AION BIOSTYEMS, INC. TEMPSHIELD

A prospective, interventional study assessing the effectiveness of the AION BIOSTYEMS, INC. tempshield ("Shield") for continuous temperature monitoring device in the Pediatric Emergency Department.

Protocol ID: STUDY00000455

NCT Number: NCT07145541

Principal Investigator: Sephora Morrison, MD

Sponsor: AION BIOSYSTEMS, INC.

Funded by: AION BIOSYSTEMS, INC.

Version Number: 2.13

1 May 2024

INVESTIGATOR PROTOCOL SIGNATURE PAGE

I agree:

- To conduct the study in compliance with this Clinical Investigational Plan (CIP), with the terms of the clinical trial agreement and with any other study conduct procedures and/or study conduct documents provided by AION BIOSTYEMS, INC.
- To promptly report to the Ethics Committees (ECs)/Institutional Review Boards (IRBs) according to local regulations. Additionally, I will not make any changes in the protocol without ECs/IRBs approval, except where necessary to ensure the safety of study participants.
- To assume responsibility for the proper conduct of the study at this site.
- To ensure that all associates, colleagues, and employees assisting in the conduct of this study are informed about their obligations in meeting these commitments.
- To conduct the study in accordance with Good Clinical Practice (GCP), the Declaration of Helsinki, and the moral, ethical, and scientific principles that justify medical research. The study will be conducted in accordance with all relevant laws and regulations relating to clinical studies, the protection, and the privacy of subjects.
- To maintain adequate and accurate records and to make those records available for audit and inspection in accordance with relevant regulatory requirements.
- To co-operate with a representative of AION BIOSTYEMS, INC. in the monitoring process of the study and in resolution of queries about the data.
- To provide AION BIOSTYEMS, INC. with an updated Curriculum Vitae and other documents required by regulatory agencies for this study.

CIP Title:	A prospective, interventional study assessing the effectiveness of the AION BIOSTYEMS, INC. tempshield (“Shield”) for continuous temperature monitoring device in the Pediatric Emergency Department.
Investigational Device:	AION BIOSTYEMS, INC. tempshield FLL Class II medical device Submitted to FDA for approval.

Principal Investigator:

Date	Name and Signature

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Table of Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
CIP	Clinical Investigation Plan
CRF	Case Report Form
CTA	Clinical Trial Agreement
EC	Ethics Committee
eCRF	Electronic Case Report Form
ED	Emergency Department
GCP	Good Clinical Practice
HCP	Healthcare Professional
HIPAA	Health Insurance Portability and Accountability
IFU	Instructions for Use
ISF	Investigation Site File
ID	Identification
IRB	Institutional Review Board
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
USADE	Unanticipated Serious Adverse Device Effect

1. General

1.1 Background and Purpose

Fever is the most common reason for children to be brought to an emergency department (ED) with causes ranging from self-limiting illnesses of childhood to serious bacterial infections (SBIs) that can prove fatal. Vital signs can help clinicians identify children at risk of serious illness.

Early detection and treatment of fever in pediatric patients is important because fever can be a sign of a serious infection or other underlying condition. If left untreated, these infections or conditions can lead to more serious complications, such as organ damage or failure.

Fever in pediatric patients can be caused by a wide range of underlying illnesses, including infections, inflammation, and other medical conditions. Some common causes of fever in children include:

1. Infections: Fever can be a sign of an infection, such as a cold, flu, pneumonia, or urinary tract infection.
2. Inflammation: Fever can also be caused by inflammation, such as from an injury or autoimmune disorder.
3. Other medical conditions: Other medical conditions that can cause fever in children include certain types of cancer, metabolic disorders, and medication reactions.

Early detection of fever can enable healthcare providers to promptly diagnose and treat the underlying cause of the fever. This can help prevent the development of complications along with the worsening of an infection.

