussion of specific directive counseling topics.*)

### **Part 3: For Study Participants with hyperacusis.**

For Study Participants with hyperacusis, the retest of pure tone thresholds and LDL/UCLs performed at each follow up visit, beginning at T2, is used during counseling until normal LDL levels and complaints about reduced sound tolerance are no longer present.

If initial volume levels for SGs were just slightly above hearing threshold, volume can be increased slightly toward the "mixing point" (*Make sure to avoid effects of stochastic resonance which will inhibit progress*).

For hyperacusis subjects, progress is checked by asking:

- Are you more comfortable in certain situations that were previously uncomfortable?

- Are you doing things you could not do before?

If LDL /UCLs have improved, this can be pointed out to the Study Participant. In this case, we know there are changes taking place in the “gain” of the auditory system, even if there are no subjective changes noted by the subject.

Discuss the use of ear protection. Is there overprotection? If the Study Participant needs to wear ear protection in loud situations, ear muffs can be put on over SGs. This allows the ears to continue to be exposed to soft sound while being protected from loud sounds (e.g., mowing the lawn).

As hyperacusis is less of an issue, tinnitus may become the major problem. If so, repeat directive counseling emphasizing tinnitus more directly. For other Study Participants, as hyperacusis becomes less of an issue, tinnitus also becomes less of an issue.

Almost all individuals with hyperacusis have some degree of misophonia, the dislike of sound or the concern that external sound will damage their hearing. This concept is common when symptoms may have been initially triggered by a loud noise. The treatment for hyperacusis involves changes in the auditory pathways. The treatment for misophonia addresses changes in the limbic and autonomic nervous system. Active Extinction (*see Appendix C, Handout 2*) can be described to the Study Participant and they can be given the handout with instructions to do over the following several weeks.

#### **Part 4: (to use if indicated)**

Elements of the initial TRT directive counseling may be reviewed, depending on the individual patient’s questions, concerns, and progress. Some of these concepts are:

- Auditory Gain
- The Heller Bergman Experiment
- The Neurophysiological Model of Tinnitus (*You could ask the Study Participant to explain the model to you to make sure s/he understands it.*)
- Conscious Loop
- Subconscious Loop
- Classification of New Sound as “Important” or “Unimportant”
  - Reclassification of Sound
  - Habituation of Reaction
  - Habituation of Perception
  - Reducing Contrast = Reducing strength
  - Sound Therapy
  - Habituation Takes Time

Examples used during Directive Counseling may be to help clarify these concepts for the Study Participant (*see Appendix B*).

**Part 5. Determining the end of treatment** (*See Section 11.4 for determining point at which to end treatment* )

Some Study Participants may feel that they have made sufficient progress in their treatment and that tinnitus and/or hyperacusis is no longer a significant issue in their life. There is no precise way to identify the end point or decide when a significant therapeutic effect has been achieved, but because this can occur sooner than the 18 months allotted by the TRTT, this must be considered.

The time to end treatment must be agreed upon between the Study Participant and the Study Audiologist. This point can occur after about one year of treatment or occasionally sooner. For the purposes of TRTT, if the Study Participant reaches the point where the tinnitus and/or hyperacusis is no longer an issue in his or her life, s/he may be instructed in how to reduce the use of the SGs and enriched environmental sound. Study Participants will, however, be required to continue to complete all TRTT Follow-up Visits and required ATH evaluations and psychometric measures.

The Study Participants's responses to the Follow-up TRT Interview provide a guide to whether tinnitus and/or hyperacusis is no longer clinically significant. In addition to change in the TRTT Follow-up Interview, Study Participants may report the following:

- The Study Participant may say, “Tinnitus is no longer an issue, what should I do?”
- The Study Participant may report they s/he has forgotten to wear the instruments for three or more weeks. This suggests that the Study Participant is forgetting about the tinnitus and is probably ready to stop wearing them.
- The Study Participant may go for long periods of time when s/he is not aware of the tinnitus; even if s/he is aware of it, s/he is not bothered by it.
- Occasionally, individuals may be unable to hear the tinnitus, even with “hard listening”. (*This is not a goal of TRT, but happens to some people.*)
- The Study Participant reports that s/he is aware of tinnitus less than 10% of the time (*habituation of perception*).

- The Study Participant reports being annoyed/distressed/irritated by tinnitus as close to zero as possible over the past 1 to 2 months (*habituation of reaction*).
- The Study Participant reports that the “effect on life” of tinnitus and/or hyperacusis is as close to zero as possible.
- The Study Participant reports very few or no activities affected or prevented by tinnitus and/or hyperacusis over the past one to two months.
- The Study Participant reports very few or no bad days over the past one to two months and, if they occur, they are not as bad as they were originally.

**Review of standardized test results** at follow-up should indicate significant improvement compared to initial tests.

### **Reducing Sound Therapy**

*(End of treatment, in this case, will mean reducing the use of SGs and enriched environmental sound. Study Participants will, however, be required to continue to complete all TRTT Follow-up Visits and required ATH evaluations and psychometric measures. This also allows the Study Audiologist to monitor the stability of the treatment effects.)*

To terminate treatment, it is important not to make rapid changes. In stopping the use of SGs, it is important to let the Study Participants know not to wear them intermittently, i.e., for several shorter periods each day (on/off) (*This draws attention to the symptoms*). Rather, they should stop wearing the devices certain days of the week (e.g., weekends) and then gradually stop the use of sound enrichment in the same way.

Finally, Study Participants can stop the use of enriched sound at night, although many individuals prefer to continue use of enriched sound at night as it helps them to sleep. They can continue to use the instruments periodically if considered necessary.

For Study Participants with tinnitus and hyperacusis, the hyperacusis is treated first with generally good results within the first 6 months. For some Study Participants with tinnitus and hyperacusis, when the hyperacusis is no longer an issue, the tinnitus is significantly improved.

If Study Participants reach this point before nine months of full TRT treatment, they should be required to wear the SGs and use enriched environmental sound for at least nine months.

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## Chapter 12

### Protocol for Sound Therapy

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#### 12.1 Introduction

Sound therapy (ST) is an integral component of the Tinnitus Retraining Therapy (TRT) treatment (Jastreboff *et al.*, 1996). The goal of ST is to facilitate the habituation process, which is initiated by directive counseling (DC; described in Chapter 11). ST is hypothesized and intended to decrease the contrast between tinnitus-related neuronal activity and background neuronal activity, to interfere with the detection of the tinnitus signal, and to decrease the gain within the auditory pathways. ST is implemented with a low-level, relatively broad-band, neutral sound. The most convenient way to provide this sound is to use commercially available sound generators (SGs) fit to both ears, supplemented by environmental sound. The Tinnitus Retraining Therapy Trial (TRTT) will test the efficacy of using ST as an adjunct to DC in TRT. Study Participants will be randomized to use of a standard or placebo SG.

#### 12.2 Sound Generators

We will use a digital equivalent of the Tranquil model sound generator, manufactured by General Hearing Instruments, Inc. (GHI), as the SG for the TRTT. The new digital devices will be implemented with added features including data-logging capability to enable the Study Audiologist to monitor the Study Participant's use of and compliance with the SG. Additionally, each participant's sound-level exposure will be monitored and logged to determine whether the SGs or environmental sound is the primary sound exposure and the nature of the sound-exposure properties. The SG will be housed either in a behind-the-ear (BTE) instrument or in an all-in-

the-ear (ITE) non-occluding device, both of which will offer adjustment of the output volume to a “zero” (fully quiet) noise floor. GHI will provide both the standard and the placebo SG devices. The placebo SG will have specially designed sound properties, closely resembling key properties of the standard SG, and a physical appearance identical to the standard (conventional) instrument so that neither the Study Audiologist nor the Study Participant will be aware of which sound treatment the participant is receiving.

### **12.2.1 Sound Generator Assignment**

Subsequent to completion of the baseline testing and determination of eligibility of the Study Participant, including informed consent, the Clinical Center will request from the DCC the randomized treatment assignment for the Study Participant using the online randomization protocol. At randomization, the Randomization Registration Form will include a kit ID. SGs will be assigned to Study Participants assigned to TRT. If the assigned SG is a BTE device, the pair of SGs will be included within the kit. The serial number of the devices will be located on the box containing the BTE devices. If the assigned SG is an ITE device, the kit will contain a Sound Generator Order Form with the serial number printed on the form and the Clinical Coordinator or Study Audiologist will order custom SG treatment devices from GHI for the Study Participant. The ordering and production of ITE devices requires the making of outer-ear impressions for the customized SGs, as described in Section 12.2.2. The assigned pair of SG devices will be fitted to the Study Participant and activated at Treatment Visit 1 (T1), immediately after the DC session as described in Section 12.2.3. The Sound Generator Issue Form documents which pair of devices is issued to the Study Participant and should be completed at T1. T1 may follow on the same day as randomization, if time permits.

### **12.2.2 Ear Canal Impressions**

Most Study Participants who meet eligibility criteria for inclusion in the study and who willingly agree to participate will have outer-ear-canal impressions made bilaterally subsequent to completing informed consent. This activity may be performed at the Baseline Visit or during a subsequent Randomization Visit at the discretion of the Study Audiologist.

The Study Audiologist will take impressions of both of the Study Participant’s outer-ear canals following the checklist and protocol outlined in Table 1. The first step in taking the impressions is to explain to the Study Participant how an impression is made and the purpose of taking an impression. This explanation will allay any fears that he or she may have about the procedure. The Study Audiologist will inform the Study Participant that the impression of the outer-ear canal is made with a soft material that must set up for about ten minutes. It also is important to explain that in some cases the first impression of the ear canal with the jaw open will not produce a good fit, and that a second impression will be taken with the jaw closed to

assure a good and comfortable fit with one of the two sets of impressions. The Study Participant will be instructed to continue to wear his or her glasses and dentures, if these are present, during the impression-taking protocol. Occasionally, it may be necessary to make a second impression for one or more of these opened- or closed-jaw conditions. If the definition of the completed impression does not adequately capture the anatomy of the outer ear and ear canal.

The Study Audiologist will then gather the materials and tools needed to take the impression, and place a bite-block between the molars for the open-jaw impressions. Next, an examination of the ear canal will be conducted using an ear light or an otoscope to assess the:

- Size of the impression needed;
- Length, direction, and diameter of the ear canal;
- Shape and contours of the external ear and canal; and
- Presence of any impediment to taking an impression (e.g., wax, enlargement, trauma, etc.).

If there is hair growth in the ear canal, it should be trimmed with scissors. A foam ear-canal block is then placed in the ear canal to extend just beyond the second bend of the canal. The ear-canal block must completely occlude the full diameter of the ear canal. If the Study Participant has a surgically altered ear canal, then the ear block must be placed by a physician before taking the impression. The ear-canal block serves to:

- Prevent impression material from reaching the eardrum;
- Acts as a safety catch if impression material sticks in the canal; and
- Assures a completed canal cross-section.

Ear-canal blocks may be trimmed with scissors for narrow ear canals. For large ear canals, larger ear canal blocks or sometimes more than one are block may be used. The ear canal block must be compressed for a proper fit with the attached removal thread extending past the outer ear. Blocks for both ears may be prepared and inserted at this point to expedite the placement of the impression material in each ear as described below.

The Study Audiologist then prepares the material used to make the impression. In the TRTT, silicone will be used to make the impressions for the SGs. Silicone is flexible yet has total memory, does not sag or collapse, and generally is not damaged by handling or shipping. Silicone also is easy to manipulate and to insert. Silicone impression material supplied by GHI will be

used in the TRTT. The manufacturer's directions for mixing the material should be carefully followed and the silicone loaded into a syringe or "gun" for placement of the impression material in the ear. The quicker the material can be placed in the syringe and the procedure started, the better the impression.

After placing the silicone material in the barrel of the syringe, the Study Audiologist will insert the plunger and force a small amount of the material into the nozzle to remove air pockets. The Study Audiologist will then place the syringe near the canal block and begin to inject the material. The tip of the syringe must be kept in the impression material at all times. As the impression material becomes visible, the syringe is slowly withdrawn simultaneously with injection of additional material. The process of inserting the impression materials continues until the helix and concha areas are completely covered and then the tragus is covered.

When the external ear has been filled completely, the Study Audiologist will use his or her finger (not palm) to touch and gently smooth the impression material in the concha and helix areas. It is critical to fill the helix, but care should be taken not to overfill the impression material, which may distend the outer ear and confound the mold of the outer ear and ear canal. Subsequently, an impression is made immediately for the opposite ear so that both impressions can cure simultaneously. After an adequate period to allow the impression material to set, the ear canal impression should be removed.

To remove an impression, the Study Audiologist will gently press the ear away from the impression; remove the helix curl slightly and bring the impression straight out while holding the ear canal block thread. It is best to pull gently and steadily so as not to distort the impression. After the cured impressions are removed from the ears, and otoscopic examination should be performed to ensure that all impression material has been removed from each ear and confirm that there are no abrasions of the ear canals or ear drum as a consequence of performing the protocol.

The Study Audiologist will then check to make sure that the impression adequately mirrors the outer-ear canal and that each helix and concha are well-formed along with the external ear canal portion. If an impression is flawed, then it will be necessary to take a second impression. If it is adequate, then the impression will be labeled and prepared for shipping to GHI. The protocol then will be repeated for the closed-jaw condition, but with the bite-block removed from the mouth.

Each impression should be labeled either either "opened-jaw" or "closed-jaw" and either "left" or "right" ear. The shipment of the impressions to GHI will therefore include two sets of impressions for each ear as well as a Sound Generator Request Form identifying the Study Participant and including the address to which the devices should be sent. Impressions will be

shipped by Federal Express overnight delivery to ensure preparation and return of the SG from the manufacturer to the Clinical Center in time for the Initial Treatment Visit (T1). At the time the impression is sent from the Clinical Center, both the DCC and GHI will be notified and, similarly, upon return of the SGs to the Clinical Center, the DCC and Clinical Center will be notified of shipment.

### **12.2.3 Fitting the Sound Generator**

The fitting/activation of and orientation to the SGs will take place after the DC session has been completed at T1. Typically, fitting of the SGs requires about one hour, and includes instruction to the Study Participant on the use and care for the instruments, correct volume settings, schedule of use, and insertion and removal of instruments. Because treatment counseling also takes place at this visit, a minimum of three hours should be allotted to complete T1. A checklist of the fitting protocol is included in Table 2 and a more detailed summary in Appendix A. A script for the fitting protocol, including recommendations for using SGs is included in Appendix B.

The Study Audiologist will fit the SG to each ear of the Study Participant using the instructions and protocol described below. An optimal fit will be achieved by ensuring that each instrument is seated comfortably and securely on the top of the ear for the BTE devices. There should be no gaps between the ear, the BTE sensing plate, and the head. The thin tube dome for the BTE should seat at the top of the ear canal, and the retention tubing should loop up the posterior of the concha. On very rare occasions, for patient comfort, the retention tubing may be clipped shorter. It should never be completely removed.

Similarly, the Study Audiologist will evaluate the fit of the ITE instruments to each ear of the Study Participant. The optimal fit requires the SG case to be well molded to the participant's ear, yet to be non-occluding so as to allow a pathway for environmental sound to enter and pass through the ear canal. The Study Audiologist should insert the SGs in both ears and check the fit. The SGs should comfortably and snugly fit within the ear canals so as not to dislodge when the Participant moves or shakes his or her head. Neither should the SGs be too long nor skewed. A reported sensation of discomfort from the Participant indicates an unacceptable fit, requiring repositioning of the SG within the ear or an adjustment of the SG. The Study Participant may be more aware of one device than the other; this is normal. In most cases, the Study Participant will adapt to the wear of both devices within a week. If the Study Audiologist finds that the instruments do not fit the Study Participant appropriately, then the devices will be returned to GHI for modification. New impressions must also be sent so that customized shells can be remade if necessary.

#### **12.2.4 Instructions to Study Participant**

The Study Audiologist will instruct the Study Participant in the proper care and use of the SGs. The Study Audiologist will describe the parts of the instrument to the Study Participant at T1. It is important that the participant is comfortable with inserting and removing each SG from his or her ear, is knowledgeable about replacement of batteries and their use, and understands how the Study Audiologist adjusted the volume settings for his or her SGs to achieve the “mixing point.” The Study Participant should practice fitting the devices and adjusting them to the “mixing point” with the Study Audiologist so that both have confidence that the Study Participant knows and understands this setting.

The Study Audiologist will use a sample instrument to review the key parts of the SGs and their care, including the following:

- Battery compartment
  - battery insertion and removal
  - battery size
  - estimated battery life (about 180 hours)
  - battery replacement
  - batteries cannot get wet, so cannot shower with SGs in place
- Storage materials
  - box for nighttime storage, when at home
  - bag for daytime storage, when not at home
- Maintenance. The Study Audiologist will instruct the Study Participant on how to clean the instrument. Brushes used for cleaning the instrument will be provided, as well as a jar with dessicant, (i.e., the Dri-Aid Kit in which to store the SG between daily use). The Study Audiologist will demonstrate to the Study Participant the correct method to clean the SG to remove debris and cerumen.
- SG toggle adjustments for control of the volume setting will be reviewed.
- Repairs occur infrequently, but if necessary are completed by the manufacturer, GHI. The Study Participant is instructed to call the Study Audiologist if a repair is necessary.

Because each Study Participant is seen individually, instructions can be tailored to the individual's needs. It is not uncommon for patients to have more specific questions after they have worn their instruments for a while. The Study Audiologist will ensure that the Participant

has no difficulty inserting and removing each device. When the Participant and the Study Audiologist are both satisfied that the Study Participant can reliably insert and remove the instruments from both ears and replace the batteries, then the next step is adjusting the volume of each SG to achieve the “mixing point.”

### **12.2.5 Volume Control of the Sound Generator**

The critical step in the fitting process, after the SGs are properly positioned, is for the Study Audiologist to work with the Study Participant to adjust the volume of each instrument to the “mixing point.” For the TRTT, the “mixing point” is defined as that volume setting for which the sound from the instrument just starts to mix or blend with the Study Participant’s most bothersome tinnitus sound, does not change the characteristic of the tinnitus, is not annoying, and does not mask the tinnitus. The “mixing point” setting will be unique for each person. The SG volume setting will be programmed by the Study Audiologist so that the Study Participant reports that he or she can hear, but barely distinguish the sound of his or her tinnitus from that of the instruments. According to Jastreboff et al. (1996), it is important in TRT theory that the sound from the instrument not mask the tinnitus, but rather blend with the tinnitus sound. Otherwise, the habituation process may not be facilitated nor progress by ST. It is also important that the sound levels not be set too close to the threshold of hearing, so there is no effect of stochastic resonance.

If the tinnitus is “worse” in one ear, then begin the process of finding the “mixing point” with that ear. The volume should be set at, or just below, the “mixing point”, the point where the sound of the instrument **starts** to mix or blend with the tinnitus. The two sounds do not have to be equal. The subject should be able to separate the tinnitus from the sound of the instrument. Key factors in setting the volume should be:

- The sound of the instrument should not change the characteristics of the tinnitus signal.
- The sound of the instrument should not be above the mixing point.
- The tinnitus should not be masked because the brain cannot learn to ignore something it cannot detect and habituation will not occur.
- The loudness or quality of the instruments should not induce any negative reaction or annoyance. This would enhance activation of the limbic and autonomic nervous systems and hinder habituation.

- If there is any question concerning the correct volume setting of the instruments, it is better to be just below the level that will induce annoyance or change the characteristics of the tinnitus.

Once the volume has been set in the “worse” ear, then begin the same adjustment process to match the volume (or loudness) in the second ear. If, when the volume in both instruments has been set, the sound seems too loud, the characteristics of the tinnitus has changed, the tinnitus is masked, or the sound induces any kind of negative reaction or annoyance, then reduce the volume in **both ears** slightly. It is better to be slightly below the mixing point if any of these factors are present. The volume should still be fairly equal in both ears. It is acceptable that a less bothersome tinnitus, if present, may be partially or completely suppressed. The procedure for programming the SG volume settings is described below.

#### **12.2.5.1 Setting the Sound Generator Volume for Tinnitus**

Instrument volume settings will be performed via programmable software, per the programming procedure outlined in Table 2, followed by “fine-tuning” manual adjustments. Subsequent to establishing the reliability of the “mixing point” volume, that setting and volume settings 2 and 4 dB below the “mixing point,” will be programmed into the SG memory. The Study Audiologist and the Study Participant will work together to set the SG initially for the ear with the most troublesome tinnitus. In adjusting the volume setting for each SG, the Study Audiologist will ask the Study Participant to indicate when s/he just starts to hear the sound of the instrument. At that point, the programmable volume setting should be increased until the sound of the instrument blends with, but does not mask, the tinnitus. The Study Participant should be able to distinguish between the tinnitus sound and the instrument sound. The Study Audiologist and Study Participant should repeat the adjustment to the “mixing point” setting to assess the participant’s reliability in reporting the “mixing point.”

The volume setting then should be set for the SG in the opposite ear. To the extent possible, the output of the two devices should be matched for loudness, while continuing to maintain the “mixing point” settings. The “mixing point” may change slightly with the fitting of the second device. This change may require programmable re-adjustment of the volume setting of the device fitted in the first ear to maintain the perceived “mixing point” and re-balance loudness between ears. Ultimately, some titration of the volume settings for both devices may be necessary to achieve final settings.

After the programmable volume setting for the “A” memory setting (i.e., mixing point for both ears) is agreed upon by the Participant, the Study Audiologist will instruct the Study Participant on how to decrease the volume settings for each SG using the switchable toggle settings on the top of the SG case. The Study Participant will be able to decrease the volume of

each SG by manually switching from the “A” pre-set memory setting (mixing point) to the setting designated as “B” (- 2 dB from the mixing point) or the “C” setting (-4 dB from the mixing point). The Study Participant will be instructed to switch the SG volume manually so that he or she just starts to hear the sound of the instrument (i.e., nominally setting for position “A”, corresponding to mixing point setting). It is important that the setting not be adjusted to the point where the Study Participant just starts to hear the sound output from the SG (at the threshold of hearing). When the sound level from the SG is close to the threshold of hearing, this situation may enhance tinnitus through stochastic resonance. After this point has been made, the Study Audiologist should then confirm with the Participant that the sound output level at the “mixing point” volume setting (i.e., “A”) is not equal to the tinnitus level and that he or she is able to separate the tinnitus sound from the sound of the instrument.

The Study Participant should practice manipulating the volume-switch settings by toggling through the three memory settings on the two SG devices and, when satisfied with the “mixing point” settings, should inform the Study Audiologist.

#### **12.2.5.2 Sound Generator Volume for Hyperacusis**

A different volume-setting protocol is used for Study Participants with hyperacusis. For these patients, the programmable volume setting is increased gradually until the Study Participant just starts to hear the sound of the instrument. The Study Audiologist then sets the output of the device to a tolerable, but comfortable setting (i.e., using the memory “A” volume setting). The second device then is set accordingly in the other ear. The Study Audiologist may need to titrate the programmable settings further to match the loudness between ears at tolerable levels. Memories B and C should be set as usual, i.e., 2 and 4 dB softer than A, respectively. If the C setting is less than 6 dB above threshold, however, stochastic resonance could develop, and so the Study Audiologist should use judgment as to the best length of the intervals between the memory settings. Over time, the Participant’s sound tolerance is expected to improve and greater output levels from the SGs will be better tolerated by the Study Participant, allowing him or her to use a higher “mixing point” setting in memory “A” with corresponding changes in the B and C memory settings.

Study Participants with hyperacusis, who are concerned about being in louder situations with no ear protection, such as parties, supermarkets, sports events, or shopping malls, can increase the volume level of the sound generator so that the “outside sound” is no longer uncomfortable. The sound generator acts as a buffer. The increase in volume can be set only during the period of time they are in the louder situation.

### **12.2.5.3 Use of Sound Generators for Tinnitus**

After the volume settings for each SG are programmed appropriately for the Study Participant, the Study Audiologist will give the Study Participant a handout of the Guidelines for Instrument Use (Appendix C). The Study Audiologist will answer any questions that the Study Participant may have about the information presented in the DC session and continuously reinforce the DC information during the treatment and subsequent follow-up visits.

The instrument fitting portion of T1 takes about 1 hour. It is important to tell the Study Participant that the amount of sound generated by the SGs is a very small amount of sound and that it can not hurt them. During the fitting the Study Audiologist will review guidelines for using the instrument in the TRTT. Instructions include:

- The “mixing point” volume setting is correct for you now, but it may require change over time. If so, then you can switch from memory “A” to memory “B” or “C” to decrease the sound level. That memory level should then be maintained throughout the day.
- Set your SGs once for the day and forget them. Try not to focus on the sound from your instruments. You may not always hear the instrument sound, especially in noisier settings.
- As you become accustomed to the sound from the instrument you will start to “tune it out” and may be unable to hear the instrument sound even in a quiet setting. In fact, for some persons, adaptation to the instrument sound will occur almost immediately and the sound will be undetectable. This is normal for many patients and should be expected.

The Study Audiologist will encourage the Study Participant to use the sound instrument as much as possible during waking moments. It may be necessary for some persons to build up gradually for extended daily use of their SGs. A minimum of 8 hours of SG use per day is essential, and longer time periods are optimal. Instructions for the use of the SGs include the following:

- Eventually you should be wearing the instruments as much as possible throughout your waking moments. If you can’t wear them all day, then try to wear them at least 8 hours each day. That does not have to be all at one time. You can break the use periods into two sessions throughout the day, but preferably not more than two sessions. It does not have to be the same schedule every day, but both instruments must always be used and worn together.

- You can build up the wearing time over the first few weeks of use (like contact lenses). You can wear them to sleep, if they are comfortable, but the sleep time does not count toward the 8 hours. Get in the habit of putting the instrument on as soon as you wake up, unless you take a shower. If so, dry your ears, and then put on the instruments, set them and forget them. (Stress the latter instruction of “setting and forgetting”.)
- Do not remove the instruments after you are satisfied with the “mixing point” settings unless you intend to stop using the devices for a prolonged period. You should **not take the devices in and out repeatedly** to check the output levels because this process will disrupt your treatment. Do your best to maintain the casing of each SG, especially the sensing plate for the BTE devices, firmly behind your outer ear and securely positioned next to your head. Minimize conditions that create gaps between your SG case and the ear and head.
- The instruments offer a steady, stable sound. The SGs move with you wherever you go to facilitate your treatment.
- In addition to wearing the instruments, keep a low level of sound on at all times, day and night. The sound does not have to be loud. You are not trying to mask the tinnitus. Use a fan, a computer, sound machine, fountain, aquarium, air conditioner, nature tapes, car noise, sound pillow, humidifier, etc. Any kind of neutral, low-volume sound is appropriate. Do not use TV or talk radio at night so that your brain does not “tune in” to something it finds interesting. Your SGs are being used in an open-ear-canal fitting protocol, which allows low-frequency sounds to escape from your ear canal or as behind the ear devices. The additional environmental sound will broaden the frequency spectrum of the ST background.

Participants should be advised not to engage in activities that increase their attention on their tinnitus. The Study Audiologist will instruct them as follows:

- Do not keep diaries or journals related to your tinnitus.
- Ask your family members and friends not to ask you about the instruments you are wearing or how you are doing with your “tinnitus problems.”

Finally, the Study Audiologist should ask the Study Participant if he or she has any questions about the use of the SG. The Study Audiologist also will assure the Study Participant that he or she is available by telephone at any time between now and the next study visit for questions or concerns about the use of the SG.

Study Participants will receive a copy of Guidelines for Instrument Use to take with them. (see Appendix C).

### **12.3 Second Treatment Visit and Subsequent Care**

The second treatment visit (T2) occurs one month after T1 and is designed to ensure that the Study Participant is wearing and using the SGs as instructed. The Study Audiologist will discuss the following points at the T2 visit:

- Each SG's physical fit;
- Volume setting at mixing point;
- Compliance and use of the SGs by the participant (using downloadable data-logging history to check device use and compliance); and
- Any Study Participant problems or concerns associated with the SGs or their use.

If the Study Participant with hyperacusis has been comfortable with the volume setting of the SG for the previous month, then the volume setting will be increased to the mixing point (if tolerable). If not, then the volume setting of the SG will be incremented by programmable adjustment toward the “mixing point” level or continued at the original setting until the next scheduled follow-up visit, at which time the Study Audiologist will discuss with the Study Participant increasing the sound level of the device to a higher level.

The Study Audiologist will answer any questions that the Study Participant has about the use of the SG at this time, and again emphasize his or her availability, to address questions and concerns.

At each subsequent Follow-up Visit, the Study Audiologist will check on the condition of the SGs, the participant's schedule of use, and re-confirm appropriate “mixing points” for the participant. The data-logging memory for each SG should be downloaded to evaluate the compliance history and sound-level exposure history, and this information sent to the Data Coordinating Center for evaluation and storage. This data-logging information can be used to encourage and counsel the participant if his or her compliance is problematic. Typically, there would be no further instruction on use of the SGs, although the Study Participant will continue to be encouraged to use the devices for the minimum 8 hours each day.

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References:

Gatehouse, S. (1999). Glasgow Hearing Aid Benefit Profile. Derivation and validation of a client-centered outcome measure for hearing aid services. *Journal of the American Academy of Audiology*, 10, 80-103.

Jastreboff PJ, Gray WC, Gold SL. Neurophysiological approach to tinnitus patients. *Am J Otol*. 1996; 17:236-40.

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**Table 1**  
**Ear Impression Guidelines**

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All ear impression sessions should be preceded by routine hygienic procedures and an explanation of the purpose and nature of the process and protocol. The opened-jaw impression should be obtained first, as follows:

**A. Opened-jaw impressions**

1. Place the bite-block between the molars.
2. Inspect the ear canal thoroughly.
3. Insert the ear-dam and ensure that there are no gaps between the dam and the canal wall.
4. Mix the silicone impression material per manufacturer's instructions, load into the syringe, and inject the material into the ear canal and pinna completely.
5. Ensure that the bowl and the helix are completely filled, but not distended.
6. Once cured, the impression should be removed by having the Study Participant open his or her jaw widely. Upon opening the jaw, the impression should be removed with a slight forward rotation.
7. Perform a post-impression otoscopic examination to ensure that all material has been removed and to rule out bleeding or swelling.
8. Inspect the impression to ensure full definition of the canal, helix, and concha. Repeat the process if there are gaps, creases, or lack of definition. Note any moles, scars, or other imperfections.
9. Repeat the opened-jaw procedure in the opposite ear.

**B. Closed-jaw impressions**

1. Remove the bite-block and repeat all steps outlined above, ensuring that the same landmarks described above are fully defined.

**C. Shipments**

1. Label impressions by "opened-jaw" or "closed-jaw" and "right" or "left" ear.
2. Ship impressions to General Hearing, Inc. along with a TRTT Sound Generator Order form, specifying color and address to which devices are to be shipped.

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**Table 2**  
**Instrument Fitting Checklist**

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**First Treatment Visit (T1)**

1. Prior to fitting the instrument on the patient's ear, the output of the instrument should be set at minimum for each ear.
2. Select the appropriate set of Sound Generators (SGs) based on the corresponding kit ID assigned at randomization.
3. The Study Audiologist will fit the Sound Generator (SG) to each ear of the Study Participant.
4. Insert a fresh battery into each of the instruments.
5. Insert the programming flex strips into the slots at the top of the battery doors.
6. Establish interaction of the software with the devices.
7. Verify the serial numbers.
8. Fill in the Study Participant's ID number.
9. For the worse ear, set volume for "A" setting.
10. Volumes for "B" (-2 dB from setting "A") and "C" (-4 dB from setting "A").
11. Repeat the process for the other ear.
12. If necessary, adjust sound level binaurally.
13. Change battery, if indicated.
14. Click on the Disconnect button.

*At this point, the instruments are now set up for the Study Participant to use.*

**T2 and Follow-up visits**

1. At follow-up visit, when and if any appropriate changes to the mixing points are made, the “Disconnect” button must be used to permanently save any changes.
2. The Datalog information stored on the computer must be uploaded to the Data Coordinating Center for proper collection and analysis.

**Guidelines for Instrument Use**

1. Give the Study Participant a copy of the handout “Guidelines for Instrument Use”
2. Review instrument use and volume setting (determined by Jastreboff Category)
3. Set it and forget it
4. Avoid silence. Tell Study Participants that when they are surrounded by normal environmental sound, they may not be aware of the sound of tinnitus.
5. Keep the focus off the tinnitus.
6. Six-week effect
7. Rough patches
8. Review of goals
9. Review of habituation process
10. Inform Study Participant of follow-up procedures and schedule.

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## Appendix A Fitting the Sound Generators

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### **A. General Hearing Instruments, Inc. (GHI) fitting protocol**

Each instrument is equipped with three memories or options (designated A, B, and C). Prior to fitting the instrument on or in the Study Participant's ear, the output of the instrument should be set at minimum for each memory. (See Table 2 for programming procedure). The Randomization Registration Report, generated and printed out during web-based randomization, will display a kit ID. For Study Participants assigned to TRT, the kit will either contain a pair of BTE Sound Generators (SGs) or a Sound Generator Request Form for the Study Audiologist to use when ordering a pair of ITE SGs. Either the BTE or the ITE devices will be fitted to the Study Participant at the first treatment visit (T1) and a Sound Generator Issue Form completed at that time to document which devices have been assigned to the Study Participant.

The Study Audiologist will fit the SG to each ear of the Study Participant. Optimal fit will be achieved by ensuring that the BTE instruments are seated comfortably and securely on the top of the ear or the ITE instruments are comfortably and snugly fitted within the outer ear. There should be no gaps between the ear and the BTE sensing plate. The thin tube dome should sit at the top of the ear canal, and the retention cord should loop up the posterior of the concha. On very rare occasions, for comfort, the retention cord may be clipped shorter, but should never be completely removed.

### **B. Fitting the Sound Generators: First Treatment Visit (T1)**

1. Insert a fresh battery into each of the instruments.
2. With programming cables attached to the programming interface, insert the programming flex strip into the slots at the top of the battery door, and then close the battery doors completely.
3. After starting the software, the Study Audiologist will be able to establish interaction with the devices by clicking on the "Connect" button located on the left side of the software screen. During the time that the software connects to the device and pertinent information is downloading, an hourglass symbol will replace the usual mouse pointer on screen. Blinking lights on the interface box indicate that communications are taking place.

