

Use of a novel average-geometry nasal cast for the development of Instructions For Use for Nose-to-Brain administration

INTRODUCTION

Nemera has developed its proprietary nasal cast, **CUBO**, built on an average anatomy from the scans of 25 healthy patients [1]. The olfactory region is defined as one third of the height of the posterior nasal cavity. The cast is 3D-printed in rigid, transparent SLA material with a soft silicone nostril, and has been used to characterise deposition in the olfactory area with Nemera's **Guided Stream Technology (GST)** device under fully controlled in vitro conditions [2].

CUBO was used to develop the **Instructions For Use (IFU)** for early clinical studies targeting delivery to the olfactory area by Healthcare Professionals. Several rounds of user studies were run; this poster presents the final study, in which **four IFUs (A-D) were evaluated**.

MATERIALS

- GST nasal devices filled with a placebo formulation (water, 0.8% w/w xanthan gum, fluorescein 5 g/L); Fluorescein improves qualitative assessment of the deposition pattern. In addition, GST devices both empty and filled with water was used in the stimuli phase to familiarise the user with the device manipulation.
- The **CUBO** nasal cast fitted with a 3D-printed human face replica (soft upper lip and philtrum) and a wig, forming a realistic human head replica (Figures 1 & 2), was fixed to a support positioned at the height of a seated patient.
- The 'seated-patient' environment was further enhanced by placing a chair below the head to represent the patients' leg space, thereby creating a distance between the HP and the patient, which obliged the HP to simulate the physical inclined posture necessary to administer the device to the human face replica.
- The GST device was equipped with an accelerator-inclinometer sensor (Ref WIT WT9011DCL) and video camera recording equipment was used for visual assessment of deposition in the nasal cast.
- HPs performed three consecutive administrations with the GST in three individual nasal casts
- The emitted dose and deposited mass characterized by gravimetric methods.
- 4 IFUs providing different instructions to the user for administration were provided. The IFU's varied in the explanation of the insertion parameters (i.e. the center of the forehead for IFU A as show in Figure 3 with the aim of achieving targeting deposition in the CUBO olfactory zone.

