SaliPen - Human Factors Study for OTC labeling

Test Product:	**SaliPen**
Sponsor's Name: **Sponsor's Address:**	**Saliwell Ltd.** **65 Hatamar St.** **Harutzim 6091700** **Israel**
Sponsor's Telephone Number: **Sponsor's Fax Number:**	**Tele# (+972).3.534.7592** **Fax# (+972).77.353.4338**
Study Number and version: **Version Date:**	**1** **August 31, 2021**

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1. Investigators' Statement

I have read the protocol:

A Clinical Study Evaluating the SaliPen Usability Engineering Study for OTC labeling

that contains all the information necessary for the conduct of the study. I agree to conduct the study as outlined therein and in accordance with to the Declaration of Helsinki 1964 and all its updates.

The undersigned confirms that I agree to conduct the study under the conditions described in this protocol:

_____ |__| |__| / |__| |__| / |__| |__|

Principal Investigator (Print Name) Date (dd / mm / yy)

_____

Principal Investigator's Signature

2. Study Synopsis

Protocol Number	21-D-246
Study Title:	SaliPen Human Factors Study for OTC labeling
Number of Centers:	One center
Countries:	USA
Study Duration:	The expected duration of the study for each subject on each Phase is about one day.
Total Study Duration:	TBD
Expected Subject Enrollment:	The total expected enrollment is 16 subjects for Phase I and 16 for Phase II.
Study Population:	Subjects attending an oral health clinic.
Study Objectives:	The primary objective of this research is to assess the human factors in relabeling the SaliPen from a prescription-based device to an OTC. Primary performance endpoints: • The user can select the device properly. • The user can use the device as instructed in the IFU.
Study Design:	This will be a single-center, prospective, open-label study. Screening: Eligible subjects will be included in the study.
Test Participant Recruitment Plan:	Patients visiting the participating clinic will be asked to participate in the study sequentially (by order of recall or arrival at the clinic). For Phase I, enrollment will be stopped once the goal of eight (8) subjects with xerostomia and eight (8) subjects without xerostomia has been reached. For Phase II, 16 subjects with xerostomia that are evaluated or treated at the clinic will be enrolled sequentially (by order of recall or arrival at the clinic). Patients that have participated in Phase I and have xerostomia will be invited to participate in Phase II, as well. Participants will receive $25 cash for participating in either phase of this study. Participants in both phases will receive $50 cash.

	Participants in Phase II will be given the option to keep the SaliPen device they will use in the study.
Inclusion Criteria:	Phase I: Any adult person that is 18 years old or older Phase II: Subjects with xerostomia that are 18 years old or older
Exclusion Criteria:	Phase I: • Children and adolescents (persons under 18 years of age) • Persons with experience in the use of SaliPen Phase II: • Persons with experience in the use of SaliPen • Children and adolescents (persons under 18 years of age) • Epileptic disorder • Persons that are allergic to the surface materials of the device ○ Electrodes: coated with gold ○ Body: made of methyl vinyl silicone rubber • Use of a pacemaker • Pregnancy • Psychiatric or psychological disorders • Involuntary muscle movement disorder (such as Parkinson's) • Neurologic disorder in head and neck area
Medical Device Description:	Electrical salivary stimulator system.
Study Endpoints:	<u>Performance Endpoints</u>: • Correct selection of the product. • Product use in accordance with the IFU.
Statistical Analysis	A simple descriptive statistical analysis will be utilized to calculate the percentage of correct answers and the percentage of subjects that passed the evaluation in each phase of the study.

3. Study Objective and Rationale

3.1. The study objective

This is a Summative Evaluation aimed at evaluating the use of SaliPen (the study product) as an Over-The-Count (OTC) device rather than as a prescription device.

3.2. The study rationale

- Xerostomia (dry mouth) is the subjective feeling of oral dryness. The diagnosis by the practitioner is mostly relying on the patient's feeling.
- Most patients are elderly, many of them with limited mobility.
- Nowadays, those patients are at high risk for COVID-19 infection, morbidity and even mortality.
- The fear of exposure at the practitioner's clinic to obtain an Rx inhibits them from treating their xerostomia with the SaliPen.
- The cost of getting a prescription is an additional burden.
- The SaliPen is an OTC in other parts of the world for years.
- The performance of potential American users of an OTC SaliPen device will be evaluated in this usability study.

As a result, many patients leave their oral dryness untreated, with the well-known consequences of poor oral functions, oral health, daily suffering, and more.

4. Brief Study Description

This Human Factors Validation Testing will assess user interactions to verify the capability of potential users to assess if the study product fits their needs and if they can use it correctly based on the provided Information For User (IFU)?