4. Upon successful connection to the devices, the screen will be updated to show the serial numbers of the devices connected. The Study Audiologist should verify that these correspond to the serial numbers of the devices provided for that Study Participant. (*Note: the function of the button used to establish connection has now been changed to that of a "Disconnect" button.*)
5. If this is the first connection to the instruments, the Study Participant's ID number field will be blank. The Study Audiologist will complete this field so that on subsequent visits the Study Participant ID number can be used to identify the device instead of referring to the serial number only. (*Note: this identification information will be stored in the SGs themselves as part of the disconnection process.*)
6. The SG provide the Study Participant with three levels of sound generator output from which to choose a volume setting on a daily basis. The first choice (memory "A") is set at the mixing point, Memory "B" is set 2 dB softer than the mixing point and memory "C" is set 4 dB softer than the mixing point.
7. Beginning with the ear with the most troublesome tinnitus, the Study Audiologist selects either the left or right ear for adjustment. Moving the A slider makes changes to the output level to achieve the mixing point setting for the selected ear. The ideal setting is considered to have been reached when the audibility of the noise "blends" with the subjective level of the tinnitus itself ( the "mixing" point).
8. During adjustment, the sliders for memories "B" and "C" will automatically track the movements of the primary mixing point adjustment at memory "A". The initial offset of these other slider positions is either 2 dB below (memory "B") or 4 dB below (memory "C") the mixing point (memory A), but can be manually adjusted by moving each slider position to the desired level. These new offsets will be used until a change is made to their value either during the present visit or subsequent visits. The output noises for memories "B" and "C" are only audible after disconnection and the user presses the memory selector on the SG instrument itself.
9. Having now established the mixing point for the ear with the most troublesome tinnitus, the Study Audiologist will repeat the process for the other ear. (*Note: Activating the device in one ear mutes the noise in the opposite ear*). Once the volume has been set in the "worse" ear, match the volume in the opposite ear. If, when the volume in both instruments has been set, the sound seems too loud, the characteristics of the tinnitus has changed, the tinnitus is masked, or the sound induces any kind of negative reaction or annoyance, then reduce the volume in **both ears** slightly. It is better to be slightly below the mixing point if any of

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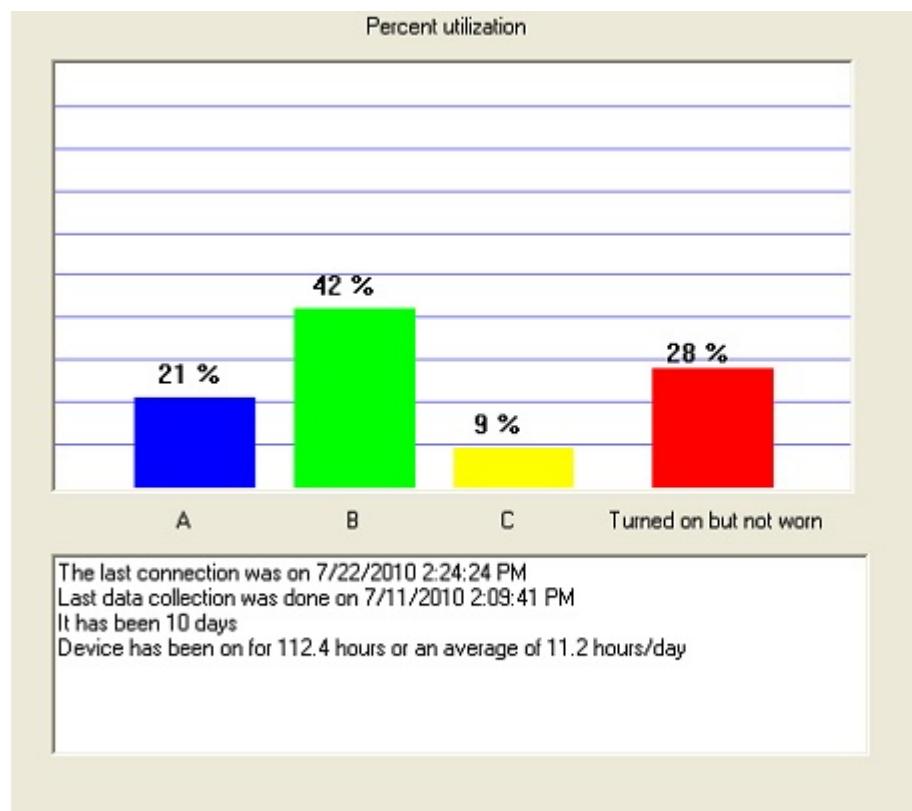
these factors are present. The volume should still be fairly equal in both ears. It is acceptable if any less bothersome tinnitus is covered.

10. Being a battery powered device, it will be necessary during the trial period to occasionally change the battery for each SG. The devices will produce an audible indicator sound when self diagnostics determine that a fresh battery is required. As part of instructing the Study Participant on the use of the devices, the Study Audiologist may click “Demonstrate Low Battery Sound” button to familiarize the Study participant with the indicator.
11. Having now configured the output levels for the Study Participant, the Study Audiologist clicks on the “Disconnect” button. At this point, the mouse arrow will appear as an hourglass shape. During the period that the hourglass mouse pointer is displayed (*Note: communication lights will be blinking on the interface box*), all relevant settings are being permanently stored into the devices. After the hourglass returns to the usual arrow, the SGs may be removed from the Study Participant’s ears, the battery doors can be opened, and the programming cables removed from the device.
12. The instruments are now ready for use.

### **C. Fitting the Sound Generators: Second Treatment Visit (T2)**

During the follow up visit the programming cables are reconnected to each instrument, taking care to match the cable to the appropriate ear.

1. Upon starting the software and clicking “Connect”, information will be retrieved from the device. After a successful connection is established the serial number and Study ID fields will be populated on screen.
2. Compliance and history-of -use are stored within the device while the SGs are operational. To download this information from the devices, click on the “Get Datalog” button. This action will download these data from the devices and store it as a file on the computer for subsequent transmittal to the Data Coordinating Center. Upon successful harvesting of the data, the Study Audiologist will be presented with a summary data display of the hours of use in each memory (i.e., “A”, “B”, and “C”, or “turned on, but not worn”). The sample data shown below indicates that for 28% of the time this individual had the devices turned on, but they were not worn. Information such as this can be useful when counseling the Study Participant about compliance with the TRT protocol.



The other information immediately visible in this example is that the device usage is primarily set for memory “B”, instead of the mixing point setting at “A”. If usage is skewed to memories “B” or “C”, as is shown here, then changes to memory “A” are necessary to reset the mixing point.

3. After making any appropriate changes to the mixing points, the “Disconnect” button must be used to permanently save any changes.
4. The datalog information stored on the computer must be transmitted to the Data Coordinating Center from each Clinical Center for proper collection and analysis. Clicking the “Upload to DCC” button will perform this operation automatically. It is not necessary for the Study Participant’s SGs to be connected to the computer for the data transmission to occur. This operation will upload all saved data, including any from previous visits.

**D. Fitting the Sound Generators: Follow-up Visits**

The process of using “Connect” to hook up to the devices and using “Get Datalog” to retrieve data will be repeated for each subsequent study visit. If the summary data indicates that fine tuning of the noise levels is warranted, adjustments may be made before using the “Disconnect” procedure described in Step 2 of the second treatment visit. **It is important for the Study Audiologist to perform the “Disconnect” procedure at the end of each study visit. Otherwise, the programmed changes will not be retained in the SGs.** This process is also followed during the final study visit.

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## Appendix B

### Script for Instrument Fitting for TRTT

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*(After the GHI fitting protocol is completed, the Study Audiologist will answer any questions that the Study Participant may have during T1 or subsequent visits. The information presented in the Directive Counseling session is also continuously reinforced during treatment and follow-up visits. The instruments offer the most direct way to give a steady, stable signal that will interfere with the brain's ability to detect the tinnitus. It is important to tell the Study Participant that the sound from the instruments is a very small amount of sound that cannot hurt them and should not interfere with communication. T1 includes the initial instrument fitting and takes about 1 hour to complete. The Study Audiologist will give the Study Participant a handout of Guidelines for Instrument Use in TRTT (see Appendix C) at the beginning of T1 to keep. The Study Audiologist will have a copy of these guidelines and review these topics.)*

**Volume setting for tinnitus** – Insert both instruments. If the tinnitus is “worse” in one ear, begin with that ear and match the volume in the other ear. **The volume should be set at, or just below, the “mixing point”, the point where the sound of the instrument starts to mix or blend with the tinnitus.** The two sounds do not have to be equal. The Study Participant should be able to separate the tinnitus from the sound of the instrument. Key factors in setting the volume should be:

- The sound of the instrument should not change the characteristics of the tinnitus signal. If it does, reset the volume.
- The sound of the instrument should not be above the mixing point (*partial suppression occurs*).
- The tinnitus should not be masked (*The brain cannot learn to ignore something it cannot detect and habituation will not occur.*)
- The loudness or quality of the instruments should not induce any negative reaction or annoyance. (*This would enhance activation of the limbic and autonomic nervous systems and hinder habituation.*)
- If there is any question concerning the correct volume setting of the instruments, it is better to be just below the level that will induce annoyance or change the characteristics of the tinnitus.

- The sound of the instruments should not be too close to the threshold of hearing. (*When the sound level is close to the threshold of hearing, tinnitus can theoretically be enhanced through stochastic resonance or a “straining to hear” effect.*)

After the volume has been set in the “worse” ear, work together with the Study Participant to match the perceived volume in the second ear. If, when the volume in both instruments has been set, the sound seems too loud, the characteristics of the tinnitus has changed, the tinnitus is masked, or the sound induces any kind of negative reaction or annoyance, then reduce the volume in **both ears** slightly. It is better to be slightly below the mixing point if any of these factors are present. The volume should still be fairly equal in both ears.

- **Set it and forget it.** Once the volume has been set in both ears, do not keep adjusting it. Readjusting attracts attention to the instruments. Do not take the instruments in and out repeatedly. This will disrupt the treatment. We want the focus off the ears and off the tinnitus.
- **Volume setting for hyperacusis** – the sound is turned up to the point where the Study Participant just starts to hear it (threshold). The volume is then increased to a soft sound. The perceived volume should be the same in each ear. The initial sound levels are determined by the Study Participants’s annoyance level. The sound should never be annoying, painful, or uncomfortable. If it is, reduce the volume slightly to the point where there is no discomfort. Monitor the sound volume at follow-up visits to determine whether the sound output can be increased. The volume level may be increased up to the start of the perceived “mixing point” at follow-up visits. Depending on the status of the hyperacusis, the sound of the SGs should never be annoying or uncomfortable. Typically, as the Study Participant with hyperacusis hears a steady, stable sound, the brain responds by turning down the “gain” of the auditory system, both at a cochlear level (OHC) and in the central auditory system. As treatment progresses, the Study Participant finds that s/he is more comfortable with environmental sounds in situations that s/he could not previously tolerate. Loudness discomfort levels (LDLs) may be improved during audiological testing at certain follow-up visits. As the hyperacusis condition improves, most people will find that the tinnitus also is not as intrusive.
- **Schedule of use** – Wear the instruments as much as possible throughout the day. If you can’t wear them all day, wear them at least 8 hours. That does not have to be all at one time and it does not have to be the same schedule every day. The wearing time can be built up over the next few weeks. Wear the instruments even if the tinnitus is not present. You can wear them to sleep, if they are comfortable, but the sleep time does not count toward the 8 hours. Put the instruments on as soon as you wake up unless you shower in the

morning. Dry your ears and put them on after that. At any time, if the instruments are physically uncomfortable, at any time, contact the Audiologist.

- **Avoid silence** – It is important to keep a low level of **neutral** environmental sound on at all times in addition to the SGs. The background sound does not have to be loud and should not mask the tinnitus. The sound should not be annoying. Use a fan, computer, nature tapes, sound machine, car sound, humidifier, aquarium, or other low level constant sound. A sound machine, sound pillow ([www.soundpillow.com](http://www.soundpillow.com)) fan, or humidifier can help during sleep. Try not to use TV or talk radio at night so that your brain does not “tune in” to something that is interesting. **When you are surrounded by normal environmental sounds, you may not be aware of the sound from the instruments.**
- **Keep the focus off the tinnitus.** Do not keep diaries or journals. Tell family and friends not to ask how you are doing. Do not worry about normal fluctuations in tinnitus from caffeine, wine, alcohol, chocolate, exercise, naps, etc. These can make the tinnitus **worse or better**, but these changes are typically temporary. Do the things you want to do and live your life without worrying about these fluctuations.
- **Six-week effect** – Do not worry if the tinnitus gets “worse” after a few weeks of wearing the instruments. It is very common and very temporary. The brain may be adjusting to this new signal.
- **Rough patches** – In the best situations, there will be periods of time when you will be more or less aware of the tinnitus. These “rough patches” will occur and they are normal and temporary. The tinnitus is not getting worse. We are trying to “grow” the better periods when you are less aware of the tinnitus. Tinnitus awareness is related to a dynamic relationship between the ear, the auditory neural pathways, the brain, the emotions, the biochemistry, the neurophysiology, what you ate, what you drank, how much sleep you got, the stresses you are under, etc. The awareness is more like a kaleidoscope with many factors coming into play that can not be controlled.
- **Goals** – Habituation is the natural process of the brain if it does not care about something (neutral) or give it importance (good or bad). The habituation process in TRT depends on neutralizing negative emotional association of the tinnitus (habituation of the reaction) and reducing the contrast between background sound and the tinnitus. The use of low-level sound makes it harder for the brain to keep track of the tinnitus. The brain is very plastic and under constant reconstruction. We can’t force the tinnitus out of existence, but we can “set things up” so that the brain will begin to filter it out (habituation of perception).

- **Habituation** – We are not looking for any changes in the first few months. At best, the changes will be slow, incremental, and subtle. The process of habituation can take about a year to 18 months. Our goal is for you to get to the point where the tinnitus and/or hyperacusis is a “non-issue” in your life. You will not generally think about it, and even if you notice it, the tinnitus will not trigger negative emotional reactions. This does not mean the tinnitus is not there. For example, it is like the refrigerator noise. If you stop to listen for it, you can hear it, but usually it is “tuned out”. At the point when the your tinnitus becomes like refrigerator noise, you will no longer need to wear the instruments.

*(The Study Participants are given a handout “Guidelines for Instrument Use” and information and equipment regarding the instruments. The Study Audiologist will also inform the Study Participants of follow-up procedures and visits.)*

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**Appendix C**  
**Tinnitus Retraining Therapy Trial**  
**Handouts**

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**HANDOUT: Guidelines for Instrument Use**

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**1. Volume Setting:**

The volume of your instruments will be set at one of three volume settings (A, B and C) that will be initially set by the Study Audiologist. The levels will be:

- A. “Mixing point” the point where you hear the sound of the instrument and it is increased slightly until the sound **starts** to mix or blend with the tinnitus. The two sounds do not have to be equal. You should be able to separate the tinnitus from the sound of the instrument. **The tinnitus should not be masked or changed by the sound of the instruments. The sound of the instruments should not be uncomfortable or annoying and should not interfere with communication.** If that occurs, reduce the sound.
- B. The volume is slightly softer than level A.
- C. The volume is slightly softer than level B.

Position or insert the instruments. The volume of the instruments should be fairly equal in both ears. If the tinnitus is “worse” in one ear, begin with that ear and match the volume in the other ear. If the sound is uncomfortable or annoying or the quality of the tinnitus is changed, reduce the volume slightly to just below the “mixing point.” You will be instructed in how to reduce the volume slightly when you first insert the instruments, if necessary. The preferred volume levels might be changed at future follow-up visits.

**2. SET IT AND FORGET IT!** Once you have set the volume, do not keep adjusting it. Do not take the instruments in and out repeatedly. This will disrupt the treatment. We want the focus off the ears and off the tinnitus.

**3. Schedule of Use:** Eventually, you should be wearing the instruments as much as possible, even all your waking moments. If you can’t wear them all day, wear them at least 8 hours a day. That does not have to be all at one time, and it does not have to be the same schedule every day. You can build up the wearing time over the next few weeks. Wear the instruments every day, even if the tinnitus is not present. You can wear them to sleep, if they are comfortable, but the sleep time does not count toward the 8 hours. Put the instruments on as soon as you wake up or after you shower in the morning. Reset the volume of the instruments if they are removed and reinserted during the day.

**4. Avoid Silence.** Keep a low level of **neutral** sound on at all times, day and night. The sound does not have to be loud. You are not trying to mask the tinnitus. Use a fan, computer, nature tapes, sound machine, car noise, humidifier, aquarium (you do not even need fish.), etc. A sound machine, sound pillow, fan, or humidifier is helpful during sleep. Try not to use TV or talk radio at night so that your brain does not “tune in” to something that is interesting. **When you are surrounded by normal environmental sounds, you may not be aware of the sound from the instruments**

**5. Keep the focus off the tinnitus.** Do not keep diaries or journals. Tell family and friends not to ask how you are doing. Do not worry about the normal fluctuations from caffeine, wine, alcohol, chocolate, exercise, naps, etc. These cause normal fluctuations in the body biochemistry. These changes can make the tinnitus better or worse, but these changes are temporary. Live your life without worrying about these fluctuations.

**6. Six-Week Effect:** Do not worry if the tinnitus gets “worse” after a few weeks. It is very common and very temporary. The brain may be adjusting to this new signal.

**7. Rough Patches:** In the best situations, there will be periods of time when you are more aware and less aware of the tinnitus. It is important for you to know that the “rough patches” will occur, and that they are normal. The tinnitus is not getting worse. We are trying to “grow” the better periods when you are less aware of the tinnitus. Tinnitus awareness is related to a dynamic relationship between the ear, the brain, the emotions, the biochemistry, the neurophysiology, what you ate or drank, how much sleep you got, the stresses you are under, etc. The rough patches are typically temporary.

**8. Goals:** Habituation is the natural process that occurs when your brain does not notice something. The habituation process in TRT depends on neutralizing the negative emotional associations of the tinnitus, and the use of low-level sound to reduce the contrast and make it harder for the brain to keep track of the tinnitus. The brain is very plastic and under constant reconstruction. We can’t force the tinnitus out of existence, but we can “set things up” so that the brain will begin to filter it out.

**9. Habituation:** We are not looking for any changes in the first few months. At best, the changes are slow, incremental, and subtle. The process of tinnitus habituation usually takes about a year to 18 months. Our goal is for you to get to the point where the tinnitus is a “non-issue” in your life. You do not generally think about it, and even if you notice it, it does not trigger negative emotional reactions. It does not mean the tinnitus is not there. For example, it is like the refrigerator noise, if you stop to listen for it, you can hear it, but you usually “tune it out”. At that point you will no longer need to wear the instruments.

**Remember that the use of controlled sound is how the brain knows the ears are “working.”**

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## Chapter 13

### Standard of Care

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#### **13.1 Introduction**

In the Tinnitus Retraining Therapy Trial (TRTT), the efficacy of the Tinnitus Retraining Therapy (TRT) will be compared with the standard of care counseling (SC) protocol that is independent of specific tinnitus theories or treatments. The SC protocol is consistent with information typically provided to patients with severe tinnitus at the TRTT's participating military medical centers and with professional guidelines for tinnitus management as outlined in the document *Preferred Practice Patterns (PPPs) in Audiology* (ASHA, 2006). According to the PPPs, tinnitus management is based on the patient's complaints, history, audiology evaluation, and self-assessment, and should include family and/or care givers. Tinnitus management is provided to reduce negative cognitive, affective, physical, and behavioral reactions to tinnitus and to improve the patient's well-being and quality of life. In addressing the individual's specific counseling needs, the PPPs cite the following topics to be considered when addressing a tinnitus patient's specific counseling needs:

- Cause, source, and audiology significance of tinnitus;
- Use of hearing protection in noise;
- Use of environmental sounds or devices to reduce tinnitus perception;
- Identification of factors that may exacerbate tinnitus;
- Adaptive coping behaviors
- Stress reduction; and
- Strategies to minimize sleep difficulties related to tinnitus.

SC, as described in this chapter, includes the above points. Unlike TRT, which is quite didactic and theory-driven, SC is interactive and patient-driven. The individual patient's condition, concerns and questions guide the counseling process. As with the Directive Counseling (DC) component, SC will be provided as individual counseling with the participation of the family members and/or significant others strongly encouraged to be present.

The Study Audiologist's role in SC is to be responsive and reassuring in order to achieve the following goals:

- Communicate concern and understanding to Study Participants. Study Participants should have the distinct impression that the Study Audiologist not only understands their problem, but also understands how it makes them feel.
- Determine Study Participant's own understanding of his or her tinnitus. Verify that he or she understands the problem and clarify any doubts and misunderstandings regarding the implications of having tinnitus.
- Engage the Study Participant in the management of his or her tinnitus problem by providing strategies appropriate to his or her own lifestyle and abilities – that will enable him or her to minimize the specific effects of tinnitus and thereby learn to cope with it.
- Reassure Study Participants that in time they will be able to manage their tinnitus.

### **13.2 Initial Counseling Session**

Prior to the counseling session, the Study Audiologist will prepare and review all materials needed to evaluate and counsel the participants. The materials will include the Baseline TRT Interview Form, all audiological/tinnitus/hyperacusis (ATH) evaluation tests, and the visual aids typically used when counseling patients during their evaluations. A three-dimensional model of the ear and illustrations of the auditory and vestibular anatomy will be used to explain hearing loss and to identify regions in which tinnitus and balance problems originate. The Study Audiologist also will prepare copies of the Study Participant's hearing test results for use when discussing the findings during the counseling session. Each Study Participant will receive a copy of his or her hearing test results. Finally, the Study Audiologist will prepare a copy of the Standard of Care Checklist by completing Sections A and B before counseling begins and completing the remainder of the form during and after counseling takes place.

A checklist included in Table 1 and a script included in Appendix A are available for use during the SC counseling session. Copies of handouts for the Study Participants are included in Appendix B.

### **13.2.1 Eliciting the Patient Narrative**

The first step in SC is to elicit a **narrative** that describes the Study Participant's experience of tinnitus. The narrative should be allowed to unfold without interruptions and with minimal prompting or interrogation. The purpose of the narrative is to establish a **mutual understanding** of the Study Participant's tinnitus problem that permits the Study Audiologist to **empathize** with the Study Participant and to facilitate an accurate understanding of tinnitus.

The Study Audiologist and Study Participant will sit face to face. An appropriate statement to initiate the narrative interview is, "Tell me about your tinnitus." The Study Audiologist will maintain eye contact with the Study Participant, and listen intently to all that he or she says. Active, reflective listening skills should be used to communicate that one understands what the Study Participant is saying. This may include nodding one's head or making simple statements such as "I see," "I understand," or "OK," to convey that one is following and understanding the comments. More specific questions should be used only when clarification or verification is necessary. If a Study Participant is withdrawn or reticent, additional questions can be posed to prompt a more extensive description of his or her tinnitus experience. The Study Audiologist will also acknowledge the Study Participant's affective/emotional reactions to tinnitus. This can be done by facial expressions as the Study Participant is speaking and by commenting after he or she has spoken. "I can see that tinnitus has been very troubling for you," or "It sounds like your tinnitus has been causing you stress." It is important that the statement accurately reflect the Study Participant's expressed feelings and/or demeanor.

Following the Study Participant's description of his or her tinnitus experience, the Study Audiologist will briefly summarize what the Study Participant has said to convey that s/he has been understood. To engage the Study Participant further, additional specific questions can now be asked to obtain information that has not been provided. This may include when the tinnitus problem began, what caused it, what aggravates/alleviates it, when is it most noticeable, etc. This aspect of the session should end with a question such as, "Is there anything else about your tinnitus that you would like me to know?"

### **13.2.2 Explaining Tinnitus**

The Study Audiologist will then ask the Study Participant if he or she worries about tinnitus and if so, what aspects of it are the most concerning. After listening to the Study Participant's response, the Study Audiologist will explain that there are some basic facts about tinnitus that makes it less worrisome for most individuals who have it. The following points should be covered:

Tinnitus refers to sounds that are perceived in the ear or brain that do not originate outside one's body. Tinnitus may be perceived differently from one person to another or even one time to another (e.g., ringing, buzzing, hissing, chirping, etc.).

- There are several different theories about what triggers tinnitus from a physiologic standpoint. Most theories associate tinnitus sounds with trauma to the nerve endings in the inner ear or somewhere along the pathway to the brain as will be discussed.
- Almost everyone notices such sounds from time to time.
- Ironically, people with hearing loss can be more annoyed by tinnitus because sounds in the world around them are not masking – or drowning out – the tinnitus.
- The vast majority of people who experience tinnitus are not bothered by it.
- Loud noise, certain medications, illness, head trauma, and stress can cause and aggravate tinnitus.
- The tinnitus may get worse, it may stay the same, or it may go away.
- Tinnitus may result from damage to the hearing system and may or may not be associated with measurable hearing loss.
- Tinnitus by itself will **not** damage your hearing.
- Tinnitus is **not** a health threatening condition.
- Many people learn to ignore their tinnitus.
- There is no known or proven medical treatment for tinnitus.
- Tinnitus is very common among military personnel who have been exposed to loud noise.
- Focusing on one's tinnitus can make it more noticeable.
- One can learn to ignore tinnitus just as one ignores the sound of one's own breathing, the hum from a fluorescent light or the refrigerator, or even the ongoing tick-tock of a grandfather's clock.
- Other sounds in the environment make it easier to ignore tinnitus.

The Study Audiologist will discuss these points and answer any questions the Study Participant may have.

### **13.2.3 The Hearing Mechanism**

A basic premise underlying TRT and most counseling theory is that understanding a problem lessens the likelihood that individuals will worry about it or catastrophize it. Hence, an explanation of the hearing mechanism and hearing disorders is an important aspect of tinnitus management. In SC, the description of the hearing mechanism, hearing loss, and tinnitus, will be tailored to the individual's current understanding of his or her problem and his or her level of inquisitiveness. A simplified explanation of the anatomy and physiology of the hearing mechanism will be presented as standard. A Study Participant's questions, interest level, and grasp of the information may prompt elaboration. Because SC is patient-driven, the level of explanation should be determined on a case-by-case basis. In SC, the hearing mechanism and hearing problems are reviewed first to facilitate understanding of the Participant's specific hearing test results.

Following, are the basic points to be covered in reviewing the hearing mechanism.

#### Outer Ear:

- The pinna, or auricle, directs sound waves through the ear canal to the eardrum - the tympanic membrane.
- Sound waves impinge upon the eardrum causing it to vibrate.

#### Middle Ear:

- The middle ear is an air-filled cavity just beyond the eardrum that is lined with mucous membrane.
- The middle ear is ventilated via the Eustachian tube.
- On the other side of the eardrum, are three small bones known as the ossicles or the ossicular chain. The three bones are the hammer, anvil, and stirrup, which are also called the malleus, incus, and stapes.

- When sound waves cause the eardrum to vibrate, the vibration is transmitted to these three bones causing a mechanical action that is a leverage system to transmit sound energy into the inner ear.
- When there is a problem associated with the outer or middle ear, the parts of the ear that conduct sound waves, the type of hearing loss is called a conductive hearing loss.
- The most common causes of conductive hearing loss include excess wax in the ear canal, perforated eardrum, middle ear infections, and otosclerosis. Most conductive hearing losses can be successfully treated medically or surgically.

### Inner Ear

- The inner ear consists of two sensory organs: the semicircular canals, which are responsible for balance, equilibrium, and our orientation in space; and the cochlea, which is the sensory organ for hearing.
- The cochlea consists of three fluid filled chambers, the middle one of which contains a long membrane along which are rows and rows of hair cells that protrude from nerves
- The footplate of the stapes, or stirrup, is attached to an opening to the cochlea and when the ossicular chain vibrates, the footplate rocks back and forth, which causes wave motions in the fluids in the inner ear.
- The wave action causes motion along the hair cells to generate an electrical impulse which is transmitted to nerve endings that send the impulse along nerve fibers that combine to form the auditory nerve – VIII cranial nerve - that sends the signal to the brain where it is perceived as sound.
- The hair cells and nerve endings at the outer end are the ones responsible for the perception of high frequency sound. The ones at the far tip perceive low frequency sounds.
- When there is a hearing problem associated with the inner ear or the VIII nerve and pathway to the brain, the loss is called a sensorineural hearing loss.
- The most common causes of sensorineural hearing loss include noise exposure, diseases (e.g., measles, mumps, meningitis, cytomegalovirus (CMV)), ototoxic drugs, aging, skull fracture or other head trauma. The vast majority of sensorineural hearing impairments are permanent.

- Many of these same factors are associated with tinnitus.
- Most theories of tinnitus involve damage to the nerves in the inner ear.

The Study Audiologist will conclude this portion of the session by engaging the Study Participant in a discussion. It is important to ascertain that the participant has understood and assimilated the review. The Study Audiologist will provide complete responses to any questions the participant may have and provide reassurance about his or her condition.

#### **13.2.4 Audiologic/Tinnitus/Hyperacusis Evaluation**

The next step in SC is to review and explain the results of the Study Participant's ATH evaluation. Using copies of the audiogram and results of the patient's ATH evaluation, the objective for the Study Audiologist is to help the patient to understand the nature of his or her hearing status, tinnitus perception and, if present, hyperacusis. Copies of the audiogram and results of the participant's ATH evaluation will be enlarged using a photocopier for easier viewing and explanation. It is particularly important to gauge the Study Participant's ability to understand the terminology and implications of hearing test results and to present this information at a level that is meaningful to him or her.

The Study Audiologist will present the patient's audiometric results and provide an explanation of the hearing sensitivity for each ear. Study Participants will have functionally normal hearing that does not require amplification to benefit daily listening and communication. The Study Audiologist will review the patient's pure tone thresholds at each audiometric frequency and explain the results of speech audiometry. Among the things the Study Audiologist may highlight are asymmetries in the audiometric results and results consistent with specific etiologies (e.g., high-frequency audiometric notches or declining high-frequency hearing sensitivity, typical of the onset of noise induced hearing impairment), and results warranting further evaluation.

Results of the Loudness Discomfort Level (LDL) test are then reviewed. The Study Audiologist describes the test, reviews the Study Participant's test results, and compares his or her findings with results considered to be within normal limits. If hyperacusis is indicated, by a subjective complaint and/or by reduced LDL values, then the Study Audiologist will explain to the Study Participant how the results indicate the presence of a sound tolerance problem.

Next, the Study Audiologist will describe the Tinnitus Pitch Match, emphasizing that the pitch obtained may not be an exact match, but a "snapshot" of the tone or pitch closest to that of the Study Participant's tinnitus. The Study Audiologist will explain that the way tinnitus sound

varies by individual; it may be a hissing, ringing, buzzing, or chirping sound. The Study Audiologist will also explain the Tinnitus Loudness Match, and explain that the loudness of the tinnitus sound is usually only a few decibels above the threshold of hearing identified at the pitch of the tinnitus sound.

As appropriate, the Study Audiologist will briefly review the results of impedance audiometry and otoacoustic emissions tests and explain that these tests help rule out significant hearing problems and/or identify the type of hearing problem.

The Study Audiologist will conclude this portion of the counseling by ensuring that the Study Participant has a good understanding of his or her hearing test results, the stability of his or her hearing over time in the past, and what to watch for in terms of further hearing loss, particularly from further noise exposure.

### **13.2.5 Coping with Tinnitus**

During this portion of the SC session, the Study Audiologist will highlight the effective ways in which the Study Participant has coped with tinnitus in the past and emphasize additional ways in which he or she may try to minimize the impact of his or her tinnitus in the future. This discussion should be tailored to the individual's specific complaints, problem situations, coping strategies used to date, personal preferences, and feasibility. The following points should be considered.

**Environmental Sounds:** Identify the situations in which environmental sound can be utilized to alleviate tinnitus. This should include a demonstration of environmental and bedside sound generators and provision of literature on a variety of available devices with purchasing/ordering information.

**Stress Reduction:** Review the importance of stress reduction/relaxation to minimize the aggravating effects of tinnitus and discuss a variety of relaxation exercise programs including Tai chi, yoga, meditation, progressive muscle relaxation, and visual imagery. If the Study Participant is not aware of such programs, provide appropriate handouts and conduct a short relaxation exercise such as visual imagery or progressive muscle relaxation. The Study Audiologist will also provide information regarding relaxing background sounds (e.g., small water fountains, and environmental sound CDs.

**Sleep Aids:** The Study Audiologist may address sleep issues by reassuring the Study Participant that many people with tinnitus experience sleep problems and that there are many ways in which these problems can be alleviated if not eliminated. The Study Audiologist will review normal sleep patterns, emphasizing that the best sleep is 8 hours of uninterrupted

sleep. The Study Audiologist will also discuss factors that affect sleeping, including stress and emotional upheaval, environmental variables (noise, light, temperature), irregular schedules, jet lag, medications, caffeine, nicotine, and alcohol. The Study Participant will be encouraged to identify the different variables that may play a part in his or her sleep difficulties. If the Study Participant reports significant sleep problems that may be related to his or her tinnitus, or that aggravate his or her tinnitus, the following recommendations are provided:

- During the day, exercise and avoid naps to promote healthy sleep.
- In the evening, avoid stressful activities and strenuous exercise; avoid caffeine, alcohol, large meals, and spicy foods close to bedtime; and go to bed when tired.
- Maintain a consistent sleep-wake pattern, (i.e., get up and go to sleep at the same time every day).
- Optimize sleeping conditions by eliminating distractions such as TV, computer, food/drink); add comfortable mattress, pillow and comforters; darken the bedroom; set temperature between 58° to 68° F.
- Add soothing, low-level background sounds such as music, nature sounds, broadband/white noise, fan, etc.
- A sound device/noise maker that produces a variety of rushing or roaring sounds.
- If sounds bother partner, consider a pillow speaker.
- Practice progressive relaxation exercises and visual imagery if needed.
- Provide literature and resources including [www.soundsleeping.com](http://www.soundsleeping.com)

**Concentration:** If a Study Participant reports that tinnitus interferes with his or her ability to concentrate, the Study Audiologist will explain that concentration affects performance and memory so it is important to enhance concentration skills and learn to ignore the tinnitus. Factors that affect concentration will be reviewed including noise, temperature, distractions, lighting, hunger, fatigue, health, boredom, stress, depression, and tinnitus. To enhance concentration, the Study Audiologist should recommend:

- Adding environmental sound to reduce tinnitus perception.

