Prospective non-interventional evaluation of insertion and sealing performance of AuraOnce Disposable Laryngeal Mask US Version

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INTRODUCTION

The AuraOnce is a class IIa disposable (single use, sterile) flexible supragottic airway device intended to maintain control of the airway during routine and emergency anaesthetic procedures in fasted patients. The AuraOnce was the first single moulded laryngeal mask with a curvature of the airway tube simulating the anatomy of the throat and was launched in 2004.

This study is initiated to ensure that the device continues to perform as intended.

The CIP was made according to the Council Directive 93/42 EEC of 14 June 1993 and amendment 2007/47/EC (1), the guidelines set out in ISO 14155 (2), ISO 14971 (3), the Helsinki Declaration (4) and the European Commissions General Data Protection Regulation (GDPR) (5).

1. IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

1.1 Description

The Ambu AuraOnce is intended for use as an alternative to a facemask for achieving and maintaining control of the airway during routine and emergency anaesthetic procedures. The Ambu AuraOnce may also be used where unexpected difficulties arise in connection with airway management. It is only intended for use by medical professionals trained in airway management.

It is a laryngeal mask consisting of a tube with a specially shaped inflatable cuff distally, which conforms to the contours of the hypopharynx and with its lumen facing the laryngeal opening. The distal tip of the cuff presses against the upper esophageal sphincter and the proximal end of the cuff rests against the base of the tongue.

The Ambu AuraOnce contains different versions of "U" and "EU". The only difference between "U" version and "EU" version is that "U" version of AuraOnce does not have an enforced tip on the top of the cuff while "EU" version of AuraOnce has the enforced tip.

The product is single use and delivered sterile.

The product concept comprises eight sizes of laryngeal masks. The correspondence between the product sizes and patient size is as stated in the table:

Mask size	Patient weight	Maximum cuff inflation volume
#1 / #1U	<5 kg	4ml
#1½ / #1½U	5-10 kg	7ml
#2 /#2U	10-20 kg	10ml
#2½ / #2½U	20-30 kg	14ml
#3 / #3U	30-50 kg	20ml

#4 / #4U	50-70 kg	30ml
#5 / #5U	70-100 kg	40ml
#6 / #6U	>100 kg	50 ml

1.2 Manufacturer

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1.3 Models/type of the investigational device

The product concept comprises eight sizes of laryngeal masks. The Ambu AuraOnce is a sterile and single use device. The product specifications are described in the table below.

	Mask size							
	#1	**#1½**	**#2**	**#2½**	**#3**	**#4**	**#5**	**#6**
① Airway connector	15 mm male (ISO 5356-1)							
② Min. I.D. Tube	5,2 mm	7,3 mm	8,6 mm	8,5 mm	8,5 mm	9,6 mm	10,6 mm	11,3 mm
③ Max. O.D. Tube	10,5 mm	13 mm	15 mm	17,5 mm	17,5 mm	20 mm	22,5 mm	25 mm
④ Inflation Valve	Luer cone compatible with ISO 594-1							
Appropriate storage temperature	10 °C (50 °F) to 25 °C (77 °F)							
Dimensions (mm) (length x width x height)	97x 24x70	112x 29x82	128x 34,5x95	148x 41x109	148x 49x116	168x 56x132	187x 64x148	200x 69x165
Weight	9,8 g	13,5 g	19,4 g	28,1 g	30,8 g	44,2 g	62,3 g	76,6 g
Internal volume of ventilatory pathway	5,5 ml	8 ml	11 ml	15 ml	16 ml	21 ml	30 ml	38 ml
Pressure drop	<1,2 cmH_2O at 15 l/min	<0,8 cmH_2O at 15 l/min	<1,0 cmH_2O at 30 l/min	<0,8 cmH_2O at 30 l/min	<2,0 cmH_2O at 60 l/min	<1,2 cmH_2O at 60 l/min	<0,8 cmH_2O at 60 l/min	<0,5 cmH_2O at 60 l/min
Min. interdental gap	15 mm	17 mm	19 mm	21 mm	25 mm	29 mm	31 mm	32 mm
⑦ Internal pathway	10,3 cm	12,0 cm	13,8 cm	15,9 cm	15,9 cm	17,8 cm	20,0 cm	22,0 cm

1.4 Device traceability

The site included in the study will make their daily used bronchoscopes available for the procedure.

The site will free of charge receive 20 Ambu® AuraOnce devices in each adult size (size 3, 4 and 5). Any devices remaining after the end of the study will be accounted for and shall be returned to Ambu®.