Sepsis is a complex clinical syndrome resulting from a systemic inflammatory response to infection. Each year, there are approximately 72,000 children hospitalized for severe sepsis in the United States, resulting in significant morbidity and mortality, and nearly $4.8 billion in U.S. health care expenditures.[1–3] There have been significant advances in early recognition and overall approach to sepsis over the past decade, which have demonstrated improved patient outcomes with protocol-driven treatment in patients with sepsis.[1–5]

An important limitation to widespread implementation of protocol bundles for pediatric sepsis is the challenges of early and accurate identification of patients with potential sepsis who may benefit from these intensive therapies.[7] This identification process is particularly problematic in the pediatric ED, where there is a high prevalence of fever with signs of the systemic inflammatory response syndrome (SIRS), despite the fact that the vast majority of these patients are not seriously ill.[8-9]

Remote and continuous temperature monitoring can be beneficial for pediatric patients because it allows healthcare providers to continuously monitor a child's temperature remotely, which can help to detect fever and other changes in temperature early on. This can be particularly useful for children who are at high risk for fever or other medical conditions, or for those who are unable to communicate their symptoms effectively.

There are several benefits to using remote temperature monitoring for pediatric patients, including:

1. Early detection: Remote temperature monitoring can help to detect fever and other changes in temperature early on, allowing healthcare providers to promptly diagnose and treat the underlying cause of the fever.
2. Continuous monitoring: Remote temperature monitoring allows healthcare providers to continuously monitor a child's temperature, which can provide a more comprehensive view of the child's health and help to identify any changes or trends.
3. Convenience: Remote temperature monitoring can be performed from the child's home, which can be more convenient for both the child and the healthcare provider.
4. Improved outcomes: Early detection and treatment of fever and other changes in temperature can lead to improved outcomes for pediatric patients and can help to prevent serious complications.

The purpose of this research study is to evaluate the effectiveness of the AION BIOSTYEMS, INC. tempshield ("Shield") temperature monitoring device and platform in detecting body temperature for children 2-4 years old. The ED Research team will be deploying this device on all qualified patients who are awaiting inpatient admission from the emergency department and who have consented to participating in the study. Patients will be asked to keep the device on for a maximum of 7 hours during their stay in the emergency department. There is a potential clinical benefit that fevers will be detected earlier in subjects wearing the AION BIOSTYEMS, INC. tempshield. It is hoped that information gained from the study will help assist clinical care workflow and the treatment of future patients.

AION BIOSTYEMS, INC. is currently seeking FDA approval for the tempshield; this study will support the company's clinical validation in pediatrics.
The objectives of the validation study are to:

1. Collect human test data using tempshield to comply with ISO 80601-2-56 for a digital thermometer per FDA guidance for children.

2. To compare the collected tempshield data against a Welch Allyn 901053 Electronic Thermometer as used in clinical settings.

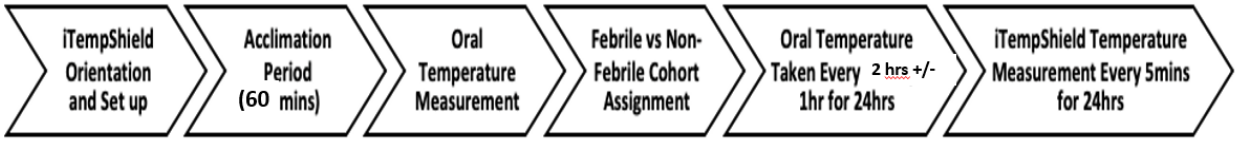
1.3 Sponsor Information

Sponsor	Name	AION BIOSTYEMS, INC.
	Address	12 Plymouth Road, Darien, CT

1.4 Clinical Investigational Plan

A prospective, single site, interventional study assessing the effectiveness for use of the non-invasive wireless temperature monitoring device and platform in detecting body temperature of young children during 1st 7 hours of their stay in the emergency department for patients, between 2-4 years of age.

1.5 Study Design Workflow



2 Identification and Description of the Investigational Device

2.1 Investigational Device

The AION BIOSTYEMS, INC. tempshield is a skin-applied, continuous temperature monitor. It is battery powered, communicates using Bluetooth LE to a smartphone, then to a clinician dashboard, and is designed to be worn continuously for up to 60 days. Its primary use is for patient monitoring in hospital or post-discharge from a healthcare facility. Through the tempshield system, clinicians can be notified if a patient's temperature exceeds a given threshold.

The tempshield system is centered around a non-invasive temperature sensor placed against the patient's skin, in the pectoral region just below the collar bone. The temperature sensor is held in place with a silicone adhesive tape similar to a custom shaped piece of medical tape. The silicone adhesive tape is hypoallergenic.