- Working in shorter spans and taking breaks.
- Optimizing external/environmental conditions to maximize overall comfort.
- Practicing attention shifting exercises (from one object to another, from tinnitus to other sounds, etc.).
- Staying focused by actively participating, taking notes, asking questions, repeating information, and organizing and categorizing important points.

#### **13.2.4 Treatment Recommendations**

The treatment recommendations for each Participant should reflect a summary of the interactive counseling session and a mutual understanding of the Study Participant's concerns, needs, and ability and willingness to engage in relevant treatment options. The recommendations should reflect the Study Participant's engagement in the decision-making process regarding treatment options. A written outline of the recommendations will be presented to each Study Participant based on the summary discussion. The following general recommendations will also be included:

- Avoid loud noises. If exposure to noise is unavoidable, properly fitted earplugs and/or other hearing protection should be used.
- Avoid caffeine, alcohol, aspirin, and other foods, drinks, and drugs that may affect tinnitus.
- Reduce exposure to identified situations that cause or increase stress.
- Initiate activities that lead to relaxation or reduction of tinnitus perception.

#### **13.3 Conclusion of Initial Counseling Session**

At the conclusion of the SC session, the Study Audiologist will provide a copy of the handouts on tinnitus facts; environmental sound devices, tips for enhancing sleep, relaxation, and concentration, and websites with additional resources. The Study Participant will also be given a copy of his or her hearing test results, and a summary of the agreed upon treatment recommendations. The Study Audiologist will advise the Study Participant that a follow-up visit will be scheduled in approximately one month to monitor treatment progress. The Study Participant will also be told that he or she may contact the Study Audiologist before then if so

desired. The schedule for subsequent evaluation follow-up visits at the Clinical Center is also provided to the Study Participant.

### **13.4 One Month Follow-up Visit**

The purpose of the one-month follow-up visit is to review the specific recommendations that were made during the initial counseling visit and to promote self-efficacy beliefs by reinforcing the Study Participant's awareness that he or she can manage tinnitus by incorporating those recommendations into daily living. Detailed instructions, a script, and a checklist are included in Appendix B.

The Study Audiologist will ask the Participant to describe his or her experiences and progress with tinnitus management since the initial counseling session. As in the initial session, this narrative should be allowed to unfold with minimal interruptions. To monitor specific issues, the Study Audiologist will then summarize the specific problem situations cited by the Study Participant during the initial session and verify that the recommended environmental sound devices are being utilized on a regular basis in those situations. The Study Participant's perception of benefit from environmental sound will be discussed. The Study Audiologist will recommend continued use and/or modifications to environmental sound devices based on the Study Participant's progress to date.

The use of recommended coping strategies to alleviate problems related to sleep, stress, or concentration will also be discussed in relation to the Study Participant's specific areas of difficulty and recorded on the Follow-up Standard of Care Form. The Study Audiologist will confirm that coping strategies are being utilized, ascertain the frequency with which the strategies are used, and made further recommendations based on the Study Participant's progress or lack thereof. Strategies that have been unsuccessful or difficult to incorporate into the Participant's lifestyle should be modified as necessary.

The Study Audiologist will focus on the positive changes made thus far and emphasize the Study Participant's ability to effect change and manage tinnitus thereby promoting the his or her self-efficacy beliefs. An essential aspect of this counseling session is to provide reassurance and encouragement, to remind the Study Participant that change takes time, and that progress is not always a linear process; fluctuations in benefit are common.

The follow-up counseling session will typically range from 30 to 60 minutes although additional time can be allotted if there are significant questions or issues that warrant discussion to ensure compliance with treatment recommendations. It is essential that the Study Audiologist re-emphasize the importance of consistent use of environmental sound devices and the recommended coping strategies for problem situations.

After verifying that the Participant has no additional questions or concerns, the Study Audiologist will advise the Participant of the follow-up evaluations that are scheduled for the TRTT and verify that the Participant's contact information is accurate.

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References:

American Speech-Language-Hearing Association 2007. Preferred Practice Patterns in Audiology. ASHA Practice Policy. Available at: <http://www.asha.org/docs/html/PP2006-00274.html>

**Table 1**  
**Checklist for Standard of Care Counseling**

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1. Review and prepare materials
2. Elicit patient narrative. Tell me about your tinnitus.
3. Summarize cognitive/affective key points in Study Participant's narrative to communicate mutual understanding and empathy.
4. Is there anything else you would like me to know about your tinnitus?
5. Do you worry about your tinnitus? What worries you?
6. Review key points about tinnitus to make it less worrisome. (2 Slides)
  1. What it is and what it isn't
  2. Noticing it and ignoring it
7. Hearing mechanism: does Study Participant have a good understanding of hearing mechanism and hearing loss?
8. Hearing mechanism: Outer ear
9. Hearing mechanism: Middle ear
10. Hearing mechanism: Conductive hearing loss
11. Hearing mechanism: Inner ear- vestibular system
12. Hearing mechanism: Inner ear - cochlear & VIII N
13. Hearing mechanism: Sensorineural hearing loss
14. Hearing mechanism: Tinnitus
15. ATH Evaluation: what is Study Participant's current understanding of hearing status?
  1. Pure tone audiogram
  2. Speech tests
  3. LDL
  4. Tinnitus pitch and loudness match
  5. Tympanometry, Reflexes
  6. OAEs
16. Verify comprehension of hearing status, counsel to monitor hearing levels.
17. Identify effective ways Study Participant has coped with tinnitus in the past.
18. Review main problem areas identified by Study Participant
19. Identify situations that would benefit from environmental sound device.
20. Review/demonstrate relevant environmental sound devices.
21. Provide literature, information on appropriate sound devices as needed.
22. Review stressful situations if identified by Study Participant.
23. When indicated, discuss stress reduction programs, demonstrate relaxation exercise, provide reference literature if indicated.

**Table 1, Checklist for Standard of Care Counseling, continued**

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24. If Study Participant has identified sleep problems, review; if not, verify if problem exists.
25. Review healthy sleep patterns.
26. Identify variables that interfere with sleep. Which apply to Study Participant?
27. Review general recommendations for sleep environment.
28. Review recommendations for sound therapy to enhance sleep.
29. Identify changes Study Participant thinks would be most helpful to minimize tinnitus interference with his/her sleep.
30. Provide sleep literature, as appropriate.
31. Has Study Participant indicated that tinnitus interferes with concentration? If not, verify that it does not.
32. If concentration is a problem, review importance of ability to concentrate: memory, productivity, job performance.
33. Discuss use of environmental sounds to enhance concentration ability by reducing tinnitus.
34. Demonstrate attention sifting, conduct shifting visual and auditory attention exercise.
35. Recommend change in work habits and environment, including short breaks.
36. Recommend tips for staying focused, engaged.
37. Summarize Study Participant's areas of concern.
38. Identify Study Participant's choice of treatment options for target areas.
39. Provide Study Participant with copies of audiogram, literature, treatment recommendations, and follow-up instructions.
40. Advise Study Participant of follow-up appointment and follow-up evaluations for TRTT.

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**Appendix A**  
**Tinnitus Retraining Therapy Trial**  
**Script for Standard of Care Counseling**

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The counseling component in tinnitus retraining therapy (TRT), directive counseling (DC), is by definition a didactic procedure designed to teach tinnitus patients the principles and techniques of TRT. The content of DC is theory driven and does not vary from patient to patient. The counseling protocol for the standard of care (SC), on the other hand, is independent of specific tinnitus theories or methods. It is a composite of the counseling content and practices already utilized (most or all of the time) by (half or more of) the audiologists participating in the TRTT. It is embedded in a framework that reflects audiologists' basic counseling role and responsibilities and the following Preferred Practice Patterns for Audiology (ASHA, 2006):

*Tinnitus management is based on the patient's complaints, history, audiology evaluation, and self-assessment, and, ideally, includes family/care givers.*

*Tinnitus management reduces negative cognitive, affective, physical, and behavioral reactions to tinnitus and improves the patient's well-being and quality of life.*

In the TRTT, SC counseling is patient- rather than theory-driven. Each patient is viewed as an individual with unique complaints. The patient's concerns and needs guide the SC counseling process. The goals of SC counseling are the following:

1. The audiologist communicates concern and understanding to patients. Patients should have the distinct impression that the audiologist not only understands their problems, but also understands how those problems make them feel and how the problems affect their well-being and quality of life. **(Validation)**
2. The audiologist assesses patients' understanding of their tinnitus, verifies that they understand the problem, and clarifies any doubts or misconceptions regarding the implications of tinnitus. **(Verification and clarification)**
3. The audiologist reassures patients that, in time, they can learn to tolerate their tinnitus. **(Reassurance/Promote Self-efficacy)**

Appendix A, Script for Standard of Care counseling, continued

4. The audiologist engages patients in the management of their tinnitus problem by providing them with strategies – appropriate to their complaints, lifestyle, and abilities – that will enable them to minimize the effects of tinnitus and thereby learn to cope with it.

**(Engagement)**

The following is provided to guide the SC counseling session. Because each patient's complaints and clinical needs determine the specific areas of emphasis, this should be viewed as a minimal or skeleton script from which additions are encouraged to ensure that each patient's specific complaints are acknowledged and addressed as needed. The SOC counseling session should take 1.5 to 2.5 hrs depending on the patient's questions and needs.

**Elicit patient narrative:** My goal is to make it possible for you to cope with tinnitus so it does not have negative effects on your well-being and your life. To do that, it is important that I understand how your tinnitus affects you every day and how you feel about it. So, please tell me all about your tinnitus.

*(Listen actively and paraphrase periodically to communicate your understanding of what the patient is saying. Encourage further disclosure as necessary to obtain a comprehensive perspective of the patient's tinnitus experience and to provide insight into coping strategies used to date. If necessary, elicit additional information by asking for clarification or examples or gently prod by asking, "How do you feel when that happens?" or "What do you generally do when that happens?" For participants who are withdrawn, any of the following questions can be asked to elicit further disclosure: What kinds of things aggravate your tinnitus? What seems to reduce your tinnitus? When is it most noticeable? When is it least noticeable? What is the most bothersome about your tinnitus? How do you react to your tinnitus? What do you do to cope with your tinnitus?*

*\*If tinnitus effects on stress, sleep, and concentration ability have not been mentioned, ask if problems exist in these areas.)*

**Summarize cognitive (thoughts)/affective (feelings) key points in patient's narrative to communicate mutual understanding and empathy:** From what you are saying, I can tell that tinnitus has been interfering in some important aspects of your life... (identify situations) and that you feel (identify emotions cited) as a result.

*(Allow participant to elaborate further as appropriate to clarify and verify your observations and foster mutual understanding of the problems and their extent.)*

Appendix A, Script for Standard of Care counseling, continued

After we have talked a little bit more about your tinnitus and tinnitus in general, I want to discuss these situations and how you have coped with them some more because I have some suggestions for other things that will help. For now though, is there anything else you would like me to know about your tinnitus?

*(If there is, verify/clarify as needed and allow patient to elaborate, then say....)*

Ok, that's good. That helps me understand your situation better too. We'll discuss that more when we review the different strategies I want you to start using to minimize the effects your tinnitus is having on you.

**Tinnitus Facts:** Do you worry about your tinnitus? What worries you about it?

*(Acknowledge and identify sources of worry.)*

People often have misconceptions about tinnitus that make it more worrisome, so I'd like to review some facts with you to make sure you don't have any unnecessary concerns that make your tinnitus even more stressful.

*(Provide Handout: Key Points about Tinnitus and review.)*

- Tinnitus refers to sounds that you hear that do not originate outside your body.
- It may be a ringing, buzzing, hissing, or chirping sound.
- Tinnitus results from nerve activity in the inner ear.
- It can be triggered by noise, some medications, disease, head trauma, and stress.
- Tinnitus may or may not be associated with hearing loss.
- It will not damage your hearing.
- Tinnitus is not a health threatening condition.
- It may get worse, may stay the same, or it may go away.

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Appendix A, Script for Standard of Care counseling, continued

*(Review each point and assess participant's accurate understanding of each.)*

You may not realize it, but tinnitus is actually a common condition. Here are some other points about tinnitus that I want you to know and understand.

- Almost everyone notices tinnitus from time to time.
- People who have some hearing loss may notice it more because they hear less sound around them.
- Tinnitus is very common among those who have been exposed to very loud noise.
- Most people who have tinnitus aren't bothered by it.
- Focusing on tinnitus can make it more noticeable.
- Many people learn to ignore their tinnitus.
- You can learn to ignore tinnitus.
- Other sounds in the environment make it easier to ignore tinnitus.

*(It is critical that the participant grasp that you believe it is possible to ignore tinnitus and that you believe he or she can do so by learning the strategies you will discuss. This step is essential in promoting self-efficacy.)*

**Hearing mechanism:** I will discuss some of these points about tinnitus in more detail in a few minutes, but first, I also want to be sure that you do not have any questions or concerns about your hearing or the results of the tests that you have had. How much do you know about how the hearing mechanism?

*(Discussion of hearing mechanism should be contingent upon participant's understanding of hearing already, his or her interest level, grasp of information, and specific questions. Using the model of the ear, explain hearing mechanism in a manner and at a level appropriate for the individual.)*

Let me review the basic parts of the ear for you and explain how we hear.

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Appendix A, Script for Standard of Care counseling, continued

- This is the outer ear also called the pinna or auricle, followed by the external auditory canal, and at the end, the tympanic membrane or eardrum, which is sensitive enough to vibrate as sound waves traveling through the air strike it.
- The middle ear (an air-filled cavity ventilated by the Eustachian tube) includes the ossicular chain - a leverage system that transfers the vibrations of the eardrum into mechanical energy to transmit the sound signal into the inner ear.
- The inner ear includes the cochlea, a fluid filled system in which the nerve endings for hearing are encased; the vibration of the ossicular chain causes wave motion in these fluids which displaces the hair cells along the inner chambers of the cochlea.
- This displacement causes an impulse, a neural impulse that is like an electrical charge that is transmitted along the VIII cranial nerve – the acoustic nerve - to the brain, which is where sound is actually perceived.
- The inner ear also consists of the vestibular or balance system, which includes the semicircular canals, the utricle and the saccule.

*(Explain the types of hearing/auditory problems associated with the parts of the ear emphasizing the issues that are relevant to the participant.)*

- When there is a blockage or mechanical breakdown to some portion of the outer ear or middle ear, the result is a conductive hearing loss. This might be excess wax, a perforation in the eardrum, fluid in the middle ear, or discontinuity of the ossicular chain. Often this type of hearing loss can be medically treated and resolved.
- Damage to the nerve endings in the inner ear from noise exposure, illness, or even aging can result in a sensorineural hearing loss. Hearing problems resulting from problems with the acoustic nerve or in the brain itself are also usually referred to as sensorineural in nature.
- There's no reason that more than one problem can't occur in the ear. If different problems cause a conductive and a sensorineural loss of hearing, it is called a mixed hearing loss.
- Tinnitus, another problem that can be related to problems with the inner ear is the ringing, buzzing, or chirping sound people sometimes hear. It appears to be related to activity from hair cells in the inner ear.

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Appendix A, Script for Standard of Care counseling, continued

**ATH Evaluation:** You have probably had your hearing tested several times in the past. Everyone in our project has hearing that is still quite good, but I would like to review your hearing test results briefly so you understand the results and can monitor any changes that might occur in the future.

*(Using the participant's audiogram, briefly review his or her results to ensure comprehension of any existing hearing problems, and the significance of the test results, e.g. 4k notch from noise exposure, etc.). Extent and complexity of the discussion of ATH Evaluation results should be based on the participant's interest level, grasp of information, and specific questions. As with the explanation of the hearing mechanism, present this material in a manner and at a level appropriate for the individual.)*

- Your hearing is tested using tones of different pitches. We test to see how loud a particular tone has to be before you can just barely detect it. That is called your threshold for that tone and is represented on the graph as a red circle for sounds in your right ear and blue X's in your left ear. The graph represents tones ranging from low frequency or low-pitched sounds to high frequency or high-pitched sounds. As the loudness increases, the decibel level increases. Theoretically, the average normal ear detects sounds around 0 dB in intensity but anything better than 20 dB is considered to be essentially within normal limits. If we test your hearing with sound coming through a set of earphones, that is called air conduction testing and your entire hearing mechanism is involved. If a small vibrator is placed against your skull behind your ear, the inner ear is being tested directly by causing vibrations to the fluids in the inner ear. That is called bone conduction testing. If your air conduction thresholds reveal a hearing loss but bone conduction thresholds are normal, then we would assume that there is a problem causing a conductive hearing loss somewhere in the outer or middle ear but that your inner ear is functioning normally. If both sets of pure tone results indicate a problem but are the same, then we know the problem is in the inner ear.
- Two different speech tests are a standard part of the audiologic evaluation. One measures how loud speech has to be before you are able to hear it and the other measures how clear speech is to you when it is around a normal conversational level.
- Acoustic immittance testing provides a graph showing us if your eardrum is intact and if the air pressure in the middle ear cavity is normal. The loud sounds that you hear during that test are a test of a reflex – a muscle contraction that helps protect the ear from sounds that are too loud. These tests all help us determine the type of hearing problem someone may have.

Appendix A, Script for Standard of Care counseling, continued

- You also had some tests to give us an idea of what your tinnitus sounds like to you. One is a match of the pitch or frequency of your tinnitus. For example, is it a high-pitched ringing or more of a low-pitched hum? The other test gives us an idea of how loud your tinnitus seems to you.

*(If patient has a hearing loss, review type, extent, and possible etiology. Recommend: (a) annual evaluations to monitor hearing levels and (b) use of hearing protection when around occupational or recreational noise. Ensure that the participant has no questions about his or her hearing status or hearing test results. If you have a break planned, this would be an appropriate time to do so.)*

**Coping with Tinnitus:**

- **Environmental Sound:**

Now, I want to focus on the situations in which tinnitus has been bothersome for you, and ways that will help you make it less noticeable and less bothersome.

*(Here, you will summarize the specific situations that the participant has identified as problematic. Review the strategies that have been used that were effective in reducing the awareness of tinnitus or the extent to which it was bothersome and encourage more frequent use of those strategies. Emphasize what has been done thus far that has been effective to make participant aware of the efficacy of his/her coping strategies. It is important to build on this efficacy.)*

One of the most effective ways to minimize the perception of tinnitus is to introduce other sounds to your surroundings. So, let's talk about ways to do this in the situations that you're in when tinnitus is bothersome. This is the most important thing you can do to make sure that tinnitus is not as noticeable and bothersome. There are many devices available that you can use to accomplish this. It is extremely important that you find sources of environmental sound for the situations that have been problems for you because your tinnitus will be less noticeable when there is other sound going on around you. When it is less noticeable, it will be less bothersome. And, interestingly enough, when it is less bothersome, you will start noticing it even less often too. Ideally, you should select sounds that you find enjoyable or relaxing and soothing. Let's decide what kinds of sounds and which devices you will get for the environments that are problematic for you.

Appendix A, Script for Standard of Care counseling, continued

*(Provide participant with Handout on Sound Devices and establish which are most appropriate for the situations in which problems have occurred. Review devices on the Handout and mention options that may already be available in the home such as fans, music, etc. Devices appropriate for sleep, work, and living environments should be covered as they apply to the participant.)*

- **Stress.**

Having other sounds in your environment will make your tinnitus less noticeable and that will help you ignore it so you will find that it is less stressful for you. I would also like to talk to you about ways to reduce stress. This is very important not only because tinnitus can be stressful, but also because, for some people, stress seems to aggravate tinnitus. Medical personnel, educators, and counselors are now recommending a variety of ways in which we can all reduce stress. Deep breathing, progressive muscle relaxation, and visual imagery are very effective techniques. Yoga, tai chi, and meditation are other options that involve more time but are also very effective. Have you used any of these techniques before?

*(Provide Tips for Relaxation Handout to patient. Conduct short deep breathing exercise and progressive muscle relaxation exercise if participant is not familiar with these procedures. If participant has identified situations that are especially stressful, discuss appropriateness of various techniques for use in those settings and recommend soothing, relaxing environmental sound options.)*

- **Sleep**

*(If patient has identified sleep problems, review; if not, verify that there is no problem. Provide sleep handout.)*

If you find it difficult to fall asleep because you tend to notice your tinnitus then, always use environmental sounds that you find soothing and relaxing. Also, it is important to improve your overall sleep habits because a lack of sleep increases stress, fatigue, and irritability, plus it negatively affects overall health. Ideally, we should get 8 hours of uninterrupted sleep every night. Stress and emotions; environmental variables such as noise, light, and temperature; irregular schedules, jet lag, medications, caffeine, nicotine, and alcohol can all disrupt sleep. Are there things that you know keep you from getting a good night's sleep?

Appendix A, Script for Standard of Care counseling, continued

*(Depending on the participant's needs, review tips on handout including the following):*

- Promote healthy sleep: During the day avoid naps and get some exercise. In the evening, avoid stressful activities and strenuous exercise; go to bed when you're tired; avoid caffeine, alcohol, large meals, and spicy foods close to bedtime.
- Optimize sleeping conditions: Eliminate distractions (TV, computer, food/drink); add comfortable mattress, pillow, comforters; darken the bedroom; set temperature between 58° to 68° F.
- Add soothing background noise: music, nature sounds, broadband noise.
- If sounds bother your partner, consider a pillow speaker.
- Practice progressive relaxation exercises and visual imagery if needed to help you fall asleep.

- **Concentration**

*(Has participant indicated that tinnitus interferes with concentration? If not, verify that it does not. As appropriate, focus on situations in which he or she has difficulty concentrating and discuss the implications of the inability to focus. Provide handout on concentration.)*

If you find that tinnitus interferes with your ability to concentrate, it is important that you do what you can to minimize your perception of tinnitus in those situations. Environmental sounds that you enjoy will be extremely beneficial in those settings. Here are some reasons this is so important and some other things you can do to help you stay focused and concentrate better.

- Concentration is important to complete daily tasks, job, etc.
- Inability to concentrate affects performance and productivity.
- Inability to concentrate causes stress and irritability.
- Good concentration enhances memory.

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Appendix A, Script for Standard of Care counseling, continued

- Could some of the following variables be affecting your ability to concentrate too? Temperature, distractions, lighting, hunger, fatigue, health, boredom, stress, depression.
- To enhance concentration: Eliminate distractions, adjust work habits/conditions, stay focused.

*Demonstrate attention-shifting exercise as follows:*

I want you to listen to your tinnitus now. Continue to listen to it for a bit... Ok, now I want you to listen to the sound of my nails. (If there is an appropriate ongoing ambient sound, name that, otherwise, tap your nails repetitively on the table. Continue the tapping sound and instruct the participant to shift his attention back to his tinnitus, and then back to the nail tapping sound a couple of times.) When you notice your tinnitus, stop yourself and shift your attention to the sound of the sound device you have going or to some other sound in the environment. If you practice this routinely, you will learn to shift your attention away from the tinnitus quite readily until it becomes almost automatic.

- **Summary and Recommendations**

*(This element of the counseling session is highly individualized. It should reflect the participant's specific problems and the specific recommendations for intervention. Review the participant's areas of concern, the selected treatment choices, and expected outcome. Provide participant with handout on additional resources.)*

I want to review the problems you have identified and the decisions we've made about how you can start managing these situations. Here's what we have planned: (List and review, ask participant to identify any remaining concerns and questions.)

In a month, we will meet again to discuss your progress. By then, you will have been using the sound devices and doing the other things we've discussed. By then, I also want you to check out the websites on the additional resources list as they apply to your specific problems and we'll discuss which ones have been helpful to you. The visit is mostly to make sure you have been able to incorporate these recommendations into your daily routine. You will also be scheduled for follow-up visits after 3, 6, 12, and 18 months. I know that the more time goes by, the more you will find you are able to ignore your tinnitus. Don't expect this to occur overnight. It will take a little time and practice. But, the more sound you have to distract you initially, and the less stress you are feeling as a result, the more things will continue to improve. I am confident that this is something you are able to do! If you have questions or concerns in the meantime, please feel free to call me.

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**Appendix B**  
**Tinnitus Retraining Therapy Trial**  
**Standard of Care Counseling One Month Treatment Visit**

**A. Instructions for One-Month Treatment Visit (T2)**

The purpose of the one-month follow-up visit is to review the recommendations that were made during the initial clinic visit and to promote self-efficacy beliefs by reinforcing the participant's awareness that he or she can manage tinnitus by incorporating those recommendations into daily living. This second counseling session should include the following:

- Mini-narrative from participant describing experience since first session
- Review of the specific tinnitus problems cited by the Study Participant
- Verification that the environmental sound devices selected for each of those situations have been obtained and are being utilized routinely
- An assessment from the participant of the progress (or lack thereof) experienced thus far in each situation based on use of environmental sound therapy
- Ascertain use of recommended strategies to alleviate problems experienced, e.g., sleep, stress, concentration.
- Modify treatment recommendations if specific strategies have been unsuccessful or difficult to adapt to participant's lifestyle.
- Focus on the positive changes made thus far and emphasize the participant's ability to effect change and manage tinnitus thereby promoting his or her self-efficacy beliefs.
- Remind participant that change takes time and that progress isn't always without occasional setbacks.
- Re-emphasize the importance of consistent use sound devices and of recommended strategies for problem situations.
- Provide reassurance and encouragement as well as praise for progress thus far or for attempts at change.
- Advise participant of follow-up evaluation appointment to be scheduled in two months.

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Appendix B, Standard of Care Counseling One Month Treatment Visit, continued**B. Standard of Care Counseling Follow-up Visit Script**

The purpose of this session is to review the issues we discussed during your clinic visit last month. I have some specific questions relative to how you are managing your tinnitus, but before we get to those, I'd like you to tell me how things have been going for you.

*(Regardless of the participant's response, your goal is to be reassuring and encouraging so you are promoting self-efficacy and engaging participant in the management of his/her tinnitus. Depending on how the participant responds, select from the following to proceed.)*

- **Participant reports little or no progress to date:** I know that may be discouraging to you, but don't forget, I explained that this is a gradual process. This is normal. That's why we have this follow-up call a month later: to remind you that change will occur gradually, and that it is important for you to continue to do the things we discussed so the gradual progress can occur. Now let's review what we decided you would do and how you have incorporated those strategies so far.
- **Participant reports some help in some situations or a little improvement:** I'm glad to hear you're making progress. Don't forget that I told you this would be a gradual process. It's very encouraging that you're making progress already. That tells me you're definitely on the right track. Let's review what we decided you would try to do and see what seems to be helping the most, and talk about the things you need to keep doing so change can continue to occur.
- **Participant reports significant improvement in general:** That's great to hear. I'd like to hear which things have been helping you the most.

When we met last month, we focused on the problems you have had. *(Summarize participant's specific issues and the cognitive/affective reactions experienced because of these problems.)*

We talked about the benefits of using environmental sound devices for these situations. Have you obtained these devices? *(If participant has not obtained devices, determine why not.)*

Are you using the devices routinely in each situation? *(If participant is not using devices routinely, determine why and encourage regular use and/or suggest modification to resolve any issues related to non-use.)*

Appendix B, Standard of Care Counseling One Month Treatment Visit, continued

Do you have any questions about these devices, or any of the other devices that might be of help to you?

We also discussed some strategies you can use to minimize problems related to some problems you experienced because of tinnitus. (*Review the specific problems with respect to sleep, relaxation, or concentration and the strategies suggested.*)

Have you been using these strategies? (*If not, review purpose of strategies, reiterate importance of using them, explore reasons for not using strategies, and if appropriate, suggest alternates. Determine which strategies are being used and how frequently they are used. If strategies are being used, provide positive feedback and encourage continued use.*)

Using these strategies will help you overcome these problems so it is important that you start/continue using them. Do you have any questions about any of the strategies we discussed?

I also gave you a list of additional websites with suggestions for these situations. Have you visited these websites? Have you learned anything that was particularly helpful on any of these sites? (*If not, remind participant to check the websites for additional help with sleep, relaxation, concentration, focusing, etc. If he or she has checked websites, ascertain which have been helpful, etc.*)

Is there anything else you would like to discuss about your tinnitus? Do you have any other questions or concerns that I can help you with today?

Before we finish, let's review what we've covered. (*Summarize and review recommendations.*)

You are doing great so far and I know you'll continue to make progress as time goes on. This is a gradual process. Just keep using the environmental sound devices to help minimize the tinnitus in those situations that are troublesome, and use the strategies we've discussed. You will continue to make progress.

Please feel free to contact me if anything comes up. We'll be in touch to schedule your next evaluation, which will be in two months.

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Appendix B, Standard of Care Counseling One Month Treatment Visit, continued**C. Checklist for Standard of Care Counseling One-month Treatment Visit**

1. Review and prepare materials
2. Elicit mini-narrative. Tell me how things have been going.
3. Summarize specific tinnitus problem discussed during intitial clinical visit with Study Participant
4. Has Study Participant obtained the recommended environmental sound devices?
5. Assess frequency of sound device use in each recommended situation.
6. Assess adjustment to and benefit from devices
7. Does Study Participant have questions about these devices, other potential devices?
8. Review the spiecific problems with respect to sleep,relaxation, or concentration and the strategies suggested.
9. Have strategies been used? Determine which strategies are being used and how frequently they are used.
10. If not, review purpose of strategies, reiterate importance of using them, explore reasons for not using strategies, and if appropriate, suggest alternates.
11. If stratigies are being used, provide positive feedback and encourage continued use.
12. Has Study Participant visited additional resource websites?
13. Were websites helpful? How so?
14. Does Study Participant have any other questions or concerns?
15. Summarize and review recommendations?
16. Focus on progress and provide reassurance and encouragement.

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Appendix C  
**Tinnitus Retraining Therapy Trial  
Handouts**

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**HANDOUT 1: Key Points about Tinnitus****Tinnitus: what it is and what it isn't**

- ◆ Tinnitus refers to sounds that you hear that do not originate outside your body.
- ◆ It may be a ringing, buzzing, hissing, or chirping sound.
- ◆ Tinnitus results from nerve activity in the inner ear.
- ◆ Tinnitus can be caused by noise, some medications, disease, head trauma, and stress.
- ◆ Tinnitus may or may not be associated with hearing loss.
- ◆ It will not damage your hearing.
- ◆ Tinnitus is *not* a health threatening condition.
- ◆ There is no proven medical treatment for tinnitus.
- ◆ It may get worse, may stay the same, or it may go away.

**Tinnitus: Noticing it and ignoring it**

- ◆ Almost everyone notices tinnitus from time to time.
- ◆ People with hearing loss may notice tinnitus more because they hear less sound around them.
- ◆ Tinnitus is very common among those who have been exposed to very loud noise.
- ◆ Most people who have tinnitus aren't bothered by it.
- ◆ Focusing on tinnitus can make it more noticeable.
- ◆ You can learn to ignore tinnitus.
- ◆ Other sounds in the environment make it easier to ignore tinnitus.

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## HANDOUT 2: Sleep Tips from the Mayo Clinic

1. **Go to bed and get up at about the same time every day, even on the weekends.** Sticking to a schedule reinforce your body's sleep-wake cycle and help you fall asleep more easily.
2. **Don't eat or drink large amounts before bedtime.** Eat a light dinner at least two hours before sleeping. If you're prone to heartburn, avoid spicy or fatty foods, which can make your heartburn flare and prevent a restful sleep. Also, limit how much you drink before bed. Too much liquid can cause you to wake up repeatedly during the night for trips to the toilet.
3. **Avoid nicotine, caffeine and alcohol in the evening.** These stimulants can keep you awake. Smokers often experience withdrawal symptoms at night, and smoking in bed is dangerous. Avoid caffeine for eight hours before your planned bedtime. Your body doesn't store caffeine, but it takes many hours to eliminate the stimulant and its effects. And although often believed to be a sedative, alcohol actually disrupts sleep.
4. **Exercise regularly.** Regular physical activity, especially aerobic exercise, can help you fall asleep faster and make your sleep more restful. However, for some people, exercising right before bed may make getting to sleep more difficult.
5. **Make your bedroom cool, dark, quiet and comfortable.** Create a room that's ideal for sleeping. Adjust the lighting, temperature, humidity and noise level to your preferences. Use blackout curtains, eye covers, earplugs, extra blankets, a fan or white-noise generator, a humidifier or other devices to create an environment that suits your needs.
6. **Sleep primarily at night.** Daytime naps may steal hours from nighttime slumber. Limit daytime sleep to about a half-hour and make it during mid-afternoon. If you work nights, keep your window coverings closed so that sunlight, which adjusts the body's internal clock, doesn't interrupt your sleep. If you have a day job and sleep at night, but still have trouble waking up, leave the window coverings open and let the sunlight help awaken you.
7. **Choose a comfortable mattress and pillow.** Features of a good bed are subjective and differ for each person. But make sure you have a bed that's comfortable. If you share your bed, make sure there's enough room for two. Children and pets are often disruptive, so you may need to set limits on how often they sleep in bed with you.
8. **Start a relaxing bedtime routine.** Do the same things each night to tell your body it's time to wind down. This may include taking a warm bath or shower, reading a book, or listening to soothing music. Relaxing activities done with lowered lights can help ease the transition between wakefulness and sleepiness.
9. **Go to bed when you're tired and turn out the lights.** If you don't fall asleep within 15 to 20 minutes, get up and do something else. Go back to bed when you're tired. Don't agonize over falling asleep. The stress will only prevent sleep.
10. **Use sleeping pills only as a last resort.** Check with your doctor before taking any sleep medications. He or she can make sure the pills won't interact with your other medications or with an existing medical condition. Your doctor can also help you determine the best dosage. If you do take a sleep medication, reduce the dosage gradually when you want to quit, and never mix alcohol and sleeping pills. If you feel sleepy or dizzy during the day, talk to your doctor about changing the dosage or discontinuing the pills.