More specifically, this is a non-comparative case series study and is subdivided into two major parts. Those parts are:

1- Phase I: aimed at testing if, based on the IFU, the potential subjects can decide whether the study product is or is not appropriate to treat their condition and,
2- Phase II: aimed at assessing whether the users can use the study product correctly without counseling by a health care provider.

Condition or disease	Intervention/treatment
Xerostomia	SaliPen

5. Detailed Study Description

5.1. Phase I

To simulate an OTC setting, potential subjects will be requested to read the label text on the outside of the study product package (external labeling) and determine whether the study product addresses their needs, without a provider direction or assistance.

5.2. Phase II

The study product will be dispensed only to those subjects who will indicate that they voluntarize to participate in this phase of the study.

At Phase II subjects with xerostomia and that are willing to try the study product, will be requested to use it with no training, except for their understanding of the User Manual (internal labeling). Those subjects will use the study product in a supervised clinical setting. Subjects who report any discomfort will be offered the option to pause and remove the device upon such a request.

Correct use verification will be performed by the study investigators. Subjects will answer questions regarding product use, clarity of the IFU, ease of use, etc. Subjects will also receive an exam of their oral cavity.

6. Study Design

Study Type:	Interventional (Clinical Trial)
Enrollment:	Phase I: 16 participants, 8 with xerostomia and 8 without xerostomia Phase II: 16 participants with xerostomia (may include participants in Phase I with xerostomia)
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Human Factor Validation - Usability Engineering assessment for OTC labeling
Official Title:	SaliPen Usability Engineering Study for OTC labeling
Study Start Date:	TBD

According to the FDA Guidance document “Applying Human Factors and Usability Engineering to Medical Devices”, a sample of 15 people to detect most of the problems in a user interface constitutes a practical minimum number of participants for human factors validation testing. This sample size theoretically provides the best possibility of detecting user interface design flaws while limiting the amount of resources required.

7. Arms and Interventions

Arm	Intervention/treatment
Experimental: Use of SaliPen medical device	Use according to self-decision.

8. Features to be studied

The points of interaction between the user and the device (User Interface) will be evaluated, including:

- the elements of the device with which the user interacts (i.e., those parts of the device that users see and touch), and
- the IFU (including packaging, labeling, User Manual, etc.).

The following parameters will be studied:

- Hazard: Potential source of harm, if any.
- Use error: User action or lack of action that was different from that expected by the manufacturer.

9. Outcome Measures

1. Percentage of participants who appropriately will self-select the study product for use under simulated OTC conditions [Phase I]. Following the standard norms for the Rx-to-OTC switch process, this outcome is a validation of potential consumers' ability to self-diagnose the condition and to decide that treatment with the product is appropriate for them.
2. Percentage of participants who correctly will use the study product when dispensed under simulated OTC conditions [Phase II]. Correct use means that the participants will demonstrate the use of the study product according to the guidelines outlined in the User Manual.
   Following the standard norms for the therapy of Rx-to-OTC switch process, this outcome is a validation of potential consumers' ability to self-treat with the product according to the product's supplied IFU.

10. Eligibility Criteria

Ages Eligible for Study: 18 years of age and older for Phase I and Phase II

Genders Eligible for Study: Female and male

10.1. Inclusion criteria:

1- For Phase I: 8 subjects with xerostomia and 8 without that are 18 years old or older

2- For Phase II: Subjects with xerostomia that are 18 years old or older

10.2. Exclusion criteria:

1- For Phase I:

- Children and adolescents (persons under 18 years of age)
- Persons with experience in the use of SaliPen

2- For Phase II: Subjects for them the study product is not indicated and/or do not agree to participate in Phase II. For the avoidance of doubt, the following conditions are exclusion criteria:
    - Persons with experience in the use of SaliPen
    - Children and adolescents (persons under 18 years of age)
    - Epileptic disorder
    - Persons that are allergic to the surface materials of the device
        - Electrodes: coated with gold
        - Body: made of methyl vinyl silicone rubber
    - Use of a pacemaker
    - Pregnancy
    - Psychiatric or psychological disorders
    - Involuntary muscle movement disorder (such as Parkinson's)
    - Neurologic disorder in head and neck area

11. Reportable Events

An adverse event (AE) is defined as any untoward medical occurrence in a subject during the investigation. Any findings will be documented on the AE CRF.

Serious AEs include any events resulting in death, decreased life expectancy, life-threatening situations, persistent or permanent disability/incapacity, hospitalization, or congenital anomaly/birth defect or other important medical event. Within 24 hours, the Investigator will submit a written report documenting the circumstances of the serious AE.

