A Prospective, Post-Market, Multi-Center Study Evaluating ViBone® in Cervical and Lumbar Spine Fusion

Clinicaltrials.gov Identifier:

NCT03425682

Original Protocol Version Date: 11/17/2017

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Protocol Synopsis

Company:	Aziyo Biologics, Inc.
Protocol Number:	CLP-0001
Product:	ViBone® Viable Bone Matrix
Protocol Title:	A Prospective, Post-Market, Multi-Center Study Evaluating ViBone in Cervical and Lumbar Spine Fusion
Treatment Indication:	Spondylosis, spondylolisthesis, degenerative disc disease, or herniated nucleus pulposus affecting either 1 to 3 contiguous levels between C2 and C7 (for cervical patients) or L1 and S1 (for lumbar patients).
Purpose:	The purpose of this study is to assess clinical and radiographic outcomes in patients who undergo 1-3 level anterior cervical discectomy fusion (ACDF) or lumbar interbody fusion (TLIF, PLIF, ALIF, LLIF) using ViBone. Subjects will be followed for 12 months following surgery to determine the number of study subjects that are solidly fused at or before 12 months postoperatively. The data for cervical and lumbar fusions will be analyzed separately and will be compared to published and/or retrospective data for autograft or other similar graft materials.
Design:	Up to 50 patients undergoing ACDF using ViBone will be enrolled. Up to 50 patients undergoing lumbar interbody fusion using ViBone will also be enrolled. Subjects will be followed via the enrolling center's standard of care for the procedure. Data from patients meeting the study criteria will be gathered at baseline, 6 months, and 12 months post-surgery.

Patient Population:	Included are both male and female patients, 18-80 years of age with spondylosis, spondylolisthesis, degenerative disc disease, or herniated nucleus pulposus affecting 1, 2, or 3 contiguous levels of the spine between C2 and C7 (for cervical patients) or L1 and S1 (for lumbar patients). Patients must be undergoing ACDF or lumbar interbody fusion using ViBone to be eligible for the study.
Outcome Measures:	Primary: • Incidence of successful fusion measured radiographically by 12 months post-surgery Secondary: • Incidence of successful fusion measured radiographically by 6 months post-surgery • Oswestry Disability Index (ODI)/Neck Disability Index (NDI) relative to baseline. • Visual Analog Scale (VAS) relative to baseline. • Incidence of subjects experiencing ViBone-related serious adverse reactions.
Duration:	Subjects will be evaluated via routine follow up visits through 12 months post-surgery.
Centers:	Up to 20 centers in the U.S.

Study contact for discussion of protocol-specific issues:

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SAFETY REPORTING CONTACT INFORMATION: REPORTING OF SAFETY INFORMATION TO SPONSOR

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1 ABBREVIATIONS

AATB	American Association of Tissue Banks
ACDF	Anterior Cervical Discectomy and Fusion
ALIF	Anterior Lumbar Interbody Fusion
Aziyo	Aziyo Biologics, Incorporated
BMI	Body Mass Index
BMP	Bone Morphogenetic Protein
C	Celsius
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
cm	Centimeter
CMS	Centers for Medicare and Medicaid Services
CRF	Case Report Form
CT	Computed Tomography
CV	Curriculum Vitae
DBM	Demineralized Bone Matrix
DDD	Degenerative Disc Disease
DMARD	Disease-Modifying Antirheumatic Drugs
DMSO	Dimethyl Sulfoxide
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EoT	End of Treatment
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
GCP	Good Clinical Practice
HCT/P	Human Cellular and Tissue Based Product
HIPAA	Health Insurance Portability & Accountability Act
HIV	Human Immunodeficiency Virus
ICBG	Iliac Crest Bone Graft
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IRB	Institutional Review Board (includes ethics committee)
LLIF	Lateral Lumber Interbody Fusion
NaCl	Sodium Chloride
NDI	Neck Disability Index
ODI	Oswestry Disability Index
PHI	Protected Health Information
PI	Principal Investigator
PLIF	Posterior Lateral Interbody Fusion
SOP	Standard Operating Procedure
TLIF	Transforaminal Lateral Interbody Fusion
VAS	Visual Analog Scale
WBC	White Blood Count

2 TRADEMARK STATEMENTS

Aziyo® and ViBone® are registered trademarks of Aziyo, Inc.

3 INTRODUCTION

3.1 Spine Fusion

Degenerative disorders of the spine can lead to a multitude of clinical problems including pain, weakness, numbness, tingling and deformity. When conservative (non-surgical) treatment fails after at least a 6-month period and/or non-operative treatment is not indicated, patients and physicians may turn to a surgical solution. Surgical options consist of decompressing nerves, correcting and/or stabilizing deformities if required and fusing the segment, depending on the clinical situation. The "gold standard" for aiding healing in spinal fusion surgeries is the harvesting of autograft from the patient's iliac crest and placing it in and around the segments of the spine that are intended to be fused. Autograft is considered the "gold standard" because it contains the essential elements required for successful bone grafting: osteogenesis, osteoconduction, and osteoinduction.

However, the morbidity of harvesting autograft has been well documented and includes chronic donor-site pain, infection, neurologic injury, blood loss, deformity, bowel injury, hernia, and prolonged surgical and hospitalization time. There are now a number of products on the market to minimize or replace the use of autograft. However, few of these products contain all three essential bone-forming elements (osteogenesis, osteoconduction, and osteoinduction).

3.2 Viable Bone Allografts

ViBone is a human tissue allograft consisting of cryopreserved bone matrix that is aseptically processed to preserve native factors that support bone repair. ViBone is a Human Cellular and Tissue Based Product (HCT/P) per 21 CFR Part 1271. It is restricted to homologous use for transplant in procedures on a single occasion by a licensed physician or surgeon.

3.3 Description of ViBone

ViBone provides all three components critical for bone regeneration: osteoconductivity, osteoinductivity, and osteogenicity. It is a next generation cellular bone matrix that has been optimized to preserve the health of native bone cells and yield more readily available bioactive agents to enhance new bone formation while ensuring a safe allograft tissue for transplantation.

ViBone is supplied ready to use and must be stored in its original packaging at -75°C to -85°C until prepared for use. It is the responsibility of the transplant facility or clinician to maintain the allograft intended for transplantation in the appropriate recommended storage conditions prior to transplant. Refer to the package insert (Appendix 4) for warnings and precautions and usage instructions.