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### HANDOUT 3: Relaxation Tips from [helpguide.org](http://helpguide.org)

1. **Deep breathing** is a simple, yet powerful, relaxation technique. It's easy to learn, can be practiced almost anywhere, and provides a quick way to get your stress levels in check. All you really need is a few minutes and a place to stretch out.

The key to deep breathing is to breathe deeply from the abdomen, getting as much fresh air as possible in your lungs. When you take deep breaths from the abdomen, rather than shallow breaths from your upper chest, you inhale more oxygen. The more oxygen you get, the less tense, short of breath, and anxious you feel. So the next time you feel stressed, take a minute to slow down and breathe deeply

- ◆ Sit comfortably with your back straight. Put one hand on your chest and the other on your stomach.
- ◆ Breathe in through your nose. The hand on your stomach should rise. The hand on your chest should move very little.
- ◆ Exhale through your mouth, pushing out as much air as you can while contracting your abdominal muscles. The hand on your stomach should move in as you exhale, but your other hand should move very little.
- ◆ Continue to breathe in through your nose and out through your mouth. Try to inhale enough so that your lower abdomen rises and falls. Count slowly as you exhale.

If you have a hard time breathing from your abdomen while sitting up, try lying on the floor. Put a small book on your stomach, and try to breathe so that the book rises as you inhale and falls as you exhale.

2. **Progressive muscle relaxation** is another effective and widely used strategy for stress relief. It involves a two-step process in which you systematically tense and relax different muscle groups in the body.

With regular practice, progressive muscle relaxation gives you an intimate familiarity with what tension—as well as complete relaxation—feels like in different parts of the body. This awareness helps you spot and counteract the first signs of the muscular tension that accompanies stress. And as your body relaxes, so will your mind. You can combine deep breathing with progressive muscle relaxation for an additional level of relief from stress. Most progressive muscle relaxation practitioners start at the feet and work their way up to the face.

- ◆ Loosen your clothing, take off your shoes, and get comfortable.
- ◆ Take a few minutes to relax, breathing in and out in slow, deep breaths.
- ◆ When you're relaxed and ready to start, shift your attention to your right foot. Take a moment to focus on the way it feels. Slowly tense the muscles in your right foot, squeezing as tightly as you can. Hold for a count of 10.
- ◆ Relax your right foot. Focus on the tension flowing away and the way your foot feels as it becomes limp and loose.
- ◆ Stay in this relaxed state for a moment, breathing deeply and slowly.
- ◆ When you're ready, shift your attention to your left foot. Follow the same sequence of muscle tension and release.
- ◆ Move slowly up through your body — legs, abdomen, back, neck, face — contracting and relaxing the muscle groups as you go.

### HANDOUT 4: Concentration Tips from the University of Cambridge

Concentration has been defined as "the ability to direct one's thinking in whatever direction one would intend". We all have the ability to concentrate some of the time. But at other times our thoughts are scattered, and our minds race from one thing to another. To deal with such times, we need to learn and practice concentration skills and strategies. To concentrate, we have to learn a skill, and as with any skill this means practice repeated day after day until we achieve enough improvement to feel that we can concentrate when we need to. Our ability to concentrate depends on:

- ◆ commitment
- ◆ enthusiasm for the task
- ◆ skill at doing the task
- ◆ our emotional and physical state
- ◆ our psychological state
- ◆ our environment

### **Expanding your concentration span**

People sometimes refer to a "concentration span" : this is the time we can concentrate on a specific task before our thoughts wander. In learning concentration skills, we aim to extend our concentration span - bearing in mind that we will have a different span for different tasks. It cannot be expanded to infinity! Most people find their level for most tasks to be about an hour, but for some people and some tasks it will just be a few minutes, while for others it might be two or three hours.

The main barriers to concentrating are boredom, anxiety and day-dreaming. Thus in improving our concentration skills we need to counteract these barriers. The following skills are basic to concentration: if you want to improve your concentration, start by practicing them.

#### **1. STOP!!!**

This sounds very simple, but it works. When you notice your thoughts wandering, say to yourself STOP and then gently bring your attention back to where you want it to be. Each time it wanders bring it back. To begin with, this could be several times a minute. But each time, say STOP and then re-focus. Don't waste energy trying to keep thoughts out of your mind (forbidden thoughts attract like a magnet!), just put the effort into STOP and re-focus. To begin with you will do this hundreds of times a week. But you will find that the period of time between your straying thoughts gets a little longer each day, so be patient and keep at it.

#### **2. Attending**

This is about maintaining concentration and not giving in to distractions. It could be described as a sort of tunnel-vision, or as being focused: you keep your concentration on what is in front of you. If you are distracted, use the STOP technique to regain concentration. You can practice attending in many situations:

- ◆ In a lecture, if people move or cough, ignore them, don't look at them, actively exclude them from the link or tunnel formed between you and the lecturer.

HANDOUT 4: Concentration Tips from the University of Cambridge, continued

- ◆ In a social situation, keep your attention solely on one person - what they say, how they look etc. - and ignore what is going on round about.

### 3. Worry time

Set aside one or more specific periods in the day when you are allowed to worry. It can help to set them just before something that you know you will do, to ensure that you stop worrying on time - e.g. before a favorite TV program, or a meal-time. Whenever an anxiety or distracting thought enters your mind during the day, banish it until your next worry time, and re-focus on what you are supposed to be doing. Some people find it helpful to write down the banished thought: it is easier to banish a thought if you are sure you won't have forgotten it when you get to your worry time. It is important that you keep your worry time(s), and make yourself worry for the full time. If you find that you can't fill the time available, then make a conscious decision to reduce it. You may notice, particularly if you keep a list, that certain things keep reappearing: this is a fairly clear indication that you need to do something about them.

#### Other Tips:

- ◆ In between periods of concentration, do things to change your physical and mental activity. You could move around or go for a quick walk to boost your circulation if you have been sitting, or you could think about something completely different - and fun - to give your brain a new focus.
- ◆ Give yourself incentives and rewards appropriate to the level of concentration you have had to maintain. Quite often they can be linked to the things that usually distract you. If you dream of sitting out in the sun when you are trying to work make your reward a period of sun-worshiping with the appropriate sun-screen lotion, of course!)

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**HANDOUT 5: Environmental Sound Devices**

A wide variety of environmental sound devices exist that help mask tinnitus. These can be used in your normal work, living, and sleep environments. Devices that emit a white noise signal are available as are those that produce simulated sounds such as rain, a stream, and other nature sounds. Recorded nature sounds are also available from many sources on CD or for MP3 or iPOD downloads. Another popular device is the tabletop water fountain that provides an ongoing background sound appropriate for an office or living room setting. You can easily access information about such devices on the internet and search for white noise, nature sounds, or sleep devices. Below are just a few examples of available devices that you can find on the websites listed in the resource handout.

[Sound Oasis Sound Therapy System](#)[Marpac Sleep-Mate/Sound Screen](#)[Sound Oasis Sound Therapy Pillow](#)[Marsona Travel Sound Conditioner](#)[Alpine Eternity Tabletop Fountain](#)[Homedics Portable Sound Spa](#)

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## HANDOUT 6: Website Resources

### Sleep

<http://www.mayoclinic.com/health/sleep/HQ01387>  
[http://www.helpguide.org/life/sleep\\_tips.htm](http://www.helpguide.org/life/sleep_tips.htm)  
<http://www.sleepfoundation.org/article/sleep-topics/healthy-sleep-tips>  
<http://www.selfhelpmagazine.com/article/insomnia>

### Relaxation

[http://helpguide.org/mental/stress\\_relief\\_meditation\\_yoga\\_relaxation.htm](http://helpguide.org/mental/stress_relief_meditation_yoga_relaxation.htm)  
<http://www.mayoclinic.com/health/relaxation-technique/SR00007>  
<http://www.squidoo.com/7relaxationtips>  
<http://www.webmd.com/balance/stress-management/features/blissing-out-10-relaxation-techniques-reduce-stress-spot>

### Concentration

<http://www.counselling.cam.ac.uk/concen.html>  
<http://zenhabits.net/5-tips-to-maximize-your-ability-to-concentrate/>  
<http://www.lumosity.com/>  
<http://www.getselfhelp.co.uk/docs/ATT.pdf> (attention training techniques)

### Environmental Sound Devices

<http://www.sleepwellbaby.com/Natural-Sound-Machines-s/462.htm>  
<http://www.serenitysupply.com/>  
<http://www.target.com/> (Search on “white noise” for many of these devices)  
<http://www.soundmachinesdirect.com/>  
<http://www.white-noise.us/>  
<http://www.sound-oasis.com/>  
<http://www.marpac.com/>

### Nature Sound Downloads

<http://www.calmsound.com/>  
<http://www.naturesounds.ca/>  
<http://www.soundsleeping.com/>  
<http://itunes.apple.com/us/artist/nature-sounds/id188943426>

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## **Chapter 14**

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## **14.1 Introduction**

Data collection forms comprise the main source of data flowing from the Clinical Centers to the Data Coordinating Center (DCC). The uniform collection of data from Clinical Centers is crucial to the overall quality of the trial. The data collection forms have been developed to obtain information in an unambiguous, straightforward manner. In the following pages, information about the general format of the Tinnitus Retraining Therapy Trial (TRTT) data collection forms is provided, along with instructions for how forms will be filled out for each patient during the eligibility visit, treatment, and during treatment follow-up.

## **14.2 General Information**

### **14.2.1 Obtaining Forms**

Forms are developed by the DCC in conjunction with the TRTT database that will be used for analyses. The forms are reviewed by both the Steering Committee (STC) and the Data and Safety Monitoring Board (DSMB), and then tested at selected Clinical Centers prior to general use.

Printable copies of each data collection form will be available on the TRTT website. Data collection forms will be organized by type of visit on the TRTT website. In preparation for a study visit, Clinical Center Coordinators should print out the required forms. As revised forms are generated, these will be posted on the TRTT website to replace the original version of the form. The revision number and date of revision for every form is found both in Section A and at the bottom of each page of the form. The DCC will notify each Clinical Center by email memorandum whenever a more recent revision is to be used. The Clinical Coordinator is responsible for seeing that all forms used are the most current version.

### **14.2.2 General Guidelines for Filling Out Forms**

Only fully certified TRTT Clinical Center staff may fill out TRTT data collection forms. Non-certified personnel and personnel certified for only certain procedures may not complete TRTT forms. Restricting completion of forms to TRTT certified personnel will maintain the same level of quality in data collection throughout all Clinical Centers and the integrity of the data. Since Clinical Center staff will be entering the data online at the TRTT website, it is important that all entries are legible. For questions in which there is a series of yes/no answers, and all responses are yes or no, vertical lines may be drawn through the appropriate answers as a quicker alternative to checking each line individually. A blue or black pen should be used to fill out forms (never a pencil). If an error is made in filling out a form, then corrections may be made using a different colored (e.g., red) pen. Do not use white-out or try to erase or obliterate the original answer. Cross out the incorrect answer with a single line, write the correct answer in a space near the incorrect answer, and initial and date the new entry. Both the correct and the incorrect answer should be legible.

While entering dates, Clinical Center staff must make every attempt to obtain an accurate date. Sometimes, however, the Study Participant may not remember an exact date (e.g., when a medication was last used). For example, the Study Participant may be able to remember the year of an event, but not recall the month or day. If this is the case, first probe for the month by asking the Study Participant to try and remember the season, then the month, and finally the day.

If the Study Participant is unable to remember the year, probe by asking the Study Participant to try and remember some other event that took place about the same time or ask the Study Participant to recall about how many years ago the event took place. Enter only the date components that the Study Participant is able to recall.

All forms should be checked for accuracy and completeness before being entered on the TRTT website. A thorough review of the form before it is entered on the TRTT website will increase efficiency at the Clinical Center. Because correcting omissions or errors found at the time of data entry uses tremendous resources, the Clinical Coordinator should attempt to make sure forms are complete and correct before beginning the data entry process.

All forms except the first page will have a space on the top right-hand corner in which to enter the Patient ID. This information must be entered on every page of all forms, so that if the pages of a form become separated, it is clear to whom the data refer. The reference number on the first page is used to record the data entry confirmation number when the form is data entered in the TRTT database.

The person responsible for obtaining the information on the form is the one whose name should be provided as the person completing the form. That person's certification number must also be on the form. The certification number comprises a series of three digits and is assigned at the time of certification.

Some data collection forms are completed by the Study Participant. The Clinical Coordinator or Study Audiologist should complete the administrative Section A before providing the self-report form to the Study Participant with appropriate instructions. After completion of a self-report form, the Clinical Coordinator should review the form for completeness and attempt to obtain responses for any missing values. The Clinical Coordinator should then complete the final administrative section on the self-report form. In cases where a Study Participant is not available for completion of a study visit, then copies of all self-report forms should be sent to the Study Participant by U.S. Postal Service for completion along with a stamped self-addressed envelope to return completed forms.

#### **14.2.3 Transmitting Data to the Coordinating Center**

Once a form is completed, signed, and checked for accuracy and completeness, it is ready for data entry using the TRTT website. The Clinical Coordinator will enter all forms into the website following the procedures outlined in the TRTT Website Use Handbook and described during training. In general, data entry is restricted to individuals who have completed training in using the website and been assigned usernames and passwords to access the data entry portion of

the TRTT website. The Eligibility Checklist is used to “register” a Study Participant in the data system. It must be completed and entered in the data system before any other data collection forms can be entered, including those used to request a randomized treatment assignment. All other Study Forms must be entered within a week following completion of the Study visit.

There will be occasions when TRTT staff at the Clinical Center need to change or update a data item. These types of changes are implemented by accessing the data system, calling up the original data entry screen by use of the reference number assigned to that form, and changing or entering the correct variable.

#### **14.2.4 Filing Forms**

Each Clinical Center must maintain a file for TRTT materials. Included in the file is correspondence from and to the Coordinating Center, General Hearing Instruments, Inc., and the Study Chair’s Office. Materials related to the Cooperative Research and Development Agreement (CRADA) and the Institutional Review Board (IRB) correspondence should also be included. There should be locked files for Study Participant files. It is important that participant confidentiality be preserved and access to the locked participant files be restricted to study personnel. The Clinical Coordinator should maintain the files.

### **14.3 Instructions for Eligibility Forms**

The following will provide detailed instructions for completion of data collection forms related to screening and determining eligibility of potential study participants. The forms are in approximate sequential order relative to enrollment and follow-up. The Eligibility Screening Form serves to “register” a potential study participant in the TRTT and must be entered before any other data collection form can be entered online.

If it is determined that a potential participant is ineligible at any point in the process of completing the baseline eligibility forms, no further forms need be completed. Rather, the Eligibility Checklist is completed, indicating the reason(s) for ineligibility. Partially or fully completed forms on ineligible individuals, except for the Eligibility Screening Form, should not be entered in the TRTT online database nor kept in the TRTT Clinical Center participant files.

Descriptions of some of these forms and instructions for completion are also included in Chapters 5, 6 and 9.

### **14.3.1 Eligibility Screening Form**

The Eligibility Screening Form (ES) is used to screen potential study participants with tinnitus on a few easily determined eligibility criteria and determine potential eligibility for the TRTT. The Eligibility Screening Form is completed by the Clinical Coordinator over the telephone or in-person for persons who have been referred to the TRTT. The namecode and study ID that is used throughout the study is assigned at screening by obtaining a pre-printed label from the sheet of study IDs provided by the DCC and affixing the label to the ES form. If the individual fails any of the eligibility criteria in Section B, then he or she is not eligible for the TRTT. If the individual fulfills all the eligibility criteria, a Baseline Eligibility Visit is scheduled. The Eligibility Screening Form must be entered on the online database regardless of eligibility because it “registers” the individual and also provides demographic information of all persons considered for the study.

### **14.3.2 Patient Locator Form**

The Patient Locator Form is used to record the Study Participant’s contact information for clinic records. It is completed for all eligible Study Participants at the Baseline Eligibility Visit and at any subsequent visit as needed to update information. The Clinical Coordinator completes the form, recording various information such as the Study Participant’s contact information, primary physician contact information, and emergency contact(s). The form is not entered online or ever sent to the DCC, but is filed in the Study Participant’s TRTT file at the Clinical Center.

### **14.3.3 Tinnitus Questionnaire**

The Tinnitus Questionnaire (TQ) is completed by the Study Participant at the Baseline Eligibility Visit to evaluate eligibility and provide the baseline value for comparison at follow-up. It is also completed at all subsequent follow-up visits. The TQ evaluates five domains of health related quality of life affected by the presence of tinnitus. The TQ is scored using a separate scoring sheet provided to Clinical Centers because not all items are scored in the same direction. A score of less than 40 on the TQ at the initial screen will exclude the potential participant from the TRTT. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, study visit dates, and review the completed form to make sure all items have been completed. The TQ is described in detail in Chapter 9.

#### **14.3.4 Beck Depression Inventory Fast Screen**

The Beck Depression Inventory Fast Screen (BD) is completed by the Study Participant during the Baseline Eligibility Visit as a screen for clinical depression. A total score of 4 or greater or a score of either 2 or 3 on item 7 will signal the need for further evaluation of the potential Study Participant for the presence of clinical depression. This form is also completed at each Follow-up Visit as a means to monitor depression as an Adverse Event. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed.

#### **14.3.5 Tinnitus History Form**

The Tinnitus History Form (TH) is completed by the Study Audiologist or the Clinical Coordinator at the time of the Baseline Eligibility Visit for each individual who is being considered for entry into the TRTT. Information collected on this form includes data on inclusion and exclusion criteria and also baseline tinnitus variables.

#### **14.3.6 Medical History Form**

The Medical History Form (MH) is completed by the Study Otolaryngologist, Study Audiologist, or the Clinical Coordinator at the time of the Baseline Eligibility Visit for each individual who is being considered for entry into the TRTT. If the form is not completed by the Study Otolaryngologist, it must be provided to him/her for review. Information collected on this form includes data on inclusion and exclusion criteria and also baseline health and medical variables.

#### **14.3.7 Baseline Tinnitus Retraining Therapy Interview Form**

The Baseline Tinnitus Retraining Therapy Interview Form (BT) is completed by the Study Audiologist at the time of the Baseline Eligibility Visit for each individual who is being considered for entry into the TRTT. Text in *italics* is read by the interviewer to the individual to guide him or her through the interview. This form is used to obtain a description of the individual's tinnitus, sound tolerance, and hearing status and the impact of each of these components on the Study Participant's health-related quality of life. Results from the interview serve as the basis to categorize each Study Participant into one of Jastreboff's TRT patient categories. Details for completing this form are included in Chapter 6.

### **14.3.8 Audiological/Tinnitus/Hyperacusis Form**

The Audiological/Tinnitus/Hyperacusis Form (BA) is completed by the Study Audiologist at the time of the Baseline Eligibility Visit for each individual who is being considered for entry into the TRTT. Data on the Study Participant's audiological testing, tinnitus characteristics, and sound tolerance are recorded on this form as well as results of tests related to exclusion criteria based on objective tinnitus.

### **14.3.9 Physical Examination Form**

The Physical Examination Form (PH) is completed by the Study Otolaryngologist at the time of the Baseline Eligibility Visit for each individual who has completed the Medical History and is being considered for entry into the TRTT. Results of measures related to inclusion and exclusion criteria obtained on the physical examination are recorded on this form.

### **14.3.10 Laboratory and Other Tests Form**

The Laboratory and Other Tests Form (LO) is completed by the Study Otolaryngologist at the time of the Baseline Eligibility Visit for each individual who has completed the Physical Examination, to record whether additional tests were required, including blood tests, imaging tests, or tests to assess emotional, psychological, or psychiatric health. Results of measures related to inclusion and exclusion criteria obtained on these tests are recorded on this form.

## **14.4 Instructions for Forms used to Summarize Eligibility Status**

### **14.4.1 Eligibility Checklist Form**

The Eligibility Checklist Form (EC) is completed by the Clinical Coordinator to assess the eligibility of every potential Study Participant for randomization to the TRTT. The numbers in parentheses at the end of each question refer to the number of the corresponding question of the data collection form that is recorded as the section heading. A "Yes" or "No" response is checked for each eligibility criterion. If no shaded boxes are checked, then the patient is eligible for randomization and a randomized treatment assignment may be requested using the online randomization process provided by the DCC.

Any response in a shaded box indicates that the patient is not eligible for randomization or not eligible at this time, i.e., pending eligibility. The Clinical Coordinator should complete those sections of the Eligibility Checklist corresponding to those parts of the Baseline Eligibility Visit

that had been attempted or completed. At least one reason for ineligibility must be checked, but all known reasons should be entered.

#### **14.4.2 Pending Study Participant Status Form**

A Pending Study Participant Status Form (PE) is used to notify the DCC that a potential Study Participant is not eligible at this time due to the presence of one or more pending eligibility criteria. This form records the date when the potential Study Participant will have fulfilled that criterion and may be re-evaluated for participation in the TRTT, and is used by the DCC to send reminders to the Clinical Center when the pending criterion may no longer apply.

### **14.5 Instructions for Self-Report and Cognitive Forms Completed at Randomization**

#### **14.5.1 Tinnitus Handicap Inventory**

The Tinnitus Handicap Inventory (TI) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. This form evaluates health-related quality of life domains affected by tinnitus in addition to those assessed by the TQ, and is also completed at all subsequent follow-up visits. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed. A full description of this form is included in Chapter 9.

#### **14.5.2 Tinnitus Functional Index**

The Tinnitus Functional Index (TF) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. This form evaluates health-related quality of life domains affected by tinnitus in addition to those assessed by the TQ, and is also completed at all subsequent follow-up visits. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed. A full description of this form is included in Chapter 9.

#### **14.5.3 Digit Symbol Substitution Task**

The Digit Symbol Substitution Task (DS) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. This form is also completed at the 6-month and 18-month follow-up visits in the TRTT. The DS is a neuropsychological test that assesses the ability of the

Study Participant to concentrate on a psychomotor task. The Clinical Coordinator or Study Audiologist must administer this test to the Study Participant. The DS is described further in Chapter 9.

#### **14.5.4 Hearing Handicap Inventory**

The Hearing Handicap Inventory (HH) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. This form is also completed at the 6-month and 18-month follow-up visits in the TRTT. The HH is a measure of the impact of hearing difficulties on the quality of life. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed. The HH is further described in Chapter 9.

#### **14.5.5 State-Trait Anxiety Inventory**

The State-Trait Anxiety Inventory (SA) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. The SA is a measure of anxiety and anxiety proneness. The SA is further described in Chapter 9. The SA is also completed by the Study Participant at the 6 and 18 months follow-up visits. Only the state component of the full State-Trait Anxiety Inventory is collected (the first 20 questions) at follow-up. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed.

#### **14.5.6 Positive and Negative Affect Schedule**

The Positive and Negative Affect Schedule (PA) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. The PA is a scale that consists of a number of words that describe different feelings and emotions. This form is also completed at the 6-month and 18-month follow-up visits in the TRTT. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed. The PA is further described in Chapter 9.

#### **14.5.7 Life Events Checklist**

The Life Events Checklist (LE) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment

is requested. This form is also completed at the 6-month and 18-month follow-up visits in the TRTT. The LE records the occurrence of important life events in the preceding year or the preceding 6 months, and both versions are included in the form. For the Baseline Visit and the 18 month visit, the version requesting information about the preceding year should be administered to the Study Participant. For the 6 month visit, the version requesting information about the preceding 6 months should be administered. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed.

#### **14.5.8 EuroQOL**

The EuroQOL (EQ) is completed by the Study Participant after indicating his/her agreement to allow randomization in the TRTT, but before the randomized treatment assignment is requested. The EQ measures health related quality of life. This form is also completed at the 6-month and 18-month follow-up visits in the TRTT. The Clinical Coordinator or Study Audiologist should enter the ID codes for the Study Participant, enter the study visit dates, and review the completed form to make sure all items have been completed.

### **14.6 Instructions for Forms used to Monitor Adherence to Treatment Protocol**

#### **14.6.1 Treatment Start-up Form**

The Treatment Start-up Form (TS) is completed by the treating Study Audiologist or Clinical Coordinator at time of the first treatment visit. This form is a record of when treatment began. Because the target date for all follow-up visits is linked to the date that treatment was begun, this form is used as the reference to mark the beginning of the follow-up period.

#### **14.6.2 TRT Checklist**

The TRT Checklist (TC) is completed by the treating Study Audiologist during the first treatment visit (T1) for Study Participants assigned to Directive Counseling (DC). The treating Study Audiologist checks whether each task and topic area required by the DC protocol was covered or completed during the DC Session.

#### **14.6.3 Standard of Care Checklist**

The Standard of Care Checklist (SC) is completed by the treating Study Audiologist during T1 for Study Participants assigned to Standard of Care (SC). The treating Study Audiologist checks whether each task and topic area required by the SC protocol was covered or completed during the SC Session.

#### **14.6.4 Sound Generator Issue Form**

The Sound Generator Issue Form (SI) is completed by the Study Audiologist when the sound generator assigned to the Study Participant at randomization is issued to the Study Participant. This form is completed at T1 when a pair of assigned sound generators is obtained from the assigned kit at the Clinical Center and given to the Study Participant. A different form , the Sound Generator Replacement Form (SR)is used to record instances when a replacement sound generator is required, including cases of malfunction, loss, or damage.

#### **14.6.5 Loudness Discomfort Level Assessment for Treatment Form**

The Loudness Discomfort Level (LDL) Assessment for Treatment Form (LD) is completed by the Study Audiologist who is not involved in the treatment of the Study Participant (i.e., who is blinded to the TRTT assignment). It is used to measure the LDL in order to provide information for treatment. It is completed at the second treatment visit (T2) and at the 3-month Follow-up Visits (F1). The Follow-up ATH form includes LDL measurements and is completed during subsequent Follow-up Visits.

#### **14.6.6 Sound Generator Use Form**

The Sound Generator Use Form is completed by the Study Audiologist at T2, and at each follow-up visit. This form is used to record compliance of the individual with the recommended use of the sound generator; record change in volume setting, if required; and discontinuation of sound generator use at the end of treatment.

#### **14.6.7 Follow-up Standard of Care Form**

The Follow-up Standard of Care Form is completed by the Study Audiologist at T2. This form is used to record compliance of the individual with the recommendations given during the standard of care counseling.

## **14.7 Instructions for Forms Completed at Follow-up**

### **14.7.1 Follow-up Medical History Form**

The Follow-up Medical History Form (FM) is completed by the Study Audiologist at the 3, 6, 12, and 18 months Follow-up Visits. Data on the Study Participant's medical condition, medication use, and current noise exposure are recorded on this form.

### **14.7.2 Follow-up Tinnitus Retraining Therapy Interview Form**

The Follow-up Tinnitus Retraining Therapy Interview Form (FT) is completed by the Study Audiologist at the 6, 12, and 18 months Follow-up Visits. This form is used to document perceived changes in the individual's tinnitus, sound tolerance, and hearing status and the impact of each of these components on the Study Participant's health-related quality of life.

### **14.7.3 Follow-up Audiological/Tinnitus/Hyperacusis Form**

The Follow-up Audiological/Tinnitus/Hyperacusis Form is completed by the Study Audiologist at the 6, 12, and 18 months Follow-up Visits. Data on the Study Participant's audiological testing, tinnitus characteristics, and sound tolerance are recorded on this form.

### **14.7.4 Other Follow-up Forms**

All additional follow-up forms are identical to those collected at the Baseline Eligibility Visit (see Sections 14.3 and 14.5). The following forms are collected at all Follow-up visits:

- Tinnitus Questionnaire (TQ)
- Tinnitus Functional Index (TF)
- Tinnitus Handicap Inventory (TI)
- Beck Depression Inventory Fast Screen (BD)

The following forms are collected only at the 6 and 18 months follow-up visits.

- Digit Symbol Substitution Task (DS)
- Hearing Handicap Inventory (HH)
- State Trait Anxiety Inventory (SA)
- Positive and Negative Affect Schedule (PA)
- EuroQoL (EQ)

## **14.8 Instructions for Forms used to Document Study Events**

### **14.8.1 Adverse Event Form**

The Adverse Event Form is completed by the Clinical Center Director (or Study Audiologist, in his or her absence) when an adverse event is identified during the study. If the event has been determined to be a Serious Adverse Event, then this form must be immediately entered into the TRTT online database and the Study Chair notified. If the Adverse Event is not a Serious Adverse Event, then this form must be entered into the online database within one week of becoming aware of the event. Instructions on reporting Adverse Events are included in Chapter 15.

### **14.8.2 Unscheduled Contact Form**

The Unscheduled Visit Form (UC) is completed anytime study-relevant information is obtained outside of a scheduled study visit. Relevant information may include additional information related to counseling or about a Study Participant's status. The Study Audiologist completes this form by recording the topics of conversation covered during the contact. This form is not used to record information related to an adverse event; if an adverse event takes place, an Adverse Event form should be completed.

### **14.8.3 Sound Generator Replacement Form**

The Sound Generator Replacement Form is completed by the Study Audiologist whenever a replacement sound generator is provided to the Study Participant for reasons of malfunction, loss, or damage. It is completed by the Study Audiologist and records the acoustic output of the replacement sound generator

### **14.8.4 Missed Visit/Forms Form**

The Missed Visit/Forms form is used to document a missed Study Visit that will not be able to be re-scheduled and the reason for the missed visit. This form is also used to document if a specific form or forms within a completed Study Visit were not able to be completed and the reasons the forms were not completed.

### **14.8.5 Study Termination Form**

The Study Termination Form is used to document that the status of a Study Participant has changed from active to permanent inactive status (e.g., withdrawn consent to participate) and the

reason for permanent inactive status. This form also documents the death of a study participation and if known, the reason for death.

#### **14.8.6 Participant Transfer Form**

The Participant Transfer Form is used to document when responsibility for a Study Participant is transferred from one Clinical Center to another, along with the reason for the transfer.

#### **14.8.7 Protocol Deviation Form**

The Protocol Deviation Form is used to document any departure from study protocol, the persons responsible, and steps developed to prevent such a departure in the future.

### **14.9 Instructions for Worksheets and Logs**

Worksheets are used to record information that is used within the study, but is not entered online. Logs are forms used to document events that are not entered into the online database.

#### **14.9.1 Audiogram Worksheet**

The Audiogram Worksheet is used as a graphical representation of the audiometric pure tone thresholds, loudness discomfort levels, and tinnitus pitch and loudness match tones and threshold. This worksheet is used for both Directive Counseling and Standard of Care counseling to describe an individual's hearing, tinnitus, and hyperacusis values obtained during an ATH examination.

#### **14.9.2 Baseline and Randomization Checklist**

The Baseline and Randomization Checklist is a worksheet that is comprised of a list of all procedures and forms to be completed at the Baseline Visit and a list of all eligibility criteria. The Clinical Coordinator may use this form to confirm eligibility and completion of all baseline and randomization procedures during and after the Baseline Visit. Because it is a worksheet, it is not entered into the data system.

#### **14.9.3 Kit Log**

The Kit Log is used to document receipt of kits containing the randomized treatment assignment to standard of care or a pair of sound generators (SGs) that have been shipped to the Clinical Center from the DCC. This log is also used to document which kits have been assigned to which Study Participants and the date of assignment. The Kit Log is also used to document the return of malfunctioning and re-issue of devices. This log will be reviewed during Clinical Center site visits (see Chapter 16, Section 16.3).

#### **14.9.4 Shipping Log**

The Shipping Log accompanies any shipment of materials that is sent to another party. It is expected that the shipping log may be used to document shipping CDs or other media with voice recordings of counseling sessions or datalogging files downloaded during sound generator measurement to the DCC. The shipping log may also be used to document shipping a damaged or malfunctioning SGs to GHI

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## **Chapter 15** **Reporting Adverse Events**

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### **15.1 Introduction and Definitions**

An adverse event is defined as any unfavorable deviation from baseline health occurring at any time following randomization to the Tinnitus Retraining Therapy Trial (TRTT). Adverse events may be physical, emotional, psychological, or social and may include any illness, sign, symptom, or clinically significant laboratory test or abnormality that has appeared or worsened during the course of the TRTT. The event may or may not be causally related to the treatment intervention.

An *unexpected* Adverse Event is any adverse reaction that has not been previously observed, whether or not the event is anticipated because of the biological properties of the study agent. An *expected* Adverse Event is any adverse reaction whose nature and severity have been previously observed and documented for the study product. There are no known risks for either tinnitus retraining therapy or the standard of care for severe tinnitus, and so there are no expected Adverse Events.

A Serious Adverse Event (SAE) is further defined as meeting one of the following conditions:

- Death;
- Life threatening;
- In-patient hospital admission, or prolongation of an existing hospitalization;
- Results in congenital anomaly or birth defect;
- Results in a persistent or significant disability or incapacity; or
- Results in need for medical intervention.

Important medical events that may not result in death, be life threatening, or require hospitalization, may be considered an SAE when based on appropriate medical judgment, as they may jeopardize the Study Participant and may require surgical, medical, or psychological intervention to prevent one of the outcomes listed in this definition.

Events not considered to be an SAE are hospitalization occurring under the following circumstances:

- Planned before entry into the TRTT;
- For elective treatment of a condition unrelated to the Study Participant's tinnitus;
- Take place as an emergency, outpatient basis and do not result in admission; or
- Are part of the normal treatment or monitoring of an existing condition.

There is a distinction between an SAE and a severe adverse event. An SAE is a regulatory definition as described above. The severity of an adverse event is an intensity classification and may be mild, moderate, severe, or life threatening. The following definitions apply:

**Mild:** Transient or mild discomfort (<48 hours); no medical intervention/therapy required

**Moderate:** Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required

**Severe:** Marked limitation in activity, some assistance usually required; medical intervention/therapy required; hospitalization possible

**Life threatening:** Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care possible

An Adverse Event is also defined by its relation with the treatment intervention, as follows:

**Definite:** Clear-cut temporal association, and no other possible cause

**Probable:** Clear-cut temporal association, and a potential alternative etiology is not apparent

**Possible:** Less clear temporal association; other etiologies are also possible

**None/Not Related:** The adverse event is completely independent of intervention administration; and/or evidence exists that the event is definitely related to another etiology.

