Using a digital spacer for inhaler technique education in pediatric asthma

PanamaID: 23081

Non-WMO study protocol

Date of document: 25-03-2026
Protocol version number: 2.0

CONTENT

1. Study organisation 3
2. Protocol Signature Sheet 6
3. Study summary 7
4. Study design 9
5. Population 10
6. Study data and analysis 11
7. Recruitment and informed consent/objection 13
8. Only complete in case of collaboration with parties outside of the UMCG (also called: third parties) 16
9. Data Management Plan (DMP) 17
10. FAIR Data and Data Sharing 18
11. Management of Biomaterials (either newly collected or from an existing biobank) 19
12. Burden, Risks & Benefits 19
13. Incidental findings 19
14. References 20
15. Appendices 20

1. Study organisation

Study title:	Using a digital spacer for inhaler technique education in pediatric asthma		
Planned start date and estimated completion date *Please note that the study may only start <u>after</u> approval and that the start date should allow for time needed for the approval process.*			*1-1-2026 to 30-6-2027*
Members of the *UMCG* study team. *Please extend section if there are more than 9 members in the study team.* *Please note that this is not a delegation log.*	**Information** *Name/ function/ department / center*		**Role in study** *E.g: Principal investigator, coordinating investigator, researcher, research nurse.*
	1	*Job van Boven/ Associate Professor/ Clinical Pharmacy & Pharmacology/ UMCG*	Co-Principal Investigator
	2	*Annelies Zwitserloot/ Pediatric pulmonologist/ Dept of Pediatrics/ UMCG*	Co-Principal Investigator
	3	*Amber Eikholt/ PhD student/ Clinical Pharmacy & Pharmacology/ UMCG*	Coordinating investigator
	4	*Anneke Salier- Tjoelker/ Dept of Pediatrics/ UMCG*	Research nurse
	5	*Kim van der Klei/ Dept of Pediatrics/ UMCG*	Research nurse
	6	*Yvonne Weesepoel/ Dept of Pediatrics/ UMCG*	Research nurse
	7		
	8		
If applicable: **Senior members of the *non-UMCG* study team(s)**	**Information** *Name/ function/ department / centre*		**Role in study** *Limit to: Principal investigator, coordinating investigator.*

Please limit to the principal and coordinating investigators for each centre. Extend section if there are more than 7 non-UMCG members in the study team(s). *Please note that this is not a delegation log.*	**1**	*Paul Hagedoorn/ Senior inhalation technologist/ Pharmacy/ RUG*	Investigator
	2		
	3		

Principal investigator , *contact information* *(The Principal Investigator heads the research team. Is responsible for planning and conducting the scientific study. The role is akin to that of a project leader. In Dutch, also 'hoofdonderzoeker'.)*	Name	Job van Boven
	E-mail	j.f.m.van.boven@umcg.nl
Corresponding researcher UMCG, *contact information*	Name	Amber Eikholt
	E-mail	a.a.eikholt@umcg.nl
	Telephone	+31 6 52474707
Sponsor (Dutch: verrichter/opdrachtgever)	UMCG: ☒	Other: ☐ If other, please note name of sponsor:
Financial support / subsidy provider	NA	☐
	Aflo Respiratory Analytics	Contact: Susan Kelly
Collaboration with non-profit Laboratory / **research sites** **(in- and outside UMCG)**	NA	☒
	Organisation name	
	Contact person	
	Email	
	Telephone	
	NA	☐

Collaboration with for-profit / commercial parties / companies **(in- and outside UMCG)**	Aflo Respiratory Analytics			
	Contact person	Susan Kelly		
	Email	susan@afloanalytics.com		
	Telephone	07730348303		
Is this study connected to a previous non-WMO or WMO application	Yes ☐	No ☒		
If yes, please provide the following information and/or documentation regarding the previous application.	Please add the name of the previous study.	/		
	Please add the PaNaMa number of the previous study.	/		
	Has the ethical approval of the previous application been added to the current application	NA ☐	Yes ☐	No ☐
	Has the study protocol of the previous application been added to the current application	NA ☐	Yes ☐	No ☐
	Has the patient information (DIF) of the previous application been added to the current application	NA ☐	Yes ☐	No ☐
	Has the Informed Consent form (IC) of the previous application been added to the current application	NA ☐	Yes ☐	No ☐

2. Protocol Signature Sheet

The undersigned principal investigator (NL: hoofdonderzoeker) UMCG and head of department UMCG confirm that the study protocol is compliant with the UMCG research code, the non-WMO Kaderreglement UMCG, and other legislation (such as the (U)AVG and WGBO).