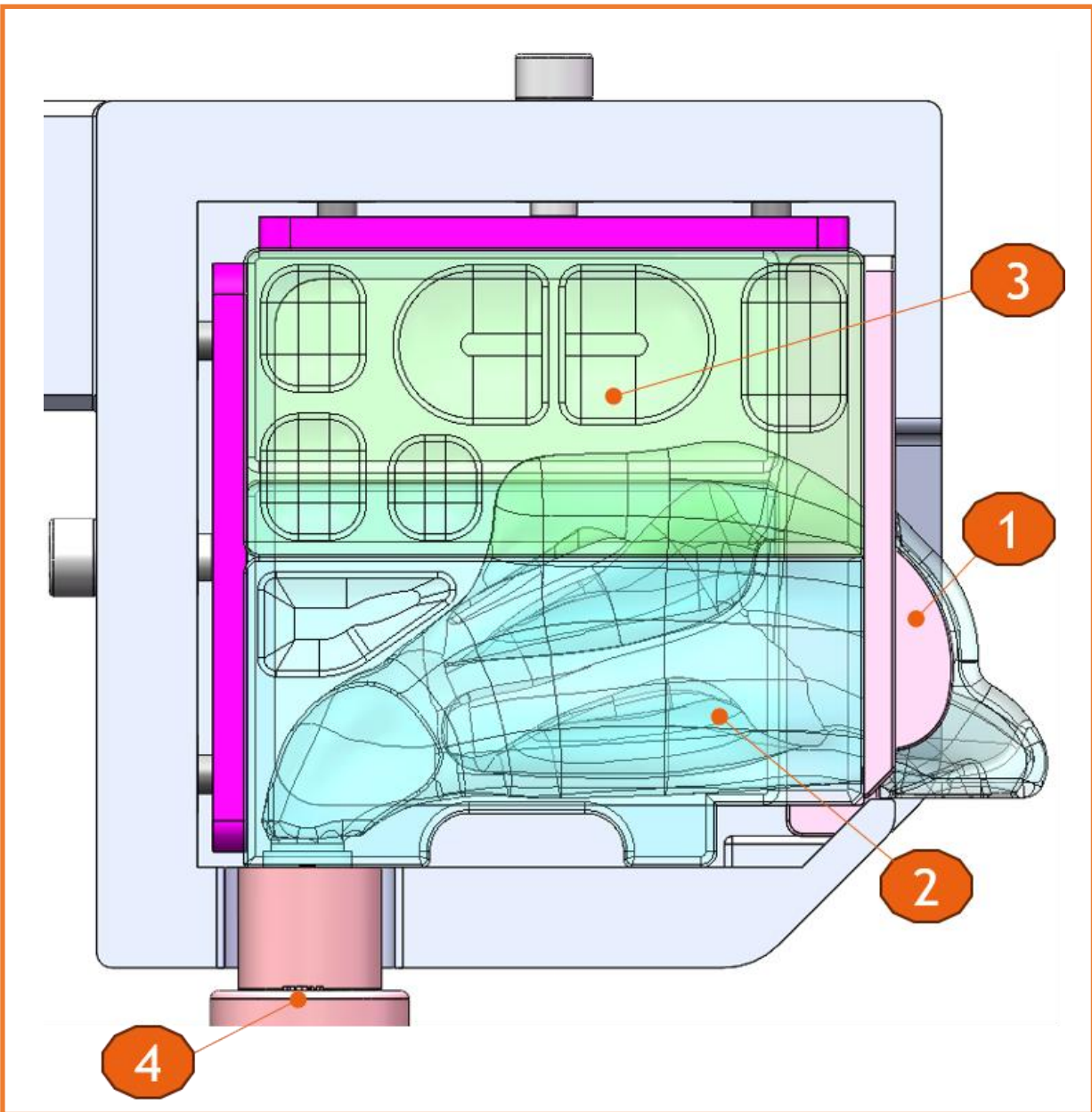


Figure 1 : CUBO Nasal cast

Regions of interest:

- 1- Nasal vestibule
- 2- Respiratory region
- 3- Olfactory region
- 4- Filter connection / lower respiratory track



Figure 2: Administration on the head replica.

AIMS & OBJECTIVES

- Development and optimization of the **Instructions For Use (IFU)** enabling Healthcare Professionals to reliably target the olfactory area with the GST device.
- Evaluation of **four candidate IFUs (A, B, C, D)** through moderated user studies, measuring deposition performance in an anatomically relevant nasal cast.

STUDY DESIGN

- Conducted at Nemera facilities in France: a moderator introduced the device, the IFUs and the study goals in a usability research room; actuations into human head replica and debriefing took place in the R&D laboratory.
- **Sixteen HP participants**, split into two groups:
 - Group 1 - IFU A then B, counterbalanced (A-B / B-A).
 - Group 2 - IFU C then D (IFU D identical to IFU C with additional guidance).
- Details of the study sequence are provided in Figure 4