## 15.2 Reporting Procedures for All Adverse Events

### 15.2.1 Serious Adverse Events

Individual cases of SAEs or unexpected adverse events requiring medical or psychological intervention must be reported promptly to the Study Chair and Data Coordinating Center (DCC).

The Clinical Center Director is responsible for reporting each SAE within 2 working days of knowledge of the event to the Study Chair and DCC by telephoning the Study Chair, completing an Adverse Event Form, and entering it online in the TRTT database. The Study Chair, in consultation with the Study Otolaryngologist, will discuss the event with the Clinical Center Director and prepare a narrative summary describing the event. The Study Chair will send the narrative summary to the DCC and the reporting Clinical Center. The Study Chair will also report each SAE, whether related to the treatment intervention or not, to all Clinical Center Directors, the NIDCD Project Officer, and the Chair of the Data and Safety Monitoring Board (DSMB) within one week of receipt.

It is expected that the DSMB Chair will review the case and advise the Study Chair and NIDCD whether further information or action is required , including whether 1) the available data should be reviewed at the next regularly scheduled DSMB meeting or 2) an *ad hoc* meeting should be called as soon as possible to review the SAE.

Each Clinical Center Director will also submit a letter to his/her local Institutional Review Board (IRB) or Ethics Committee, informing them of the SAE, if required by the Clinical Center's IRB or Ethics Committee.

### **15.2.2 Adverse Events**

In addition to SAEs, Clinical Center directors and staff also report all other adverse events by completing an Adverse Event Form. An Adverse Event Form is completed when at least one of the criteria below have been met.

- The event was unexpected, even if it is not an SAE.
- The adverse event was not listed as a risk in the informed consent and may have been caused by the study intervention, even if it is not an SAE.
- There is doubt as to whether to file a report with the IRB. It is better to file a report that may be unnecessary than to fail to file a required report.

The DCC and Study Chair will prepare a report of all non-serious adverse events as well as all intervening SAEs for review by the DSMB at its regularly scheduled meetings.

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## **Chapter 16** **Monitoring for Adherence to Protocol**

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### **16.1 Introduction**

Multi-center research studies require a variety of quality assurance procedures to insure compliance with the study protocol and collection and reporting of quality data. It is important that these procedures are incorporated into the design of the study. The quality assurance procedures of the TRTT are designed to assure data quality throughout the course of the study and to insure the validity and interpretability of results.

Specific quality assurance procedures include:

- Multi-center organization and committee structure (see Chapter 3);
- Standard protocol for all procedures and treatments as documented by a Manual of Procedures;

- Standard data collection forms;
- Standard eligibility and exclusion criteria (see Chapter 4);
- Standard treatment protocol (see Chapters 11, 12, and 13);
- Standard schedule for patient followup; (see Chapter 10)
- Central allocation of random treatment assignment (see Chapters 5 and 18);
- Guidelines for informed consent (see Chapter 25);
- Certification of Clinical Center personnel (see Chapter 17);
- Centralized data processing (see Chapter 22);
- Centralized evaluation of recorded treatment sessions;
- Quality Assurance Committee (QAC);
- Periodic performance reports; and
- Review of data by a Data and Safety Monitoring Board (DSMB).

Initially, TRTT instructional documents and materials will be prepared by the Data Coordinating Center (DCC) and the Chair's Office with input from the Clinical Centers. These will include:

- Manual of Procedures: A detailed description of the study design, organization, definitions, treatments, policies, clinic examination procedures, and certification procedures, with charts and tables for clarification;
- Data collection forms book: Collection of all TRTT data forms used in data collection;
- Visual aids (a flip-chart presentation) to be used during directive counseling (DC) and standard visual aids (models, brochures, etc.) to be used during the standard of care clinical consultation (SC)
- Videotapes demonstrating study procedures for DC, SC, and fitting of sound generators;

- Standardized handouts for Study Participants as part of either intervention; and
- Standardized patient consent statements.

## **16.2 Quality Assurance Committee**

The QAC has overall responsibility for monitoring the performance of all study centers in the TRTT. See Chapter 3 for a description of the membership and general function of QAC. This committee also reviews site visit reports and monitors all deviations from protocol.

The QAC is responsible for designing and implementing the procedures to be used for monitoring adherence to treatment protocol through review of voice recordings produced during counseling sessions.

## **16.3 Site Visits**

For any multi-center study such as the TRTT, it is necessary to assure that:

- There is standardization of all procedures, including patient examinations and treatment;
- Clinical Center personnel have been adequately trained to carry out these activities;
- There is adequate and continued adherence to the protocol; and
- The procedures performed are reasonably reproducible.

Periodic site visits by independent observers provide one effective way to achieve these goals.

### **16.3.1 Scheduling**

All TRTT Clinical Centers are visited at periodic intervals. The first round of visits will take place in the year recruitment has begun and will include performance monitoring and assessment of the overall operations of each Clinical Center, including recruitment, implementation of procedures, data collection, and follow-up. Additional goals may include in-person detailed training of Study Audiologists in performing DC and SC as well as study-specific methods for performing audiological measurements. There will be three site visits in succeeding years to

continue monitoring Clinical Center performance and trouble-shoot problem areas. Visiting teams will include individuals from the DCC, Chair's office and a member of the Quality Assurance Committee.

### **16.3.2 Preparation**

Before a site visit, the DCC is responsible for assembling an agenda of topics for discussion, facilities to be examined, and examinations to be performed. If necessary, a Site Visit Committee will be organized.

The Clinical Center staff prepares for the visit by having all study operations in place and study materials available. All TRTT staff must be available at some time during the course of the visit.

### **16.3.3 Conduct**

The site visit usually requires one working day. The goal is to review all aspects of Clinical Center operations.

### **16.3.4 Site Visit Reports**

Written reports by the visiting team will be submitted to the Steering Committee (STC) and a summary of the site visit given to DSMB. Concerns or problems regarding the stability of a Center and/or its capabilities of functioning properly in the study will be referred to the QAC for consideration and for a recommendation concerning corrective action. Further recommendation may be requested from the DSMB or the STC. Corrective action may include termination or replacement of a center. A copy of the site visit report and any recommendations of the QAC are sent to the Clinical Center Director and Clinical Coordinator of the Clinical Center visited.

## **16.4 Quarterly Telephone Calls**

Each quarter, a scheduled telephone call will be placed from the DCC to the Clinical Coordinator at each Clinical Center. The purpose of this telephone call is to assess Clinical Center performance and discussion of aspects and problems experienced by the Clinical Center in the conduct of the TRTT protocol between site visits. Topics covered are:

- Study Participant related issues;
- Clinical Coordinator problems;

- Status of study personnel;
- Recruitment;
- Protocol violations; and
- Study forms.

## **16.5 Monitoring of Protocol Within the Clinical Center by the Data Coordinating Center**

With the assistance of the Study Chair's Office, the DCC assesses adherence both to certification requirements for study personnel (see Chapter 17) and to study examinations and procedures. Clinical Centers in which uncertified personnel repeatedly administer TRTT functions are subject to corrective action by the STC.

### **16.5.1 Monitoring Incoming Data**

Data processing at the DCC proceeds in parallel with data collection at each Clinical Center in order to:

- Identify problems with design of data collection forms;
- Identify individuals who do not understand the protocol;
- Identify misunderstandings regarding form completion;
- Identify missing information and provide a timely opportunity to retrieve it;
- Identify questionable data for the Clinical Center staff to confirm or correct;
- Provide "clean" current data for analysis and reporting to the DSMB;
- Monitor adherence to TRTT procedures concerning eligibility criteria, randomization, treatment, certification, and patient follow-up; and

- Maintain an inventory of all information currently available for TRTT patients at any point in time.

Any problems identified through data processing are called to the attention of the appropriate personnel for handling, correction, and prevention of future recurrences.

### **16.5.2 Monitoring Administration of Treatment**

To maintain the validity of the TRTT, it is critical that adherence to protocol is strictly followed for the DC counseling and SC arms of the treatment. In the TRTT this adherence could be difficult because Study Audiologists are permitted to administer both types of treatment, DC and SC. In addition, there is a some slight overlap in the topics to be covered in the two types of treatments (e.g., recommendation for ambient low level noise) .

The TRTT will institute three procedures designed to facilitate compliance with the protocol by Study Audiologists.

- Study Audiologists will be required to use treatment-specific visual aids during the counseling session that is matched to DC or SC;
- Study Audiologists will complete a checklist during each DC and SC session, indicating topics covered or discussed in the session.
- Treatment sessions will be voice recorded. Files generated by voice recorders will be submitted to the DCC along with the checklist for review for compliance with the assigned treatment study protocol.

Recordings of the first two treatment sessions of each type of counseling for each Study Audiologist will be reviewed by the Training/Protocol Monitors for adherence to protocol. If no deficiencies are noted in these sessions, then one recording from among the next five counseling sessions will be randomly selected for review by the DCC. This pattern will continue for Study Audiologists who maintain adherence, i.e., one recording of every five treatment sessions will be reviewed as long as the Study Audiologist continues to adhere to protocol.

If, following review of the first recordings, the Study Audiologist is found not to adhere to the treatment protocol, deficiencies will be identified and discussed in a formal telephone conference call including the Training/Protocol Monitors, the Project Coordinator, and the Study Audiologist. The next two treatment sessions of that Study Audiologist will then be reviewed to ascertain adherence to protocol. If the treatment session still does not adhere to protocol, then the

Study Audiologist will be de-certified and not permitted to conduct treatment sessions for the TRTT until he or she has undergone in-person re-training with the Training/Protocol Monitor.

### **16.6 Protocol Deviations**

A violation of the TRTT protocol occurs whenever any procedure or event takes place that is contrary to that specified by the protocol. The operational provisions of the protocol are detailed in this Manual of Procedures. Examples of violations include treatment of a patient in any manner other than that assigned at the time of randomization, enrollment of ineligible patients, and inaccurate or incomplete baseline data.

Many violations are detected by the computerized data edit program at the DCC. However, the DCC investigators depend upon the Project Coordinator and the Clinical Coordinators to identify and document all non-protocol treatment events. The Project Coordinator is responsible for identifying and documenting those data edit messages that specify protocol violations. The Project Coordinator identifies all protocol deviations taking place within each Clinical Center on a monthly basis and sends a report to the Clinical Coordinator with suggestions to avoid similar protocol deviations in the future.

Protocol deviations are documented in a data file maintained at the DCC. They are reported to the STC and to the DSMB.

### **16.7 Monitoring Reports**

At each of the meetings of the STC, Full Investigative Group (FIG), DSMB, and QAC, the DCC prepares information related to performance of individual Clinical Centers. Reports consist of information on adherence to the TRTT protocol, completeness and quality of data and materials submitted to the DCC, and findings from site visits to the Clinical Centers or other communications with them. These reports are important not only for study administration but also for providing feedback to the collaborating Clinical Centers. The QAC uses these reports to target Clinical Centers where special training or assistance is required.

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## Chapter 17

### Certification Procedures

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#### **17.1 Introduction**

The purpose of the certification requirements in the TRTT is to assure that, to the extent possible in a multicenter study, procedures are being performed in the same way and in accord with the study protocol in all Clinical Centers in which similar activities are carried out. The certification program is supervised by the Quality Assurance Committee (QAC). The Training/Protocol Monitors are responsible for training and certification for all clinical activities, and are located at the Study Chair's Office. The Project Coordinator, located in the Data Coordinating Center, works closely with the Training/Protocol Monitors and is responsible for training and certification related to data collection and study conduct for the TRTT. All materials and documents are submitted to this individual who monitors the status of certifications in progress, issues certification numbers, forwards certification documents to the appropriate central units or committee chairpersons for approval, and reports to the QAC any problems or deviations from established procedures.

#### **17.2 Personnel Certification**

##### **17.2.1 Positions Requiring Certification**

TRTT certification is required for each of the following study roles:

- Clinical Coordinator;
- Data System Operator;

- Study Otolaryngologist; and
- Study Audiologist.

Two Study Audiologists at each Clinical Center will be required to allow one to conduct the counseling session (directive counseling (DC) or standard of care clinical consultation (SC)) for a particular Study Participant while the other will remain blinded to that participant's treatment assignment.

### **17.2.2 Procedures for Personnel Certification**

Staff at all Clinical Centers, the Study Chair's Office, and Data Coordinating Center (DCC) are required to undergo a certification process before patient recruitment can begin. The certification process includes:

- Completion of a form by each Clinical Center detailing a variety of characteristics of the Clinical Center related to space, staffing, equipment, etc;
- Review and approval of the consent process proposed, including the proposed consent statement (review to be done by the DCC in conjunction with the Data and Safety Monitoring Board (DSMB)) and associated HIPAA statement;
- Fully executed Cooperative Research and Development Agreement (CRADA) among the Clinical Center, University of Alabama, and the Johns Hopkins University; and
- Review and understanding of the TRTT protocol and study procedures.

Personnel at each site involved in data collection, including the Study Otolaryngologist, Study Audiologists, Data System Operator and Clinical Coordinator, are required to undergo a certification process that includes passing an online knowledge assessment test on TRTT procedures, and participation in appropriate training sessions conducted by the DCC and Chair's Office. A Clinical Center will not be cleared to recruit patients until all necessary personnel have been trained and certified. All new personnel recruited after the initial training session will receive training from certified staff at a TRTT center as part of their initial certification process, but may require more extensive training by the DCC or Study Chair's Office staff.

Data collection personnel (i.e., Study Audiologists, and Clinical Coordinators) may be required to undergo re-certification periodically. The re-certification process involves tests

aimed at assessing knowledge of TRTT procedures, as well as demonstrations of skills required for execution of specified duties and responsibilities.

The DCC is responsible for implementation and maintenance of certification procedures. All certification documentation, including that prepared by the Training/Protocol Monitors, is submitted to the Project Coordinator, who is responsible for recommending certification. Materials are reviewed by the DCC staff. The designated reviewer recommends certification if satisfied with the quality of materials submitted. After satisfactory completion of all requirements, a certification number is issued by the Project Coordinator. This number is used to identify the study personnel on all forms submitted from the Clinical Center.

At each Clinical Center, two Study Audiologists, a Study Otolaryngologist, a Data System Operator, and a Clinical Coordinator must be certified for that Center to enroll, treat, enter Clinical Center data, and follow TRTT patients. The Clinical Center Director may take responsibility for filling any of these positions. A single individual may fill more than one position if qualified for two or more roles, except that two individuals must be certified as Study Audiologists. Additional Study Otolaryngologists or Audiologists may be certified for the convenience or need of a Clinical Center. Any problems with meeting certification requirements are resolved by the DCC investigators in consultation with the Center Director and the candidate.

### **17.2.3 Clinical Coordinator**

The Clinical Coordinator is a key member of the research team in each Clinical Center. This individual must not only be knowledgeable concerning the duties specifically assigned to the Clinical Coordinator, but also must function as the local TRTT expert for other Clinical Center staff. This individual plays an important role in assuring the quality and integrity of the data provided by the local Clinical Center.

The requirements for certification as a TRTT Clinical Coordinator are to:

- Attend a TRTT training session conducted centrally, concerning:
  - TRTT design and methods;
  - Clinical Center management for the study;
  - Study Participant enrollment and randomization;
  - Study Participant care and follow-up;
  - Audiological/tinnitus/hyperacusis (ATH) evaluation measurements; and
  - Data collection instrument completions.
- Read the TRTT Manual of Procedures;

- Review the TRTT data collection forms;
- Work with each member of the TRTT Clinical Center staff in completing two sets of Baseline Eligibility Visit and Randomization Visit data collection forms and other required material for Study Participants;
- Work with each member of the TRTT Clinical Center staff in completing requests for certification;
- Complete an online TRTT Knowledge Assessment test; and
- Complete and submit a Personnel Request for Certification form.

#### **17.2.4 Study Audiologist**

At least two Study Audiologists must be certified for each TRTT Clinical Center. One of these may serve as Clinical Center Director, Study Otolaryngologist, or as the Clinical Coordinator. The requirements for TRTT certification as Study Audiologists are to:

- Attend a TRTT training session concerning:
  - TRTT design and methods;
  - Study Participant recruitment;
  - Study Participant enrollment and randomization;
  - Study Participant education and informed consent;
  - Study Participant care and follow-up;
  - Clinical Center management;
  - Forms completion; and
  - ATH evaluation protocol.
- Read the TRTT Manual of Procedures;
- Review TRTT data collection forms;
- Have completed at least one year of clinical experience (post-clinical fellowship year) as an audiologist;
- Attend a TRT training session, comprised of training in directive counseling (DC) and use of sound therapy;

- Attend a training meeting on components comprising standard of care treatment (SC) from the SC Training/Protocol Monitor;
- Review the directive counseling DC technique videotape;
- Review the SC technique videotape;
- Review the sound generator (SG) fitting technique videotape;
- Submit one voice recording of a DC counseling session with a non-study (or dummy) patient;
- Submit one voice recording of an SC session with a non-study (or dummy) patient;
- Work with other TRTT personnel to complete two sets of Baseline Eligibility Visit and Randomization Visit data collection forms and materials for non-study patients;
- Complete an online TRTT Knowledge Assessment test; and
- Complete and submit a Personnel Request for Certification form.

### **17.2.5 Study Otolaryngologist**

At least one Study Otolaryngologist must be certified for each TRTT Clinical Center. The requirements for TRTT certification as Study Otolaryngologist are to:

- Read the TRTT Manual of Operations;
- Review TRTT data collection forms;
- Submit two TRTT baseline medical examination data collection forms;
- Complete an online TRTT Knowledge Assessment test; and
- Complete and submit a Personnel Request for Certification form.

### **17.2.6 Data System Operator Certification**

At least one person must be certified as a Data System Operator. The requirements for certification as a TRTT Data System Operator are to:

- Read the TRTT Manual of Procedures;
- Establish a working knowledge of the TRTT data collection forms;
- Data enter dummy TRTT data collection forms provided by the DCC;
- Complete an online TRTT Knowledge Assessment test; and
- To complete and submit a Personnel Request for Certification form.

### **17.3 Clinical Center Certification**

Certification of Clinical Centers in the TRTT is required to be permitted to enroll, treat, or follow Study Participants. The purpose of certification is to document that the Clinical Center has:

- The required TRTT certified personnel;
- The required Manual of Procedures, study forms, and other materials for performing TRTT procedures;
- Received approval from local officials to participate in the TRTT
- Received approval from the local Institutional Review Board of the informed consent procedures and protocol;
- Completed execution of a Cooperative Research and Development Agreement (CRADA) among the Clinical Center, University of Alabama, and the Johns Hopkins University;
- Contacted all referral sources to notify them of the TRTT and to request assistance in referring and enrolling eligible Study Participants; and
- The required facilities and equipment to conduct TRTT procedures.

To be certified as a TRTT Clinical Center, the following requirements must complete a Request for Clinical Center Certification Form. This form documents that the following criteria have been met:

- Certified TRTT personnel with individuals certified for each of the following positions:
  - Clinical Coordinator;
  - Data System Operator;
  - Study Otolaryngologist; and
  - Two Study Audiologists.
- Affiliated with clinical or medical centers having facilities and equipment for hospitalization and laboratory work;
- Facilities for audiological measurement according to TRTT procedures;
- Local approval of participation in the TRTT; and
- Approval of the TRTT informed consent procedures by the local Institutional Review Board filed with the Data Coordinating Center.

Immediately following completion of these requirements, each Clinical Center is provisionally certified. Provisional certification allows the Clinical Center to begin screening individuals for the TRTT. The Clinical Center is also permitted to begin enrollment of Study Participants. To obtain final certification, the Clinical Center is required to submit paper copies of all data collection forms completed for the first Study Participant randomized at that center. These forms will be audited, with the data on the paper forms compared with that entered into the TRTT online database. Following a successful audit the Clinical Center will obtain final full certification.

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## Chapter 18

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## **18.1 Introduction**

The Clinical Centers serve a vital role in the Tinnitus Retraining Therapy Trial (TRTT). Clinical Centers serve as the sites for participant recruitment, treatment, follow-up, and concomitant data collection for the TRTT. Each Clinical Center will have the requisite staff, equipment, and patient caseload necessary to accomplish these critical activities. It is anticipated that each Clinical Center will begin active participation by Year 02 when all necessary administrative and clinical preparations and training at the site have been completed.

## **18.2 Responsibilities of the Clinical Center**

Responsibilities of a participating TTRT Clinical Center include:

- Attending all requisite sessions conducted by the Chair's Office and Data Coordinating Center (DCC) and its staff for training, quality assurance, certification, and re-certification purposes;
- Following all certification and re-certification procedures to ensure the quality of all study activities;
- Providing appropriate representation at meetings of the Full Investigative Group (FIG);
- Allocating the requisite clinical space and equipment necessary to complete the diagnostic and treatment procedures included in the TRTT;
- Maintaining and calibrating all equipment in accordance with TRTT or manufacturer's standards;
- Maintaining adequate quantities of appropriate supplies required for the TRTT;
- Providing an easily accessible location for secure, confidential maintenance of Study Participant records;
- Determining eligibility of potential Study Participants for the TRTT and maintaining a record of all individuals screened for participation, which will include the outcome of screening and where appropriate, the reason for those deemed ineligible for participation;
- Recruiting approximately 10 Study Participants per year over the period of the study;

- Monitoring and fulfilling target goals for recruitment of women and minorities;
- Conducting Study Participant education and consent process;
- Obtaining random treatment assignments from the Coordinating Center for eligible, consenting individuals and ensuring adherence to those assignments;
- Maintaining complete current residency, employment, and general health information for each Study Participant for the duration of the TRTT;
- Examining each Study Participant enrolled in the TRTT according to the established schedule;
- Obtaining the requisite audiometric and other data at each designated evaluation period and completing the appropriate study and data collection forms;
- Conducting evaluation and fitting of tinnitus sound therapy devices (sound generators (SGs) as indicated by protocol;
- Evaluating the performance of SGs;
- Obtaining replacement SGs in the case of malfunction or damage;
- Following the assigned treatment protocol for each Study Participant and completing the appropriate data collection forms;
- Verifying completeness of all forms and completing online data entry in the TRTT database maintained by the DCC within the designated time period;
- Responding promptly to requests from the DCC.

### **18.3 Required Equipment and Materials**

To conduct the appropriate diagnostic, fitting, and follow-up evaluations required in the TRTT, each Clinical Center must have the following equipment and materials:

- A diagnostic audiometer;

- Immittance/impedance equipment meeting ANSI standards
- Visual aids for directive counseling (DC) and standard of care (SC) treatment sessions;
- Computer for data logging of sound generators;
- Computer with internet access for data entry; and
- Equipment for voice recording each counseling session.

## **18.4 Personnel**

### **18.4.1 Clinical Center Director**

#### **18.4.1.1 Qualifications**

The Clinical Center Director (Clinical Center Principal Investigator) will oversee the management of all administrative, clinical, and research aspects of the TRTT at the Clinical Center. The Director must have a thorough understanding of the TRTT and the scientific implications of adherence to the research protocol.

#### **18.4.1.2 Responsibilities**

The Clinical Center Director's responsibilities will include executive decision making regarding hiring, purchasing of equipment, allocation of Clinical Center personnel and resources, authorizing staff travel for TRTT meetings, and monitoring the integrity of the TRTT within his or her Center. The Clinical Center Director will be responsible to the Study Chair and will maintain direct communication with the DCC. He or she will attend all TRTT FIG meetings. The Clinical Center Director may hold any study position, but typically will be either a study-certified Study Audiologist or Study Otolaryngologist. The Clinical Center director will work with the other members of the Clinical Center to facilitate Study Participant recruitment and follow-up throughout the TRTT. The Clinical Center director is also responsible for ensuring that all adverse events are reported promptly to the Study Chair and DCC.

### **18.4.2 Clinical Research Coordinator**

#### **18.4.2.1 Qualifications**

The Clinical Coordinator must have a thorough understanding of the audiological, clinical and research implications of the TRTT. In addition to organizational skills, the Clinical Coordinator must have excellent interpersonal skills so as to maintain each Study Participant's cooperation and participation in the trial. The Clinical Coordinator may also serve in any study role, but typically as a Study Audiologist and/or a Data Systems Operator.

#### **18.4.2.2 Responsibilities**

The Clinical Coordinator, together with the Clinical Center Director, is responsible for ensuring that the Clinical Center is ready for participation in the TRTT. Specific duties of the Clinical Coordinator related to preparation and ongoing maintenance of Clinical Center activities include:

- Attending scheduled TRTT training sessions;
- Ensuring all Study Audiologists have the requisite training and competence necessary for the provision of DC and sound therapy in accordance with the trial protocol;
- Ensuring all Study Audiologists have the requisite training in SC treatment to ensure uniform administration across all Clinical Centers;
- Serving as a resource for other study personnel regarding the details of the TRTT protocol;
- Initiating and maintaining all required communications with the relevant institutional review board concerning the TRTT protocol implementation at the Clinical Center and documentation for informed consent and HIPAA;
- Monitoring levels of supplies to guard against shortages during the data collection process; and
- Maintaining all Clinical Center communication including correspondence, e-mail, and telephone inquiries regarding the TRTT.

Responsibilities of the Clinical Coordinator include tasks related to participant interactions, include:

- Implementing methods for recruitment of appropriate Study Participants;
- Verifying each participant's eligibility for participation in the trial;
- Ensuring that sufficient numbers of Study Participants are being recruited;
- Maintaining documentation related to Study Participants, including:
  - appointment notebooks with each participant's follow-up schedule; and
  - log book with Study Participant ID numbers, and namecode;
- Conducting the necessary Study Participant education and obtaining informed consent from Study Participants;
- Coordinating the treatment modules for Study Participants following their randomized assignments;
- Overseeing administration of self-report measures upon enrollment in the trial;
- Sending Study Participants appointment reminders with date and time noted;
- Updating each participant's records with change of address, employment site and other relevant contact information;
- Contacting Study Participants to maintain their interest in the trial between scheduled visits, thereby demonstrating the investigator's ongoing concern for the Study Participant;
- Communicating with Study Participants who have missed scheduled visits to encourage them to complete the remainder of their follow-up appointments.

The Clinical Coordinator also provides the primary interface between the Clinical Center and the DCC. In this capacity, the Clinical Coordinator is responsible for;

- Attending annual meetings of the TRTT FIG;

- Maintaining all study documents, including updates to the Manual of Procedures as provided by the Coordinating Center;
- Updating the TRTT website regarding personnel changes affecting conduct of the trial;
- Communicating with the DCC regarding problems with data quality, recruitment progress, and attrition rates;
- Serving as a resource for other study personnel regarding the details of updates or changes to the protocol, and as directed by the DCC; and
- Monitoring evaluations, treatment, and follow-up procedures to ensure compliance with the protocol for quality assurance purposes.

#### **18.4.2.3    Interactions with the Data Coordinating Center**

To assist Clinical Coordinators in integrating the TRTT protocol into their Clinical Center routine, the DCC has scheduled a training session for the Clinical Centers in conjunction with the FIG meeting. At this time, DCC staff shall provide each Clinical Coordinator with a copy of the TRTT Manual of Procedures and the TRTT Data System Manual.

The Clinical Coordinator should set up two loose-leaf binders at the beginning of the study: one for the Manual of Procedures and one for the Log Book. The log book is a permanent record containing the signed Informed Consent Forms and the Patient Locator Forms for each Study Participant. Since this book contains the only identifying information for each Study Participant, a duplicate log book is to be kept in another location, preferably in another building. The duplicate log book should be updated each time a new participant is entered into the study and should be reviewed for completeness at least monthly.

Study data collection forms and instruments are developed by the DCC with assistance from the Chair's office and will be downloadable from the TRTT website (<http://www.TRTT.org>). Data collection forms will be grouped by study visit in the TRTT website and can be printed immediately before each study visit. Individual forms may also be printed.

If there is a change in study protocol, or when a study form has been revised, the DCC will issue a Policy and Procedure Memorandum (PPM). The PPM will become part of the Manual of Procedures and should be included in the looseleaf binder with the Manual of Procedures. The DCC will also update the TRTT website with the revised data collection form. The Clinical

Coordinator is responsible for determining that the new version of the data collection form is used on all subsequent study visits. Under no circumstances should outdated forms be used. The Clinical Coordinator is responsible for explaining to other Clinical Center staff any changes in procedures that are described in the PPM or that are required by form revisions.

### **18.4.3 Study Audiologists**

#### **18.4.3.1 Qualifications**

Study Audiologists participating in the TRTT are American Speech-Language Hearing Association or American Academy of Audiology certified audiologists with a demonstrated interest in clinical research activities. Each Study Audiologist must be proficient in audiological assessment and management procedures, assessment of loudness discomfort levels, matching of tinnitus pitch and loudness, and otoacoustic emissions and acoustic immittance measurement.

#### **18.4.3.2 Responsibilities**

Responsibilities of the Study Audiologists include:

- Completing the requisite clinician training for the TRTT;
- Attending DC and SC training sessions for the TRTT;
- Facilitating recruitment of Study Participants through grand rounds or in-service presentations about the TRTT to local area referring physicians or audiologists;
- Completing audiological/tinnitus/hyperacusis (ATH) evaluations for Study Participants;
- Conducting DC and SC sessions;
- Fitting and checking of SGs;
- Conducting ST across the various arms of the trial as assigned by randomized treatment assignment;
- Conducting necessary measurement and duties at treatment follow-up visits at the Clinical Center; and

- Completing the necessary study forms for each Study Participant, examining the forms for accuracy and completeness, and giving them to the Clinical Coordinator for data entry in a timely fashion.

#### **18.4.4 Data System Operator**

##### **18.4.1.1 Qualifications**

The Data System Operator must be certified and have a thorough knowledge of the TRTT protocol, data forms, and the web-based data entry system.

##### **18.4.1.2 Responsibilities**

The Data System Operator is responsible for timely and accurate data entry of all required forms, including audiometric testing forms, into the online TRTT study database, including data entry and data edits (see Section 18.5). Responsibilities include to:

- Complete training in the web-based data system;
- Transmit evaluation and treatment data to the DCC upon verification of validity and completeness;
- Work with other member of the Clinical Center to facilitate data flow to the DCC; and
- Respond in a timely manner to data queries received from the DCC.

#### **18.4.5 Study Otolaryngologists**

##### **18.4.5.1 Qualifications**

Participating physicians are Attending Otolaryngologists at each Clinical Center. Study Otolaryngologists must be certified and agree to refer Study Participants to the TRTT and to facilitate recruitment of Study Participants from local area military physicians.

##### **18.4.5.2 Responsibilities**

Study Otolaryngologists will have the following responsibilities in the TRTT:

- Refer ear, nose and throat patients who report tinnitus to the Clinical Coordinator for determination of eligibility for participation in the TRTT;
- Facilitate recruitment of Study Participants;
- Complete physical examinations, and order and evaluate laboratory, imaging, or other tests on potentially eligible Study Participants, ruling out medical conditions that would compromise the potential Study Participant's eligibility for the trial;
- Complete data collection forms documenting the physical examination, laboratory and other tests, and eligibility of Study Participants to the TRTT; and
- Consult with the Clinical Coordinator on cases that may require medical evaluation or intervention.

## **18.5 Data Management**

### **18.5.1 Data Collection Forms**

Data collection forms containing information on a participant's identification are not sent to the Coordinating Center. These include the Patient Locator Form, Informed Consent Form, and HIPAA forms, which are photocopied for the duplicate log book and then carefully filed in the original log book.

All information recorded on study data collection forms is entered into the web-based TRTT study database; paper data collection forms are not usually transmitted to the DCC but should be retained with the Study Participants file for review at site visits or for verification of data queries. Information obtained during audiometric testing is also entered into the TRTT database. Exceptions are data collection forms completed during baseline and randomization of the first Study participant enrolled, which are sent to complete certification requirements, or forms requested by the DCC for routine audits.

In general, data collection forms should be entered into the online TRTT database within one week of completing the Study Visit. The only exceptions are at the Baseline Eligibility visit - the Eligibility Screening Form, the Tinnitus Questionnaire and the Eligibility Checklist must be entered immediately before requesting a randomized treatment assignment. In addition, an adverse event (if serious) must be filed within 2 days using the Adverse Event Form. A tracking system, available on the TRTT database, will show which data collection forms have been entered and which are still outstanding.

### **18.5.2 Data Entry of Forms**

Before the data forms are entered, each form should be carefully checked by the Clinical Coordinator, especially if completed by someone other than the Clinical Coordinator. This process is extremely important, because correcting errors that have entered the data system is far more time-consuming and expensive than taking the appropriate steps to prevent errors. Forms completed by the Study Participant should be checked for missing responses at the time of completion. Self-report forms completed by the Study Participant with missing responses cannot be corrected at a later date. Every answer on the form is to be checked for each of the following criteria:

- Completeness: If any required item is unanswered or has a question mark for an answer, the form "fails edit." If there is doubt about how an item is to be answered, the DCC should be contacted, by telephone if necessary. Each form is extensively edited by computer as it is being entered, and the cost of correcting any errors at a later date is almost certain to exceed the cost of a telephone call;
- Consistency: If so noted, some questions should be answered only for certain Study Participants. If the question does not apply, it should be left blank; the TRTT database will be programmed to skip items that do not apply.
- Legibility: Write-in responses should be printed so that they are clearly legible, so that the person completing data entry can determine the appropriate response.

In order to enter data in the TRTT web-based database, the Data System Operator will be required to log in with a username and password, and access the relevant screen by entering the Study Participant ID, namecode, and visit. The Data System Operator will then choose from the list of data collection forms associated with the relevant visit. Following successful data entry for a particular form, a reference, or confirmation, number will be given that can be used to re-access that particular form in the future.

### **18.5.3 Data Edits and Corrections**

The data recorded on the study visit forms are entered directly into the online TRTT database. During data entry, real-time validation performs formatting and ranged checks on the currently active field. Errors during data entry are displayed using a pop-up box and may include invalid formatting of dates, text, or numbers, and also responses that fall outside of a predetermined range. Other types of errors include validation checks (e.g., illogical responses) and are

displayed upon submitting the form. These types of checks include skip pattern violations, skipping key items, and/or providing other unreasonable responses.