Name	Signature	Date
Principal Investigator UMCG:	Job van Boven, Associate Professor	24-10-2025
Head of the department UMCG:	Jos Kosterink, Professor, Head of Clinical Pharmacy & Pharmacology	
Departmental Scientific Review Board (if applicable)	NA	
If tissues are requested from a biobank or data from a databank, please add a signature from the biobank administrator (NL: beheerder) here.	NA	
If tissues are requested from the UMCG biobank pathology, please add a signature from the tissue review board pathology here.	NA	

3. Study summary

3.1 Introduction and rationale

Asthma is one of the most prevalent chronic diseases in the pediatric population. Effective inhaled treatments, such as inhaled corticosteroids, are available. However, the World Health Organization estimates that up to 50% of patients have suboptimal medication adherence. Importantly, non-adherence to asthma medication has been associated with poor clinical and economic outcomes.[1]

To be most effective, interventions focusing on enhancing adherence should be evidence-based and provided in a personalized manner. Electronic monitoring may offer such opportunities. A UK study found that the average adherence rate for children with asthma was 49% for those who were monitored but received no reminders, and 70% for those who received reminders to take their medication.[2] While the number of puffs taken improved, asthma control did not improve, likely due to a lack of inhaler technique improvement. Whilst inhaler technique is sometimes checked in clinics, this aspect of adherence is much more difficult to monitor remotely.

Most children use pressurized Metered Dose Inhalers (pMDIs) in combination with spacers to assist optimal drug delivery to the lungs. Especially for younger children, an adequate inhaler technique is difficult to achieve, thereby hampering asthma control. Understanding if critical errors in administration of inhaled medications are occurring is vital if healthcare professionals are to be able to effectively educate children with asthma and make informed follow-up treatment decisions. Until recently, the use of pMDI's with spacers has been difficult to measure. Smart inhalers can be of help, but current ones are typically designed for dry powder inhalers, unsuitable for children. This study intends to use a novel Smart Spacer device linked with the aflo™ platform, which simultaneously measures adherence and technique of pMDI's with spacer. Notably, the aflo™ platform automates and measures/prompts the 6 steps of correct inhalation technique for pMDIs when used with a spacer (shake inhaler, breathe out, place to mouth, press inhaler, breathe in slowly and evenly until dose is completed, hold breath for 10 seconds, modified from the UK Inhaler Group Inhaler Proficiency Checklist Score), gives real-time inhaler technique feedback, provides daily medicines adherence reminders, collects daily patient reported symptom control and monthly Asthma Control Test scores and shares real time geolocated air quality data. The platform functionality was evaluated in a 20-patient usability study (IRAS 300542) which demonstrated the functionality capability, user willingness to share their data with their clinician and high levels of user satisfaction. Its use in pediatric care has not been evaluated yet.

3.2 Design (including population, method, confounders, and outcomes)

Study design

Single-center, single-arm pre-post pilot study of 3 months performed in pediatric secondary care

Inclusion criteria

(1) children between 6 and 18 years;
(2) the physician diagnosed asthma;
(3) using ICS (+/-LABA+/-LAMA+/- SABA) administered by pMDIs and spacer, suitable for the aflo™ device;
(4) uncontrolled asthma defined as ACT score <19 AND/OR recent exacerbation AND/OR suspicion of nonadherence/poor technique;

(5) have an Apple and/or Android smartphone with an operating system 4.3 or above and a data plan for the duration of the study period ;
(6) and willingness to sign informed consent (child>12 years and parents).

Exclusion criteria
(1) other chronic lung or cardiac disease;
(2) inability to adequately understand or communicate in Dutch

Sample size
12 patients [3-5]

Smart spacer
The study will pilot the use of an electronic medication sensor and an accompanying mobile application, designed and developed by Respiratory Analytics, known as aflo™. The sensor appends between a pMDI on one side and a 'spacer' on the other. It automates all of the correct steps required to optimise the use of a pMDI, recording and storing every actuation of the inhaled medication. The device does not interfere with the administration of medication. Data is encrypted and transmitted to a secure, HIPAA-compliant cloud environment using Bluetooth Smart, and can be accessed by patients through the accompanying mobile application. The app is programmed to provide scheduled reminders for daily medications, daily patient-reported symptom control reports, weekly spacer and removable device insert wash reminders, and monthly Asthma Control Test scores. A single device will be used for all pMDIs required by each patient.