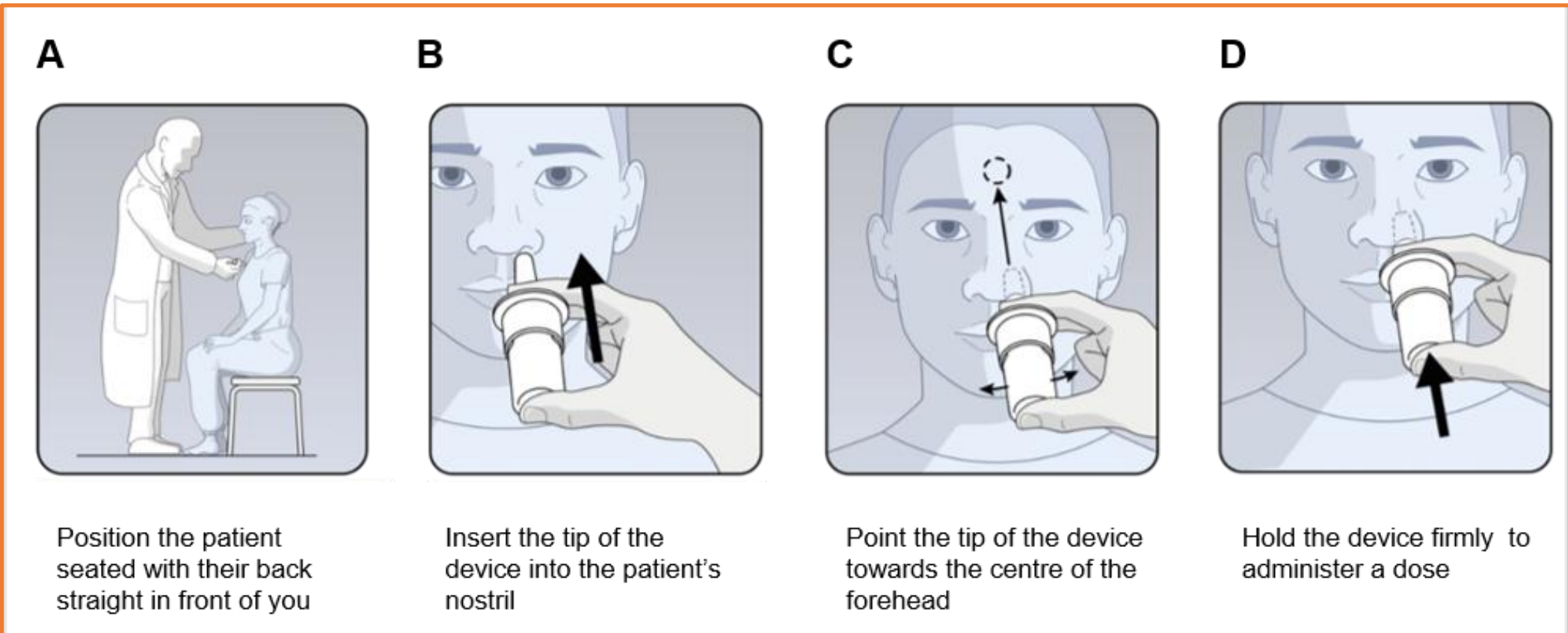


Figure 3: Instruction For Use 'A'