Most forms will require double data entry (two “passes”). A warning or error is displayed when the entries are not the same between the two passes. When the Data System Operator receives an error display, she or he should review the Study Participant's records and determine the correct answer for each item listed. It may be necessary to consult with the Clinical Coordinator, Study Otolaryngologist or Audiologist who examined the Study Participant for specific medical or audiological information.

On occasion, Clinical Center personnel may discover errors on forms in addition to those detected by the computer edit or may need to update data. When this occurs, previously entered data may be modified by editing or replacing an existing form using the TRTT online data system. Error correction using the TRTT database is made by using the original reference number (received at original data entry submission) to bring up original form to be corrected. The original paper data collection form should also be corrected. When making corrections, clinic staff should never obliterate the original response. A single line should be drawn through the incorrect response and the corrected response should be recorded beside it, above it, or below it. Both the incorrect and correct responses should be clearly legible. The individual recording the correction should initial and date it. It is important that an "audit trail" be present in case there are questions about the accuracy or integrity of data reported by the study or from an individual clinic.

Should any questions arise regarding the completion of an edit message or a suspected reporting error, a phone call to the Coordinating Center is strongly encouraged.

## **18.6 Study Participant Interactions**

### **18.6.1 Personal Interactions**

One of the most important duties of the Clinical Coordinator is generating and maintaining good rapport with all Study Participants and assuring that each enrolled participant remains in the trial. The Clinical Coordinator fosters the attitude that the Study Participant is a critical member of the trial team. This may be accomplished by taking time to ensure that all Study Visits are positive experiences for the Study Participant and through regular contact by telephone calls between regularly scheduled visits. Finally, Study Participants shall be informed of study results by personal letter as they are published.

### **18.6.2 Scheduling and Coordination of Study Visits**

The Clinical Coordinator should be thoroughly familiar with the materials pertaining to missed visits, telephone contacts to be made between visits, and procedures to be followed for inactive or transfer participants. (See Chapter 10 for details of these procedures). The participant's study Appointment Schedule is generated online by the DCC shortly after a treatment assignment for the Study Participant has been issued and the Initial Treatment Visit (T1) completed. The appointment schedule is also posted on the TRTT website. The clinical coordinator should print out the Appointment Schedule for each Study Participant as it becomes available. This schedule is to be consulted whenever the Study Participant is given an appointment for a follow-up visit. It is especially important to refer to the Appointment Schedule when an appointment date is changed. Ideally, an appointment should be scheduled as closely as possible to the expected appointment date. This procedure allows time for rescheduling broken appointments within the permissible time limits for the examination, thereby decreasing the number of missed visits. If a visit is completed near the end of a time window, an attempt should be made to get back on schedule by making the next appointment as close as possible to the target date. The date each visit is actually completed should be written on the Appointment Schedule in the appropriate place. A copy of the Appointment Schedule should be kept in the Study Participant's clinic chart.

The following steps should be taken before the Study Participant appears for a scheduled visit:

- Remind the Study Participant of the scheduled appointment by telephone or mail in advance of the date;
- Retrieve the Study Participant's medical file;
- Complete Section A on the first page and place the Study Participant's ID number on all subsequent pages of the forms pertinent to the scheduled visit;
- If necessary for that particular visit, schedule appointments for audiology; and
- Put the Patient Locator Form in the folder as a reminder to review and update the information.

### **18.6.2 Updating the Study Participant's Medical File**

The following steps should be taken to keep the Study Participant's medical file as complete and up-to-date as possible:

- The personal information on the Study Participant, such as telephone numbers, place of employment, persons who can be contacted about his or her whereabouts, etc., should be updated at least annually. Contacts already listed should be confirmed;
- If necessary, have the proper releases signed by the Study Participant to perform treatment or tests, or to obtain medical records from other hospitals or physicians. Continue to contact these hospitals or physicians until all required information has been received; and
- Be sure to have copies of those forms and other information which were transmitted to the DCC in the Study Participant's file.

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## Chapter 19

### Data Coordinating Center Operations and Procedures

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#### **19.1      Introduction**

The Data Coordinating Center (DCC) in a multi-center trial performs essential functions from the earliest design stages to the final closeout, analysis and publication of results. This chapter describes those functions as related to the Tinnitus Retraining Treatment Trial (TRTT) and that

range from providing scientific leadership and creativity to providing detailed administrative and data management services.

In its daily work, the DCC has responsibility for fostering collegiality, cohesion, and cooperation among the investigators of the trial, including the committees, Clinical Centers, resource centers, and sponsoring agency.

The general duties and functions of the DCC are to:

- Serve as a collaborating partner with the other investigators in the organization, design, execution, and analysis of the trial;
- Provide biostatistical and epidemiologic expertise to the trial regarding the design and operation of the trial;
- Provide expertise in the area of data processing and biostatistics;
- Develop study forms, documents, and protocols and serve as a repository for trial documents;
- Develop and implement all data processing procedures;
- Develop, implement, and maintain quality control procedures for the detection and correction of any deficiencies in data collection, processing, and analyses;
- Function as the study communications center; and
- Prepare progress reports and assist with the preparation of publications.

## **19.2 Organization and Staffing**

The TRTT DCC is located at the Center for Clinical Trials at the Johns Hopkins Bloomberg School of Public Health (CCT). The DCC Director is represented on the TRTT Executive Committee (EC), Steering Committee (STC), and Data and Safety Monitoring Board (DSMB).

Staffing of the DCC varies with time and the demands of each phase of activity. From its inception, the TRTT DCC staff will be headed by a Director. A Biostatistician and Director of Information Management with expertise in clinical trials will serve part-time. A Co-Investigator with experience in interpretation of psychometric instruments will also serve part-time. A Project Coordinator, Database Programmer, Statistical Programmer, and Research Assistant

devote greater percentages of time to the TRTT. Office management, administrative, and clerical services are supported as needed.

Specific responsibilities for the individual DCC staff members are listed below.

**Principal Investigator.** She will be responsible, along with the Study Chair, for the overall scientific direction of the trial. She will work with other senior personnel in directing the scientific and administrative activities of the DCC. She will provide expertise in coordinating the preparation and planning of the protocol and the Manual of Procedures, developing certification and training programs, and designing and implementing quality control mechanisms for this study. She will be a member of the EC, STC, and DSMB, and will chair the Quality Assurance Committee (QAC). She will also be a member of the Coordinating Center Data Analysis Committee.

**Study Biostatistician.** The Study Biostatistician has overall responsibility for the statistical analysis of all study data. As such, he will be actively involved in decision making early on in the study with regard to study outcomes, recruitment progress, and statistical considerations, as well as selection and possible modification of analysis methods. The Biostatistician will have primary responsibility for statistical analyses of the study outcomes, as well as analyses related to quality control and assurance.

**Director of Information Management.** The Director of Information Management will be responsible for the study information system design and for supervision of system development and maintenance. He will implement and maintain the data system including data acquisition, data editing procedures, all data integrity safeguards including passwords, rights, and data views, and creating and maintaining transaction logs which enable error recovery. Together with the Database Programmers, he will be responsible for recommending, configuring, and testing hardware and software and consults on matters of networking and interfacing computer systems within the DCC sites. He will also be responsible for implementing the TRTT website, including the programming interface to allow online data forms completion by Study Participants and Clinical Center staff.

**Co-Investigator.** The Co-Investigator will be responsible for the acquisition of copyrighted psychometric forms that must be purchased. She will also be responsible for training investigators in the proper use of the psychometric instruments and for interpretation of results related to psychological testing. The Co-Investigator will also assist with the tinnitus health-related quality of life instrument interpretation.

Statistical Programmer. She or he will work with the Study Biostatistician and will execute all data analyses of this trial and assist the Project Coordinator in data monitoring and reporting. She or he will be a member of the Coordinating Center Data Analysis Committee.

Project Coordinator. She will coordinate and supervise the day-to-day management activities related to the trial. Her responsibilities include: preparation of study protocols, instructional documents, monitoring quality of data collected, overseeing preparation of initial reports, certification of study personnel, and preparation of data analyses and paper writing activities. She will also be responsible for monitoring the web-based randomization and treatment allocations for eligible Study Participants to Clinical Center staff.

Research Assistant: S/he will assist the database programmer to perform the duties of data cleaning, dataset compiling, database updating and implementation of data security procedures for the dataset. In addition, s/he will assist with inventory all data collection forms, code, edits, and log in the forms into the database. She will also assist the Project Coordinator to coordinate, schedule and maintain quality checks on study treatment sessions and in preparation of materials, including graphs and tables, for DSMB and other Committee meetings and for final publications.

Administrative Assistant. S/he will provide secretarial and clerical support for the professional staff at the DCC. S/he will be responsible for the typing, reproducing, and mailing of all material for the study, including correspondence, master copies of study documents, reports, minutes, manuscripts, requisitions, etc. S/he will also be responsible for making travel arrangements for DCC personnel.

### **19.3 Responsibilities of the Data Coordinating Center**

Responsibilities of the DCC begin with support of the design phase of the study and include:

- Preparation and distribution of TRTT trial documents and support materials;
- Design of the data system and associated forms for the collection of study data;
- Training and certification of staff;
- Development of randomization procedures;
- Data entry, management, and analysis;
- Generation of data and safety monitoring reports;
- Production of all analyses required for publication;

- Participation in the preparation and review of papers for publication; and
- Preparation of funding applications.

### **19.3.1 Study Design**

Although study design was formulated prior to grant approval and the initiation of funding, refinement of that design to address newly surfaced questions is required as the project enters its post-funding planning phase. The DCC provides epidemiologic and biostatistical support during this process, helping the STC address issues as they arise. The DCC is responsible for assessing whether proposed changes can be successfully implemented and what will be their impact on data analysis. The TRTT design and data collection requirements are complex. The TRTT is designed as a three-arm trial, stratified by Clinical Center. Steps in the treatment process require standardized monitoring for follow-up. The TRTT design, treatment, and data collection, described in previous chapters of this Manual, reflect that complexity and dedication to responsible patient care and research.

### **19.3.2 Development of Protocols**

In the planning phase of the trial, the DCC devotes much of its time and effort to refine the protocols to meet the needs of the TRTT study design. Rules and guidelines for the operation of the study organization, recruitment and training of staff, equipping and supplying of each Clinical Center, examination schedules, conduct of clinical examinations, and data collection activities must also be refined. Measures for quality control shall be formulated. These protocols shall be drafted by the DCC staff, given preliminary review by the Study Chair, and then given final review by the TRTT STC.

Policy and procedure changes are issued in numbered memoranda and revisions to the Manual of Procedures, data forms, and standard procedure documents as required. Revisions are issued only when absolutely necessary.

In addition to study protocol, the DCC is responsible for designing the protocol for quality assurance, as described in Chapters 16 and 17.

### **19.3.3 Forms Design**

Development of TRTT data collection forms runs parallel to the development of the TRTT procedures and protocol design. The creation of a form is given considerable time and effort because reliable data collection is heavily dependent on the quality of the associated forms. The TRTT will use a web-based data system, requiring clear easy-to-use data collection forms and web screens.

All TRTT patient forms are designed to include the following:

- Identifying information coded to protect the confidentiality of the Study Participant's name;
- Data collection items ordered on the form according to the order of procedures as they occur during the clinic visit;
- Instructional prompts for activities to be performed during the data entry process or the study visit; and
- Documentation indicating who performed each procedure and when the procedure was performed.

There are TRTT forms to support the following activities: training and certification of personnel and clinics; recruitment and randomization activities; scheduling of appointments; collection of data for the Baseline Eligibility, Randomization, Treatment, and Follow-up Visits that document the timing and circumstances for each step the Study Participant takes along the treatment protocol and the results of such procedures as audiological testing, directive counseling (DC), sound generator (SG) fitting, standard of care treatment session (SC), recording locator information, or data editing.

Study forms will be designed according to specifications developed by the STC and constructed by the DCC. As forms are web-based, it will be easy to modify forms in the event that changes may be required during the study. Completed forms prototypes will be printed and submitted in turn for approval by the Director of the DCC, the Study Chair's Office, and finally the STC. After each form is approved, it will be tested by local audiologists. After required corrections and approval, the study forms will be uploaded on the TRTT website at the DCC for access by the Clinical Centers.

#### **19.3.4 Preparation, Distribution and Archival of TRTT Documents and Support Materials**

The DCC has full responsibility for organizing its work on the study design, procedures, and forms into what become the main documents of the study. This includes ongoing revisions and updates and the reliable dissemination of such modifications to all appropriate personnel. Periodically, certain study documents, such as this Manual, shall be reviewed, updated, and reissued in total. The DCC is responsible for the final copy of all official study documents with the exception of communications forms. Current versions of all study documents, including data collection forms, will be available for printing following download from the TRTT website.

The DCC is the official study archive. Originals of the data forms, and copies of all correspondence, meeting materials, and study documents will be kept by the DCC for inclusion in their file systems which will be organized chronologically and also by subject.

#### **19.3.4.1 General Principles**

Each TRTT document prepared by the DCC should serve a valuable function, be written as clearly and as succinctly as possible, and be tested and evaluated by study leaders and those staff who will use it on a daily basis. Each document is updated as needed, distributed to all personnel or made available online to whom it might prove specifically useful or generally educational. Documents shall be retired when no longer of value.

#### **19.3.4.2 Design Summary**

Prepared as a brief description of the TRTT trial, the Design Summary shall state the study objectives, major design features including inclusion and exclusion criteria, treatment alternatives, the participating Centers, and the study timetable. The Design Summary, provided as a paper document and also as a PowerPoint presentation, can be used to explain the study to potential cooperating investigators in areas where there are participating Clinical Centers.

#### **19.3.4.3 Manual of Procedures**

Preparation of the TRTT Manual of Procedures is a major DCC responsibility in association with other members of the TRTT team. This document shall be closely linked with the development of many of the TRTT procedures. The essential features of the trial, which are explained in the Manual, shall be indicated by its Table of Contents.

#### **19.3.4.4 Patient Consent Statement**

The DCC, along with the Study Chair and advice of other TRTT investigators, shall develop the Patient Consent Statement. It will serve as the official approved document for educating candidates about the purpose, methods, possible risks and benefits of the TRTT. In addition to acceptance by the STC and the DSMB, the Patient Consent Statement shall be submitted for approval to the Institutional Review Board associated with each Clinical Center. Any textual changes required by the home institution shall be evaluated by the TRTT STC and the DSMB and approved if acceptable. The general principle is that material may be added according to trial requirements, but may not be deleted.

The informed consent statement shall explain the alternative treatments, the process that determines which treatment will be administered to the Study Participant, the role of the Clinical Center in delivering patient care, and the Study Participant's responsibilities for following the

treatment regimens and for being available for at least two years of follow-up data collection visits.

An assurance of confidentiality shall also be clearly stated, both at the Clinical Center and in the handling of the accumulated group results. Patients shall be given information about whom to contact should they have complaints about the study or the care they are receiving. The consent statement, intended to help candidates make an informed decision about participation in the TRTT trial, is designed to provide an honest representation of what the study involves.

#### **19.3.4.5 Forms Book**

All forms and charts that are developed for the operation of the trial shall be organized and collected into a Forms Book. The forms shall be updated when changes are made in existing forms and as new forms are developed to support successive stages of the trial. All forms will be uploaded for distribution to Clinical Centers on the TRTT website (<http://www.trtt.org>) organized by study visit.

#### **19.3.4.6 Address and Telephone Directory**

Creation of a directory of the names, addresses, telephone numbers, and e-mail addresses of the members of all TRTT trial committees and staff at all Centers shall initially be the responsibility of the DCC. The Directory will be uploaded on the TRTT website and each Center will add and delete staff as staff changes occur and also maintain the contact information for each of its members. Regular updates of the directory are an important tool in successful internal communications among the TRTT collaborators.

#### **19.3.4.7 Standard Procedures**

The DCC bears the responsibility of seeing that standard procedures are developed. Every clinical examination procedure followed in the TRTT shall be defined in the Manual of Procedures. This is accomplished cooperatively between DCC staff and professionals from the Study Chair's office, who are experienced at carrying out each procedure.

There shall be TRTT standard procedures for the following activities:

- Directive counseling (DC);
- Standard of care (SC);
- Sound Generator (SG) fitting;

- Audiological/Tinnitus/Hyperacusis (ATH) evaluation; and
- Physical examinations.

#### **19.3.4.8 Numbered Memos**

Changes in policies and procedures, as may be required, shall be communicated from the DCC to all appropriate participating Centers through the use of numbered Policy and Procedures Memoranda (PPM). These PPMs are part of the official records of the TRTT and are used for transmitting information about changes that should be instituted immediately. Among other things, they cover changes to the Manual of Procedures or other documents, as well as revisions to data collection forms.

#### **19.3.4.9 Administrative Aids for Clinical and Reference Centers**

The DCC staff shall develop administrative tools for the Clinical Centers. Such aids will include forms for scoring the Tinnitus Questionnaire, providing a form for audiograms, etc. These forms, which will not be collected at the DCC, shall be maintained at each Clinical Center and referred to as logs or worksheets.

#### **19.3.4.10 TRTT Publications**

Publications which emanate from the TRTT research group must be submitted to the DCC and approved by the STC prior to submission to journals or professional meetings. All members of the TRTT Full Investigative Group (FIG) are encouraged to collaborate in the process of informing the medical community about the design, methodology, baseline patient characteristics, and, in time, the results of the trial. However, all studies central to the trial and all proposed ancillary studies will require STC approval and DCC review.

The DCC shall be responsible for cooperating with authors by preparing the needed data and sharing its expertise gained in the coordination of the trial.

#### **19.3.4.11 TRTT Archives**

The TRTT library is housed in the DCC offices. In it are contained all current and previous versions of all study documents, printed copies of data forms, computer tapes of study data, all TRTT DSMB Reports, a collection of associated books and journals and most correspondence for the trial. A public use dataset will be developed during the trial and will be available after publication of the main results.

At the close of the TRTT trial, all participating centers will be directed to store study documents as determined by the STC or legal regulations.

### **19.3.5 Certification**

The process of certifying Clinical Centers and staff is the ongoing responsibility of the Director and Project Coordinator at the DCC with advice and council of the Quality Assurance Committee. This process is described in detail in Chapter 17 of this Manual.

### **19.3.6 Study Meetings**

The planning, scheduling and execution of all TRTT meetings, with the exception of the DSMB meetings, shall be handled by the Study Chair's Office in conjunction with the DCC staff and with help from Clinical Center staff as needed. Such meetings shall be devoted to Clinical Center staff training, to the work of TRTT committees, or for the purpose of site visits to TRTT Clinical Centers.

#### **19.3.6.1 Training**

The integration of new Clinical Centers is closely tied to the process of training the Clinical Center staff. The DCC staff shall design and conduct training sessions in conjunction with the Study Chair's office, as required to prepare Clinical Center staff for the certification process and participant enrollment. This may entail on-site training sessions conducted by DCC staff, or on-site training sessions conducted by certified personnel from other TRTT centers.

Ongoing training shall also occur at TRTT Full Investigative Group (FIG) meetings at which professional staff from the different TRTT Clinical Centers and reference Centers meet and have the opportunity for group sharing of experiences, learning new skills, and improving existing skills.

#### **19.3.6.2 Site Visits**

One of the TRTT quality assurance tools is the site visit. Each visit involves a group of TRTT staff members who visit one of the Clinical Centers for the purpose of observing its operation, looking for solutions to any problems that surface, and making suggestions for general improvement. Site visits shall be held regularly. Reports of these visits shall be written by a DCC staff member who has participated in the site visit. The resulting reports shall be distributed to site visit participants and to the Center that is visited. Summaries of reports are presented to the STC and the DSMB for review.

### **19.3.7 Randomization**

Randomization is the computer-assisted process chosen by the TRTT trial for generating a treatment assignment for a patient. It is described in detail in Chapter 5. The DCC will develop and maintain the central computer software to implement and document the process.

### **19.3.8 Analysis of Data and Report Generation**

The DCC is responsible for producing several types of reports periodically. These reports are described below. The DCC is also responsible for conducting data analyses needed for publication of results or for other purposes as determined by the study leadership.

#### **19.3.8.1 Data and Safety Monitoring Reports**

Every six months a report shall be prepared for the DSMB. The main purpose of this report is to assess adverse or beneficial effects of the TRTT treatments to date. The reasons for this documentation are two-fold. One is to determine if any treatment arm is causing significant adverse reactions or side effects that would warrant discontinuing that treatment. The second is to determine if one treatment is significantly more effective than the other so as to warrant stopping the study and making the results known to the scientific community. The report will be formatted so that the DSMB can readily examine the information necessary to make such decisions and will be modified according to the information needs of the DSMB. Highlights of the data analysis for preparation of monitoring reports and publications are shown in Table 1.

#### **19.3.8.2 Performance Monitoring Reports**

Every six months, the DSMB will also examine data pertaining to the performance of all the centers involved in the TRTT trial. This is done so that the DSMB can assess the quality of the treatment data being presented and make recommendations concerning areas where improvements can be made. The report will evaluate data quality at the Clinical Centers and the DCC. Topics will include completeness of study data, adherence to protocol, quality of clinical procedures, quality of form completion, and quality of data processing.

#### **19.3.8.3 Recruitment Reports**

Counts of the numbers of patients recruited at each Clinical Center will be generated online following enrollment of each Study Participant. This recruitment report will be available to all Clinical Coordinators and Center Directors. A monthly report will be printed and e-mailed to all DSMB members. These reports will give the number of patients recruited in each of the last three months and the cumulative total prior to the last three months. These reports will also convey the number of women and minorities recruited to the TRTT by Clinical Center to encourage fulfillment of targeted enrollment goals.



Table 1  
Highlights of Data Analysis for Monitoring Reports and Publications

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- **Performance monitoring**
  - Rates of patient recruitment
  - Rates of compliance with treatment protocol
  - Measures of quality of data collection
- **Description of study population**
  - Demographic characteristics
  - Medical History
  - Tinnitus History
  - Audiological characteristics
  - Health Related Quality of Life
  - Burden of disease
- **Treatment effects**
  - Comparisons between treatment groups for outcome variables
  - Interrelationships among outcome variables
  - Risk factor analysis of data collection at baseline

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## **Chapter 20** **Chair's Office Operations and Procedures**

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### **20.1 Introduction**

The Chair's Office is responsible for the overall scientific and administrative conduct of the TRTT, along with the coordination and management of the project. All technical questions with regard to treatment and complications shall be directed to the Chair's Office. In addition, preparations for meetings shall also be arranged through the Chair's Office. The Study Chair's office also has responsibility for recruiting, organizing, and managing the Clinical Centers and subcontracting for services in the Clinical Centers.

### **20.2 Responsibilities**

The Chair's Office is responsible for the overall scientific and administrative conduct of the trial. Specific duties include:

- Planning, developing, and refining the TRTT design, including cooperation with the Director of the Data Coordinating Center (DCC) in preparing the Manual of Procedures and necessary institutional review board protocols for the Chair's Office, Coordinating Center, and Clinical Centers;
- Developing the placebo sound generator (SG) and process for coordination of production and delivery of conventional and placebo SGs;
- Recruiting, organizing, and supervising all Clinical Centers;
- Developing and maintaining a three-party contract, including the University of Alabama (UA), Johns Hopkins University (JHU), and each clinical site as the parties. Cooperative Research and Development Agreements (CRADAs) have been prepared by the UA legal office in conjunction with Naval and Air Force officials and reviewed and signed by UA, JHU, and each clinical site.
- Organizing training sessions for Study Audiologists to learn the principles, theory, and practice of TRT and consensus standard of care (SC) across the military Clinical Centers;
- Resolving all technical questions with regard to treatment and complications;
- Making meeting arrangements for the Steering Committee (STC), Executive Committee (EC), and the Full Investigative Group (FIG);
- Preparing and distributing meeting minutes to the appropriate committee members;
- Preparing the training videotapes for directive counseling (DC), SC, and SG fitting;
- Coordinating publicity on a local and national level to enhance patient recruitment;
- Monitoring target enrollment and recruitment of minorities and women at each Clinical Center in collaboration with the DCC;
- Monitoring adherence to protocol at each Clinical Center through regular communication, evaluation of voice recorded counseling sessions, and site visits at each Clinical Center;
- Assisting with preparation and assembly of reports;

- Developing scientific publications and presentations in conjunction with the Coordinating Center and other TRTT investigators;
- Preparing continuation grant proposals with other TRTT investigators; and
- Supervising closeout of each TRTT Clinical Center at the end of the study.

## **20.3 Organization**

### **20.3.1 Introduction**

The Chair's Office is located on the Campus of the University of Alabama within the Department of Communicative Disorders.

### **20.3.2 Personnel and Their Responsibilities**

#### **20.3.2.1 Study Chair**

The Study Chair is responsible for the overall scientific and administrative conduct of the trial. He is responsible for:

- Ensuring that the objectives of the project are met.
- Maintaining Institutional Review Board compliance, budgeting and accounting of Military Clinical Centers via a sub-contractual arrangement;
- Training, coordination and oversight of the Study Audiologists who will provide the assigned treatments at the Clinical Centers; and
- Supervision of personnel and consultants in the Study Chair's Office.

He shall serve as Chair of the EC and the STC, as a voting member of the Quality Assurance Committee (QAC), and the FIG. He will also serve as a non-voting member of the Data and Safety Monitoring Committee (DSMB). He will correspond regularly and be in close contact with the chairs of all standing committees and will appoint new committees as the occasion arises during the conduct of the study. The Study Chair will participate in the protocol monitoring visits to all Clinical Centers and his office has responsibility for general oversight of each Clinical Center and their clinical activities as part of the TRTT. All issues including study design, eligibility, exclusion criteria, therapeutic considerations, etc. shall be addressed by the Study Chair. He also has primary responsibility, along with the Director of the DCC in publishing and presenting the findings of the TRTT.

### **20.3.2.2 Training/Protocol Monitor**

The Training/Protocol Monitors are responsible for the training programs and for monitoring adherence to the directive counseling (DC) and standard-of-care (SC) protocols. One Training/Protocol Monitor will have expertise with DC, and a second Training/Protocol Monitor will have expertise with SC. Both will have responsibility for relevant training and quality control. The former Training/Protocol Monitor will be responsible for instructing Study Audiologists in the fitting of sound therapy (ST) devices and follow-up care. The study responsibilities for the Training/Protocol Monitors include:

- Training and certifying Study Audiologists to provide the TRTT treatments;
- Working with the Study Chairman in preparing the DC, SC, and sound generator (SG) fitting training videotapes;
- Talking and corresponding with the Study Otolaryngologists and Audiologists regarding study protocol, especially with respect to clinical measures and DC and SC;
- Participating in site visits and monitoring for adherence to protocol at the Clinical Centers; and
- Monitoring adherence to DC and SC protocols by reviewing voice recordings of TRTT treatment sessions.

### **20.3.2.3 Study Otolaryngologist**

The roles of this physician, who has experience in participating as a member of a clinical team providing TRT, are to:

- Train Clinical Center Study Otolaryngologists in medical evaluation of tinnitus patients and determination of eligibility;
- Assist the Study Chair's Office in medically related matters pertaining to patient eligibility for the TRTT and treatment-related complications; and
- Serve as a general medical resource to Study Otolaryngologists.

#### **20.3.2.4 Administrative Assistant/Meeting Coordinator**

The Administrative Assistant/Meeting Coordinator assists the Study Chair in all aspects of the study. This individual shall have the following specific duties and responsibilities:

- Attending all technical group meetings and preparing minutes of the meetings for subsequent editing and distribution by the Study Chair and DCC Director;
- Arranging meetings of the EC, STC, QAC, and FIG, making technical, travel, and food arrangements, assisting chairpersons of these committees, and preparing and distributing minutes to members of the appropriate committee;
- Arranging scheduled telephone and conference calls;
- Maintaining office supplies for the Chair's Office; and
- Typing and distributing study correspondence, relevant reports, and/or manuscripts.

In addition, s/he will assist the Study Chair in budgeting and accounting activities of the Study Chair's office. These activities will include:

- Coordinating execution of the CRADAs among the University of Alabama, military Clinical Centers, and the Johns Hopkins University;
- Payments and tracking of expenditures for personnel, equipment, supplies, etc., associated with the Study Chair's office;
- Payment or reimbursement of travel expenses for committee and group meetings, training meetings, site visits, etc.
- Payment for all meeting expenses (e.g., food and audiovisual equipment);
- Purchase and accounting of all SGs for Clinical Centers; and
- Day-to-day financial operations of the Study Chair's office.

## **20.4 Preparations for Study Meetings**

The Chair's Office prepares and arranges for meetings of the EC, STC, QAC, and FIG. These preparations shall include setting an agenda, selecting a location, and managing details for accommodation. EC meetings are held on a monthly basis via conference telephone call. Face-to-face meetings of the STC and QAC are scheduled to coincide with meetings of the FIG, which are held annually. The STC meets by conference call at least monthly between face-to-face meetings.

## **20.5 Preparation of Recruitment Materials**

The Study Chair's Office will work closely with the individual Clinical Centers to market the TRTT and enhance participant recruitment. Relevant marketing materials will be prepared by the Study Chair's Office in conjunction with local Clinical Centers. National presentations with Military Clinical Center Directors will be coordinated to promote the TRTT at annual Tri-Care meetings of military audiologists and physicians who may be potential sources of participant referrals. Initially the Study Chair will describe the purposes and objectives of the study at training and orientation meetings for participating Clinical Center members in the TRTT. Topics included will be randomization, treatment options, length of follow-up, outcome measures, and local recruitment issues specific to participating Clinical Centers. Topics for subsequent years include baseline features of enrolled Study Participants, which will be monitored closely with each Clinical Center to ensure fulfillment of target enrollment of minority and women participants.

## **20.6 Preparation of Training Videotape**

Standardization of the treatment sessions including DC, SC, and SG fitting sessions, will be accomplished in part through viewing study video tapes prepared by the Training/Protocol Monitors. These tapes will review the steps to be performed in the counseling and ST fitting sessions, as well as follow-up counseling sessions. Use of these tapes should enhance standardization across Clinical Centers and minimize confounding problems or extraneous matters being introduced into a given session. Copies of videotapes will be distributed to each of the Clinical Centers.

## **20.7 Publication and Presentation of Study Findings**

The Study Chair's Office will work with the DCC and TRTT investigators to prepare publications and scientific presentations to report the findings of this study and the TRTT design.

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## **Chapter 21** **General Hearing Inc. Operations**

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### **21.1 Introduction**

General Hearing Instruments, Inc.(GHI), located in New Orleans, Louisiana, will provide the sound therapy devices used for sound therapy in the Tinnitus Retraining Therapy Trial (TRTT). Sound therapy (ST) is an integral component of Tinnitus Retraining Therapy (TRT) and aims to facilitate the habituation process by decreasing the contrast between tinnitus-related and background neuronal activity. GHI manufactures the sound generator (SG) that will be used to provide sound therapy in the TRTT. This instrument is the digital equivalent of the Tranquil model SG. The digital devices will be implemented with added features including data-logging capability to enable the Study Audiologist to monitor the Study Participant's use of the SGs and ST protocol compliance.

### **21.2 Organization**

Mr. Roger Juneau, President of GHI, will oversee manufacturing and quality control of the devices together with Mr. Ed Desporte, Director of Product Development. They will ensure the acoustic output characteristics of all devices used in the TRTT. Generally, Clinical Centers will not contact GHI directly, but will contact the TRTT Data Coordinating Center (DCC) if any problems arise with respect to supply or distribution of original or replacement devices. Direct contact with GHI may be necessary when questions or problems arise which are related to the data-logging capabilities of devices.

### **21.3 Responsibilities**

GHI will work in coordination with the Study Chair and the DCC to facilitate custom device production and timely delivery of the SG devices for each Study Participant assigned to ST at all

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six (6) Clinical Centers. GHI also will provide the necessary hardware and software to download and analyze each Study Participant's ST usage pattern and sound exposure history. The usage pattern will be used by the Study Audiologist at follow-up visits to assess ST compliance and for counseling of non-compliant participants.

### **21.3.1 Manufacture of Devices**

GHI will manufacture all devices used in the TRTT. Approximately half the manufactured devices will be configured as conventional SGs and the remainder will be configured as placebo SGs. Although it is expected that about 76 participants will be randomized to each type of device, additional devices of each type (conventional and placebo) will be required when a device needs to be replaced because of loss or damage. Devices will be manufactured and packaged as pairs (one for the left ear and one for the right ear) and lost or damaged devices will be replaced as pairs. Each pair of devices will be identified using sequential serial numbers and packaged in a kit which itself has a kit ID. The serial numbers for the devices for the right and left ear will be identical except that the last digit will be "R" or "L", respectively.

### **21.3.2 Randomization of Devices**

GHI will provide the TRTT DCC with a block of at least 600 serial numbers (300 pairs) that will be used to identify and represent the full set of instruments for the study, including those to be used as randomly assigned devices as well as replacement devices. The DCC will randomly designate which sets of serial numbers will be used for the conventional devices and which for the placebo devices. The DCC will also generate randomization assignments by kit ID, and matching conventional devices with assignment to full TRT and placebo devices with assignment to partial TRT. Because randomization is stratified by Clinical Center, randomization will also determine which devices will be sent to which Clinical Center.