2.2 Manufacturer

The legal manufacturer of the system is AION BIOSTYEMS, INC.. The production of the AION BIOSTYEMS, INC. device components are done by qualified and certified sub-contractors with extensive experience.

2.3 Identification of the Investigational Device

The following table lists the devices that will be used during this clinical trial. Device identification and traceability can be done using their serial number.

AION BIOSTYEMS, INC. tempshield FLL Class II medical device

Table 1: Device Identification

System Part	Identification	Software Version
AION BIOSTYEMS, INC. tempshield Device	Each Device has a Unique ID	3.2.14
Study Dedicated Samsung Phone (incl. charger)	Will Set Study Serial number prior to study	N/A
AION BIOSTYEMS, INC. Clinical Trial App	NA	2.22.0

2.4 Traceability during the Clinical Investigation

The AION BIOSTYEMS, INC. device with relevant accessories will be provided by the Sponsor.

Each AION BIOSTYEMS, INC. tempshield Device will have a unique serial number. Delivery/return forms as well as the accountability log will be filled out and filed in the Investigator Site File (ISF), each time equipment and devices are dispensed to caregivers or returned/replaced.

2.5 Intended Use of the Investigational Device in the Clinical Investigation

During the AION BIOSTYEMS, INC. study, the efficacy of the AION BIOSTYEMS, INC. tempshield device in continuous temperature monitoring of young children will be assessed.

2.6 Intended Use of the Investigational Device

The sensor on the AION BIOSTYEMS, INC. tempshield device passively collects temperature readings every 5 minutes and transmits the temperature data to the AION BIOSTYEMS, INC. mobile application via Bluetooth.

The AION BIOSTYEMS, INC. tempshield is not an approved medical device and therefore, does not:

- Diagnose, cure, lessen, monitor, treat or prevent disease or injury,
- Affect body functions/structures,
- Achieve primary intended purposes through chemical action,
- Monitor patients clinical or at-home temperature

2.7 Description of the Investigational Device

The testing system AION BIOSTYEMS, INC. tempshield device consists of 2 elements:

- An **electronic temperature sensor,** a non-invasive, wearable, wireless measuring device positioned on the child's pectoral region just below the collar bone
- A Samsung A13 Mobile phone configured to run the AION Biostyems, Inc. Shield Application 2.22.0 or greater. This device must be within 30 feet of subject.

The following accessories will be used for placement of the device on subject:

- Silicone adhesive tape (attachment and retention of the sensor to the patient's skin), a silicone adhesive tape similar to a custom shaped piece of medical tape. The actual adhesive tape is 3M Micropore™ S.

2.8 Training

2.8.1 Site Initiation Visit

Study team will be trained by AION BIOSTYEMS, INC. at the site initiation visit on the protocol, recruitment plan, data collection, device use, safety reporting and the study monitoring plan. This training will be documented and conducted prior to the first patient being enrolled.

2.8.2 Ongoing Training

The study team will receive ongoing training for any major changes to the study protocol. Additionally, new staff added during the course of the study will also need to complete training on all study related procedures and will be documented.

2.9 Description of the Medical Procedures involved in the Use of the Device

The use of the AION BIOSTYEMS, INC. tempshield requires research staff to place the shield onto the subject's chest, directly in contact with the skin. The AION BIOSTYEMS, INC. tempshield is worn by the subject at all times for a maximum of 7 hours and removed by research staff at the end of the study period.

Initiation of physiological parameters recording is activated by the research staff via the AION BIOSTYEMS, INC. mobile App installed on the provided study-dedicated Samsung phone.

During the recording, the guardians can view the measured physiological parameters in real time via the AION BIOSTYEMS, INC. mobile App.

Oral temperatures will be taken using a Welch Allyn 901053 oral thermometer and input into the AION BIOSTYEMS, INC. mobile app via research staff.

2.10 Addition Supplemental Study Materials

Refer to Annex A for the AION BIOSTYEMS, INC. system IFU, study information sheet, and device video.