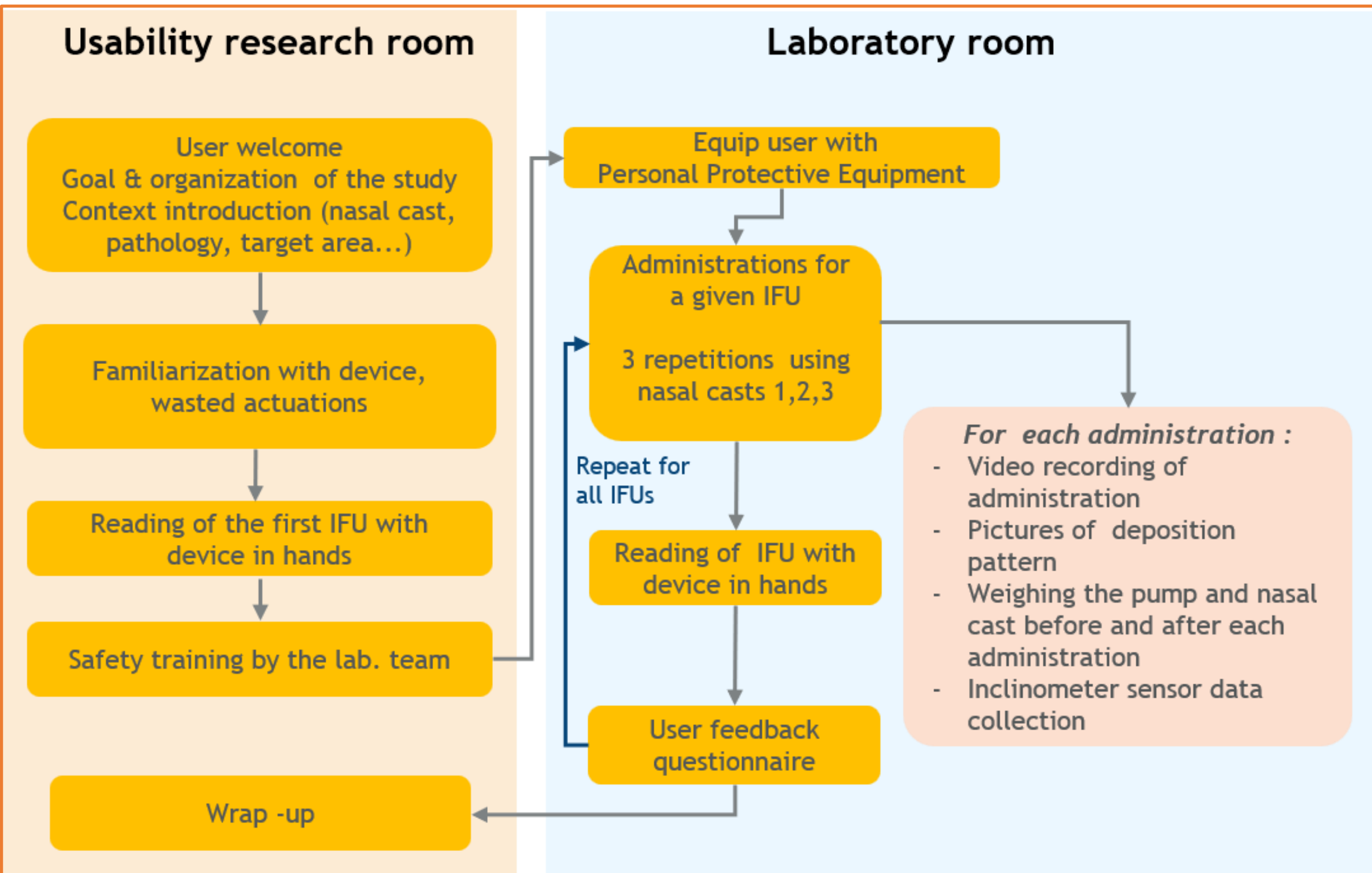


Figure 4 : Usability study overview

RESULTS

A **successful outcome** was defined as administration resulting in **more than 50% of the emitted dose delivered to the olfactory area**. Success rate varied with the IFU: **IFUs A and B produced the highest success**, while IFU D gave the lowest success rate, (matrix 1).

Task0	IFU A	IFU B	IFU C	IFU D
Score	(16/24)	(17/24)	(14/24)	(10/24)
Success rate	67%	71%	58%	42%

Matrix 1: Success rate of administrations with deposition in the olfactory area above 50%.

The deposition-pattern images (Figure 5), the administration videos and the inclination-sensor data were analysed to establish correlations between the administration conditions and the resulting deposition pattern. For intellectual-property reasons, these results cannot currently be published.

In addition, user feedback was collected to identify which areas of the IFUs required further refinement.