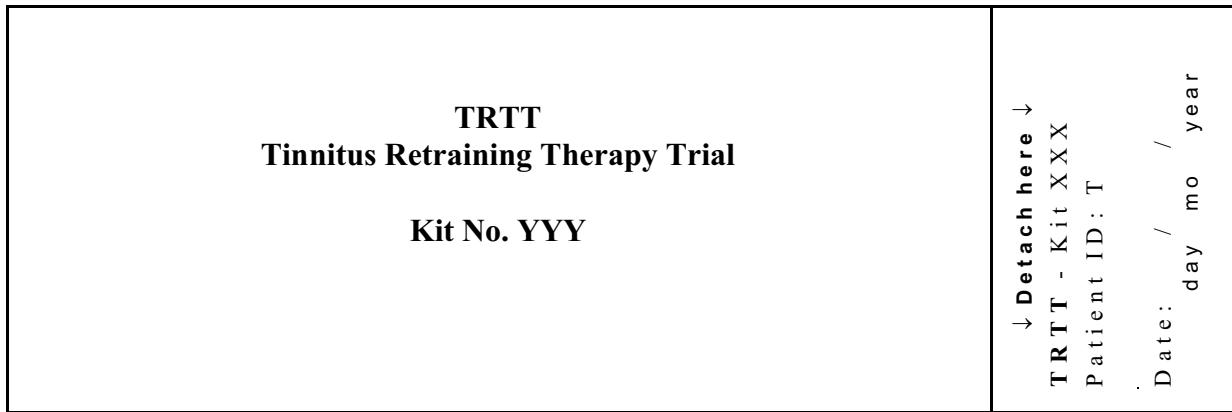
### **21.3.3 Distribution of Devices**

At the beginning of the study, the TRTT used behind-the-ear devices and the DCC was responsible for distribution of devices to Clinical Centers. GHI sent a sufficient number of pairs of SGs to the DCC to supply all 6 Clinical Centers with the first 6 randomized treatment assignments. Each SG pair is housed in a single container.

The DCC placed each container within a box having a kit ID. Each box had a sheet of paper noting the treatment assignment, either TRT (Directive Counseling and Sound Therapy) or Standard of Care (SC). Boxes for Study Participants assigned to TRT also contained the pair of SGs assigned to that Study Participant. The DCC affixed a tear-off label to each kit. The label included the kit ID and a tear-off portion to be affixed to the Sound Generator Issue Form for

Study Participants assigned to TRT or to the Standard of Care Checklist for Study Participants assigned to SC.

Figure 1. Sample tear off label



In order to maintain a constant stock of SG pairs at each Clinical Center, after a series of randomized treatment assignments involving an SG, the DCC sent an email to GHI requesting replenishment of the stock at the DCC. GHI sent the requisite SGs within two business days.

Part-way through the trial, it became obvious that for some Study Participants, the behind-the-ear devices failed at an unacceptable rate and the decision was made to preferentially use non-occluding in-the-ear devices from that point forward. The DCC will continue to send kits with tear-off labels to the Clinical Centers, but instead of including a box containing the sound generators, the kit will include a sheet of paper noting the treatment assignment, either TRT or SC, and a Sound Generator Order Form. The Sound Generator Order form will include the serial number of the assigned device and a place for the Clinical Center to indicate the preferred color for the device. When the impressions for in-the-ear devices have been obtained and are ready to be shipped to GHI, the Sound Generator Order Form is completed and faxed to both GHI and the DCC. This action notifies GHI about the requisite sound generators to be manufactured. A copy of the Sound Generator Order Form is included in the Study Participant's file, and the original placed in the box with the impressions to be shipped to GHI.

When the manufacture of the devices has been completed, GHI will notify the DCC by email on the day the sound generators are shipped to the Clinical Center.

At the end of the trial, if TRT proves to be successful, any unused devices will be offered to Study Participants assigned to SC.

### **21.3.4 Replacement Devices**

If, during the course of the trial, the Tranquil device(s) assigned to a Study Participant are damaged or malfunction, the Study Participant will be asked to contact the Clinical Center staff to report the problem, arrange to return the set of devices to the Clinical Center, and receive a replacement pair from the Clinical Center. For behind-the-ear devices, the Clinical Center staff will contact the DCC who will send a replacement pair of devices from the stock on hand to the Clinical Center using overnight delivery. The Clinical Center staff will return the pair of devices (which includes the damaged or malfunctioning device(s)) to GHI directly. For in-the-ear devices, the Clinical Center will contact the DCC but send the malfunctioning devices directly to GHI, who will send a replacement pair.

### **21.3.5 Data Logging**

Each Tranquil device will be engineered with data-logging capabilities. Data that are captured include:

- Sound output of the device (encrypted to preserve blinding at the Clinical Center);
- Intensity of ambient sound;
- Total times used and average number of hours per use that the Study Participant has worn the device;
- Total number of times the Study Participant has removed and re-inserted the device;
- Length of intervals when participant has not used the device per interval and day; and
- Low battery indicator.

Data will be downloaded from the devices onto a laptop or tower computer supplied to each Clinical Center for that purpose. The downloaded data will be used to generate reports on the use of the SG devices to aid the Clinical Centers in monitoring protocol compliance. These and additional data will also be sent to the DCC. Instructions for downloading the data are described in Chapter 12, Protocol for Sound Therapy.

The DCC will send data related to the function of each device directly to GHI. This information will be encrypted and not available to the Clinical Centers. GHI will be responsible for reviewing the data within three days of receipt. If GHI determines that any device is not operating properly (i.e, a conventional device is not generating a sound signal or a placebo device continues to generate a sound signal for a longer period of time than expected), GHI will immediately notify the DCC, so that a properly working replacement device can be issued to the Study Participant.

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## **Chapter 22** **Data Management**

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### **22.1 Introduction**

The Data Coordinating Center (DCC) is responsible for providing for study design, study information management design, data analysis, and interpretation. The goal and responsibility of the DCC is to work with the Clinical Centers to ensure that appropriate, complete and high quality data are assembled and that a study data base is developed and maintained throughout the course of the study that allows for appropriate and correct analyses of the interim and final data. Study information management includes database design and administration, forms development and data acquisition, data and forms tracking, quality assurance, and data security. The TRTT database will be web-based and managed at the Center for Clinical Trials at the Johns Hopkins Bloomberg School of Public Health.

### **22.2 Database Design, Development and Administration**

The major functional features of the proposed data management system include mechanisms for data acquisition, management, and transfer; a monitoring system to track participant visits and data collection forms, and completion of study milestones (e.g., accrual of participants, inventory of data completed); quality assurance procedures to insure validity and integrity of data

entered into the central research information system; and security features to insure the integrity of data. Detailed descriptions of each feature are explained below.

### **22.2.1 Design and Development**

Study database design consists of defining each of the data sources and the relationship between data sources and then constructing a database structure that efficiently stores and maintains the data inter-relationships of data elements. This generally begins with defining at least one data table per data source and defining key variables that will be used to preserve the ability to uniquely access each data record and link each to other records as study needs dictate. The standardized indices in the TRTT data management system will include the site ID, participant ID and alphabetical ID code ( name code), and date of visit. This infrastructure provides for data management, efficient tracking of Study Participant status, and development of performance monitoring and other quality assurance reports.

To facilitate design of data collection tools, a comprehensive data dictionary will be constructed to capture information about each data item. The item designator, item name, description, valid ranges or contents, width, format (i.e., date, numeric, text), item skip patterns based on data responses, and cross-item logical checks will be entered into the data dictionary, using manually defined definitions. The data dictionary will be maintained in both hard copy and electronic database formats at the DCC.

### **22.2.2 Database Administration**

Database administration includes the management of hardware and software components that comprise the system, implementation of back-up and recovery of data, and assignment of account privileges to control the functions each user is permitted to perform. These services will be regularly performed by the Director of Information Management.

### **22.2.3 Participant Status Tracking**

The database tracking system will monitor and record the Study Participant status as he or she moves from initial screening through randomization, enrollment, and follow-up study visit completion. Whenever there is a status change, the date and result, (e.g. eligible, yes or no) will be recorded, along with room for a comment. These procedures provide an historical record to track each recruit's status, and are especially important in tracking the status of those individuals whose eligibility is pending (see Chapter 5, section 5.3.2).

On-demand reports of the status of Study Participants using the participant status tracking module will enable study staff to monitor recruitment progress closely and compare it against

TRTT recruitment goals. If recruitment is lagging, the DCC staff can readily see at what stage the problem exists. With this information, the Steering Committee (STC) can then make informed decisions about modifications to the design, such as relaxation of certain eligibility criteria. This early warning system will maximize the opportunity to correct recruitment problems in the initial phase of the study.

#### **22.2.4 Randomization**

During the study database design, tables of randomized treatment assignments will be created. These tamper-proof tables will contain already generated random assignments that will be allocated at the time of randomization. These tables will contain randomly permuted blocked allocations, stratified by Clinical Center, and will be accessible online or by DCC staff if and when a Clinical Center telephones for a randomized treatment assignment.

A standard report will be generated at randomization, which will be available online immediately following randomization. It will designate the kit ID assigned to the Study Participant. The actual assignment, TRT (Directive Counseling (DC) and sound generator (SG)), or the standard of care (SC), will be contained within the kit itself. If assigned to TRT, the kit will also include the pair of Sound Generators to be used for Study Participants assigned to TRT.

#### **221.2.5 Scheduling Study Visits**

The database will be designed to assess the date of the Initial Treatment Visit (T1) to determine the dates and acceptable windows for Follow-up Visits for each Study Participant. A personalized study schedule will be generated for each Study Participant. Separate schedules will be generated for the treatment visits occurring at one month following T1, and for follow-up visits taking place at 3, 6, 12, and 18 months after T1. These schedules will serve to inform Clinical Center staff of the appropriate dates to schedule upcoming visits as specified in the protocol. In addition to the appointment schedules, email reminders will be generated at least one month before a study visit is due and sent to the Clinical Center staff scheduling the study visits. These reports will also be available on the TRTT website.

### **22.3 Processing Data Collection Forms**

TRTT Clinical Coordinators will collect TRTT data on paper data collection forms and enter this data online at the TRTT website. Data entry screens will have the same fields and prompts that are recorded on the paper data collection forms. Integrity checks are implemented at the database level as data is being entered. The database will highlight missing and questionable (e.g., out-of-range) data entries, including those related to user-defined dictionary look ups, numeric range tests, date, currency and character-specific formatting. Staff at the DCC will also

perform data checks to correct data following receipt of data feedback information from Clinical Centers.

### **22.3.1 Validation of Data Collection Forms**

All data items will be validated against criteria specified in the data dictionary. Validation includes checks for consistency with other responses and completeness. These errors will be flagged during the data entry process and may include coding for cross-edits, across forms edits, and any special edits. The cross-edits can be as simple as comparing one variable with another or they can be more difficult such as checking a calculated score and then making certain decisions based on the score.

Data errors or inconsistencies will be flagged and displayed immediately online during the data entry process. Data flags will either require ‘immediate correction’ or may be set as “warnings” (e.g., missing data). Immediate correction is required before the form is allowed to be submitted. The presence of warnings will not disallow submission of the form, but must be addressed in a timely manner. Errors that are warnings are entered into an error log and an error report will then be produced by the system. This report includes the error in the error log, its nature, the offending record ID, the data item ID, and the offending data value along with room to record the data correction. Any variables that are questioned as possibly being in error will be reported back to the Clinical Centers in a report called the Edit Report/Clarification Request. These reports will be site specific. This report will give the identification information for the variable in question (site number, patient code, form number, rating period), the variable name of the variable in question, the reason the variable is being questioned, the variable’s current value, and a space to correct the variable or indicate that the variable is correct as is. Sites will complete this report by accessing the TRTT website database and making the corrections or returning a report to the DCC verifying that the data as entered is correct.

Any new errors generated during editing are added to the error log. Errors that are corrected no longer appear in the error report but nevertheless remain in the error log to be used for monitoring, e.g. detecting error patterns. The process continues until there are no errors in the error report. Before the data may be used for interim or final analysis, all errors must be corrected or a decision to over-ride must be recorded. Unless authorized by study role, data corrections may only be applied to records and items flagged in the error log.

### **22.3.2 Data and Forms Tracking**

The TRTT forms tracking system updates the status of data collection forms as they proceed through all data processing steps. It will be used to generate monthly online reports of the status of all forms received that month and to assess enrollment milestones. Reports will be generated

from this tracking system and posted on the Clinical Center specific area of the TRTT website and also sent to the Clinical Center Coordinator on a monthly basis. Reports will monitor data collection forms expected from scheduled study visits, and will provide notification on the status of specific data collection forms (e.g., expected, completed, pending, missing). Updates can be completed if the key identifiers for a data collection form already exist in the database.

Reports generated on a monthly basis may include a:

- Missing Forms report that lists all expected forms that have not yet been entered;
- Outstanding Clarification Report that indicates the number of Edit Report/Clarification Requests that have not been received within 30 days of the date initiated;
- Expected Study Visits by participant visits; and
- Participant Status Report that lists all individuals whose eligibility remains pending.

This combination of reports will allow the Clinical Centers and DCC to monitor the quality of the data, as well as determine whether a Clinical Center is falling behind in the submission of data and corrections. The Project Coordinator will serve as a first-line resource for the Clinical Centers, working closely with them to help them understand the problems that the reports detect and correct the problems.

At the end of the study, the DCC will complete a final clean-up of the study database, working closely with Clinical Centers to ensure that all collected data have been entered into the database and that all entered data are as correct as can be made possible.

## **22.4 Quality Assurance**

For quality assurance, the following procedures will be monitored:

- Enrollment, including eligibility and randomization;
- Progression of Study Participants throughout the follow-up period;
- Data collection activities including completeness of data for each visit;
- Data capture during the data entry process;
- Visits scheduled within allowable time limits;

- Collection and submission of all expected data collection forms at study visits;
- Error trapping; and
- Error correction or data updates.

## **22.5 Confidentiality, Security, and Data Integrity**

To safeguard the confidentiality of Study Participants, at initial contact each participant will be assigned a unique, sequential Patient ID and a name code ID. Identifiers for potential participants from each Clinical Center will be generated before the study begins. As participants are screened, each ID number will be retrieved in sequence from the label sheet provided to each Clinical Center and assigned to potential Study Participants. The name code will be chosen by the Clinical Center. These IDs will be used to identify the study participant for the duration of the trial and must be entered to register the individual as a Study Participant. These identifiers must also be entered to access an online data collection form. To distinguish between identical data collection forms that are completed at different time points in the study (e.g., the Tinnitus Questionnaire), a date will be used as an additional ID field.

Security measures include password protection to block unwarranted intrusion into the database. In order to gain access to the system, the user must have a valid account and password and must be listed in the key staff list created at the time the study design and protocol are established. This list is accessible to the Database Programmer to allow for additions and deletions of an individual. When an individual has been deleted from the list, that person will no longer have access to study data even though he or she may have a valid account and password. If either component fails the lock and key check at entry, the user will receive a message to contact the database administrator by e-mail or telephone and will be blocked from entering the study database. In addition, to protect against unauthorized entry, each user will be granted privileges and views that allow access and limit function based purely on need. For instance, only those authorized users granted update authority will be permitted to change data.

Data integrity features include all procedures designed to protect the validity of the content and structure of data items, such as steps to protect against accidental errors at data entry, and update and policies and procedures designed to protect the structural integrity of the database system. Since relationships between tables (components) of a relational database are important, the database will be set up to enforce referential integrity that prevents breaking certain linkages e.g., deleting a record on which other records depend. In order to provide added protection, requests for record updates and deletions will be systematically implemented by the Database

Programmer. In addition to a restricted password, deletion control requires that the participant ID and form number be verified by duplicate entry before the deletion is executed. A record of the deletion will be maintained in the transaction log, and a copy of the deleted information will be retained in a deleted records log to allow for recovery of data if necessary.

All elements of the database will be backed-up daily and weekly onto high capacity cassette tapes and monthly backups will be transferred to CD media. In addition to those kept on site, copies of weekly backups will be stored off-site in a fireproof safe to permit retrieval of the data in the event of a total loss of information on site.

The database is a moving target, such that it is burdensome to attempt to reproduce snapshots of it at later points in time. “Frozen”, or official interim datasets, containing data entered “as of” a given date, will be created for monitoring purposes in conjunction with Data and Safety Monitoring Board interim monitoring report generation. These datasets will be archived for reference, and in order to duplicate analyses.

## **22.6 Data Sharing with Outside Investigators**

The TRTT data will become available to outside investigators at the conclusion of the trial and following publication of the main study findings (see Chapter 24). To facilitate sharing of data collected by the TRTT, an informational web-page will be added to the TRTT website by the DCC. The web-page will provide the following:

- Instructions for obtaining data;
- An application for data usage;
- A set of forms with an explanation of variable naming conventions;
- A data dictionary; and
- A data use agreement in PDF format.

The website will not be used for direct distribution of data but rather will be used only as a mechanism for informing researchers of the availability of the data, the potential for collaboration with the Center investigators, and the procedures for obtaining data for analysis.

Investigators requesting data for secondary analysis purposes will be asked to provide a proposal for the intended use of the data, and a list of the variables requested. All users will be

expected to enter into a data use agreement. Release of datasets to secondary users will be subject to approval of the TRTT Steering Committee.

To protect the confidentiality of participant data, only de-identified data will be made available for secondary analysis. Data records will be free of the personal identifiers specified in section 164.514(b)(2)(I) of the federal Privacy Rule. Indirect identifiers that would potentially compromise the anonymity of participants will be suppressed in all datasets released for public use. In addition, all secondary users of data will be asked to sign a data use agreement that stipulates conditions for use of the data. The agreement will specify the confidentiality and data security standards that must be adhered to by the recipient and will expressly stipulate that:

- The data are to be used for Institutional Review Board-approved research purposes only;
- No effort will be made to identify individual participants; and
- Data will not be transferred to other users by the recipient.

The data-sharing web-page will be advertised to potential users via the TRTT website and through newsletters targeted to the scientific community. A link to the data sharing web- page also will be maintained on the Johns Hopkins Bloomberg School of Public Health Center for Clinical Trial's website.

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## Chapter 23

### Statistical Considerations and Data Analysis

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### **23.1 Introduction**

#### **23.1.1 Study Design**

The Tinnitus Retraining Therapy Trial (TRTT) is a multi-center randomized placebo-controlled trial designed to investigate the efficacy of Tinnitus Retraining Therapy (TRT) as a treatment for severe debilitating tinnitus of at least one year's duration. TRT is an habituation-based intervention that uses directive counseling (DC) and low-level sound therapy (ST) to facilitate habituation of the awareness of tinnitus, its annoyance, and impact on the patient's life. It will be compared with the standard of care (SC) as typically administered to patients with severely debilitating tinnitus in the military.

Within the trial, each Study Participant will be randomized to one of three treatment groups as shown in Table 23.1.

**Table 23.1 Schematic showing the three study groups**

	<b>Sound therapy</b>	<b>“Counseling”</b>
<b>Group 1 (TRT)</b>	Conventional Sound Generator	DC
<b>Group 2 (partial TRT)</b>	Placebo Sound Generator	DC
<b>Group 3 (Standard of care)</b>	Recommendation to use ambient sound	Standard clinical consultation as provided in the military

Randomization helps to ensure that treatment groups are balanced with respect to pretreatment characteristics, although analyses of departures from balance will be carried out with appropriate adjustment to treatment effect estimation, if needed. Randomization will be performed using permuted blocks of random size, and stratified by Clinical Center. The logistics of the randomization are described in Chapter 5, Patient Entry into the Study.

An important feature of this study is that every effort is made to keep the Study Audiologists and Study Participants blinded with respect to the type of sound generator (SG), either conventional or placebo.

### **23.1.2 Primary Objective**

The primary objective of the TRTT is to assess the efficacy of TRT, defined as DC and ST achieved through conventional SGs (Group 1) as a treatment for severe debilitating tinnitus. The primary outcome to be measured in the TRTT is the difference in scores on the Tinnitus Questionnaire (TQ) between baseline and follow-up assessed longitudinally, at 3, 6, 12, and 18 months of treatment. The corresponding hypothesis is that TRT (Group 1 in Table 22.1) compared with the standard of care (SC; Group 3) will reduce the severity of debilitating tinnitus significantly as assessed by longitudinal changes in the TQ score and at the end of treatment..

The secondary efficacy outcomes will test the following hypotheses. TRT (Group 1) compared with SC (Group 3) will reduce severity of debilitating tinnitus significantly as assessed by longitudinal changes in:

Score on the following tinnitus and functional measures:

- Sub-scales of the TQ;
- Tinnitus Handicap Inventory;
- Tinnitus Functional Index;
- TRT Visual Analogue Scale; and
- Digit Symbol Substitution Task.

and psychoacoustic measures:

- Tinnitus Pitch and Loudness Match; and
- Loudness Discomfort Level (LDL)

### **23.1.3 Secondary Objectives**

The secondary objectives are to investigate the efficacy of each of the TRT components, DC and ST achieved with conventional SGs. Specifically, we will:

1. Investigate whether ST using conventional SGs is more effective in treating Study Participants with debilitating tinnitus compared with placebo SGs given that both groups are assigned to DC (Group 1 versus Group 2).
2. Investigate whether DC is more effective in treating Study Participants with debilitating tinnitus compared with usual care (Group 2 versus Group 3). We assume that the effect of placebo ST is negligible.

The primary and secondary efficacy outcomes and hypotheses are similar to those for the primary objectives. Specifically, we hypothesize that the reduction in severity of tinnitus will be higher in Study Participants assigned to (1) Group 1 (DC + conventional SG) compared with those assigned to Group 2 (DC + placebo SG); and also in (2) Group 2 (DC + placebo SG)

compared with those assigned to Group 3 (SC) as assessed by longitudinal changes in the TQ score. Secondary efficacy outcomes are change, assessed longitudinally and also at the end of treatment in the following:

Score on the following tinnitus and functional measures

- Sub-scales of the TQ;
- Tinnitus Handicap Inventory;
- Tinnitus Functional Index;
- TRT Visual Analogue Scale; and
- Digit Symbol Substitution Task.

and psychoacoustic measures:

- Tinnitus Pitch and Loudness Match; and
- Loudness Discomfort Level (LDL)

## 23.2 Sample Size Considerations

The overall objectives of this study are thus three-fold, i.e. to assess the:

- Efficacy of TRT (DC + conventional SG) compared with SC;
- Superiority of conventional SG over the placebo SG given the patients in comparison groups are exposed to DC; and
- Superiority of DC over SC, given the assumption that there is no or little effect of placebo SG.

The primary outcome measure is change in the TQ score. Thus, the TRTT is designed primarily to have sufficient power to detect the minimal clinically important difference between these study groups as designated by clinical experts. This approach allows us to detect important differences, yet not waste resources on power to detect unimportant differences.

### 23.2.1 Determination of the Minimal Clinically Important Difference

Consultation with experts familiar with the TQ were used to estimate the change in the TQ that would be deemed clinically important. Hallam (the developer of the TQ instrument) proposed that “An effect size of 0.8 or perhaps 1.0 on the Emotional Distress subscale is a reasonable criterion for [clinically] significant change.” An effect size of 0.8 to 1.0 on the full TQ would correspond to a change of approximately 10 to 13 points. Hiller, a researcher with extensive experience using the TQ stated “I personally believe that a change of less than 5 to 6 points does not mean much.” Based on this input, the TRTT has been designed to have good power to detect a 10-point difference for the primary objective (i.e., between Group 1 and Group 3) and a 7-point difference for the secondary objectives (i.e., between Group 1 and Group 2 or between Group 2 and Group 3) with respect to the longitudinally assessed change in TQ.

A review of the literature suggests that an effect of this size is plausible. A brief review of four studies that assessed the effectiveness of the TRT or TRT-like intervention as measured by the TQ is shown in Table 23.2.

**Table 23.2. Changes in TQ Score after TRT or TRT-like Interventions**

Study	Sample Size	Length of follow-up (weeks)	Mean TQ at baseline	Mean TQ at follow-up	Change
Goebel, Rubler, Stepputat <i>et al.</i> (1999)	10	16	47.2	39.7	-7.5
Biesinger, and Greimel (1999) <sup>1</sup>	42	52	56.4	42.3	-14.2
Haerkotter (2001)	28	26	53.7	29.5	-24.2
Delb, D'Amelio, Boosten, and Plinket (2002)	27	26	46.5	32.1	-14.4
Zachriat (2003)	30	52	44.5	29.1	-15.4

<sup>1</sup> Exact numbers were abstracted from Table 4 in Goebel and Hiller (1999).

TRT or TRT-like interventions are shown in Table 23.2 to achieve substantial changes in these earlier studies, although the sample size in each study is quite small.

To estimate expected changes in TQ in the “usual” care groups, a literature survey was completed. Four studies were found using wait list controls and are summarized in Table 23.3.

**Table 23.3. Changes in TQ Score for Wait List Controls**

Study	Sample Size	Length of follow-up (weeks)	Mean TQ at baseline	Mean TQ at follow-up	Change
Goebel and Hiller, 1995	138	26 to 52	52.0	51.2	-0.8
Kroner-Herwig and Esser, 1999	20	30	38.7	35.9	-2.8
Goebel, Rubler, Stepputat <i>et al.</i> , 1999	27	26	56.1	57.1	1.0
Delb, D'Amelio, Boosten, and Plinket (2002)	27	12	48.1	47.4	-0.7

Three studies examined the effect of “education” or other types of “counseling”. These are shown in Table 23.4.

**Table 23.4. Changes in TQ Score for Counseling Controls**

Study	Sample Size	Length of follow-up (weeks)	Mean TQ at baseline	Mean TQ at follow-up	Change
Kroner-Herwig <i>et al.</i> , 1997 <sup>1</sup>	16	8	36.3	28	-8.3
Von Wedel <i>et al.</i> , 2000	49	12	47.2	42.8	-4.4
Schmidt and Kroner-Herwig, 2002	23	4	43	38	-5

<sup>1</sup> Exact numbers were abstracted from Table 4 in Goebel and Hiller (1999).

On average, there is only about a 5-point change with various types of counseling, although the studies had small sample sizes and short follow-up times.

### 23.2.2 Variation in Changes in TQ after Treatment.

We also surveyed the literature and contacted TQ experts to obtain information on variances in the changes to be expected in order to calculate power. Results are summarized in Table 23.5.

**Table 23.5. Variances of Changes in TQ in Previous Studies**

Source	Sample	Length of follow-up (months)	Standard Deviation of TQ Change Scores
Goebel and Hiller (1995)	Patients receiving in-patient treatment (n=137)	2	12.6
Delb, D'Amelio, Boosten and Plinkert (2002)	Men (n=17) Women (n=10)	8 18	11.1 11.8
Personal communication from Wolfgang Hiller	Patients with baseline TQ $\geq$ 40	8 18	15 17

Based on the evidence in Table 23.5, we will assume that, on average, the standard deviation of the TQ change scores equals 12.5. The amount is near to the average of the values reported.

### 23.2.3 Sample Size Calculations

For the sample size calculations, we have made the following assumptions:

- Type-I error rate = 0.05
- Two sided test;
- 10-point clinically significant difference in mean TQ scores for primary comparison (DC + conventional SG versus SC);
- 7-point difference for hypothesized partial comparisons: SG (DC + conventional SG versus DC + placebo SG) and DC (DC + placebo SG versus SC);
- Power of 80% of comparisons of partial interventions to drive the sample size calculations;
- Equal standard deviation of 12.5;
- Four follow-up treatment time points (3, 6, 12, and 18 months); and
- 10 % attrition rate

We used Power and Sample Size Calculations (Dupont and Plummer) to calculate an estimated sample size for the TRTT. We divided  $\alpha$  of 0.05 among the three major comparisons. Using this software, we estimate that a total of 228 Study Participants or 76 Study Participants in each of the 3 groups will be required to yield at least 80% power to detect a 7-point difference for analyses of the TRT components, ST and DC. This sample size will provide for greater than 95% power for the primary analysis (comparison of TRT (Group 1) to the standard of care (Group 3)), taking into account a 10 % drop-out rate. The sample size estimation is a conservative estimate as the primary outcome is a longitudinal analysis using data from follow-up visits at 3, 6, 12 and 18 months.

Table 23.6 illustrates the sample size sensitivities to changes in the expected differences in TQ scores using these assumptions and standard deviation of 12.5.

**Table 23.6. Sample Size Sensitivities**

Difference in TQ score	Power		
	80%	90%	95%
<b>10</b>	113	147	<b>173</b>
<b>8</b>	173	<b>223</b>	270
<b>7</b>	<b>228</b>	290	350
<b>6</b>	307	397	477

With these assumptions, we estimate that with 228 Study Participants (to allow for 10% attrition), we will have greater than 95% power to detect a difference of 10 points in the TQ score of Study Participants assigned to TRT compared with SC, either as a longitudinal analyses or if measured at a single time point at the end of 18 months of treatment . We will have 80% power to detect a 7-point difference in the TRT components i.e, efficacy of sound therapy by comparing conventional SG with placebo SG for individuals assigned to DC; and efficacy of DC by comparing individuals assigned to DC + placebo SG with SC. These sample sizes will also have sufficient power to account for an equivalent point change in the “Emotional Distress” sub-scale.

### 23.3 Data Analysis

Analyses will be performed based on the principle of intention to treat, i.e., in the analysis Study Participants will be included in the group to which they were randomized, regardless of whether they adhered to the treatment. For the primary outcome, the only participants that will

not be included will be those for whom TQ could not be assessed at any follow-up visit due to loss to follow-up. However, we anticipate that few, if any, participants will not be able to complete at least one follow-up TQ measure. In addition, we have allowed for completion of the TQ by mail. Any report of our results will include an accounting of the numbers lost to follow-up and the reasons for the loss.

### **23.3.1 Interim Data Reports**

At least twice each year, the data files at the Coordinating Center will be "frozen", i.e., a copy or "snapshot" is made of the files as they exist on a specified date, in preparation for generating reports for the Data and Safety Monitoring Board (DSMB). Every effort will be made to insure that all error corrections and updates have been applied to the analysis sample. The data for interim analysis will be extracted from the database into flat files and converted into SAS or STATA data set format. In these formats, the data may be transformed, new analysis variables computed, and subjected to a variety of statistical analyses using procedures built into these analytic programs.

The main objective of each report is to present the accumulated data with sufficient detail and clarity through appropriate statistical analysis to permit evaluation of treatment benefit or harm. These reports include information regarding progress of the study, data quality, and comparisons of participants assigned to different management strategies within the randomized trial for the outcomes of interest. The specific contents of each report are developed by the Coordinating Center statisticians in collaboration with the DSMB. The interim reports are provided only to the DSMB and not to the Study Chair's office or collaborating Clinical Centers.

The same steps will be performed prior to final analysis, except that the whole database will be utilized.

We have chosen not to specify a planned interim analysis of the primary outcome, because we believe that interim analyses should be done only when there is an opportunity to end or change a trial while there is still time to make a difference (i.e., to prevent patients from being put onto or kept on an inferior treatment). The first time point at which an interim analysis could reasonably be completed would be near to the point in time when recruitment will have been completed. We would prefer not to obtain an interim analyses rather than lose statistical power by taking this additional look at the data. However, the specific report content and any interim analyses plans will be developed by the DCC statistician in collaboration with the DSMB.

### 23.3.2 Statistical Analyses

The Data Coordinating Center will form a Coordinating Center Data Analysis Committee which will include the Data Coordinating Center Director, Study Biostatistician, and Statistical Programmer.

The Data Coordinating Center statistician will work closely with the DSMB and clinical investigators to arrive at appropriate statistical analyses, consistent interpretation of the data, and clear and unequivocal presentation of the TRTT findings to the medical community. Statistical analysis responsibilities include:

- Defining the outcome(s) to be evaluated in conjunction with clinical study investigators;
- Describing the differences between the treatment groups being compared with respect to the baseline variables which might contain prognostic information, and with outcome(s) of interest;
- Evaluating the strength of the evidence regarding differences between the treatment groups and making decisions on the basis of the evidence; and
- Recommending one of the treatment strategies or concluding that no recommendation can be made.

Initial analyses will be descriptive in nature, using means, standard deviations, and proportions to describe baseline characteristics of the sample for all participants combined and by intervention group. Distributions of continuous variables will be examined for symmetry, and transformations will be considered for seriously skewed variables. For continuous variables, one-way analyses of variance will be used to compare the intervention groups on demographic and other baseline characteristics; the purpose is to assess comparability among the randomly assigned groups. For dichotomous or other categorical variables, chi-square tests will be used to compare intervention groups, and enrolled/excluded groups. Pearson correlation coefficients will be calculated to assess the strength of the associations among the various outcome measures, and to examine associations of other covariates with outcome measures; such potential confounding variables will be considered for inclusion in secondary analyses involving regression models.

All primary analyses will be based on the “intention to treat” principle. Analyses will include the following:

### 23.3.2.1 Primary Outcome

The primary outcome variable will be change in the TQ score. We will use spaghetti plots for initial exploratory analyses and longitudinal data analyses as our primary analytic method. Longitudinal analyses allows us to account for the natural correlation which occurs with observations on the same subject over time and for the same Audiologist observing several Study Participants. Indicator variables will identify group; their coefficients in the models represent the primary focus on group differences. Adjustment for covariates such as age and sex can easily be accounted for in this class of models.

Mean TQ scores will be compared between two treatment groups using Generalized Estimating Equations (GEE) as implemented in STATA, SAS or R. The basic model is as follows:

Let  $TQ$  denote the TQ score. We expect effects of Clinical Center, Audiologist, treatment group, and possibly personality traits as measured by the State-Trait Anxiety Index (STAI) or Positive and Negative Affect Schedule (PANAS); or other factors such as hearing difficulty measured using the Hearing Handicap Inventory (HHI), or early completion of treatment. We will use models of the form:

$$TQ_{ijkgt} = \beta_0 + \beta_c C_j + \beta_a A_k + \gamma_g G_g + \tau T_t + \rho_1 PT_{1i} + \rho_2 PT_{2i} + \varepsilon_{ijkgt}$$

where:

j indexes Clinical Center;  
k indexes Audiologist;  
g indexes Group;  
t indexes Time; and  
I indexes Study Participant.

Both Study Audiologist and Study Participant are nested within Clinical Centers. The parameter of interest is  $\gamma_g$ , with  $\gamma_1$  representing the difference between Group 1 (full TRT) and Group 3 (SC). (G represents a dummy variable for Groups).  $\beta_a$  and  $\beta_c$  provide comparisons between Study Audiologists and Clinical Centers; C and A are dummy variables.  $\tau$  captures the effect of time;  $T_1$  has the values of 0, 3, 6, 12, and 18.  $\rho_1$  and  $\rho_2$  capture differences in psychometric instruments measurements, e.g., the STAI and PANAS, respectively. Other factors may also be included as necessary ( $\rho_3$ ,  $\rho_4$ , etc.).