- From 6 years to 12 years, the aflo™ app is downloaded onto a guardian's mobile device, and the child must use the guardian/ parent's (over 18 years) device to access the aflo™ platform.
- From 13 years to 15 years, the aflo™ app can be downloaded on the child's mobile device with an over-18-year-old guardian (parent/ supervisor) consent, once the guardian has downloaded the parent/ guardian version of the app. The child will use the app on their own mobile device, and the guardian/parent will have full visibility of all reminders, inhaler technique data, and air quality.
- From 16 years to 17 years, the aflo™ app can be downloaded onto the child's mobile device. The child will be asked if they wish to share data with their guardian/ parent. This is not mandatory, and the child can use it without guardian/ parent supervision, although we encourage children in this age group to share their data in the same way as the 13 - 15 year old age group.

The aflo™ Smart Spacer Platform is CE-marked and will be used within its intended use (see Attachment A: PanamaID23081_CE-marking aflo™). The University of Groningen inhalation lab (led by Paul Hagedoorn) has verified the smart spacer's inhalation parameters (e.g., impact on pressure drop) and measurements independently before the study started. Various situations were simulated to see if the aflo™ system detects these and provides the correct feedback. Additionally, the flow rate was mapped in conjunction with the aflo device to verify whether the feedback from the colored LEDs on the device aligns with the calibrated flow rate.

Training
All research staff will be trained to the relevant level of investigation conduct in device usage and clinical assessments. Training will include:

- Instructions on the use of the device
- Clinical measurements
- Health and Safety aspects

- Clinical Investigation plan and procedures therein
- Completion of investigation documentation
- Handling/reporting complaints and adverse events

Study procedures
Participants will have two clinic visits and two follow-up phone calls. Baseline data will be collected at the screening and baseline visit using standardized questionnaires. Patients will be followed up by phone at week 4 and week 8 to assess asthma control (ACT) and ensure continued interest in study participation. The final clinic visit will occur at week 12 and assess pilot endpoints.
After 4 to 6 weeks, the select group that used the 10-breath method will also be examined to determine whether the 10-breath method is necessary and whether the number of breaths can be reduced to achieve a comparable effect, based on an interim analysis.

Participants will continue to receive standard and emergency care through their primary asthma providers (primary care physician and/or specialist) through the study. Participants will be provided with a phone number to call during office hours to report any issues with the electronic sensor or mobile application.

Outcomes
Primary outcomes
- To assess the feasibility of implementing the aflo™ smart spacer platform in routine pediatric asthma care (e.g., recruitment rate, retention rate, adherence with study procedures, completeness of data).
- To evaluate the usability of the aflo™ platform among children with asthma and their caregivers, using standardized usability metrics (e.g., System Usability Scale).

Primary Efficacy Variable
The primary efficacy variable is the change in inhaler errors from baseline (mean of the first 3 days) to post-intervention after using the aflo™ platform (mean of the last 3 days of usage during the 3-month follow-up, requiring at least 1 month of follow-up).

Secondary Efficacy Variables
Secondary efficacy variables include change in the (children's) Asthma Control Test (ACT), spirometry (FEF25-75, FEF75, FEV1/FVC), FeNO, adherence (mean 3 month day-to-day usage in line with prescribed regimen, compared to historical pharmacy dispense records 1 year before), exacerbations, and SABA use.

3.3 Research question
What is usability, feasibility, and potential effectof the smart spacer aflo™ platform in pediatric practice?