3 Justification for the design of the Clinical Investigation

3.1 Review of Clinical Literature

In a study published in the Journal of Hospital Medicine in 2014, researchers found that continuous temperature monitoring was associated with earlier detection of fever and sepsis in hospitalized children. The study involved the use of continuous temperature monitoring with a noninvasive, wireless, and wearable temperature sensor. Another study published in the Journal of Pediatric Nursing in 2016 found that continuous temperature monitoring was effective in reducing the incidence of fever in children undergoing chemotherapy. The study involved the use of a wearable, wireless temperature monitoring system that allowed for continuous monitoring of body temperature.

Overall, these studies suggest that continuous temperature monitoring can be an effective way to detect and manage fever and other temperature-related issues in children. The use of wearable, wireless, and noninvasive temperature monitoring systems can provide a convenient and accurate way to monitor a child's temperature, particularly in hospital settings where frequent temperature checks may be required.

The outcomes of this study will be used to improve the AION BIOSTYEMS, INC. device and mobile app in evaluation of clinical performance with the goal of validating device with the FDA and subsequently deploying the device in pediatric hospitals.

4 Risks and Benefits of Investigational Device and Study

The study is a validation testing study for the AION BIOSTYEMS, INC. tempshield sensor and algorithm. Participation in the study poses minimal risks:

- Each participant will be administered the tempshield testing system using an AION BIOSTYEMS, INC.-provided smartphone and AION BIOSTYEMS, INC.-provided details. This will ensure that no personal information from participants will be entered into AION BIOSTYEMS, INC.'s mobile app or transmitted to AION BIOSTYEMS, INC. servers.
- All participants will have the sensor administered to an area of their skin just below their clavicle. The adhesive tape is silicone-based and hypoallergenic, but there is a small chance that the tape could cause mild skin irritation. Participants with a known allergy or sensitivity to silicone will be excluded from the study for this reason. In addition, the study moderator will instruct the participant to seek medical attention if and when any irritation occurs, whether during or after the study. All required FDA biocompatibility testing, and wear length testing has been performed by the manufacturer.
- There is a risk that study data, including personally identifiable information, could be lost, or stolen, even with the safeguards described in this protocol. If the Principal Investigator or any other study staff are made aware of a data breach involving personally identifiable data, study participants will be notified of the breach and any available remediation measures taken.
- The participant may stop the session without penalty or loss of benefits at any time. The study moderator will also stop the session if he/she judges that the participant is at risk of injury or if it is in the best interest of the participant, even if the participant wishes to continue.
- There is a risk of physical harm to the participant if the device is left on during radiology (MRI, X-ray, CT) imaging procedures. Due to this risk, study procedures ensure that the device is removed prior to the procedures.

The only minor anticipated adverse device effects are:

- Local skin irritation at sensor or adhesive location (low risk). Although, so far, skin irritation following the use of the AION BIOSTYEMS, INC. system has never been reported by any users of the AION BIOSTYEMS, INC. system, even after several days of use.

There are no direct benefits to people who participate in the study. Some participants may enjoy participating in the study or contributing to research that they may find personally interesting. The research data will be used to help extend the age range of the tempshield to an expanded age group to benefit future pediatrics.

5 Objectives and Hypotheses of the Clinical Investigation

Study Objectives	The objectives of the validation study are to: 1. Collect human test data using tempshield to comply with ISO 80601-2-56 for a digital thermometer per FDA guidance for children. In particular children under the age of 5 years. 2. To compare the collected tempshield data against a Welch Allyn 901053 Electronic Thermometer as used in clinical settings.
Study Endpoints	To collect enough data points to determine statistically if the current algorithm (5 years and up) applies to children under five. To collect enough data to age adjust the algorithm used.

6 Design of the Clinical Investigation

6.1 Study Design

This study is designed as prospective, interventional study assessing the effectiveness of the AION BIOSTYEMS, INC. tempshield (“Shield”) for continuous temperature monitoring device in the Pediatric Emergency Department.

Upon entry to the emergency department, a Children’s National study staff will be approached for interest and presented with the project and all relevant study materials/documents.

If parents/legal representatives are interested in their child’s participation in this study and following eligibility confirmation, the parent(s)/legal representative(s) will be provided with an information sheet. Patient’s caregiver will be explain the purpose of the study (to test effectiveness of AION BIOSTYEMS, INC. tempshield in continuous monitoring of temperature in an ED setting) and what the study involves (wearing AION BIOSTYEMS, INC. tempshield on participant’s chest for a maximum of 7 hours and having oral temperature taken every 1 hour). Due to age of participants (2-4years), no assent will be obtained for subjects.