There are no requirements regarding device accountability for CE marked devices. However, for logistical reasons the Sponsor will account for all devices delivered to and returned from the Investigators in a Device Accountability Form kept at Sponsor's address.

1.5 Investigational device procedures

The laryngeal mask is introduced in the routine fashion by trained staff (anesthesiologist or anesthesia nurse). It will be used in already planned diagnostic flexible bronchoscopy procedures in general anesthesia. The flexible bronchoscope is introduced through the laryngeal mask and special attention is paid to the cuff area including the tip.

2. JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

The clinical investigation is an observational study designed as quality control of the AuraOnce. Based on experience, the sample size has been judged to be adequate to provide the information necessary to show a representative picture of the product quality which is the objective of the study.

3. OBJECTIVES AND HYPOTHESES

The objective of this study is to observe the performance of the AuraOnce through clinical assessment and endoscopic imaging to ensure ongoing documentation on quality of the product in regards to correct placement remains high.

This is an observational study with no hypothesis. However, a success criterion is set saying that in 90% of the cases the AuraOnce must be correctly centred above vocal cords with no clinical significant air leak and using maximum three placement attempts.

3.1 Primary

Primary endpoint[1]:

- Leakage (yes/no), if yes insert signs of leakage

3.2 Secondary

Secondary endpoints[2]:

- Questionnaire – interview to anaesthesiologist/nurse
  - Ease of insertion (5-point scale, very difficult to very easy)
  - Ease of obtaining seal (5-point scale, very difficult to very easy)
  - Overall performance (5-point scale, very bad to excellent)
- Opening placed just above vocal cords (yes/no) correct positioning is documented by endoscopic picture (including POGO score)

[1] Primary endpoint(s) is (are) principal indicator(s) used for assessing the primary hypothesis of a clinical investigation. It is also used to calculate sample size.
[2] Secondary endpoints are indicators used for assessing the secondary hypotheses of a clinical investigation.

- Folding of tip (yes/no) - is documented by endoscopic picture

3.3 Claims and intended performance

The claims to be observed in the study is:
- Ease of insertion
- Tip resists folding over during insertion and plugs the upper oesophageal sphincter
- Sealing

4. DESIGN OF THE CLINICAL INVESTIGATION

4.1 General

This study is designed as a single-center, prospective observational, non-controlled, non-interventional study with an investigation period lasting for one day (during one bronchoscopy procedure). The study will take place in Denmark.

The study will include minimum 15 adult patients planned for a diagnostic flexible bronchoscopy procedure in general anaesthesia using a laryngeal mask.

The involved site will include subjects during a one month period, October 2019. However, the study will not be initiated before the study protocol is duly approved, i.e. by site, Ambu and Ethics Committee if relevant (if EC approval is not needed a written opinion from the EC must be obtained). If the number of subjects cannot be included in time, the sponsor will decide whether the study period should be extended, or the study should be closed.

The intention is to perform a quality assessment of the AuraOnce. Subjects will not be asked to participate in this study as it is a quality study (see section 16) where the AuraOnce is used within its intended use and according to normal clinical procedure.

4.2 Investigational devices and comparators

4.2.1 Device exposure

The subjects will be exposed to the device for less than an hour. The devices used for the study are all CE marked and used in normal clinical practice.

4.2.2 Choice of comparator

Not applicable

4.2.3 Other investigational devices or medications

Apart from the AuraOnce Laryngeal mask, the following devices can be used during the procedure:

- Flexible bronchoscope normally used for the planned bronchoscopy procedure at site.
- Syringes with saline for broncho-alveolar lavage (BAL)
- Biopsy forceps for transbronchial biopsy (TBB).

4.2.4 Number of investigational devices to be used

One AuraOnce is expected to be used for each procedure. In case of device deficiencies, the product must be replaced, and a device deficiency form must be completed.

4.3 Subjects

The clinical investigation will be conducted on minimum 15 subjects and maximum 20 subjects enrolled in one clinical investigation site.

4.3.1 Inclusion criteria

Subjects will be enrolled responding to the following criteria:

- Subjects > 18 years
- Subjects planned for diagnostic flexible bronchoscopy procedure in general anesthesia using a laryngeal mask.

4.3.2 Exclusion criteria

Subjects responding to the following criteria are excluded from participation:

- Subjects where use of AuraOnce cannot be clinically justified

4.3.3 Subject withdrawal or discontinuation

Patients not completing the clinical procedure as intended by the investigator are considered as drop-outs as the evaluation form will lack information of the device. In case of drop-outs the study will not be completed until the minimum number of subjects is included.

Subjects will be withdrawn from the clinical investigation for the following reason:

a. Withdrawal by investigator for e.g. safety reasons

The reason for withdrawal will be investigated and carefully documented in the appropriate section of the case report form (CRF).