4. Study design

4.1 Mono- <u>or</u> multicenter study.	Monocenter study ☒	Multicenter study ☐

4.2 Retrospective study (available data/ biomaterials only) **or prospective study** (data/ biomaterials from [some] participants will be collected), (click both if mixed-method).		Retrospective study ☐	Prospective study ☒
4.3 Cross-sectional or follow-up study (click both if mixed-method).		Cross-sectional study ☐	Follow-up study ☒
4.4 Quantitative or qualitative study (click both if mixed-method).		Quantitative study ☒	Qualitative study ☐
4.5 Pilot or explorative study?	Not applicable ☐	Pilot study ☒	Explorative study ☐
Explain why it is a pilot or explorative study. *We have no experience with this device yet and first need an indication of its value, and it may inform a sample size calculation for a follow up study. In the event of a positive signal, we may conduct a larger, controlled confirmatory study. This may inform wider usage and uptake in daily practice and guidelines.*			

5. Population

5.1 Research participants (tick all that apply)		
Healthy volunteers Patients		☐ ☒
5.2 Participant classification (tick all that apply)		
Participants ≥ 16 years		☒
Children between 12 and 16 years *(if applicable, written informed consent will be obtained from the child and both parents - if both have authority, or guardian [or parents/guardian only if incapacitated child])*		☒
Children < 12 years *(if applicable, written informed consent will be obtained from both parents - if both have authority, or guardian)*		☒
Explain the purpose limitation ('doelbinding' in Dutch) if you plan to include minors below 16 years of age. This means that this data may only be gathered if participation of that age group is utterly essential (Dutch: persoonsgegevens alleen verzamelen met een gerechtvaardigd doel waarvoor die leeftijdsgroep noodzakelijk is). ➢ *It is the group that most often uses a spacer in daily clinical practice and usually suffers from incorrect inhaler technique, so this is the group that may benefit the most.*		
5.3 Incapacitated adults		
Participants can be incapacitated/decisionally impaired adults *(if applicable, written informed consent must be obtained from a legal representative)*	Yes ☐	No ☒
If yes, explain the purpose limitation ('doelbinding' in Dutch). This means that this data may only be gathered if participation of this group is utterly essential (persoonsgegevens alleen verzamelen met een gerechtvaardigd doel waarvoor deze groep noodzakelijk is).		
5.4 Inclusion and exclusion criteria ***Inclusion criteria*** (1) children between 6 and 18 years; (2) the physician diagnosed asthma; (3) using ICS (+/-LABA+/-LAMA+/- SABA) administered by pMDIs and spacer, suitable for the aflo™ device;		

(4) uncontrolled asthma defined as ACT score <19 AND/OR recent exacerbation AND/OR suspicion of nonadherence/poor technique;
(5) have an Apple and/or Android smartphone with an operating system 4.3 or above and a data plan for the duration of the study period ;
(6) and willingness to sign informed consent (child>12 years and parents).

Exclusion criteria
(1) other chronic lung or cardiac disease;
(2) inability to adequately understand or communicate in Dutch

6. Study data and analysis

This section needs to be completed for both quantitative and qualitative designs.
Outcomes should be realistic, the sample size should be adequate, and sufficient data should be collected. The patient burden should be balanced with the usefulness of the outcomes, and the analysis should be appropriate. To clarify that this has been given careful consideration, completion of section 6 is required.

6.1 Data collected
For primary outcomes:
The primary feasibility and usability is measured by collecting data such as recruitment rate, retention rate, adherence with study procedures, completeness of data, and a usability questionnaire measured at the end of the study after 3 months (System Usability Scale).

The primary efficacy variable is the change in inhaler errors from baseline (mean of first 3 days) to post intervention after using the aflo™ platform (mean of last 3 days usage during the 3 months follow-up, requiring at least 1 month of follow-up).

For secondary outcomes and other outcomes:
Secondary efficacy variables include change in the (children's) Asthma Control Test (ACT), spirometry (FEF25-75, FEF75, FEV1/FVC), FeNO, adherence (mean 3 month day-to-day usage in line with prescribed regimen, compared to historical pharmacy dispense records 1 year before), exacerbations, and SABA use.

If not applicable to your study, please explain the reason and the alternative outcomes:
NA

Have all the data for the primary and secondary outcomes been described, or are alternatives provided?	Yes ☒	No ☐

6.2 Number of participants:
Target total number of participants: 12
Target number of UMCG participants: 12

6.3 Justification of sample size

Sample size justification is required according to the AVG/GDPR law. The number of subjects should always be large enough to answer the research questions reliably, but not more than necessary.

The sample size can be justified in several ways. Often, the easiest is a power analysis; alternatively, a comparison with the sample size of closely related studies may be applicable (specification is required), or a saturation design. Other options may apply.

Pilot studies and/or exploratory studies comply with different sample size rules, but for these, please also indicate on what basis the sample size has been decided.