Once enrolled, the tempshield wearable device will be placed on the upper chest with gentle, silicon adhesive tape. Study staff will ensure that the device is stable on the subject's chest. In the case that the device will not successfully adhere to the patient's chest, the research team will forego the enrollment of that specific subject due to lack of feasibility. The research team will register the wearable device and connect it to the AION BIOSTYEMS, INC. Shield app via the Samsung A13. A Samsung phone will be kept in the patient's room to track the temperature from the device. This phone is used for recording the Oral temperatures taken by the study staff.

Upon activation of the tempshield, participants will be given 60 minutes for the tempshield to acclimate to the environment before an oral temperature measurement is taken. The oral temperature will be taken by the research team using a Welch Allyn 901053 Oral Thermometer and input information into the AION BIOSTYEMS, INC. app. After the acclimation period, the first measurement of oral temperature using the Welch Allyn oral thermometer will be recorded in the AION BIOSTYEMS, INC. Shield app by the research team.

This measurement must also be >= 99.5 F for febrile participants. If it is less than 99.5F then they will be in the non-febrile cohort, unless see below.

- *The research team will take an oral temperature measurement with the Welch Allyn device every four hours. The Welch Allyn temp will be entered into the App. If the patient's measurement is 99.5 F or above, they will qualify for the febrile cohort of the study. If the patient never exceeds 99.5F and are within normal temperature range and temperature below 99.5 F, they will qualify for the non-febrile cohort*

Following this, measurements of the tempshield sensor temperature will be recorded in the AION BIOSTYEMS, INC. Shield app 1 ±5 minutes apart. Research coordinators will measure oral temperatures every 2 hours ±1 hour for up to a 24hour period, with a maximum of 6 recordings per pt.. A patient's participation will end once they are discharged from the ED or after 7 hours, whichever comes first. If the patient is moved to in-patient unit, the research coordinator will remove the device from the participant. After 7 hours or at the time of ED discharge, the device will be removed from the participant. If there is no height listed in the EMR, research staff will measure participant height.

In addition to collecting oral temperature every 2 hours, research staff will also recheck placement of AION BIOSTYEMS, INC. device in adhesive to ensure that the device is still stable in place. If adhesive is not stable, research staff will replace the adhesive with new strip. Research staff will check with LAR to make sure that device was not removed or did not fall off. If device was removed or had fallen off, research team will document estimated time of removal and replacement on CRF and the reasoning for the device displacement. If the device is damage and unable to be used, the device will be replaced, and the enrollment will continue for the duration of the 7 hours. Otherwise, the same device will be used on the subject throughout the enrollment even if it falls off or is removed from the subject.

Subjects will receive a $25 Amazon or Target card after second oral temperature is obtained. Children enrolled will also receive a small stuffed toy in the price range of $10-$20 if able to successfully complete a minimum of two oral temperatures.

AION BIOSTYEMS, INC. will have access to all oral temperatures taken during the duration of the patient's Emergency Room stay. The oral temperatures will be de-identifed and recorded by the research team from the EMR. The oral temperature data will be used to compare against the tempshield data for clinical validation.

Research staff, families, and participants will be made aware of the following precautions that will take place during enrollment:

- Avoid positioning participant directly near ventilation ducts, open windows, or forced convection of any kind (e.g., fans)
- Avoid positioning participants in direct sunlight (windows)
- Avoid allowing participants to move around excessively, leave the premises, or go outdoors
- Avoid allowing participants to drink hot or cold fluids within 5-min of an oral temperature measurement
- If participants have eaten within 30 minutes of taking oral temperature, research coordinators will note this information in the AION BIOSTYEMS, INC. app
- If participants have drinks within 5 minutes of taking oral temperature, research coordinators will note this information in the AION BIOSTYEMS, INC. app
- If any of the above cautions happen during the 4hour window the clinician staff shall record them in the mobile app. (e.g. Sitting in open sunlight 15 minutes prior to 4 hour visit.

