1.5 OVERALL SYNOPSIS OF THE CLINICAL INVESTIGATION

Clinical investigation single identification #:	Clinicaltrials.gov #NCT06085443
Clinical investigation plan #:	**23E1670**
Title of the clinical investigation:	CLINICAL STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF A AURICULARY SPRAY MEDICAL DEVICE "EAR HYGIENE"
Sponsor:	**YSLAB** **Le Forum** **2, rue Félix Le DANTEC** **29 000 Quimper** **FRANCE**
Development phase:	Post market study Device used according to IFU
Objectives:	Principal aim: SAFETY The primary objective of the study is to confirm the safety of a marketed auricular spray with reverse and microdiffusion nozzle by clinical examination by ENT specialist and by the scoring of the irritation of the ear canal at D60 in comparison with basal scoring of irritation at D0 (scale 0 to 3) such as: - 0: no irritation, - 1: slight irritation (located slight erythema and/or dryness), - 2: moderate irritation (clear erythema or dryness which may be visible on the whole treated area), - 3: severe irritation (serious erythema with potential oedema and/or scar). Potential adverse events collection. Secondary aims: EFFICACY/PERFORMANCE PREVENTION for investigational device with reverse nozzle, investigational device with microdiffusion nozzle and for control group, in comparison to the baseline (D0) and between groups: • scoring of the obstruction of ear canal by the Investigator 0: no obstruction – normal and/or no significant presence of cerumen in the ear canal. The membrane is clearly visible. 1: <25% minimal, very little and mostly insignificant impacted cerumen. The tympanic membrane is visible, but with still a little bit cerumen. 2: 25-50% mild, some excessive impacted cerumen causing partial occlusion of the ear canal. The tympanic membrane is not entirely visible, quite difficult to see. 3: 50-75% moderate, moderate and excessive impacted cerumen causing partial occlusion of the ear canal. Partial to very little of the tympanic membrane is visible. 4: 75-100% severe, severe and excessive impacted cerumen causing partial or complete occlusion of the ear canal. Little if any of the tympanic membrane is visible. • audiogram with classification of the loss or win hearing function using the following scale (only for subjects more than 6):

	No hearing function loss, hearing function loss between 5 to 10dB, hearing function >10dB (Subha et al.2006), hearing function win between 5 to 10 dB, hearing function win >10dB. Additionally, the secondary objective of this study will be to see if the investigational device is more efficient in children, adults or elderly subjects (for both nozzles - reverse or microdiffusion). • Subject's self-evaluation using a questionnaire. • Evaluation of the effect on the number of auricular affection (such as otitis) during the use period (daily log).
Design:	Open study, randomized, before / after treatment, with tested product versus control group, in parallel groups
Planned Sample Size:	99 included subjects and results delivered on 90 subjects. • 1 group of 72 included subjects in order to have results on 66 subjects (33 subjects using product with the “reverse diffuser” and 33 using the product with the “microdiffusion diffuser” • 1 group of 27 included subjects in order to have results on 24 subjects not using a spray (control group). (in case of discomfort or pain, they are allowed to use ear drops prescribed by a doctor after a medical examination)
Number of investigational study sites:	2 centers
Inclusion criteria:	1. Gender: female and/or male. 2. Age: - 30 to 40% having age between 3 to 12 yo, - 30 to 40% between 13 to 65 yo, - 30 to 40% more than 65 yo. 3. Subjects able to use the tested product. 4. Subjects having history of cerumen occlusion more than once a year with or without symptoms (reduction of hearing function, obstruction feeling of the ear canal,..). 5. Subjects having ear help system or regular users of systems such as anti-noise plugs or headsets (only for the 13yo subjects and more). 6. Subjects having a clinical score of ear canal obstruction of 2 or 3 at D0.
Exclusion criteria:	1. Subjects who had chirurgical act on the mastoïde. 2. Subjects who had severe troubles of the internal ear (severe dizziness, desorientation, nausea). 3. Subjects using regularly a ear spray for washing his/her ears. 4. Subjects having a score of ear canal obstruction at 4 at D0. 5. Pregnant or nursing woman or planning a pregnancy during the study; 6. Subject who had been deprived of their freedom by administrative or legal decision or who is under guardianship; 7. Subject in a social or sanitary establishment; 8. Subject suspected to be non-compliant according to the investigator’s judgment; 9. Subject with a condition or receiving a medication which, in the investigator’s judgment, put the subject at undue risk; 10. Subject suffering from a severe or progressive disease.
Investigational device: **Name / code**	OCEAN BIO-ACTIF Ear Hygiene (reverse nozzle) OCEAN BIO-ACTIF Ear Hygiene (microdiffusion nozzle) Bag on valve spray, with ergonomic nozzle

Galenic form **Dosage** **Duration** **Administration route**	2 sprays in ear, every 3 days at home 90 days Topical to ear canal
Endpoints:	Primary endpoints: • Clinical evaluation, • Clinical score of the irritation with structured scale, • Record of the possible adverse reactions. Secondary endpoints: • Clinical score of the obstruction of ear canal, • Results of audiogram with classification of the loss or win hearing function • Subject satisfaction survey • The number of auricular affection (such as otitis) during the use period
Study Procedures:	D0, D90
Statistical methods:	The analysis of the primary endpoint will be performed on the ITT and population. The analysis of the secondary endpoint will be performed on the population. The analysis of the safety/tolerance parameters will be performed on “safety” population. **<u>Primary endpoint:</u>** The irritation is assessed by the Laryngologist using a 4-point structured scale (from “No irritation (0)” to “Severe irritation (3)” on D0 and D90. For each product, a paired t-test will be used to test whether the change from baseline (D90-D0) differ significantly from 0. The normality assumption will be checked using a Shapiro-Wilk test (α=0.01), in case of rejection, a Wilcoxon signed ranks test will be used. To test whether the products differ statistically in terms of change from baseline (D90-D0), a *two-sided* t-test is used. If the normality assumption is not met, a non-parametric approach is used with a Wilcoxon signed rank test. **<u>Secondary endpoints:</u>** For each secondary parameter: • Clinical score of the irritation with structured scale • Clinical score of the obstruction of ear canal • Results of audiogram with classification of the loss or win hearing function. • The number of auricular affection (such as otitis) during the use period For each product, a paired t-test will be used to test whether the change from baseline (D90-D0) differ significantly from 0. The normality assumption will be checked using a Shapiro-Wilk test

	(α=0.01), in case of rejection, a Wilcoxon signed ranks test will be used. To test whether the products differ statistically in terms of change from baseline (D90-D0), a *two-sided* t-test is used. If the normality assumption is not met, a non-parametric approach is used with a Wilcoxon signed rank test. *For the subjective evaluation questionnaire:* For each item of the subjective questionnaire, the raw data will be summarized in frequency (N) and percentage (%) by group of product. All statistical tests will be assessed at α = 5% level of significance in a bilateral approach. Statistical software: SAS® v9.4.
Foreseen study duration:	Clinical investigation beginning: Q4 2023 Clinical investigation end: Q3 2024 Clinical investigation global duration:8 months Duration by subject: 90 days

FLOW-CHART

Procedure (time-points)	**V1**	**V2**
Intervals	**D0**	**D90 (+/-3)**
Informed Consent	●	
Medical exam	●	
Medical background and previous treatment	●	
Clinical scoring including irritation of the ear canal	●	●
Audiogram	●	●
Dispense product and daily log	●	
Collect product and daily log		●
Subjective evaluation questionnaire		●
Adherence control, record of AE, concomitant treatments	●	●
End of study form		●