While AE's and SAE's are not anticipated, should an incident occur during the visit or a subject report an event following the visit, the AE will be recorded in the subject's study records and followed to resolution.

12. Contacts and Locations

The subjects will randomly be recruited at clinical settings that deal with oral health, like dental or head and neck clinics. The outcome measure will be performed in this setting. Data will be collected on-site by the clinical staff.

13. Task Analysis

The Task Analysis breaks down the device use process into discrete sequences of tasks. The tasks will be analyzed to identify the user interface components involved, the use errors that users could make and the potential results of all use errors. The following task analysis is planned:

Phase	#	Task
I	1	Potential user knows the intended use of the study product.
	2	Potential user assesses correctly whether the study product is indicated for him/her.
	3	Potential user assesses correctly whether he/she can use the study product or not or conditioned to a medical advice.
II	1	User knows the maximum amount of times and the maximum length of time he/she can use the study product.
	2	User knows how to switch the study product ON and OFF.
	3	User knows how to place the study product into his/her mouth.
	4	User knows how to remove the study product from his/her mouth.
	5	Patient knows how to separate the intraoral and the extraoral units.
	6	Patients reports any significant discomfort felt with SaliPen
	7	Patients reports any significant difficultis in using SaliPen

Each task will be evaluated by the binary grading scheme satisfactory/unsatisfactory. The evaluator will be a member of the study team.

For Phase I - 100% success is needed to pass the evaluation for every subject.

For Phase II - 85% success rate is needed to pass the evaluation for every subject.

The Human Factor Study will be considered successful if 85% of the participants passed each Phase of the test.

14. Ethical and Legal Aspects

14.1. Compliance with Regulations Applicable to Clinical Trials

The study will be conducted according to the laws, regulations and administrative provisions relating to the implementation of Good Clinical Practice in the conduct of clinical trials.

14.2. Informed Consent

The principles of Informed Consent, according to the Declaration of Helsinki 1964 and all its updates, will be followed. A subject should not enter a clinical study until he/she has been properly informed, has been given time to contemplate participation, and has freely given his/her consent by signing and dating the IRB-approved informed consent form. This must be done prior to performing any study-related procedures.

The proposed consent form and any other documents relevant to the consent process must be submitted to the Institutional Review Board (IRB), together with the protocol, and must be approved prior to the study start.

A copy of the fully signed and dated Informed Consent and any other documents relevant to the consent process will be given to the subject and the original will be maintained at the site.

14.3. Institutional Review Board (IRB)

The study must have approval, in writing, by an appropriate Institutional Review Board (IRB).

Records of the IRB review and approval of all documents pertaining to this study must be kept on file by the investigator.

Serious or unanticipated adverse events (SAEs) must also be reported to the IRB by the Investigator.

14.4. Protocol Amendments

Protocol amendments must be approved by the IRB prior to implementation.

14.5. Subject Confidentiality

All subject data will be identified only by a subject identification number and date of birth.

15. Guide for participants

Phase I - Self-Administered Questionnaire

I.D.: _____DATE:_____

Please read the cover and the back cover of the device and answer the following questions:

1. **Is the device for Dry Mouth Relief?**
   - ❑ Yes
   - ❑ No

2. **Does the device fit your needs?**
   - ❑ Yes
   - ❑ No

3. **If the device fits your needs, please check a box (only one):**

   - ❑ **I can use the device.**

   - ❑ **I cannot use the device because, either:**
     - I'm under 18 years of age.
     - I suffer from epileptic disorder.
     - I'm allergic to gold or silicone rubber.

   - ❑ **I need a professional consultation before buying the device because, either**:
     - I use a pacemaker.
     - I'm pregnant.
     - I suffer from a psychiatric or psychological disorder.
     - I suffer from an involuntary movement disorder (for example Parkinson's disease).
     - I have a neurologic disorder in the head and neck area (for example trigeminal neuralgia).

Phase II - Interviewer-administered questionnaire

I.D.: _____DATE: _____

Please read the user manual and hold the device.

Firstly, your oral cavity will be examined.

Next, you will be asked the following questions and to perform the following tasks:

1. **How many times can you use the device in a day and how many minutes (maximum time) you can use the device in one session? (See page 2)**
2. **How do you turn ON and OFF the device? (See page 6)**
3. **How do you insert the device in your mouth? (See pages 7, 8 and 9 and watch the video "How to use the SaliPen device to stop dry mouth")**
4. **How do you take the device out of your mouth? (See pages 7, 8 and 9)**
5. **How do you detach and reattach the white extraoral command unit from the blue intraoral stimulating unit? (See page 6)**
6. **Did you experience discomfort with the SaliPen in your mouth?**
7. **Did you experience difficulties in using the SaliPen?**

Finally, your oral cavity will be examined again.