4 STUDY PURPOSE AND OBJECTIVES

4.1 Study Purpose

The purpose of this prospective registry is to assess clinical and radiographic outcomes in patients who undergo ACDF or lumbar interbody fusion surgery using ViBone.

4.2 Objectives

Subjects will be followed for 12 months post-surgery to determine the incidence of successful fusion at 12 months postoperatively. This data will be compared to published and/or retrospective data for autograft or other similar products.

Additional study objectives include:

- Incidence of successful fusion measured radiographically at 6 months post-surgery
- Change from baseline in Oswestry Disability Index (lumbar interbody fusion patients) or Neck Disability Index (ACDF patients)
- Change from baseline in Visual Analog Scale for back and leg pain
- Incidence of ViBone-related serious adverse reactions

5 STUDY DESIGN

5.1 Design Summary

This study is a multi-center, post-market, prospective patient registry to evaluate the clinical and radiographic outcomes of ViBone in patients undergoing cervical or lumbar spine fusion. Data will be gathered for up to 50 subjects undergoing ACDF surgery and up to 50 subjects undergoing lumbar interbody fusion surgery using ViBone. Total enrollment is expected to be approximately 200 subjects. The purpose of this study is to assess clinical and radiographic outcomes in patients who undergo 1-3 level ACDF or lumbar interbody fusion surgery using ViBone. Subjects will be followed for 12 months post-surgery to determine the number of study subjects that are solidly fused at 12 months postoperatively. This data will be compared to published and/or retrospective data for autograft or other similar products.

5.2 Patient Enrollment

All patients who sign an Institutional Review Board (IRB) approved Informed Consent Form (ICF) and an authorization for Protocol CLP-0001 for use of Protected Health Information (PHI) will be assigned a unique screening number consisting of a 4-digit sequential number assigned by Medrio EDC.

6 PATIENT SELECTION

6.1 Study Population

Up to 50 ACDF and up to 50 lumbar interbody fusion patients from up to twenty centers in the United States will be enrolled. The study population will consist of male and female patients, 18-80 years of age. Eligible patients should have spondylosis, spondylolisthesis, degenerative disc disease, or herniated nucleus pulposus. Cervical fusion patients shall undergo ACDF surgery using ViBone at 1 to 3 contiguous levels between C2 and C7. Lumbar fusion patients shall undergo lumbar interbody fusion surgery using ViBone at 1 to 3 contiguous levels between L1 and S1.

6.2 Eligibility criteria

6.2.1 Informed Consent Form

Each patient will be required to sign an IRB-approved ICF prior to enrollment in the study.

The ICF and product package insert will be used to explain the study and fully disclose known risks and benefits. Subjects will not directly benefit from being in this study; however, the results of this study may help people undergoing spine fusion in the future. As with implantation of all human allograft tissue, risks associated with the implantation of ViBone include lack of response from the recipient (e.g., lack of fusion or non-union with adjacent tissue). It is also possible for a host site to become infected or the allograft tissue may cause an inflammatory response. Current technologies may not preclude the transmission of infectious agents or disease, including hepatitis and HIV. ViBone is preserved in 5% dimethyl sulfoxide (DMSO) in a 0.9% sodium chloride solution. Povidone iodine, Dulbecco's phosphate buffered saline, sodium chloride irrigation solution, sodium phosphate, hydrochloric acid and hydrogen peroxide are all used for processing, preservation and storage of the allografts and trace amounts of these solutions may be present in the product.

There are no additional medical risks involved in participating in this study. The only additional risk from taking part in this study is that the confidentiality of subject information may be lost or compromised.

The ICF must include the elements required by the FDA in US 21 CFR 50 and International Conference on Harmonization (ICH) guidelines.

Patients will also be required to consent to the use of their PHI according to all applicable health information privacy regulations. This authorization can be part of the ICF or can be a separate document.

Each Investigator participating in the study is responsible for obtaining approval from Aziyo for any consent documents prior to their submission to their IRB and prior to their use. Each Investigator participating in the study is also responsible for ensuring that a written ICF and written authorization for use of PHI are obtained from each patient that they enroll into the study at the time of that patient's enrollment. Documentation of the informed consent process must be completed by research personnel and the patient will receive a copy of the signed ICF. No study-related activities may be performed on any patient and no data may be

collected from any subject for study purposes prior to receiving these consents and authorizations.

Subjects will be allowed to withdraw consent at any time for any reason.

6.2.2 Inclusion Criteria

In order to be eligible, patients are required to meet the following inclusion criteria:

- Male or female, 18-80 years of age
- For cervical cases – ACDF surgery at 1, 2, or 3 contiguous levels between C2-C7
- For lumbar cases – lumbar interbody fusion surgery at 1, 2, or 3 contiguous levels between L1-S1
- Patient signed Informed Consent Form with HIPAA Authorization
- Appropriate candidate for surgery
- Patient will adhere to the scheduled follow-up visits and requirements of the protocol
    - Routine patient exams include pre-operative, operative, and at least two post-operative visits (6 and 12 months post-surgery)
    - Pre-operative and post-operative visits include radiological examination (X-ray (required) and CT scan (if available))

6.2.3 Exclusion Criteria

Patients are excluded if any of the following exclusion criteria are met prior to undergoing surgery:

- Long term use of medications that are known to inhibit fusion or bone metabolism or immune suppressants 6 months prior to surgery (i.e., steroids, chemotherapy, DMARDs, etc.)
- Treatment with radiotherapy Both cervical and lumbar fusion during the same procedure
- Acute or chronic systemic or localized spinal infections
- Instability associated with major reconstructive surgery for primary tumors or metastatic malignant tumors of the cervical (for ACDF patients) or lumbar (for TLIF, PLIF, LLIF, and ALIF patients) spine
- Previous pseudoarthrosis at any level of the cervical (for ACDF patients) or lumbar (for TLIF, PLIF, LLIF, and ALIF patients) spine
- Nursing mothers or women who are pregnant or plan to become pregnant during the course of the study

- Current or recent history of malignancy or infectious disease. Patients with current or recent history of basal cell carcinoma are eligible.
- Inability to provide informed consent
- Rapid joint disease, bone absorption, osteomalacia, and/or diagnosed osteoporosis (bone density test score of ≤-2.5).
- Other medical or surgical conditions which would preclude the potential benefit of surgery, such as congenital abnormalities, immunosuppressive disease, elevation of sedimentation rate unexplained by other diseases, elevation of white blood count (WBC), or marked left shift in the WBC differential count.
- Active local or systemic infection or is undergoing adjunctive treatment for local or systemic infection.