If a subject is replaced the new subject is given a new subject number.

4.3.4 Recruitment and point of enrolment

The subjects (patients) included in this study are scheduled for a diagnostic flexible bronchoscopy procedure in general anesthesia using a laryngeal mask.

When a subject is included, the investigator assures that the subject meets all inclusion criteria and none of the exclusion criteria, by checking the relevant boxes in the CRF.

The subjects will not receive information about the study, as no patient data are obtained, and the CE-marked AuraOnce laryngeal mask is used within intended use. The only data to be obtained are evaluation forms directly related to the performance of the device, the user's perception of insertion of the laryngeal mask and pictures of the placement and sealing.

4.3.5 Duration of the clinical investigation

The data collection is expected to last three days within a two months period. The subjects are included in the study when the investigator has ensured that they fulfill the in- and exclusion criteria and they are completed when the bronchoscopist have confirmed the laryngeal mask placement (by taking a picture) and starts the planned bronchoscopy procedure. The expected duration of each subject's participation is estimated to be less than one hour.

4.4 Procedures

The site will receive the protocol, AuraOnce and case report forms (CRFs). A total of 80 Aura once products will be provided, included 20 laryngeal masks in each size (size 3, 4, 5). Any remaining products after the study will be returned to Ambu A/S.

During normal clinical bronchoscopy procedures where general anaesthesia with a laryngeal mask is needed AuraOnce will be used if the subjects fulfil the in- and exclusion criteria. The CRF must be filled in for each subject that is enrolled in the investigation.

The investigation period for each subject is within one day. The anaesthesiologist decides which size of AuraOnce should be used for each subject and places the laryngeal mask according to normal clinical practice at the site.

4.4.1 Screening

Patients planned for a diagnostic bronchoscopy procedure under general anaesthesia at the investigational site will be evaluated by the anaesthesiologist to determine if AuraOnce can be clinically justified for the procedure. If AuraOnce can be clinically justified and the subject fulfils the inclusion criteria for the study, he/she will be enrolled in the study. If AuraOnce cannot be clinically justified or if the patient does not fulfil the inclusion criteria, he/she will be excluded from the investigation and receive the standard treatment off this investigation.

4.4.2 Randomisation

Not applicable

4.4.3 Investigational procedures

4.4.4 Pre-examination of the airway

- Before inserting the AuraOnce a pre-examination will be performed to ensure that the anatomy is applicable for laryngeal mask placement.
- An examination of the airway will be performed and include the following measures:
    - Airway cleaned (yes/no)
    - Inter-incisor distance (normal/reduced)
    - Sifnificant overbite (no/yes)
    - Mandibular space (normal/reduced)
    - Cervical motion (normal/restrictede)
    - Short thick neck (no/yes)

4.4.5 Preparation for use

- The device will be prepared, and size will be chosen according to users' standard clinical procedure.

4.4.6 Insertion of AuraOnce

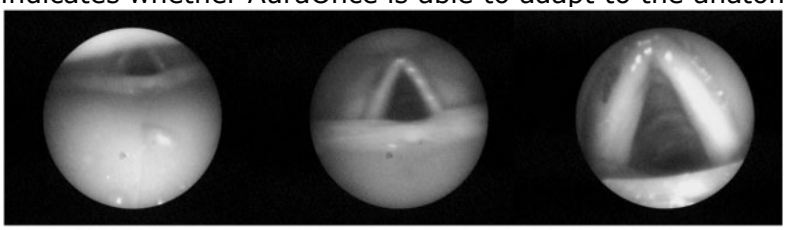
- All participants are experienced in placement of laryngeal masks and placement will be performed according to standard clinical practice.
- Number of attempts for correct placement will be noted in the CRF
- After insertion the following information is noted in the CRF:
    - Leakage (yes/no) – if yes: signs of leakage are noted
- After insertion the user perception of the AuraOnce placement is obtained regarding:
    - Ease of insertion
    - Ease of obtaining seal

- Overall performance of the product

4.4.7 Bronchoscopy procedure

Prior to the bronchoscopy procedure, which the patient is scheduled for, an assessment of the AuraOnce will be performed.

- The head of the patient is placed in neutral position.
- A lubricated flexible video bronchoscope is inserted through the AuraOnce.
- A picture is taken of the vocal cords to assess the placement of AuraOnce
  - The picture is kept with the CRF
- The percentage of glottic opening (POGO), defined on a scale from 0-100 (see figure below) is used to confirm correct placement (6). The percentage of opening seen indicates whether AuraOnce is able to adapt to the anatomy.