16. Evaluation Sheets

Phase I

Subject I.D.: _____
EVALUATOR NAME: _____
Date:_____

Step 1: **Anamnesis taken by the evaluator**

Ruling	Parameters	yes	no
Indication	Xerostomia		
Contraindications	Under 18 years old		
	Epileptic disorder		
	Allergy to gold		
	Allergy to silicone		
Precautions – medical advice recommended before purchase	Pacemaker		
	Pregnant		
	Psychiatric or psychological disorder		
	Involuntary movement disorder (e.g., Parkinson's disease)		
	Neurologic disorder in the head and neck area (e.g., trigeminal neuralgia)		

Step 2: **Self-Administered Questionnaire** - Subject pre-purchase selection of the study product

Subjects will be asked to read the cover and the back cover of the device package and answer the following questions:

Question / Statement	Participant's answer	Correct answer	Success (1) / Failure (0)
1. Is the device for Dry Mouth Relief?	❑ Yes ❑ No	❑ Yes ❑ No	
2. Does the device fit your needs?	❑ Yes ❑ No	❑ Yes ❑ No	
3. If the device fits your needs, please check a box (only one):			
I can use the device	❑ Yes ❑ No	❑ Yes ❑ No	

Question / Statement	Participant's answer	Correct answer	Success (1) / Failure (0)
I cannot use the device because, either: • I'm under 18 years of age. • I suffer from epileptic disorder. • I'm allergic to gold or silicone rubber.	❑ Yes ❑ No	❑ Yes ❑ No	
I need professional advice before using the device because, either: • I use a pacemaker. • I'm pregnant. • I suffer from a psychiatric or psychological disorder. • I suffer from an involuntary movement disorder (for example Parkinson's disease). • I have a neurologic disorder in the head and neck area (for example trigeminal neuralgia).	❑ Yes ❑ No	❑ Yes ❑ No	

Step 3: **Summary evaluation** (to be completed by the evaluator)

Total questions/statements for those **with** dry mouth: 5

Number of correct answers: _____

Total questions/statements for those **without** dry mouth: 2

Number of correct answers: _____

Passed? (all answers/statements should be correct):

❑ Yes
❑ No

Phase II

Subject I.D.: _____

Step 1: **Oral soft tissue examination**

EVALUATOR NAME: _____
DATE:_____

	Normal	Abnormal	If Abnormal, please specify findings
Labial Mucosa (including lips)	☐	☐	
Buccal Mucosa	☐	☐	
Mucogingival Folds	☐	☐	
Gingival Mucosa	☐	☐	
Edentulous Ridge/Retromolar area	☐	☐	
Tongue	☐	☐	
Sublingual Area/floor of mouth	☐	☐	
Submandibular area	☐	☐	

Step 2: **Assessment of subject performance**

EVALUATOR NAME: _____
DATE:_____

Please evaluate how the participant addresses the following questions/tasks:

Questions	Participant's answer	Correct answer	Success (1) / Failure (0)
1. How many times in a day and how many minutes (maximum time) you can use the device in one session?			
Tasks	**Evaluation**		**Success (1) / Failure (0)**
2. How do you turn on ON and OFF the device?			
3. How do you insert the device in your mouth?			
4. How do you take the device out of your mouth?			
5. How do you detach and reattach the white extraoral command unit from the blue intraoral stimulating unit?			
Subject assessment (place an x where relevant for you) Note: Success (1) is meant if options 2 or 3 were chosen Failure (0) is meant if option 1 was chosen			**Success (1) / Failure (0)**
6. Did you experience discomfort with the SaliPen in your mouth?	1- Severe discomfort		
	2- Moderater discomfort		
	3- No discomfort		
7. Did you experience difficulties in using the SaliPen?	1- Severe discomfort		
	2- Moderater discomfort		
	3- No discomfort		

Summary evaluation:

Total questions/tasks/self-assessments: 7

Number of points: _____

Passed? (minimum 6 points):

- ❑ Yes
- ❑ No

Step 3: **Oral soft tissue examination**

EVALUATOR NAME: _____
DATE:_____

	Normal	Abnormal	If Abnormal, please specify findings
Labial Mucosa (including lips)	☐	☐	
Buccal Mucosa	☐	☐	
Mucogingival Folds	☐	☐	
Gingival Mucosa	☐	☐	
Edentulous Ridge/Retromolar area	☐	☐	
Tongue	☐	☐	
Sublingual Area/floor of mouth	☐	☐	
Submandibular area	☐	☐	