Multiple methodological sources indicate that approximately 12 participants per group (or 10–15 in total for single-arm feasibility work) provide adequate precision to estimate key feasibility parameters and to identify procedural issues in pilot studies:

- Julious (2005) proposes the well-established rule-of-thumb of 12 participants per group in pilot studies aimed at estimating variability and informing feasibility procedures. [3]
- A recent methodological update (2025) similarly supports small pilot samples (≈10–15 participants) when primary outcomes concern feasibility, usability, and implementation processes rather than treatment effects. [4]
- A previous smart spacer pilot study using a digital inhalation-monitoring device successfully included 12 participants, demonstrating that this sample size is sufficient to evaluate usability, acceptability, data capture performance, and preliminary changes in inhaler technique in this specific clinical domain. [5]

These converging findings support the use of a small, focused cohort when investigating feasibility and system performance, especially in pediatric digital health interventions where participant burden should be minimized.

Additionally, to meet ethical requirements (AVG/WGBO) and to ensure that the sample is not too small to provide reliable information on the primary feasibility and usability objectives, an interim analysis will be incorporated after the first 12 participants have completed follow-up.

The interim analysis is not designed for hypothesis testing or assessing clinical effectiveness. Instead, it evaluates whether the initial sample provides sufficiently precise information regarding:

1. Feasibility indicators, such as recruitment rate, retention, completeness of data, and participant adherence;
2. Usability outcomes, including System Usability Scale scores, technical reliability, and user feedback;
3. Variability of inhaler-technique measurements, to determine whether an expanded sample is required to improve the precision of exploratory effect estimates.

Has the sample size justification been described?	NA ☐	Yes ☒	No ☐

6.4 Data minimisation

Only the essential baseline characteristics and data that are required to answer the research question will be collected:	Yes ☒	No ☐

6.5 Statistical and/or qualitative analysis

Please specify Statistical Analysis Plan (SAP):

a. Description of study population:

Children between 6 and 18 years with physician-diagnosed asthma, using ICS (+/-LABA+/-LAMA+/- SABA) administered by pMDIs and spacer, suitable for the aflo™ device, and having uncontrolled asthma defined as ACT score <19 AND/OR recent exacerbation AND/OR suspicion of nonadherence/poor technique.

b. Description of preparation of the data for analyses:

Data will be downloaded from the eCRF in RedCap and the smart spacer device and subsequently combined for analyses in an Excel file. Quality checks (e.g. checking for potential outliers, missing values etc.) will be done before database lock.

c. Specify all applicable statistical and/ or qualitative methods. This usually requires an extensive description of the planned analyses and covariates:

Data will be analysed using SPSS. Given this is a non-controlled pilot study, analyses are mainly descriptive. However, we will exploratively assess some differences in the primary and secondary outcomes between the baseline and 3-month follow-up, where feasible.

For the primary outcome: change in inhaler errors from baseline (mean of first 3 days) to post-intervention after using the aflo™ platform (mean of last 3 days usage during the 3-month follow-up will be assessed by a paired samples T-test (in case of normally distributed data) or a Wilcoxon signed-rank test (if not normally distributed).

For secondary outcomes: differences in (children's) Asthma Control Test (ACT), spirometry (FEF25-75, FEF75, FEV1/FVC), FeNO, between baseline and 3 months follow-up will be assessed by a paired samples T-test (in case of normally distributed data) or a Wilcoxon signed-rank test (if not normally distributed).

Exacerbations, SABA use, and usability of device (SUS score) will only be described for the 3 months with mean and standard deviation (or median and IQR, where applicable).

d. Clarify how this analysis plan, study setup, sample size, and design will answer the study questions:

This involves a pilot study to assess potential effect (see analysis on inhaler errors) and usability/feasibility (see analysis on SUS score) and will inform sample sizes for larger follow up studies to confirm efficacy in a controlled design.