7 STUDY PROCEDURES

7.1 Schedule of Assessments

Study assessments are summarized below in Table 1, and are further described in Section 7.2.

Table 1: Schedule of Assessments

	Pre-Surgery Screening Visit	Surgical Procedure Visit	Follow-Up Visits (+/- 1 Month)
Visit Window	Day -30 to 0	Day 0	6 and 12 Months Post Surgery
Inclusion/Exclusion Determination	X		
Informed Consent/PHI Authorization	X		
Baseline Demographics and Basic Patient Information	X		
Surgical Procedure Details		X	
Radiological Assessment (including flexion/extension)	X[1, 2]		X[3]
Oswestry Disability Index (Lumbar Fusion) or Neck Disability Index (Cervical Fusion)	X		X
Visual Analog Scale (Both Leg and Back Pain)	X		X
ViBone-Related Serious Adverse Reactions Assessment			As needed

[1] Baseline radiographs may be up to 12 months prior to the surgical procedure.

[2] Flexion/extension x-rays are not required at baseline, but will be collected if captured.
[3] Flexion/extension x-rays are required at all follow-up visits.

7.2 Study Visits

All procedures and evaluations must be performed at the study site. No study procedures can be conducted until the subject has provided written informed consent.

7.2.1 Pre-Surgery Screening Visit

The Pre-Surgery Screening Visit may take place up to and including 30 days prior to the date of the surgical procedure. The following information shall be collected during the Pre-Surgery Screening Visit:

- Inclusion/Exclusion Determination
- Written informed consent and written authorization for use and disclosure of PHI
- Demographics (age, gender, ethnicity/race)
- Medical History
- Physical Exam, including height, and body weight
- Oswestry Disability Index (lumbar fusion) (Appendix 5) or Neck Disability Index (cervical fusion) (Appendix 6)
- Visual Analog Scale (both leg and back pain) (Appendix 7)
- Radiological Assessment – at minimum, lateral and anterior/posterior radiographs are required at baseline. Flexion and extension radiographs will also be collected if captured by the investigator. If performed, CT scans will also be collected.

7.2.2 Surgical Procedure Visit

The Surgical Procedure Visit shall occur on the same day as the surgical procedure. The following information shall be collected during the Surgical Procedure Visit:

- Surgical procedure details including the type of fusion performed, spine levels involved, ViBone, and other products used.
- If another product is being used in the interbody space, at least 70% of the total volume should be ViBone.

7.2.3 Follow-Up Visits

Study-related Follow-Up Visits shall occur at 6 months and 12 months (± 1 month) after the date of the surgical procedure. The following information shall be collected at each Follow-Up Visit:

- Surgical Complication Assessment
- Oswestry Disability Index (lumbar fusion) or Neck Disability Index (cervical fusion)
- Visual Analog Scale (both leg and back pain)
- Radiological Assessment – at minimum, lateral, anterior/posterior, flexion and extension radiographs are required at each follow-up visit. If performed, CT scans will also be collected.

7.2.4 Subject Close-Out

The Subject Close-Out shall be performed for all patients enrolled, as well as if either:

(1) A subject is assigned a subject ID in the EDC, but does not undergo treatment;
(2) A subject terminates early from the study for any reason.

7.3 Study Monitoring

Individual study sites may be monitored periodically to assure satisfactory enrollment, data recording, and adherence to the protocol. The frequency of monitoring of a study site may vary depending on its enrollment rate and the quality of data collected. The Investigator and staff are expected to cooperate with the monitor at each site visit and provide all relevant study documentation upon request for review. In addition to regular visits, each site may be monitored by phone and/or fax to keep abreast of subject status and to answer questions.

7.4 Protocol Deviations

This study will be conducted as described in this protocol, except for an emergency situation in which the protection, safety, and well-being of the subject requires immediate intervention, based on the judgment of the Investigator (or a responsible, appropriately trained professional designated by the Investigator). In the event of a significant unforeseen deviation from the protocol (e.g., deviation impacting subject safety, obtaining informed consent prior to conducting study procedures, control of study product), the Investigator or his or her designee must contact Aziyo immediately by telephone. When at all possible, the deviation should also be reviewed/approved by the IRB in accordance with IRB policies.

8 STUDY PRODUCT

8.1 ViBone Formulation and Packaging

The Package Insert contains a full discussion of ViBone formulation and packaging. (Appendix 4).

8.2 Labeling and Storage

The product label contains the elements required by the code of federal regulations (CFR), the American Association of Tissue Banks (AATB) and other local authorities for tissue products.

ViBone is supplied ready to use and must be stored in its original packaging at -75°C to -85°C until prepared for use. It is the responsibility of the transplant facility or clinician to maintain the allograft intended for transplantation in the appropriate recommended storage conditions prior to transplant.

8.3 Study Treatments

8.3.1 Treatment Regimen

ViBone will be implanted at the time of surgery.

8.3.2 Study Duration

Subjects enrolled in the registry will be followed for 12 months.

9 PREMATURE SUBJECT WITHDRAWAL

Participation is voluntary and all subjects have the right to withdraw their participation from the study at any time. Subjects will be withdrawn from the study immediately if any of the following occurs:

- the Investigator determines it is in the best interest of the subject, or
- the subject withdraws informed consent, or
- the subject withdraws authorization to use protected health information.

Aziyo or its designee must be notified promptly when a subject is withdrawn. The Investigator will encourage all subjects who decide to withdraw from the study to complete all evaluations that may be necessary to ensure that the subject is free of untoward effects and to seek appropriate follow-up for any continuing problems. The date the subject is withdrawn from the study and the reason for discontinuation will be recorded in the electronic data capture system. When a subject is withdrawn from the study, regardless of the reason, all evaluations required at the final study visit should be performed.