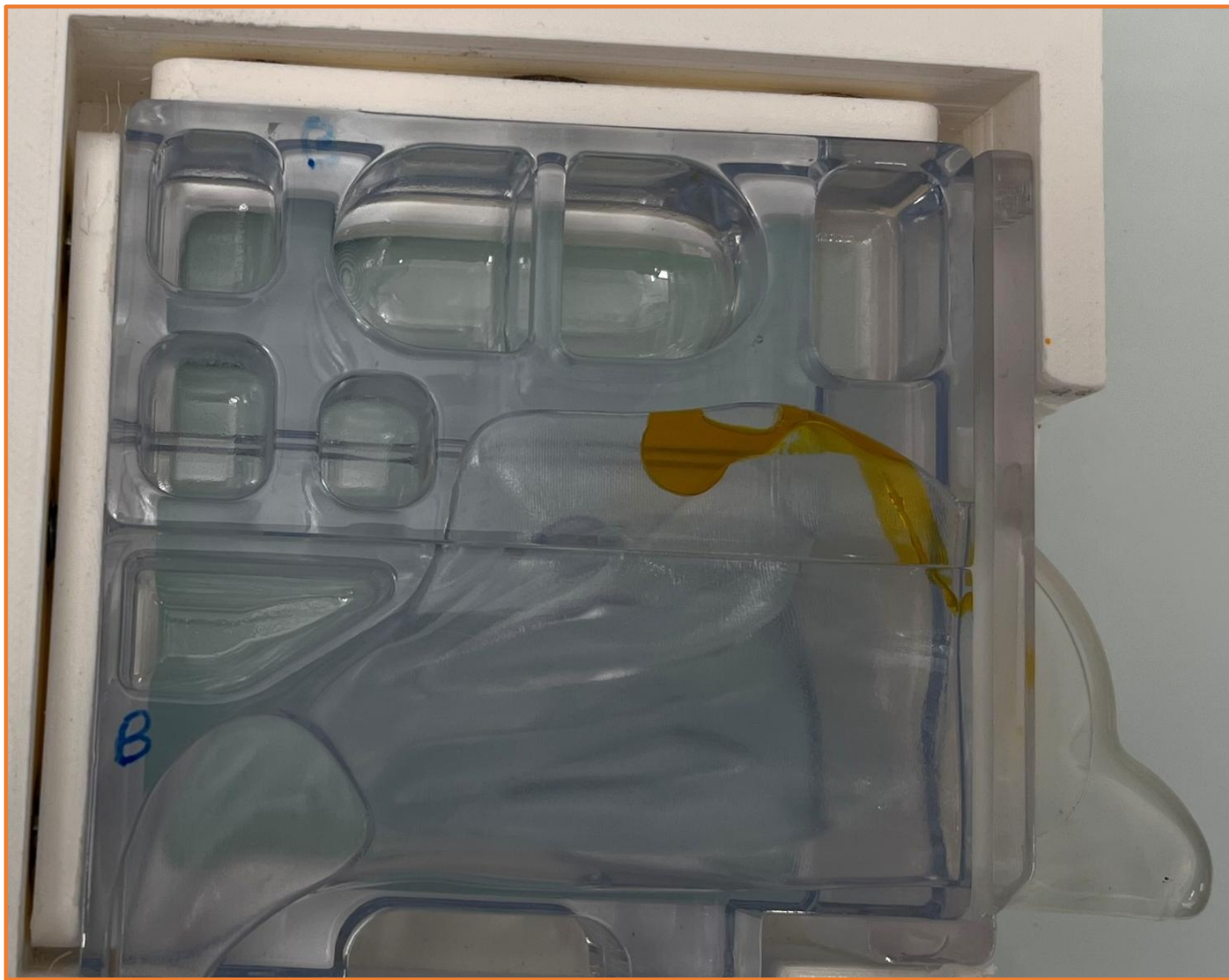


Figure 5: Typical deposition pattern in the nasal cast.

DISCUSSION & CONCLUSION

The simulated care environment with the human head replica nasal cast set-up facilitated the evaluation of the likely olfactory deposition with the GST device in a real-life situation. The IFU strongly impacts the success rate of deposition in the targeted region, with IFUs A and B showing the best results. Observing users, collecting their feedback and monitoring their deposition performance supported the definition of the optimum IFU.

REFERENCES

References
[1] Brüning J et al. Characterization of the Airflow within an Average Geometry of the Healthy Human Nasal Cavity. Sci Rep. 2020;10(1):3755.
[2] Foliard T et al. Sensitivity analysis of Guided Stream Technology for targeting the olfactory area using an anatomically relevant nasal cast. Poster, DDL 2025.