6.2 Subjects

6.2.1 Inclusion Criteria

A subject **must** meet all of the following inclusion criteria to be eligible for inclusion in this study:

1. Male or female patients between ages 2 years -4 years of age
2. Confirmed oral temperature of >=99.5 F for febrile participants OR confirmed oral temperature of <99.5 F for afebrile participants
3. Willing and likely (based on the investigator's judgement) to comply with all study requirements

6.2.2 Exclusion Criteria

Subjects meeting any of the following criteria will be excluded from participating in this study:

1. Participants who are allergic to silicone
2. Adolescents with sensory issues who may find it difficult to have a wearable device on their chest.

3. Participants presenting an anatomical limitation that would prevent the use of the wearable device

6.2.3 Deviation from Inclusion/Exclusion Criteria

The inclusion/exclusion criteria must be strictly followed. If a subject who does not meet these criteria is inadvertently included, the Sponsor or a specified designee should be immediately contacted to obtain instructions on whether the subject should be discontinued from the study.

6.2.3 Criteria and Procedures for Subject Withdrawal or Discontinuation

Subjects may be withdrawn early from the study for several reasons, including but not limited to:

- Parents/Legal representatives' request
- Investigator request
- Discharge
- Adverse Events (AEs) (e.g., intolerable AE occurrence or treatment forces subject to stop participation in the study)
- Non-compliance of protocol and required procedures

The parents/legal representatives are free to withdraw their child from this study at any time upon their request. Withdrawing from the study does not affect the access to standard treatments for their child or their relationship with the hospital and affiliated HCPs.

If a study subject is discontinued from the study early, a Note-to -File (NTF) will be written describing the reason for discontinuation.

In case of discontinuation or withdrawal of subjects who already received an AION BIOSTYEMS, INC. device, research staff will remove device and collect all study equipment. Subjects who are discontinued from the study or withdraw consent may be replaced.

6.2.5 Duration of the Clinical Study

The study is expected to last approximately no longer than 7 hours with the device.

The study is expected to last approximately 2 years.

6.2.6 Number of Study Subjects

A total of 150 participants between the ages of 2-4 years will be recruited for the study. The study will not include more than 25 nonfebrile patients. ***Febrile participants will be confirmed febrile (oral measurement with the Welch Allyn clinical thermometer >= 99.5 F) at the time of enrollment.*** Additional participants may be recruited as needed, to ensure the required sample size for clinical validation of the tempshield is met.

6.2.7 Information on Vulnerable, Pregnant or Breastfeeding Population

As the intended population of the AION BIOSTYEMS, INC. system is children < 5 years old, this study is performed on vulnerable population to assess the efficacy of using the AION BIOSTYEMS, INC. system for continuous temperature monitoring on the relevant population.

6.3 Study Procedures

6.3.1 Detailed Description of Study Procedures

Consenting and Inclusion

Waiver of documentation of consent and assent is being requested for participants because this study involves minimal risk of harm to participants and involves no procedures for which written consent is normally required outside the research context. No PHI will be sent to third parties outside of Children's National.

Procedures Following Enrollment

The tempshield wearable device will be placed on the upper chest with gentle, silicon adhesive tape. The research team will register the wearable device and connect it to the AION BIOSTYEMS, INC. Shield app via the Samsung A13. A Samsung phone will be kept in the patient's room to track the temperature from the device. This phone is used for recording the Oral temperatures taken by the study staff.

Upon activation of the tempshield, participants will be given 60 minutes for the tempshield to acclimate to the environment before an oral temperature measurement is taken. The oral temperature will be taken by the research team using a Welch Allyn 901053 Oral Thermometer and input information into the AION BIOSTYEMS, INC. app. After the acclimation period, the first measurement of oral temperature using the Welch Allyn oral thermometer will be recorded in the AION BIOSTYEMS, INC. Shield app by the research team.

Following this, measurements of the tempshield sensor temperature will be recorded in the AION BIOSTYEMS, INC. Shield app 1 ±5 minutes apart. Research coordinators will measure oral temperatures every 2 hours ±1 hour over the 24hour period, with a maximum of 6 recordings per pt. After 7 hours or at time of ED discharge, the device will be removed from the participant. The device will be removed overnight when outside of research hours. This will ensure that the research team is able to continuously monitor the participant.

Subjects will receive a $25 Amazon or Target gift card after second oral temperature is obtained. Children will receive the $10-$20 small stuffed toy after the second oral temperature reading is obtained.