10 OUTCOME MEASURES

The following outcome measures will be assessed at 6 months and 12 months and compared to published and/or retrospective data for autograft or other similar products:

Study objectives are to detect:

- Fusion rates as determined by radiographic imaging at 6 and 12 months post-surgery.
  - Fusion of the interbody space shall be deemed successful if the following radiographic endpoints are demonstrated on x-ray examination (lateral, anterior/posterior, flexion and extension): Evidence of bridging trabecular bone between the involved motion segments, translational motion <3mm; and angular motion <5º.[1]
- Changes in Oswestry Disability Index/Neck Disability Index from baseline, at all available follow-up time-points.
- Changes in Visual Analog Scale (VAS) from baseline, at all available follow-up time-points.

Safety evaluations include:

- Incidence of ViBone-related serious adverse reactions.

11 SAFETY

11.1 Reporting Serious Adverse Reactions

Adverse Reactions involving a communicable disease and are deemed related to use of ViBone, will be reported to FDA's MedWatch program and details of the event shall be documented on the applicable Serious Adverse Reaction form.[2] Per FDA 21 CFR 1271.3 (y), an adverse reaction is defined as a noxious and unintended response to any HCT/P for which there is a reasonable possibility that the HCT/P caused the response.

Per FDA 21 CFR 1271.350 adverse reactions involving a communicable disease related to an HCT/P (ViBone) must be investigated and reported to the FDA within 15 calendar days of initial receipt of the information. Adverse reactions are further defined to include the following:

A communicable disease that:

1. **Is fatal** (report if you suspect the death was an outcome of the adverse event);

2. **Is life threatening** (subject at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the subject;

3. **Results in permanent impairment of body function or permanent damage to body structure** (Report if the adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the subject's body function/structure, physical activities and/or quality of life); or

4. **Necessitates medical or surgical intervention, including hospitalization** (report if hospitalization is the result of an adverse event. Emergency department visits that do not result in admission should be evaluated for one of the other outcomes).

If an adverse reaction involving a communicable disease that is believed to be related to the use of ViBone occurs, a Serious Adverse Reaction form shall be completed. In addition to completing the form, Aziyo must be notified within 24 hours of the Investigator becoming aware of the event. All fields are required in order to provide Aziyo personnel with the required information to evaluate the reaction and complete the required MedWatch report for submission to FDA per the Sponsor's Medical Device Reporting SOP.

12 STATISTICAL CONSIDERATIONS

As this study is designed to assess the clinical and radiographic outcomes in patients who undergo cervical (ACDF) or lumbar (TLIF, PLIF, LLIF, or ALIF) spine fusion surgery using ViBone, statistics will be descriptive. Baseline demographic and clinical variables will be summarized. Frequencies and percentages with confidence intervals will be tabulated for surgical outcomes.

12.1 Sample Size

Up to 50 patients undergoing ACDF surgery using ViBone will be enrolled. Up to 50 patients undergoing lumbar interbody fusion surgery using ViBone will also be enrolled.

13 DOCUMENTATION

13.1 Source Documents

Source documents are defined as original documents, data, and records. They may include hospital records, clinical and office charts, laboratory data and information, subject diaries or evaluation checklists, pharmacy dispensing and other records, recorded data from automated instruments, microfiches, photographic negatives, microfilm, magnetic media and X-rays, or other information closest to its source. All Investigators and institutions will permit trial-related monitoring, audit, IRB and regulatory inspections, and will provide direct access to source documents.

13.2 Case Report Forms

Aziyo will provide access to electronic CRFs for the recording and collection of data via Medrio electronic data capture (EDC). These forms will be used to transmit information collected during this study to Aziyo. The Investigator must agree to complete and maintain source documents and complete CRFs for each subject participating in the study. All information entered into electronic CRFs must also be reflected in the subject source documents.

The Investigator or designated sub-Investigator will review the CRFs for completeness and accuracy and approve where indicated. CRFs will be reviewed periodically for completeness, legibility, and acceptability by Aziyo. Aziyo will be allowed access to all source documents pertinent to the study in order to verify CRF entries as needed.

14 ETHICS AND RESPONSIBILITY

This study must be carried out in compliance with the protocol and the ethical principles that have their origin in the Declaration of Helsinki; Title 21 of the Code of Federal Regulations §§ 50, 54, and 56, and ICH E6.

The Investigator agrees, when signing the protocol, to adhere to the instructions and procedures described in it.

The Investigator will supply the following to the study site's IRB:

- Protocol and any amendment(s)
- Informed consent and written authorization for use and disclosure of PHI document and updates
- Package Insert and product brochure
- Relevant curriculum vitae, if required
- Adverse reaction reports, as appropriate

The following documents must be provided to Aziyo, or its designee, prior to the start of the study:

- Current curriculum vitae (no more than two years old) and current state medical license of Principal Investigator and all sub-Investigators
- Protocol and amendment(s) signature pages
- Copy of the IRB approval letter for the protocol and informed consent and written authorization for use and disclosure of PHI document, signed by the IRB chairperson or their designee, including the name and address of the IRB
- IRB approvals of any amendments to the protocol or revisions to the informed consent and written authorization of use and disclosure of PHI document, including the IRB stamp and date
- Debarment Statement confirming that no one involved in the study is debarred
- Proof of Patient written authorization for use and disclosure of PHI, as applicable
- Stamped and dated copy of the IRB approved informed consent and written authorization for use and disclosure of PHI form and any revisions.

The following documents must be provided to Aziyo, or its designee, as applicable:

- IRB re-approval of the protocol, at least annually
- Relevant revisions to curriculum vitae signed and dated, as applicable

15 PROTOCOL AMENDMENTS

Protocol amendments will only be made by Aziyo. The IRB must review and provide approval for any amendments likely to affect the safety of the subjects or the conduct of the study. The Investigator should send a copy of the approval letter from the IRB or Independent Ethics Committee (IEC) to Aziyo or its designee.

16 USE OF INFORMATON AND PUBLICATION

16.1 Use of Information

All information concerning ViBone and Aziyo Biologics, Inc. patent applications, formulas, manufacturing processes, basic scientific data, or formulation information, supplied by Aziyo and not previously published is considered confidential information.