Has the statistical analysis section (6.5) been completed?	Yes ☒	No ☐

7. Recruitment and informed consent/objection

7.1 Data collection Please check the data source that applies to your study; more may apply:	
Data will be prospectively collected (data/ biomaterials from [some] participants will be collected)	☒

Data will be collected from (electronic) patient records (e.g. 'EPD UMCG')	☒	
Data will be collected from an already existing bio- or databank *Please add documents that demonstrate (ethical) approval at the instalment of the bio- or databank*	☐	
Data will be collected from a previous study (e.g. 'FAIR data' - internal/external). *Please note that the templates of the patient information and the (original) Informed Consent form need to be added to the application.*	☐	
7.2 Informed consent procedure		
7.2.1 Participants will be asked informed consent	Yes ☒ *If yes: please complete 7.2.2 and 7.3.*	No ☐ *If no: please complete 7.2.3 and 7.3.*
7.2.2 *If consent is asked* complete this section		
7.2.2.1 *<u>if the potential participant is a patient</u>:*		
First contact with potential participant is made by the treatment provider, either by accompanying letter or in person.	Yes ☒	No ☐
Informed consent procedure, including signing the IC, will be carried out by the research nurse/ researcher (*not the treatment provider).*	Yes ☒	No ☐
7.2.2.2 *<u>For participants that are either patients or non-patients</u>:*		
• <u>Recruitment:</u> Please describe how eligible participants will be approached and recruited: *Eligible patients will be approached only by their treating clinician. During a routine consultation, the clinician will briefly introduce the study and assess whether the patient and/or caregivers are interested in receiving further information. If the patient or caregiver expresses interest, the clinician will provide the Participant Information Form (PIF) and the Informed Consent (IC) form directly (either in print or digitally). The clinician will not share any patient contact details with the research team at this stage.* *Patients and/or caregivers may review the study materials at home. If they have questions, they may contact the research team themselves using the contact details provided in the PIF.* *If the patient and/or caregiver wishes to participate, they may sign the IC form and return it to the research team (e.g., by post, secure email, or by handing it in during a scheduled appointment). Only after the signed consent form has been received will the research team obtain access to the participant's contact information and may then reach out to schedule study procedures.*		

Participation remains voluntary, and participants may withdraw at any time without providing a reason and without any consequences for their medical care.			
• <u>Information provision:</u> The participant will *only* be contacted via telephone if they have given prior permission for this:	NA ☐	Yes ☐	No ☒
Contact via telephone only serves to provide additional information, it cannot be used to ask informed consent:	NA ☐	Yes ☒	No ☐
If either of the above 2 items are answered with 'no' please elaborate on the reason for this: *To avoid unnecessary visits beyond routine care*			
• <u>Time to consider:</u> The participant will have at least 14 days to consider participation:		Yes ☒	No ☐
If this is not the case please describe the reason for this and what time is allotted for the participant to consider participation.			
• <u>Informed consent recording:</u> Informed consent will be recorded either on paper via signature or electronically:		Yes ☒	No ☐
If no, please elaborate on how the informed consent will be recorded?			
• <u>Use of templates</u> Have the UMCG templates been used for both DIF and IC-form: *Attach participant information letter and informed consent form to the present study protocol. Please note that all sections of the templates need to be present in the file DIF and IC*.		Yes ☒	No ☐
7.2.3 *If consent cannot be asked,* please complete this section:			
Total number of participants who will not be asked informed consent: 0 Total number of *UMCG participants* who will not be asked informed consent: 0			
Which WGBO argumentation applies to your study (see SOP Obtaining Informed Consent non-WMO):			
• Asking permission **is reasonably impossible**, because it would burden the patient to such an extent that it might cause psychological distress.			☐
• Asking permission **is reasonably impossible**, because a large part of the participant group is likely deceased or cannot be located.			☐
• Consent **cannot be required** because obtaining it would entail a disproportionate amount of time and effort, such as in the case of large numbers of patients or patients who were treated a long time ago.			☐
• Consent **cannot be required** because requesting consent would lead to selective response, thereby potentially biasing the research results.			☐
• Consent **cannot be required**, because:			☐

Required: In addition to the broad categories above, please clarify *why* these arguments apply to your specific study:			
The objection registry will be checked in case one or more UMCG patients will not be asked informed consent, the data from those who objected will be excluded from the analyses.	NA ☐	Yes ☒	
7.3 Linking with (other) bio-/databank			
In case the data will be linked with a /another bio-/databank, informed consent will be/has been obtained for this linkage(s)	Yes, consent ☐	No consent ☐	Data will not be linked ☒