Similar models will be run for the secondary objectives. The mean TQ scores will be compared between the Group 1 (DC + conventional SG) and Group 2 (DC + placebo SG) for the superiority of the conventional SG; and between Group 2 (DC + placebo SG) and Group 3 (SC)

for the superiority of DC over the standard of care in reducing the severity of tinnitus among patients with severely debilitating tinnitus.

The GEE procedure has several useful features:

- It allows a flexible approach to modeling covariance structure, which results in a parsimonious covariance model.
- It uses the generalized least squares (GLS) method, which is generally superior to the ordinary least squares (OLS) method with an appropriate covariance structure.
- The presence of missing repeated measures for a subject does not result in exclusion of that subject from the analysis; instead, it uses all available data.
- It can be used to analyze different types of outcomes such as continuous, binary, or count.
- It can be used to analyze unbalanced design caused by either differing numbers of observations per person or by observations taken at different times.

We have included variables in the models to estimate the relationship between various personality characteristics and successful habituation to tinnitus in our basic model. Interaction terms between these patient characteristics and treatment group will be included to assess whether the effect of TRT is greater for certain types of patients. Personality characteristics of interest include those measured by the STAI and PANAS. Similar analyses will assess whether age, sex, or other patient characteristics are predictive of successful habituation with or without TRT.

In addition, the availability of information on the Study Participants will make it possible to learn about the impact of tinnitus in various demographic or other subgroups, and to assess whether the effect of TRT or TRT components varies between demographic subgroups and so we will perform valid analyses by gender, age, and minority status. We will also explore whether treatment with TRT or its components differentially impacts individuals with hyperacusis in conjunction with tinnitus versus those with only tinnitus, and whether and by how much initial tinnitus severity affects treatment efficacy.

### **23.3.2.2 Secondary Efficacy Analyses**

For the analyses looking at the difference between TQ score at baseline and 18 months, we will compare TQ mean scores at 18-month in the treatment phase among treatment groups using Analysis of Covariance (ANCOVA). We will adjust for Baseline TQ scores and heterogeneity of

tinnitus status in the patient population. We will also adjust for important baseline covariates and variables that may be unbalanced at baseline (even with randomization) and are potentially related to TQ score. We will also use GEE for this analysis.

The data resulting from this project will enable us to address a number of additional research questions. First, to assess the effect of the interventions on different aspects of tinnitus morbidity, we will use the approach described above with other outcome variables, including the TQ subscales, global and subscale scores of the Tinnitus Functional Index, the Tinnitus Handicap Inventory, and the visual analog scale of the TRT Interview instrument. We will also compare baseline audiometric measures, and psychoacoustic variables of Tinnitus Loudness Match and Loudness Discomfort Level to evaluate whether there is any change across time in these measures.

The secondary outcome variables are the same for both the primary objective and the secondary objectives. For both the objectives, all of the longitudinally assessed variables (for example, subscales of TQ, Tinnitus Handicap Inventory, Tinnitus Functional Index, TRT-Visual Analog Scale, Digit Symbol Substitution Task, tinnitus pitch and loudness match, and LDL) will be treated as the TQ score (primary efficacy outcome analysis) using GEE. The respective mean scores will be compared between corresponding treatment groups (as described in the previous section) over the entire treatment phase. Both the differences in mean responses between treatment groups and the rate of change over time will be of interest in these analyses.

### **23.3.2.3 Missing Value Strategy**

All primary analyses will be based on the “intention to treat” principle. Every effort will be made to secure data at the protocol-defined measurement time points, even for participants who have left the study for administrative reasons or due to adverse events. We will not exclude data from participants who have used other treatments for tinnitus, despite the request at baseline that any such treatments not be used. Indeed, our intent is that all participants randomized will be included in the analyses whenever possible.

When a patient’s data are not available, we will compare participants who are lost to follow-up by with those who complete the study on baseline characteristics and treatment assignment to assess characteristics of those who do not complete the study. We will address missing data by applying a consistent missing value strategy, multiple imputation, as appropriate to the analyses of the primary and the secondary outcome measures.

Multiple imputation (or MI) assumes that the missing data is missing at random. MI is easy to implement using SAS® procedures PROC MI and PROC MIANALYZE. The MI procedure replaces each missing value in a given data set with a set of potential values that represent the

uncertainty about the right value to impute (Rubin 1986). Multiple data sets thus imputed will be analyzed using the standard statistical procedure depending on the underlying model of the outcome measure variable involved. The estimates from all the analyzed imputed data sets will be combined using MIANALYZE procedure to produce inferential results.

We have chosen to use MI, because although random imputation does eliminate the biases that can be introduced by deterministic imputation (e.g., last value carried forward (LOCF)), it may itself create bias. If it is used only once to impute the missing values and if the resulted data set is used as if it is the real data set, the resulting standard errors are too small and the test statistics are too big. To avoid this error the data set with missing values is imputed multiple times and the variability in the estimates from each imputed data set can be used to adjust the standard errors upward (Allison, 2001).

Since GEE procedures analyze only reported data we will compare its results with the imputation methods for consistency. This comparison is a form of sensitivity analysis.

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## References:

Allison, P.D., Missing data, Sage Publications, Thousands Oaks, CA, 2001.

Delb W, D'Amelio R, Boisten CJ, Plinkert PK. [Evaluation of the tinnitus retraining therapy as combined with a cognitive behavioral group therapy]. 2002. *HNO* 50:997-1004.

Dupont WD and Plummer WD: (At:  
<http://biostat.mc.vanderbilt.edu/twiki/bin/view/Main/PowerSampleSize>, accessed September 17, 2008).

Goebel G and Hiller W, Effects and predictors of a psychotherapeutic inpatient treatment for chronic tinnitus, *Proceedings of the Fifth International Tinnitus Seminar*, (p. 568-74). 1995.

Goebel G, Hiller W. Quality management in the therapy of chronic tinnitus. *Proceedings of the Sixth International Tinnitus Seminar* (p. 357-63). London, UK. 1999.

Goebel G, Rübner D, Steppurat F, Hiller W, Heuser J, Fichter MM. Controlled prospective study of tinnitus retraining therapy compared to tinnitus coping therapy and broad-band noise generator therapy. *Proceedings of the Sixth International Tinnitus Seminar* (p. 302 – 6). London, UK. 1999.

Haerkötter C. Kognitive verhaltenstherapie bei chronischen tinnitus: Evaluation neurer Ansätze. Eine Studie zu potentiellen Therapieeffekten verbesserter Edukation und apparativer Versorgung mit therapeutischem Rauschgeneratoren. Dissertation zur Erlangung des akademischen Grades Doktor der Sozialwissenschaften in der Fakultät für Sozial -und Verhaltenswissenschaften der Eberhard-Karls-Universität Tübingen. 2001. At <http://w210.ub.uni-tuebingen.de/dbt/volltexte/2001/268/pdf/HAER>

Rubin, D. B., Multiple Imputation for Nonresponse in Surveys, New York: John Wiley & Sons, Inc. 1986.

Schmitt C, Kröner-Herwig B. Comparison of tinnitus coping training and TRT: Are they superior to education? *Proceedings of the Seventh International Tinnitus Seminar* (p 272-6). Perth, Australia. 2002.

Von Wedel H, von Wedel UC. [An assessment of tinnitus retraining therapy]. *HNO* 2000. 48:887-901

Zachriat C. Vergleichende Evalutionsstudie zur Wirksamkeit des Tinnitus-Bewältigungs-Trainings und der Tinnitus-Retraining-therapie. Dissertation zur Erlangung des Doktorgrades der Mathematisch-Naturwissenschaftlichen Fakultäten der Georg-August-Universität zu Göttingen. 2003. At <http://webdoc.sub.gwdg.de/diss/2003/zachriat/zachriat.pdf>

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## **Chapter 24** **Study and Publication Policy**

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### **24.1 Publicity**

A statement describing the study, giving a general description of its design, purpose, and methods, will be prepared for informational purposes for those individuals outside the Full Investigative Group (FIG) who request these details. Information about treatment efficacy will only be made available at the end of the study. The only exception to this policy will be if the Data and Safety Monitoring Board (DSMB) and the Steering Committee (STC) have concluded, prior to the planned termination of the study, that one treatment is clearly either superior or inferior to the other, and modify the protocol accordingly.

Publicity about the study within the local tinnitus community in areas with a Clinical Center is part of the recruitment process inasmuch as the study will depend upon referral of possible Study Participants from these communities in a timely manner. Publicity about the study also will be possible throughout the larger network of U.S. Armed Forces medical center audiologists and otolaryngologists through Tri-Service conferences and meetings held jointly across the U.S. Armed Forces annually.

## **24.2 Editorial Policy**

An editorial policy for the study will be developed by the STC in the initial stages of the study. A subcommittee of the STC with specific responsibilities for dealing with matters relating to publications and presentations will be formed if necessary. In studies such as this it is important to recognize that the study is being carried out under a collaborative arrangement among all centers, and that the study has been designed to address questions based on data from all Clinical Centers combined. This is the form in which the DSMB will examine the data. Presentations or publications based on data from individual Clinical Centers will, in general, not be appropriate. The STC will develop a policy regarding authorship of papers from the TRTT. This policy will include guidelines for whether papers will be published in the name of the research group without mention of specific authors, or using a format in which names of authors are specifically mentioned. Papers describing the main results of the TRTT (comparisons of treatment groups) will follow corporate or group authorship format. Corporate authorship will name "The Tinnitus Retraining Therapy Trial Research Group" as author and individual investigators and Clinical Center staff will be named at the end of the article.

### **24.2.1 Publication of Trial Design, Methods, and Findings**

The entire FIG and its leadership committees will be expected to provide input with regard to topics for publication particularly with regard to the area of trial design, methods, and findings. The Data Coordinating Center (DCC), in conjunction with the STC will develop and maintain a list of topics, questions, and investigations considered appropriate for publication. The STC will be responsible for providing guidance to the DCC with regard to the sequence in which the topics are to be pursued. Publications will probably include the following:

- A paper describing the design and rationale for the TRTT, including a description of followup procedures, and methods for data collection; and
- One or more papers describing the results of the TRTT as measured by comparisons between the treatment groups for differences in scores on the Tinnitus Questionnaire (TQ) during followup, as well as differences for the secondary outcomes.

Paperwriting activities involve considerable amounts of time and effort, particularly by members of the Chair's Office and DCC. All writing committees for TRTT papers will include at least one representative from the Study Chair's Office and the DCC. Other members will be picked by the Executive Committee (EC) from the membership of the FIG, as dictated by interest

and by the expertise needed for the paper. All manuscripts emanating from the TRTT will be submitted to journals complying with the NIH Public Access Policy. All publications will be archived in PubMed Central as required by this policy.

Publications using TRTT results or which are intended to describe its design or procedures will require clearance by the EC.

#### **24.2.2 Presentations**

Guidelines for preparing presentations are in general similar to those for preparing publications. Abstracts prepared for submission to program committees for local, national, or international meetings must be approved by the EC prior to submission. Abstracts may, in special cases, be submitted prior to review and approval provided the submitter is willing to withdraw the abstract after submission if it is not approved by the EC upon review.

#### **24.2.3 Publications from Ancillary Studies**

An ancillary study is defined in Subsection 24.3.1. Publications from ancillary studies will be subject to the same review as publications from the TRTT.

### **24.3 Ancillary Studies**

#### **24.3.1 Definition of an Ancillary Study**

Ancillary studies are studies that are not considered essential to the design or conduct of the TRTT but which involve patients or data collected on patients enrolled in the TRTT. An ancillary study might be carried out on all patients enrolled in the study, or on some subset of patients (e.g., patients enrolled at specific clinics or specific subgroups of patients).

Ancillary studies must not interfere with the design or conduct of the TRTT. For example, they must not involve unblinding of clinic study personnel, who are otherwise blinded as to patient treatment allocation, and must not interfere with the treatments being studied in the TRTT.

### **24.3.2 Preparation for Request for Approval for an Ancillary Study**

An investigator wishing to carry out an ancillary study must submit a short, written protocol describing the following:

- Aim of the study;
- Patient population;
- Data collection procedures and/or description of existing data to be used;
- Proposed analyses;
- Resources required, separated by use of existing resources and proposed additional resources for which additional funding will be sought; and
- Projected timetable.

The protocol must be submitted to the STC and the DSMB for review. Studies that require additional funding will not be supported with TRTT funds. The required funds will have to be raised by the proposing investigator via a separate grant application or other means.

### **24.3.3 Procedures for Obtaining Ancillary Study Approval**

After a written request for approval of an ancillary study has been received by the STC and the DSMB including a description of the protocol as outlined in Subsection 24.3.2, these two committees will vote on whether to approve or disapprove the request. Approval must be obtained from both committees. Approval by these committees does not obligate a Clinical Center to participate in the ancillary study. The proposing investigator is responsible for obtaining the necessary commitment from each of the Centers he or she wishes to involve. This approval includes both Clinical Centers and resource Centers.

If the STC and the DSMB receive several requests for approval for different ancillary studies that have the potential to conflict with each other (e.g., in terms of requirement for resources or involvement of patients) the STC will vote on the relative merits of each such study. The criteria for evaluating the proposals will include scientific contribution and relevance to the questions being addressed in the TRTT.

## **24.4 Access to Study Information**

It is important that access to study information be limited to authorized people only. Personnel should not become inappropriately unblinded as a result of access to study information. Study data will be recorded on forms and stored in data files, using only study ID numbers, not personal identifiers. Each Clinical Center is responsible for ensuring that the lists or cards on which study ID numbers are cross-referenced to personal identifiers are kept in a locked file cabinet or box so that confidentiality is maintained. No center other than the Clinical Center at which a patient is enrolled will have access to this identifying information. The appropriateness of handling study information will be one of the items evaluated during site visits to each Center (see Section 16.3). Chapter 18 describes the responsibilities of personnel at the Clinical Centers, and what components of the treatment should be blinded for these individuals.

### **24.4.1 Study Documents**

Study documents such as forms and manuals of procedures will be released for the information of individuals outside the FIG at appropriate times during the course of the study. The STC will decide which documents are to be released and the timetable for their release. Documents that are released will be placed in the library of the National Technical Information Service in Springfield, Virginia. Individuals wishing to access released study documents may apply to the NTIS using whatever application procedures are in force at the time of application.

### **24.4.2 Study Data**

Completed data collection forms will be stored at the center where the form was completed. For example, the form on which baseline medical history is recorded will be stored at the Clinical Center. Computer files containing the data for enrolled patients from all centers will be maintained at the DCC. Data at the DCC will be identified only by study identification number, and not by personal identifiers.

Access to study data by individuals outside the FIG will not be available while enrollment and follow-up of Study Participants is still underway. Any special circumstances that arise that might give rise to the requests for data before the end of the study, (e.g., if enrollment and follow-up for one or more treatment groups is discontinued but recruitment and follow-up is still continued for the remaining treatment groups) will be considered separately.

At the conclusion of the TRTT and following publication of the main study findings, the DCC will organize the TRTT data into a Public Use Dataset suitable for use by members of the research community, and prepare documentation of the Public Use Dataset. The TRTT Public Use Dataset will be:

- Preserved in an electronic format accessible to standard database/analytic software; and
- Archived at the Johns Hopkins Bloomberg School of Public Health, under the auspices of the Principal Investigator of the DCC.

Documentation for the TRTT Public Use Dataset will be developed and described in a Codebook with the following information:

- Contents of the Public Use Dataset;
- Format of the Public Use Dataset; including naming conventions;
- Methods and procedures used to collect, process, and store the data; and
- Documentation for specific study decisions related to the data taken as the project was ongoing.

The exact time at which data will be publically available as a Public use Dataset will be decided by the STC, but is expected to be at some time after analyses have been carried out to address the main study questions. Individuals, including individual investigators within the FIG or individuals outside of the group who are interested in the results of a particular analysis, or individuals wishing to have analysis carried out prior to study data having been released, may make a request to the STC. Such a request will be reviewed, and if approved, the analyses will be carried out and made available both to the FIG and to the individual requesting the analyses.

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## **Chapter 25** **Patient Informed Consent**

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### **25.1 Overview of Patient Consent and Authorization**

Each Study Participant enrolling in the Tinnitus Retraining Therapy Trial (TRTT) will provide informed consent for participation in this research and permission for their health records to be transmitted from the Clinical Center to the Data Coordinating Center (DCC) for analyses. The latter authorization will conform to regulations in the Health Insurance Portability and Accountability Act (HIPPA). Depending on local requirements, the HIPPA Compliance documentation may either be part of the informed consent statement or provided as a separate document. Each Clinical Center will determine appropriate informed consent and HIPPA authorization forms in compliance with local Investigational Review Board (IRB) requirements.

#### **25.1.2 Patient Consent**

The patient consent process involves providing the patient a clear description of:

- How the patient qualifies for the study;
- The treatments to be studied and the rationale for the choice of treatment;
- Treatment alternatives available outside of the TRTT or the lack of such alternatives;
- The method of assigning patients to treatment;
- The data collection schedule procedures and the anticipated length of follow-up;
- The risks and benefits from participation in the TRTT;

- The patient's responsibilities for participation in the TRTT; and
- Safeguards in place to protect the patient's well-being.

In addition, the consent process involves:

- Giving the patients sufficient time to review the information provided to them before being required to make a decision;
- Answering any questions that the patient has based on the information provided; and
- Ensuring that the consent, when obtained, is given voluntarily.

The sample patient consent form for this study is provided in Section 25.2. This consent allows for evaluation and entry into the TRTT and gives consent for randomized treatment assignment to one of the treatment groups (described in Chapters 2 and 5).

Each Clinical Center must obtain local IRB approval of the human subjects procedures and informed consent statements. If an IRB requires additions to the consent forms developed for the TRTT, then these revisions may be made and sent to the DCC; however, the materials contained in the consent statement developed for the TRTT must be included in the statement used at each Clinical Center. When additions or changes are made in the Clinical Center's informed consent materials, then the modified consent form should be sent to the Data Coordinating Center with Clinical Center staff highlighting the changes from the sample consent forms. The DCC staff will review these changes and present a report to the Data and Safety Monitoring Board (DSMB) indicating minor and major deviations from the sample consent forms.

### **25.1.2 HIPAA Authorization**

Individuals who are screened for eligibility or who agree to participate in the TRTT will provide permission for their data to be transferred to the DCC per HIPPA guidelines. HIPPA will be obtained in writing from the patient at each local Clinical Center.

The HIPPA authorization will inform the patient about the:

- Specific health and data information to be collected that will be used in the TRTT;
- TRTT investigators, staff, and affiliated organizations who may use or disclose the participant's health information;

- TRTT investigators and staff who will receive the patient's data or health information for analyses;
- Reasons for the use or disclosure of the patient's data or health information by the TRTT staff;
- Expiration date or termination event after which TRTT staff will cease to use or disclose relevant patient data or information
- Right to refuse to sign the authorization for release of patient information;
- Right to revoke the authorization; and
- Potential re-disclosure by the external research sponsor (NIH), which will not be covered by HIPPA privacy regulation.

A sample HIPPA authorization form for this study is provided in Section 25.4. Alternatively, the material contained in this form may be combined with the informed consent statement.

## 25.2 Sample Consent for Research Participation

This is an example of an informed consent statement for research participation. It is administered after screening and prior to eligibility evaluation at the Baseline Eligibility Visit and randomization.

Title of Research Project: Tinnitus Retraining Therapy Trial

Principal Investigator: C. Formby, Ph.D.

Phone: (205) 348-1847

Sponsor: National Institutes of Health

National Institute of Deafness and Other Communication Disorders

Please read this form carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. If there are any words or information that you do not understand, the study doctor or study staff will explain them to you. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. Before you take part in the research study, you must sign the end of this form.

### Purpose:

We are asking you to join this research study, the Tinnitus Retraining Therapy Trial (TRTT). Tinnitus is a set of symptoms that is often described as a ringing, buzzing, chirping, or roaring sound in one or both ears. Because there is currently no special treatment for tinnitus, we are conducting a research study. We will test whether TRT is a better treatment than the usual care offered to tinnitus patients. We will also test whether both parts of the costly TRT treatment are necessary for it to work. TRT includes special counseling and wearing instruments in the ear. The instruments make seashell like sounds. Although TRT appears to help many people with tinnitus, it has not yet been scientifically tested and it is unclear how it works, or if it works.

You are being asked to take part in this study because you have serious tinnitus for which TRT has been beneficial for some persons. This study includes only those people who choose to take part. Please take your time to make your decision and feel free to ask any questions that you might have.

You would be one of about 38 patients in this study at our Clinical Center. You would be one of about 228 patients in this study nationwide at 6 military Clinical Center locations.

## Procedures

You will have medical exams similar to those performed for persons with tinnitus. We will ask some questions about your tinnitus and about your medical history as it relates to your tinnitus or other hearing problems. You will have a physical examination. Your ears, eyes, head, neck, nervous system, heart, blood vessels, and lungs will be examined. You will also have standard hearing tests to examine your hearing and tinnitus. You will also be asked questions about how the tinnitus affects your daily activities. You will also be asked questions about your mental health. The total testing time will be about three hours, but may be longer if additional tests are required. Other tests that may be performed include blood tests, imaging tests, or tests for mental health. The exam and the tests will be used to see if you have a medical condition related to your tinnitus that can be treated with medicine or surgery. If you do, then you would not be eligible for this study. If none is found, then you might be eligible for the research study.

If you decide to join this study, you will receive one of three treatments. Which treatment you receive will be decided randomly using a computer in a way similar to flipping a coin. You will receive one of the three following treatments:

1. Directive Counseling + Conventional Sound Therapy: If you are assigned to this group, then you will receive information and counseling about your tinnitus. You will also receive follow-up counseling. You will be given a pair of sound therapy instruments worn in your ear that make a soft noise. Ear impressions may be required to customize the in-the-ear therapy instruments. You will be asked to wear and use one of the instruments in each ear as much as possible throughout each day.
2. Directive Counseling + Experimental Sound Therapy: If you are assigned to this group, then you will receive information and counseling about your tinnitus. You will also receive related follow-up counseling. You will be given a pair of sound therapy instruments worn in your ear that makes a soft noise. Ear impressions may be required to customize the in-the-ear therapy instruments. The noise will be like that produced by the conventional sound therapy instruments, but the dosage of the noise will be different. You will be asked to wear and use one of the instruments in each ear as much as possible throughout each day
3. Standard of Care Therapy: If you are assigned to this group, then you will receive the counseling that is usually given to tinnitus patients in most military health care settings, including follow-up care.

The conventional sound therapy and the experimental sound therapy instruments will look exactly the same. You and your doctor will not know which one you received.

You will be asked to come in to the clinic for appointments. The first appointment will be within 2 months of when you decide to join the study but could be sooner. At this visit, you will begin treatment. This visit will last about 3 hours. About a month later, you will be seen for a second visit for more counseling. You may also receive counseling at 3 and 6 months after the first visit. These visits will each last about  $\frac{1}{2}$  hour. Counseling may also be needed at other times and will also last about 15 minutes.

You will complete hearing tests at your Clinical Center at about 3, 6, 12, and 18 months after treatment begins. You will also complete a set of questionnaires at 3, 6, 12, and 18 months after treatment begins and annually until the end of the study. We also ask if we can contact you at some time in the future if we need to check information or see if your treatment is still working to help you with your tinnitus.

You will spend about 13-15 hours being in this study over the next 18 months. This includes your time for testing, treatment and completion of follow-up measurements and questionnaires. It may also include brief telephone contacts to check on your progress. This does not include your travel time to and from your clinical center visits.

After the final 18-month visit, you will enter the follow-up phase of the research study. The follow-up phase will continue until the end of the overall study, up to three years. The annual follow-up includes completion of three questionnaires about tinnitus and will take about an hour of your time to complete. The questionnaires will be mailed to you and will include a self-addressed, stamped envelope for you to return.

### **When Should You Not Take Part?**

If you have any of the following conditions or are taking any of the medicines listed below, you should not take part in this study;

- History of a head trauma within the last 24 months;
- History of multiple sclerosis;
- Use of a cancer chemotherapy drug within the past 12 months;
- Use of 325 mg of aspirin per day;
- A medical condition that is not controlled, such as diabetes, high blood pressure, thyroid problems, or an autoimmune disease; or
- Not eligible for medical care at a Department of Defense Clinical Center or Veterans medical treatment facility.

### **Risks/discomforts**

The risks from the exam are the same as those from hearing tests and general medical examinations in an ear, nose, and throat doctor's office. You may feel some discomfort when the doctor examines your head and neck areas by touching requiring some pressure. Also, there may be some risk if there is a need to draw a blood sample. Some people feel a slight discomfort or even pain when we take the blood sample from your vein. Sometimes people feel faint for a few minutes. Some people get a bruise mark on their vein after giving a blood sample. Any bruise mark should disappear in a few days.

There are no known risks to you from being in this study. You might be assigned to a treatment that is not the best treatment. None of the treatments will make your tinnitus worse. One of the treatments in this study may be better than the others. If you received a different treatment, then at the end of this study you will be offered the best treatment at no cost.

There also may be other side effects that are unknown.

### **Benefits**

There is no guarantee that you will receive any benefits from being in the study. However, you

- Will have detailed tests and examinations to check your health, hearing, and tinnitus. These test results are available to you or your family doctor on request.
- May contribute to medical research
- May benefit from the study treatment because it will help your tinnitus
- May prevent future patients from the inconvenience and expense of TRT if it does not work.

### **Confidentiality**

If you are not eligible for the study as a result of this exam, no data will be collected for the study except the reason you are not eligible.

If you are eligible for the study, we will collect research data for the study from your exam and study visits. We will make every effort to protect your privacy and keep your data confidential.

- We will use only study codes to identify your data and study records.
- The study data and records will be kept in a secure place.
- Personal information such as your name, address and telephone number will not be in the central study computer files

- The identity of all study participants is kept confidential. We will not identify anyone when we publish the findings of the study.

### **New findings**

We will tell you about any new findings from outside the study that might change your decision to continue in this study.

### **Costs**

Your insurance carriers will be asked to pay for costs for the office visits and tests that take place during the exam. You may be responsible for the deductible and/or other costs not covered by your insurance carrier.

The treatment that you receive in this study and the related follow-up will be administered at no expense to you.

### **Payment**

You will not be paid for your participation in this study.

### **Alternative treatment**

Currently there is no proven treatment for severe tinnitus. Your participation in this study will not deny you of any established alternative treatment. Choosing not to participate in this study is your alternative to volunteering for the study.

### **Compensation for injury**

It is unlikely that you will get injured as a result of participating in this study. If you are harmed as a result of your participation in this study, medical treatment is available at [name site]. All medical care (*including medical treatment for injuries related to this study and medical care unrelated to this study*) will be evaluated and provided in keeping with the benefits to which you are entitled under applicable regulations.

### **Voluntary Participation/Withdrawal**

Your participation in this study is voluntary. You have the right to decline to participate in this research. In addition, you may decline to participate in any specific study procedure or complete

any questionnaire. You may leave the study at any time without risk to you. This will not affect your current or future medical care in any way at this Clinical Center or elsewhere.

Even if you are not eligible now to join this study or decide not to join this study, then we still would like to have permission to contact you later to ask you questions that may help us to understand tinnitus. At that time, you would be asked to sign a new consent form allowing us to ask you more questions. Even if you do not allow us to contact you in the future, you may still qualify to join this study.

You have the right to decline future use of your data or information that you provided for this study, while still participating in this investigation. If you decide you do not want your information used in the study, please contact the director of the study at your participating Clinical Center.

### **Authorization to use and Disclose Information for research purposes**

[Insert local HIPAA language here]

### **Who do I call if I have questions or problems?**

- Call the principal investigator, [insert name], at [telephone number] if you have questions, complaints, or get sick or injured as a result of being in this study.
- Call or contact the [institution] IRB Office if you have questions about your rights as a study participant. Contact the IRB if you feel you have not been treated fairly or if you have other concerns. The IRB contact information

*(The name, address, and telephone number of the site's IRB)*

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all your questions.

If you agree to participate in this study, you will receive a signed and dated copy of this consent form for your records.

**Consent:** I have read the information in this consent form. All my questions have been answered. I freely consent to participate in this study. I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above. By signing this consent form I have not waived any of the legal rights, which I otherwise would have as a participant in a research study.

---

Print name of Participant

Signature of Adult Participant

---

Date

**Signature of person obtaining consent:** I confirm that I have explained the study to the extent compatible with the participant understands and that the participant has agreed to be in the study.

---

Print name of Person  
Obtaining ConsentSignature of Person  
Obtaining Consent

---

Date

**25.3 Addendum Informed Consent for Participation in Research Activities**

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This is an example of an addendum to the original informed consent statement, allowing continued follow-up in the TRTT. It is administered at any time for study participants who had not initially agreed to more than 18 months follow-up

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**Title of Research:** Tinnitus Retraining Therapy Trial

**Investigator(s):**

**IRB Approval #:**

**Sponsor: NIH/NIDCD**

You are currently taking part in the research study titled, "Tinnitus Retraining Therapy Trial." This study is being conducted at [insert name]. The purpose of this document is to provide you with more information about the study, which will be discussed with you.

Since the time you signed the original consent form for this study, a change has been made to the protocol to include the completion of annual follow-up questionnaires after you complete the final 18 month visit. The questionnaires will be administered annually until the end of the entire study; up to three years. The annual follow-up includes completion of three questionnaires, the Tinnitus Questionnaire, Tinnitus Functional Index and the Tinnitus Handicap Inventory, and will take about an hour of your time to complete. The questionnaires will be mailed to you and will include a self-addressed, stamped envelope for you to return.

Your continued participation in this research is voluntary and refusal to take part will involve no penalty to you or loss of any benefits to which you are otherwise entitled. You may withdraw from the research study now or at any time without penalty or loss of benefits to which you are otherwise entitled. You will be informed of any significant new findings developed during the course of participation in this research that may have a bearing on your willingness to continue in the study. The investigator may withdraw you from this research if circumstances arise which makes this necessary.

If you would like, the information in the original consent form may be reviewed with you.

**QUESTIONS, CONCERNS OR COMPLAINTS**

If you have questions about the study now, please ask them. If you have questions or concerns later, you can reach [insert name] at [insert telephone number].

You do not give up any of your legal rights by signing this consent form.

**STATEMENT OF CONSENT:**

**Consent:** I have read the information in this consent form. All my questions have been answered. I freely consent to participate in this study. I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above. By signing this consent form I have not waived any of the legal rights, which I otherwise would have as a participant in a research study.

---

Print name of Participant

---

Signature of Adult Participant

---

Date

**Signature of person obtaining consent:** I confirm that I have explained the study to the extent compatible with the participant understands and that the participant has agreed to be in the study.

---

Print name of Person  
Obtaining Consent

---

Signature of Person  
Obtaining Consent

---

Date

## 25.4 Sample HIPPA Form

This is an example of an authorization statement satisfying HIPPA requirements.

Health Insurance Portability and Accountability Act  
**AUTHORIZATION TO OBTAIN, USE AND DISCLOSE  
PROTECTED HEALTH INFORMATION FOR RESEARCH**

Name: \_\_\_\_\_

Date of Birth: \_\_\_\_\_ Medical Record Number: \_\_\_\_\_ SSN: \_\_\_\_\_

Federal laws require that hospitals, researchers and health care providers protect the privacy of information that identifies you and relates to your past, present and future physical and mental health or conditions, or the provision of health care. If you agree to participate in this research, protected health information will be used and shared with others. The following questions and answers provide more specific information about how your information will be used, protected and shared. In addition you should have received a “(institution) Notice of Privacy Practices.” If you have not received this notice please ask the researcher.

**The information will be used or disclosed to perform the following research study:**

*IRB Number:*

Tinnitus Retraining Therapy Trial

**The protected health information to be Used or Disclosed:**

- Health-related information you have been asked to provide for the study during interviews, via questionnaires;
- Results of hearing and other diagnostic tests obtained during the study visit relating to eligibility for the study and participation in the study; and
- Results of laboratory tests and research procedures carried out for the purposes of the study.

**The following are Authorized to Use or Disclose the Information:**

*Name of Clinical Center Principal Investigator and Co-Investigators and the Clinical Center research team*

Dr. Craig Formby at the University of Alabama and his research team

Dr. Roberta Scherer at the Johns Hopkins Bloomberg School of Public Health, Baltimore Maryland, and her research team

**The following are authorized to receive some or all of the information:**

Investigators at the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health, who are all participating in the research study.

In addition, representatives of Federal agencies, the (*Clinical Center*) Institutional Review Board, (*Clinical Center*) Research Compliance offices, (*Clinical Center*) Legal Counsel, may review records in order to meet federal or state regulations.

**For how long will your protected health information be used or shared with others?**

There is no scheduled date at which this information will be destroyed or no longer used. This is because information that is collected for research purposes may be analyzed for many more years and it is not possible to determine when analysis will be complete.

**Additional information about this authorization**

You can change your mind and not let the researcher disclose or use your protected health information (revoke the Authorization). If you revoke the Authorization, you must send a written letter to: (*Clinical Director*) at (*phone number*) to inform (*him or her*) of your decision. If you revoke this Authorization, researchers may only use and disclose the protected health information already collected for this research study. However, your protected health information may still be used and disclosed should you have an adverse event (a bad effect). If you change your mind and withdraw the authorization, you will not be allowed to continue to participate in the study.

You have the right to choose not to sign this form. However, if you decide not to sign, you cannot participate in the research. Refusing to sign will not affect the present or future care you receive at this institution and will not cause any penalty or loss of benefits to which you are otherwise entitled.

Once your health information has been disclosed to anyone outside of the (*institution*), the federal law designed to protect your privacy may no longer protect the information. The researchers and the National Institute on Deafness and Other Communication Disorders are required to take reasonable steps to protect your health information by using and disclosing it only as described in this Authorization.

Subject to certain legal limitations, you have the right to access your protected health information that is created during this research that relates to your treatment or payment, provided your right to access is not exempted by law. In some cases, you may access this information only after the study analyses are complete. To request this information, you will need to contact the (*institution*) Privacy Officer at (*phone number*)

My signature indicates that I authorize the use and disclosure of my protected health information for the purposes described above. I also permit my doctors and other health care providers to disclose my protected health information for the purposes described above.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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