The information developed during the conduct of this study is also considered confidential and will be used by Aziyo in connection with the development of ViBone. This information may be disclosed as deemed necessary by Aziyo to other Investigators, other pharmaceutical companies, and governmental agencies. To allow for the use of the information derived from this study and to ensure complete and thorough analysis, the Investigator is obligated to provide Aziyo with complete test results and all data developed in this study and to provide direct access to source data and documents for study-related monitoring, audits, IRB review, and regulatory inspection.

This confidential information shall remain the sole property of Aziyo, shall not be disclosed to others without the written consent of Aziyo, and shall not be used except in the performance of this study.

The Investigator will maintain a confidential subject identification code list of all subjects enrolled in the study by name and subject number. This list will be maintained at the study site and will not be retrieved by Aziyo. The Investigator must obtain patient written authorization for the use and disclosure of PHI according to the Health Insurance Portability Act of 1996 or other local privacy laws.

16.2 Publication

At the completion of the study, publications may be authored by specified Investigators who contribute significantly to the implementation and conduct of the study, and by non-site personnel who contribute substantially to the design, interpretation, or analysis of the study.

The outcome data for cervical and lumbar fusions will be analyzed separately and will be compared to published and/or retrospective data for autograft or other similar products.

17 STUDY TERMINATION

Aziyo may terminate this study prematurely, either in its entirety or a specific study site, for reasonable cause provided that written notice is submitted a reasonable time in advance of the intended termination. The Investigator may also terminate the study at his or her site for reasonable cause, after providing written notice to Aziyo a reasonable time in advance of the intended termination. Advance notice is not required by either party if the study is stopped due to safety concerns. If Aziyo terminates the study for safety reasons, it will immediately notify the Investigator by telephone and subsequently provide written instructions for study termination.

18 CITED REFERENCES

1. FDA. Guidance for Industry and/or FDA Reviewers/Staff. Guidance Document for the Preparation of IDEs for Spinal Systems. 2000.
2. FDA. MedWatch Form FDA 3500A: Mandatory Reporting of Adverse Reactions Related to Human Cells, Tissues and Cellular and Tissue-Based Products (HCT/Ps). 2005.
3. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine 2000 Nov 15;25(22):2940-52.
4. Vernon, H. & Mior, S. (1991). The Neck Disability Index: A study of reliability and validity. Journal of Manipulative and Physiological Therapeutics. 14, 409-415

19 APPENDICES

19.1 Appendix 1: Principal Investigator Agreement

Principal Investigator Agreement

I have read and understood the contents of this protocol and the information provided as it relates to the study product and agree to conduct this treatment protocol in compliance with the protocol, Good Clinical Practice, and other applicable regulatory requirements.

I accept the oversight of the treatment protocol monitor designated by Aziyo, and control procedures, including verification by access to source documents, as required by the protocol monitoring and audit functions of Aziyo or its designee and the audit functions of regulatory agencies in accordance with Good Clinical Practice.

Per ICH and GCP I will ensure the accuracy, completeness, and timeliness of the data reported to the sponsor in the eCRFs.

I understand that any changes to this protocol (not associated with procedures necessary for the safety of the patient) instituted by me or those I directly designate will constitute a violation of the protocol unless specifically discussed with the Aziyo Biologics, Inc. monitor or designee beforehand.

I agree that neither I nor any person employed by me in connection with any work to be performed for or on behalf of Aziyo has been debarred under Section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act, and that no debarred person will in the future be employed by me in connection with any work to be performed for or on behalf of Aziyo. If at any time after execution of this Agreement, I become aware that I or any person employed by me in connection with any work to be performed for or on behalf of Aziyo shall become or shall be in the process of being debarred, I agree to notify Aziyo at once.

I will personally conduct the treatment and follow-up as described herein, or will oversee and remain fully responsible for the treatment and follow-up as described herein if I delegate any parts of it.

Principal Investigator: _____ _____

Print Signature

Date: _____

19.2 Appendix 2: Supplemental SAMPLE Informed Consent Form for ViBone Study

Supplemental SAMPLE Informed Consent Form for ViBone Study

Title: A Prospective, Post-Market, Multi-Center Study Evaluating ViBone in Cervical and Lumbar Spine Fusion

Protocol Number: CLP-0001
WIRB® Protocol #XXXXX

Sponsor: Aziyo Biologics, Inc.

Investigator: Name
Address
City, State Zip
Country

Study Related Phone Number(s): Name
Phone number (24 hours)

Summary

You are being asked to be in a research study evaluating ViBone, a donated human tissue product, in patients undergoing cervical or lumbar spine fusion. The purpose of this consent form is to help you better understand the study purpose and requirements and to help you determine if you'd like to participate.

ViBone is processed from donated human bone. The bone is processed in a way that preserves the native growth factors and cells needed for bone formation.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn more about spine fusion in order to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- This study involves standard medical care. Standard care is the treatment normally given for a certain condition or illness.
- Your medical records will become part of the research record. Before sharing your records with the sponsor of the study, your doctor will remove any personal information (name, date of birth, etc.) that would allow you to be identified. These deidentified medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.

- Your medical insurance may be billed for any standard medical care you receive during the research study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a research study. Taking part in a research study could affect your current or future insurance coverage.

If you take part in this research study, you will be given a copy of this consent form. This consent form is a supplemental consent specifically for the study evaluating ViBone in cervical and lumbar spine fusion. You will also need to sign other consent form(s) for your surgical procedure.

What is the purpose of the study?

During your spine fusion procedure, your doctor will use ViBone, a human tissue allograft that is intended to support bone repair. ViBone is used in fusion surgery to stop motion between two or more vertebral bodies. ViBone and other bone allografts may stimulate new bone formation and may provide a foundation or scaffold on which your body can grow new bone.

ViBone is a human tissue allograft consisting of viable bone matrix that is processed in a way that preserves native factors that support bone repair. ViBone is regulated by the Food and Drug Administration as a Human Cellular and Tissue Based Product (HCT/P) per 21 CFR Part 1271.

The purpose of this study is to gather additional information on the use of ViBone when it is used in patients undergoing cervical or lumbar spine fusion.

How long will the study last and how many people will be in the study?

Your involvement in this study will last for approximately twelve months. You will have at least two routine follow-up evaluations, one at 6 months and another at 12 months after your surgical procedure. Up to 20 U.S. clinical sites will be participating in the study and approximately 200 patients are expected to be enrolled.