10% 50% 100%

- A picture of the AuraOnce cuff is taken, specially focussing on the tip
  - The picture is printed and kept with the CRF
  - If any issues with the cuff is observed (especially folding) it must be described in the CRF.

After assessing the AuraOnce the diagnostic flexible bronchoscopy procedure is performed as planned and the AuraOnce is removed after the procedure. The bronchoscopic procedure and removal of AuraOnce is not part of this investigation, and the study ends as the bronchoscope passes the vocal cords.

4.4.8 Follow-up procedures

Not applicable

4.4.9 Missed follow-up

Not applicable as no follow up is done

4.4.10 Lost to follow-up

Not applicable as no follow up is done

4.4.11 Procedures performed by sponsor representatives

Not applicable

4.4.12 Subject Identification and Confidentiality

Each subject will be given a subject number, however all data collected will be anonymized and it will not be possible to identify the subject after completion of the procedure. No patient registration list will be created to ensure patient confidentiality.

Data entered on the CRF are confidential and will only be available to the sponsor (including sponsor delegates), members of data management teams, the statistician, data monitoring

board members or clinical event committee members if involved, and if requested to regulatory authorities.

4.5 Monitoring plan

The sponsor is responsible for ensuring appropriate monitoring of the clinical investigation activities.

During the period of the investigation a representative of the sponsor, Annette Bitz, +45 2080 1620 or Anna Charlotte Lundgaard, +45 2964 3748, will act as monitor/s of the investigation. The investigator may contact Annette Bitz or Anna Charlotte Lundgaard at any time. The monitor will be the primary contact for the principal investigator and clinical investigation site personnel.

Monitoring activities are mandatory as per good clinical practice, however the extend and depth of these activities depend on the criticality of the clinical investigation, speed of enrolment, the experience of the clinical investigation site personnel in carrying out clinical investigations and specific study designs.

For the purpose of this clinical investigation the below described monitoring procedures have been determined.

4.5.1 Monitoring visits

The monitor/s is responsible for planning the monitoring visit including initiation visit, routine visit and close-out visit.

4.5.2 Initiation visit:

The initiation visit will be performed before the study is initiated. The aim of this meeting is to train the investigator(s) on the investigation procedure, perform a page-by-page revision of the CIP with emphasis on reporting of deviations, adverse events and how to complete the CRF. Moreover, contract signature and written EC opinion will be verified, and monitoring arrangements will be discussed. It is required that all investigators participating are present in this meeting.

4.5.3 Routine Visit

Monitoring of the CRFs will be performed after the first day of data collection (4-7 subjects are expected to be completed at this point). Ongoing monitoring will be performed by the observer who will be presented during all data collections. The aim of these routine visits is to corroborate the clinical investigation progress. CRF will be monitored for completeness and correctness of the data. It is required that at least one investigator is available during monitoring visits.

4.5.4 Close-out visit:

The close-out visit will be performed when the data collection has been completed. The aim of this meeting is to close financial aspects, check that all essential documents are complete and up to date, all outstanding queries are resolved, current state of all adverse events is documented, arrangement for achieving all clinical investigation documentation, device accountability and collection of the original CFR.

4.5.5 Source data verification

No source data verification will be performed for this study, as there will be no access to the patient file. Name, address/contact information and personal identification number (CPR) will not be collected for this study. To ensure correct data collection and high-quality data, an observer dedicated for the study will be available during the entire data collection to double check that all data is noted correct. It will be the same observer during the entire data collection.

5. AUDIT

Audit of the clinical investigation may be conducted by the sponsor or third parties designated by the sponsor to evaluate compliance with the CIP, written procedures and international standards (2). These audits may cover all involved parties, systems and facilities and are independent from routine monitoring. The aims of the audit are:

- to assess the effectiveness of the monitoring,
- whenever there are repetitive deviations from the CIP,
- to prepare the investigation for a regulatory inspection,
- when requested by a regulatory authority, etc.

Audits may be performed during the investigation. All parties will be informed in advance of the date and objective of the audit.

6. STATISTICAL CONSIDERATIONS

6.1 Sample size

No sample size calculations have been performed for this study as the data obtained only will form basis for quality control of the performance of the Ambu AuraOnce disposable Laryngeal Mask.

The study will include a minimum of 15 and a maximum of 20 adult patients already scheduled for a diagnostic flexible bronchoscopy procedure in general anesthesia using a laryngeal mask.

6.2 Pass/fail criteria

In 90% of the cases the AuraOnce must be correctly centred above vocal cords with no clinical significant air leak and using maximum 3 placement attempts.