8. Only complete in case of collaboration with parties outside of the UMCG (also called: third parties)

8.1 Which party is in the lead?	UMCG ☒	Not the UMCG ☐
8.2 Is the leading party a commercial party?	Yes ☐	No ☒
8.3 *Only complete if UMCG is not in the lead:* **Is the role of the UMCG limited to supplying data?**	Yes ☐	No ☒
8.4 Description of the cooperation Please describe the role and tasks that will be performed by the UMCG and by the partner(s). Please note that only the role and tasks described here can be mentioned in the contract. *The UMCG is responsible for the conduct, procedures, and scientific aspects of the study. Aflo Respiratory Analytics will provide the smart spacer devices and technical information on their use. The company does not receive any financial compensation for its involvement.* *The UMCG receives a small grant to support the execution of the study. This grant covers study-related costs, including personnel time, data management, and dissemination activities such as publication of the study results. Aflo Respiratory Analytics has no role in the study design, data analysis, or interpretation of findings.*		
8.5 Data and/or biomaterial management in combination with the partners Please elaborate on the following aspects: • Which data (and/or biomaterials) will be shared with the partners? *None, just aggregate data as to be published.* • How is the data (and/or biomaterials) saved and/or destroyed after study end? *15 years at UMCG (Research Drive)*		
8.6 With Informed consent *Please complete only if patients are asked for Informed Consent:*	Yes	No

In case of collaboration with *commercial/for-profit* organisations. Has the research participant been informed in the DIF, or will they be told, about the collaboration with commercial third parties.	☒	☐
Has or will informed consent be(en) obtained for data sharing with the third party?	Yes ☒	No ☐
8.7 Contracts For both with informed consent and without informed consent: will you contact the loket Contract Research to arrange the proper contracts?	Yes ☒	No ☐
8.8 Data Protection Impact Assessment (DPIA) Will a DPIA be drawn up?	Yes ☐	No ☒
If a DPIA will *not* be drawn up please elaborate on the reason for this: *There is no risk of data loss, as all data will remain at UMCG, initially stored in REDCap and subsequently at Research Drive. No personal data will leave the UMCG; data are pseudonymized and stored in REDCap in line with UMCG data protection policies.*		

9. Data Management Plan (DMP)

In this study, data will be collected, processed, and archived in accordance with the General Data Protection Regulation (GDPR) and the FAIR (Findable, Accessible, Interoperable, Reusable) principles, under the responsibility of the Principal Investigator, as required by GDPR law. Please note that completion of this section is *required*. A separate DMP will not be reviewed.		
9.1 Handling and storage of data		
The following are requirements with regard to handling and storage of data. Please mark all that apply:		
• Digital data will be archived following a strict security and back-up policy (akin to UMCG security level).	☒	
• Paper source data and study files will be archived according the UMCG policy	☒	
• Source data, study files and digital data will be archived 15 years after the study is completed.	☒	
• Tooling (eg. software and procedures) used for collecting, processing, analysing, and storing data will be compliant with the UMCG policy and Standard Operating Procedures in the UMCG Research Toolbox.	☒	
9.1.1 *If applicable:* Not all items in the above section 10.1 apply to my study. Please elaborate on the reason for this and the solutions.		
9.2 Anonymization and pseudonymization		
Data will be <u>anonymized</u> during data collection. *Please note that this means the data cannot be linked back to the participant, and in practice, this usually requires very large numbers of participants in the dataset.*	Yes ☐	No ☒

If data is anonymized: • Please explain what procedure is used: / • Please reflect on the applicability of K1-anonimity on your dataset: / *If anonymized data please skip the rest of section 9.*		
Data will be pseudonymized during data collection (i.e. data cannot directly be linked back to the participant).	Yes ☒	No ☐
If data is pseudonymized, please explain what procedure is used. *Study subject number in REDCAp with a code list at the Pediatrics department in a separate file with limited access for staff involved in this study only.*		
9.3 Pseudonymization requirements		
9.3.1 The following are requirements when pseudonymized data is used, please mark all that apply:		
• Indirect and direct identifiable information collected will be minimized and only collected for the purpose of this study	☒	
• Direct identifiable information (e.g. contact details, code list, encryption key, participant identification log) will be stored separately from pseudonymized data	☒	
• Direct identifiable information can only be accessed by the Principal Investigator and study delegates after authorization by the Principal Investigator.	☒	
• Pseudonymized data can only be accessed by the Principal Investigator and study delegates after authorization by the Principal Investigator.	☒	
• Data roles, responsibilities, access and authorization, during the study and after study completion, will be managed and documented (e.g. in the DMP or study delegation log).	☒	
9.3.2 *If applicable:* not all items in the above list of pseudonymization requirements apply to my study. Please elaborate on the reason for this and the alternative solutions. /		