What are the procedures required by the study and are there any extra tests or treatments required if I participate?

Your procedure will be performed per the standard of care by your physician. Although participation in the study requires no additional procedures or tests, it is important that you comply with standard of care by attending the scheduled follow-up visits as recommended by your physician. Your physician will provide the following information from your visits and your medical records:

- Demographic information (age, race, gender)
- Date and type of procedure performed
- Information on any hardware used in the procedure
- Information on ViBone implanted
- ViBone-related serious adverse reactions
- Imaging related to your procedure and details on your fusion

Are there any additional risks or discomforts associated with participation?

There are no identified medical risks involved in participating in this study. The only additional risk from taking part in this study is that the confidentiality of your information may be lost or compromised.

Please discuss the standard risks associated with your procedure and the use of allograft tissue products with your physician.

Will I benefit from participation in this study?

You will not directly benefit from being in this study. However, the results of this study may help people undergoing spine fusion in the future.

Who will pay for the surgery, associated products and follow-up care required for the fusion procedure?

You or your insurance company will be billed for your surgery, medications, visits and any other standard treatment/care.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

Will I be compensated for participation in this study?

There is no payment provided to patients for participation in this study.

Are there alternatives to participating in this study?

You do not need to take part in this research study to receive treatment for your condition. You can undergo the same surgery with the same product without taking part in this study. Your study doctor can discuss treatment alternatives and the risks and benefits of these alternatives with you. If you decide to not participate in this study, it will not affect your medical treatment in any way.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. Some of your health information from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor Aziyo Biologics, Inc.
- The Institutional Review Board (IRB) is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

Who may use and give out information?

The study doctor and the study staff.

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

How will information about me be kept private?

Your privacy is very important to the researchers. Here are a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information.
3) Information that identifies you will not be given to anyone, unless required by law.
4) If research results are published, your name and other personal information will not be used.

May I review or copy my information?

Yes, but only after the research is over.

May I withdraw or cancel my participation in this study?

Yes. You can decide to discontinue at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study. Information that has already been given to or used by researchers will not be returned.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If the study is stopped by the sponsor, IRB or FDA.

Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission.

Who pays for the study-related activities?

The sponsor, Aziyo Biologics, Inc., will pay for the data collection efforts associated with this research study.

Who can answer my questions about this study?

Contact [name] at [number(s)] (24 hours) if you have any questions or concerns about this study.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

An Institutional Review Board is a group of people who independently review research.

The Institutional Review Board will not be able to answer some study-specific questions. However, you may contact the IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

By signing this consent form, I have not given up any of my legal rights.

_____

Subject Name (printed)

_____ _____

Signature of Subject Date

_____ _____

Printed Name of Person Conducting the Informed Consent Discussion Position

_____ _____

Signature of Person Conducting the Informed Consent Discussion Date

19.3 Appendix 4: ViBone Package Insert

ViBone

THIS PRODUCT IS MANUFACTURED FROM DONATED HUMAN TISSUE, RECOVERED FROM A SINGLE HUMAN DONOR WITH DOCUMENTED AUTHORIZATION FOR DONATION AND RECOVERY. THE TISSUE IS RECOVERED AND SUPPLIED FROM U.S. TISSUE BANKS ONLY. THE RECOVERY, PROCESSING AND PACKAGING WAS PERFORMED USING ASEPTIC TECHNIQUES.

DESCRIPTION AND INDICATION FOR USE

ViBone™ is a human tissue allograft consisting of cryopreserved bone matrix that is aseptically processed to preserve native factors that support bone repair. ViBone™ is a Human Cellular and Tissue Based Product (HCT/P) per 21 CFR Part 1271. Each allograft is restricted to homologous use for transplant in procedures on a single occasion by a licensed physician or surgeon.

DONOR SCREENING AND TESTING (SUMMARY OF RECORDS)

ViBone™ was prepared from a donor determined to be eligible by the Medical Director of Aziyo or physician designee based on the results of screening and testing. Donors are screened for high risk behavior and contraindications to transplant through medical/social history interview, review of medical records, physical assessment, and review of post mortem-examination results (when applicable). Tissue from this donor has passed bacteriological testing by a CLIA Certified Laboratory. Communicable disease testing was performed by a laboratory registered with FDA to perform donor testing and certified to perform such testing on human specimens in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR part 493, or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS) and found to be negative or non- reactive for a minimum of:

- HIV type 1 and 2 antibody (HIV-1 & 2 Ab)
- HIV type 1 nucleic acid test using PCR and/or TMA format (HIV-1 NAT)
- Hepatitis B virus (HBsAg and HBV NAT)
- Hepatitis B core antibody total (HBcAb IgG/IgM or total)
- Hepatitis C virus (HCV Ab and HCV NAT)
- Syphilis by rapid plasma reagin (RPR) or other serological tests

Additional tests, including Human T-lymphotropic virus I/II, may have been performed at the time of screening, and results were found acceptable for transplantation. Any additional test(s) performed can be provided upon request. Donor eligibility determination was made by Aziyo Biologics in compliance with U.S. FDA regulations (21 CFR 1270 and 1271) and American Association of Tissue Banks® (AATB®) Standards. The Medical Director determined final eligibility and acceptability for transplantation after review of donor screening and testing records.

WARNINGS AND PRECAUTIONS

An allograft may not elicit proper response from the recipient (e.g. fusion/union with adjacent tissue). It is possible for a host site to become infected or the allograft may cause an inflammatory response. Current technologies may not preclude the transmission of infectious agents or disease, including hepatitis and HIV. ViBone™ is preserved in 5% dimethyl sulfoxide (DMSO) in a 0.9% sodium chloride solution. Povidone iodine, Dulbecco's phosphate buffered saline, sodium chloride irrigation solution, sodium phosphate, hydrochloric acid and hydrogen peroxide are all used for processing, preservation and storage of the allografts and trace amounts of these solutions may be present in the product.

TRANSPORTATION, STORAGE AND HANDLING

ViBone™ is supplied ready to use and must be stored in its original packaging at -75°C to -85°C (-103°F to -121°F) until prepared for use. It is the responsibility of the transplant facility or clinician to maintain the allograft intended for transplantation in the appropriate recommended storage conditions prior to transplant.