6.3 Statistical analyses

6.3.1 General aspects

Descriptive statistics of all measured outcomes are provided (median and range or mean and standard deviation as appropriate). The study is not sufficiently powered to explore patient characteristics related to unsuccessful placement of laryngeal mask.

6.3.2 Handling of dropouts and missing data

Patients not completing the clinical procedure as intended by the investigator are considered as drop-outs as the evaluation form will lack information of the device. Drop-outs are

compensated in the sample size estimation to ensure that a complete data set is collected for minimum 15 patients. Missing data will not be imputed.

7. DATA MANAGEMENT

A database will be set up, and two individuals at Ambu A/S will perform double data entry. Any unclear data points will be highlighted in a data clarification form that will be sent to the responsible investigator for clarification. An error list will be generated, and errors corrected by Ambu A/S staff.

7.1 Data review and cleaning

The CRF must be filled in for each subject that is included in the investigation.

The CRF is in English and should be filled in English when possible.

Missing data not recorded on the day of the procedure should be filled in later accompanied by date and signature. Data that are evaluated as incorrect by investigator should be crossed over with ink allowing the "old data" to be seen ~~(example)~~. The investigator shall then write the corrected data, signed and dated.

The principal investigator at the clinical site will perform primary data collection by entering the data into the CRF. Only the principal investigator or other pre-designated clinical investigation site personnel will be authorized to enter data.

The sponsor's designated monitor shall ensure appropriate training on data entry is provided prior to the start of the clinical investigation to all site personnel involved.

The principal investigator can delegate tasks to his/her collaborators, however the roles and responsibilities as time period of involvement for each clinical site personnel must be documented on the site personnel log as well as training received before getting involved with the clinical investigation.

Clinical site personnel not trained and not officially identified by his/her name and signature cannot enter data in the CRFs.

The principal investigator shall approve and date each CRF.

The monitor shall verify all critical data points and issue queries for the authorized clinical site personnel to answer.

A CRF section shall be considered complete when all data are completed, verified by the monitor, outstanding queries resolved and signed off by the principal investigator.

A critical quality control will be performed continuously by the designated observer at the site.

7.2 Data retention

The sponsor and principal investigator shall maintain the clinical investigation documents as required by the applicable regulatory requirements. For non-implants the investigator binder, including CIP, CIR and copies of CRF's, , must be kept on site for at least 5 years after the clinical investigation report has been signed.

The sponsor will file original CRFs for rest of the products' lifetime + 10 years. Moreover, adverse event forms, statistical analysis, agreements, approvals, investigators' CVs, CIP, and CIR will also be filed.

8. DEVICE ACCOUNTABILITY

The site included in the study will make their daily used bronchoscopes available for the procedure.

The site will free of charge receive 20 Ambu® AuraOnce devices in each of the sizes used for adults (size 3, 4, 5 and 6). Any devices remaining after the end of the study will be accounted for and shall be returned to Ambu®.

There are no requirements regarding device accountability for CE marked devices. However, for logistical reasons the Sponsor will account for all devices delivered to and returned from the Investigators in a Device Accountability Form kept at Sponsor's address.

9. STATEMENTS OF COMPLIANCE

The clinical investigation will be conducted according to the guidelines established in the Declaration of Helsinki (4). Good clinical practice

The clinical investigation processes will comply with good clinical practice as outlined in ISO 14155 (2).

9.1 Regulatory compliance

The clinical investigation processes shall be performed in compliance with all applicable regulatory requirements in addition to the above defined requirements for good clinical practices. Where regulatory requirements are less or more stringent than the requirements outlined in ISO 14155 (2) the most stringent requirements will need to be complied with.

This includes the Council Directive 93/42 EEC of 14 June 1993 and amendment 2007/47/EC (1).

9.2 Patient information

Not applicable for this study.

9.3 Informed consent

Not applicable for this study.

10. LIST OF REFERENCES

1. European Council. Council Directive 93/42 EEC of June 1993 concerning Medical Devices. Vol. L 169, Council Directive 93/42/EEC. 1993.
2. Dansk Standard. Clinical investigation of medical devices for human subjects – Good clinical practice. Vol. 3. 2012.
3. Dansk Standard. Medical devices – Application of risk management to medical devices. Vol. 6. 2012.
4. The World Medical Association. Wma Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 2013.
5. The European Parliment and The Council of the European. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural

persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Da. Off J Eur Union. 2016;(April):88.

6. Levitan, RM; Ochroch, EA; Kush, S; Shofer, FS; Hollander J. Assessment of airway visualization: validation of the percentage of glottic opening (POGO) scale. Acad Emerg Med. 1998;5(9):919–23.