10. FAIR Data and Data Sharing

10.1 FAIR data The following statements concern FAIR data, which is the UMCG policy. *Please note that FAIR is not the same as Open Access.*		
Data will be made findable by including the description of the study (and type of data (i.e. metadata) in the UMCG FAIR data catalogue and other discipline specific catalogue(s).	Yes ☐	No ☒
If 'no' is answered on the above question , please elaborate on the reason for this. *This is a clinical study. The trial will be registered in a trial registry, so it is already findable. We aim to avoid double registration. Additionally, in our publications, we will include a statement regarding data availability. Note: If the UMCG Fair data catalogue is linked (or can be linked) to clinical trial registries, the answer is yes.*		
10.2 Data Sharing		

In case data (and biomaterials) will leave or enter the UMCG, will you contact the loket Contract Research to arrange the proper contracts? (Loket_Contract_Research@umcg.nl)	Yes ☐	No ☐	No data will leave or enter UMCG. ☒

11. Management of Biomaterials (either newly collected or from an existing biobank)

11.1 Will biomaterials be collected, processed, analyzed and/or stored for the purpose of this study?	Yes ☐	No ☒ *skip and delete rest of section 11*

12. Burden, Risks & Benefits

12.1 Burden Is there a (potential) burden for the participant as a result of participating in this study? *For example: feeling tired after performing tests, reliving bad memories.*	Yes, minimal burden ☐	Yes, more than minimal burden ☐	No ☒
/			
12.2 Risk Does the participant run a risk of injuries and/or other discomfort as a result of participating in this study? *For example: risk of falling while doing exercises*	Yes, minimal risk ☐	Yes, more than minimal risk ☐	No ☒
/			
12.3 Benefits Does the participant receive benefits/reward/incentives for participating in this study?		Yes ☒	No ☐
If yes, please explain what the benefits/reward/incentives entail. *Patients (and/or their caregivers) get insights into the quality of their inhaler usage and receive feedback to optimize it. This may help gain control of their asthma. At the end of the study, the participants receive a cinema voucher.*			

13. Incidental findings

Is there a risk of incidental findings?	yes, minimal risk ☐	yes, ≥ substantial risk ☐	No ☒
For the following section, please use this SOP as a guide: SOP 4A.72193 Handling incidental findings in scientific research. Link: https://umcg.zenya.work/portal/#/document/c15161b3-476e-494b-9ebf-dc1ce47c66e8			

14. References

Klik of tik om tekst in te voeren.*[1] R Dekhuijzen, F Lavorini, OS Usmani, JF van Boven. Addressing the impact and unmet needs of non-adherence in asthma and COPD: where do we go from here? Journal of Allergy & Clinical Immunology: In Practice 2018; 6(3): 785-793*

[2] RW Morton, et al. STAAR: a randomised controlled trial of electronic adherence monitoring with reminder alarms and feedback to improve clinical outcomes for children with asthma. Thorax 2017; 72 (4): 347-354.

[3] Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharm Stat 2005; 4: 287–291

[4] Ying X, Freedland KE, Powell LH, Stuart EA, Ehrhardt S, Mayo-Wilson E. Determining sample size for pilot trials: a tutorial. BMJ. 2025 Aug 8;390:e083405. doi: 10.1136/bmj-2024-083405. PMID: 40780848.

[5] *Dierick BJH, Been-Buck S, Klemmeier T, Hagedoorn P, van de Hei SJ, Kerstjens HAM, Kocks JWH, Zijp TR, Wessels AMA, Touw DJ, van Boven JFM. Digital spacer data driven COPD inhaler adherence education: The OUTERSPACE proof-of-concept study. Respir Med. 2022 Sep;201:106940.*

15. Appendices

The following appendices are attached.

A. PanamaID23081_CE_marking aflo™

B. PanamaID23081_PIF_Caretaker_V2

C. PanamaID23081_PIF_Child_12to17years_V2

D. PanamaID23081_PIF_Child_6to12years_V1

E. Photos of the Alfo™ device