HOW SUPPLIED

ViBone™ bone allograft is supplied frozen and packaged in a polycarbonate jar placed in an outer peel pouch. The inner jar and allograft are sterile. The outer peel pouch is not sterile. Allograft volume is indicated on the package label.

STERILITY CONTROL

ViBone™ allografts have been processed under aseptic conditions to prevent contamination and cross contamination of the product. Destructive microbiological testing per USP <71> *Sterility Tests* is performed on samples from each lot and must show "No Growth" after a 14-day incubation in growth promoting media.

PRECAUTIONS

Inspect the integrity of the package upon receipt and before use. Do not use ViBone™ under the following conditions:

- The container in which the allograft is stored is damaged or the label has been damaged or defaced.
- The allograft expiration date has passed.
- Recommended storage conditions have not been maintained.

INSTRUCTIONS FOR USE

It is important to utilize aseptic techniques when unpacking the allograft.

1. Examine the labeling and outer peel pouch. Do not use if there is evidence that the integrity of the outer pouch has been compromised.
2. Aseptically present the inner jar onto a sterile field.
3. Place the unopened jar into a sterile basin and fill with warm (approximately 37°C) sterile saline to just below the jar lid.
4. Thaw ViBone™ for approximately 5-15 minutes.
5. Don sterile surgical gloves, remove the jar lid and remove the product from the jar.
6. The allograft tissue should be pliable. If the allograft is still frozen, warm by holding the allograft with sterile gloved hands until completely thawed and pliable.
7. ViBone™ should be transplanted within two hours of thawing and all unused product must be discarded. Product is intended for single use and should not be refrozen or sterilized.

TRACEABILITY

The FDA requires traceability from the donor to the recipient. The physician is responsible for completing the recipient records to ensure traceability. As a convenience, pre-printed peel-off labels are included with each allograft. Using the labels, record the allograft tissue identification information in the patient medical record.

ADVERSE REACTION

The physician must promptly report any adverse outcomes potentially attributable to ViBone™ to Aziyo at 800-922-3100.

Manufactured By:

AZIYO® BIOLOGICS

Aziyo Biologics, Inc.
880 Harbour Way S, Suite 100
Richmond, CA 94804
Phone: 800-922-3100
Fax: 510-307-9896

FDA Registration No. 1000100754
CTO Registration Certificate No. 100242
Accredited by the AATB®.

American Association of Tissue Banks® and AATB® are registered service marks of the American Association of Tissue Banks®.

IFU-0006 Rev 05

19.4 Appendix 5: Oswestry Disability Index

Oswestry Low Back Pain Disability Questionnaire

Sources: Fairbank JCT & Pynsent, PB (2000) The Oswestry Disability Index. *Spine*, 25(22):2940-2953.

Davidson M & Keating J (2001) A comparison of five low back disability questionnaires: reliability and responsiveness. *Physical Therapy* 2002;82:8-24.

The Oswestry Disability Index (also known as the Oswestry Low Back Pain Disability Questionnaire) is an extremely important tool that researchers and disability evaluators use to measure a patient's permanent functional disability. The test is considered the 'gold standard' of low back functional outcome tools [1].

Scoring instructions

For each section the total possible score is 5: if the first statement is marked the section score = 0; if the last statement is marked, it = 5. If all 10 sections are completed the score is calculated as follows:

Example: 16 (total scored)

50 (total possible score) x 100 = 32%

If one section is missed or not applicable the score is calculated:

16 (total scored)

45 (total possible score) x 100 = 35.5%

Minimum detectable change (90% confidence): 10% points (change of less than this may be attributable to error in the measurement)

Interpretation of scores

0% to 20%: minimal disability:	The patient can cope with most living activities. Usually no treatment is indicated apart from advice on lifting sitting and exercise.
21%-40%: moderate disability:	The patient experiences more pain and difficulty with sitting, lifting and standing. Travel and social life are more difficult and they may be disabled from work. Personal care, sexual activity and sleeping are not grossly affected and the patient can usually be managed by conservative means.
41%-60%: severe disability:	Pain remains the main problem in this group but activities of daily living are affected. These patients require a detailed investigation.
61%-80%: crippled:	Back pain impinges on all aspects of the patient's life. Positive intervention is required.
81%-100%:	These patients are either bed-bound or exaggerating their symptoms.

Page 1

Oswestry Low Back Pain Disability Questionnaire

Instructions

This questionnaire has been designed to give us information as to how your back or leg pain is affecting your ability to manage in everyday life. Please answer by checking ONE box in each section for the statement which best applies to you. We realise you may consider that two or more statements in any one section apply but please just shade out the spot that indicates the statement which most clearly describes your problem.

Section 1 – Pain intensity

- ☐ I have no pain at the moment
- ☐ The pain is very mild at the moment
- ☐ The pain is moderate at the moment
- ☐ The pain is fairly severe at the moment
- ☐ The pain is very severe at the moment
- ☐ The pain is the worst imaginable at the moment

Section 2 – Personal care (washing, dressing etc)

- ☐ I can look after myself normally without causing extra pain
- ☐ I can look after myself normally but it causes extra pain
- ☐ It is painful to look after myself and I am slow and careful
- ☐ I need some help but manage most of my personal care
- ☐ I need help every day in most aspects of self-care
- ☐ I do not get dressed, I wash with difficulty and stay in bed

Section 3 – Lifting

- ☐ I can lift heavy weights without extra pain
- ☐ I can lift heavy weights but it gives extra pain
- ☐ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently placed eg. on a table
- ☐ Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned
- ☐ I can lift very light weights
- ☐ I cannot lift or carry anything at all

Section 4 – Walking*

- ☐ Pain does not prevent me walking any distance
- ☐ Pain prevents me from walking more than 1 mile
- ☐ Pain prevents me from walking more than 1/2 mile
- ☐ Pain prevents me from walking more than 100 yards
- ☐ I can only walk using a stick or crutches
- ☐ I am in bed most of the time

Oswestry Low Back Disability Questionnaire

Section 5 – Sitting

- ☐ I can sit in any chair as long as I like
- ☐ I can only sit in my favourite chair as long as I like
- ☐ Pain prevents me sitting more than one hour
- ☐ Pain prevents me from sitting more than 30 minutes
- ☐ Pain prevents me from sitting more than 10 minutes
- ☐ Pain prevents me from sitting at all

Section 6 – Standing

- ☐ I can stand as long as I want without extra pain
- ☐ I can stand as long as I want but it gives me extra pain
- ☐ Pain prevents me from standing for more than 1 hour
- ☐ Pain prevents me from standing for more than 30 minutes
- ☐ Pain prevents me from standing for more than 10 minutes
- ☐ Pain prevents me from standing at all

Section 7 – Sleeping

- ☐ My sleep is never disturbed by pain
- ☐ My sleep is occasionally disturbed by pain
- ☐ Because of pain I have less than 6 hours sleep
- ☐ Because of pain I have less than 4 hours sleep
- ☐ Because of pain I have less than 2 hours sleep
- ☐ Pain prevents me from sleeping at all

Section 8 – Sex life (if applicable)

- ☐ My sex life is normal and causes no extra pain
- ☐ My sex life is normal but causes some extra pain
- ☐ My sex life is nearly normal but is very painful
- ☐ My sex life is severely restricted by pain
- ☐ My sex life is nearly absent because of pain
- ☐ Pain prevents any sex life at all

Section 9 – Social life

- ☐ My social life is normal and gives me no extra pain
- ☐ My social life is normal but increases the degree of pain
- ☐ Pain has no significant effect on my social life apart from limiting my more energetic interests eg, sport
- ☐ Pain has restricted my social life and I do not go out as often
- ☐ Pain has restricted my social life to my home
- ☐ I have no social life because of pain

Section 10 – Travelling

- ☐ I can travel anywhere without pain
- ☐ I can travel anywhere but it gives me extra pain
- ☐ Pain is bad but I manage journeys over two hours
- ☐ Pain restricts me to journeys of less than one hour
- ☐ Pain restricts me to short necessary journeys under 30 minutes
- ☐ Pain prevents me from travelling except to receive treatment

References

1. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine 2000 Nov 15;25(22):2940-52; discussion 52.

19.5 Appendix 6: Neck Disability Index

Neck Disability Index

Office Use Only
Name _____
Date _____

This questionnaire has been designed to give us information as to how your neck pain has affected your ability to manage in everyday life. Please answer every section and **mark in each section only the one box that applies to you**. We realise you may consider that two or more statements in any one section relate to you, but please just mark the box that most closely describes your problem.

Section 1: Pain Intensity

☐ I have no pain at the moment
☐ The pain is very mild at the moment
☐ The pain is moderate at the moment
☐ The pain is fairly severe at the moment
☐ The pain is very severe at the moment
☐ The pain is the worst imaginable at the moment

Section 2: Personal Care (Washing, Dressing, etc.)

☐ I can look after myself normally without causing extra pain
☐ I can look after myself normally but it causes extra pain
☐ It is painful to look after myself and I am slow and careful
☐ I need some help but can manage most of my personal care
☐ I need help every day in most aspects of self care
☐ I do not get dressed, I wash with difficulty and stay in bed

Section 3: Lifting

☐ I can lift heavy weights without extra pain
☐ I can lift heavy weights but it gives extra pain
☐ Pain prevents me lifting heavy weights off the floor, but I can manage if they are conveniently placed, for example on a table
☐ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned
☐ I can only lift very light weights
☐ I cannot lift or carry anything

Section 4: Reading

☐ I can read as much as I want to with no pain in my neck
☐ I can read as much as I want to with slight pain in my neck
☐ I can read as much as I want with moderate pain in my neck
☐ I can't read as much as I want because of moderate pain in my neck
☐ I can hardly read at all because of severe pain in my neck
☐ I cannot read at all

Section 5: Headaches

☐ I have no headaches at all
☐ I have slight headaches, which come infrequently
☐ I have moderate headaches, which come infrequently
☐ I have moderate headaches, which come frequently
☐ I have severe headaches, which come frequently
☐ I have headaches almost all the time

Section 6: Concentration

☐ I can concentrate fully when I want to with no difficulty
☐ I can concentrate fully when I want to with slight difficulty
☐ I have a fair degree of difficulty in concentrating when I want to
☐ I have a lot of difficulty in concentrating when I want to
☐ I have a great deal of difficulty in concentrating when I want to
☐ I cannot concentrate at all

Section 7: Work

☐ I can do as much work as I want to
☐ I can only do my usual work, but no more
☐ I can do most of my usual work, but no more
☐ I cannot do my usual work
☐ I can hardly do any work at all
☐ I can't do any work at all

Section 8: Driving

☐ I can drive my car without any neck pain
☐ I can drive my car as long as I want with slight pain in my neck
☐ I can drive my car as long as I want with moderate pain in my neck
☐ I can't drive my car as long as I want because of moderate pain in my neck
☐ I can hardly drive at all because of severe pain in my neck
☐ I can't drive my car at all

Section 9: Sleeping

☐ I have no trouble sleeping
☐ My sleep is slightly disturbed (less than 1 hr sleepless)
☐ My sleep is mildly disturbed (1-2 hrs sleepless)
☐ My sleep is moderately disturbed (2-3 hrs sleepless)
☐ My sleep is greatly disturbed (3-5 hrs sleepless)
☐ My sleep is completely disturbed (5-7 hrs sleepless)

Section 10: Recreation

☐ I am able to engage in all my recreation activities with no neck pain at all
☐ I am able to engage in all my recreation activities, with some pain in my neck
☐ I am able to engage in most, but not all of my usual recreation activities because of pain in my neck
☐ I am able to engage in a few of my usual recreation activities because of pain in my neck
☐ I can hardly do any recreation activities because of pain in my neck
☐ I can't do any recreation activities at all

Score: ___/50 **Transform to percentage score x 100 = %points**

Scoring: For each section the total possible score is 5: if the first statement is marked the section score = 0, if the last statement is marked it = 5. If all ten sections are completed the score is calculated as follows:

Example: 16 (total scored)
50 (total possible score) x 100 = 32%

If one section is missed or not applicable the score is calculated:

16 (total scored)
45 (total possible score) x 100 = 35.5%

Minimum Detectable Change (90% confidence): 5 points or 10 %points

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NDI developed by: Vernon, H. & Mior, S. (1991). The Neck Disability Index: A study of reliability and validity. Journal of Manipulative and Physiological Therapeutics. 14, 409-415

19.6 Appendix 7: Visual Analog Scale