AION BIOSTYEMS, INC. will have access to all oral temperatures taken during the duration of the patient's Emergency Room stay. The oral temperatures will be de-identified and recorded in the app. The oral temperature data will be used to compare against the tempshield data for

clinical validation.

If there is no height recorded in the EMR for this visit, then research staff will measure participant height.

If, at any point during study procedures, a participant is to receive radiology (CT, MRI, X-Ray) imaging, the AION BIOSTYEMS, INC. tempshield device will be removed from the participant. At start of study enrollment, radiology team will be alerted that individuals will be enrolled in a study in which a device will need to be removed prior to imaging. Upon each patient's enrollment in the study, the patient will receive a brightly colored wristband that states the patient is wearing a device that must be removed prior to radiology procedures. The child's provider will also be alerted to the child's participation in the study and the need to remove the device before imaging.

6.3.2 Study Materials and Equipment

The following study materials will be used:

- Parent/Guardian Study Information Sheet
- AION BIOSTYEMS, INC. tempshield Device is the skin applied device used for collecting and transmitting the skin temperature to the mobile device.
- Samsung A13 Phones this device will collect the skin temperature and will perform the AION Biostyems, Inc. conversion algorithm and then send the data and the unique ID to the AION Biostyems, Inc. Core.
- Welch Allyn 901053 Oral Thermometers This Thermometer has been the gold standard for AION Biostyems, Inc. in Previous studies and must be calibrated prior to service and after study for valid data verification.
- User Guide

The testing and validation systems are listed below:

AION BIOSTYEMS, INC. will provide Samsung A13 phones and 2 Welch Allyn 901053 oral thermometers. A Samsung A13 device will be placed in each patient's room to continuously track their temperature.

Additional supplies needed from Children's National includes wipes (if the patient's skin needs to be cleaned before the device application) and hand sanitizer/gloves for the person placing the device on the patient.

Availability of accompanying documentation and provision of training for the study:

The tempshield's accompanying documentation (i.e., packaging, paper IFU, in-app IFU, and User Guide) will be available to study staff as reference for device application on the subjects.

6.3.3 Study Environment

The validation study will be conducted in the Children's National Emergency Department during which the Children's National Research team will obtain participant consent and conduct the study.

6.3.4 Study facilitator inoculations

The Children's National Research team will be required to be up to date with the following inoculations:

- COVID-19 vaccinations

6.4 Monitoring

The sponsor will oversee the data collection, including managing data queries, running data reports, providing data summaries, and statistical analyses.

The sponsor will provide oversight of the regulatory aspects of the study including IRB and contracts with sites.

Any serious unanticipated problems that may occur will be reviewed and determined whether a change in the protocol is necessary. If the study exhibits an excess amount of serious unanticipated events the study will be stopped and reviewed.

6.4.1 Monitoring Plan

Study will be monitored by a monthly monitoring visit either on site or remotely to review data collection, recruitment, access the subject safety and regulatory requirements of the study.

Data is expected to be entered by the study team the same day as enrollment and queries resolved within 3 business days of the raised query.

6.5 Auditing

The Principal Investigator makes all pertinent records available, including source documentation, for inspection by the ECs/IRBs and for auditing by the Sponsor or designee after appropriate notification. The verification of data must be by direct inspection of source documents. This information will be considered as confidential. The Principal Investigator should inform the Sponsor as soon as they are made aware of the audit or inspection

7 Statistical Considerations

Raw data collected by the AION BIOSTYEMS, INC. tempshield device are stored in encrypted files and include the temperature.

The objective of this formative study is to evaluate the effectiveness of the AION BIOSTYEMS, INC. tempshield (“Shield”) temperature monitoring device and platform in detecting body temperature for children 2-4 years old.

- The sample size of “up to 130 subjects” has been defined based on the following criteria 80601-2-56 ISO standard for digital thermometers recommends that 110 study participants with 30% of them Febrile be tested. We are seeking to do 150 patients because of patient fall out and accounting for potential withdrawals

Based on all the above information, the sample size of “up to 100 subjects” should be large enough to address the study objective and study endpoints.

8 Data Management

8.1 Data Management

Data recording for this study and backend temperature data collected through the tempshield device and on the AION BIOSTYEMS, INC. Shield app sent to AION BIOSTYEMS, INC.s servers. The following data points will be recorded on AION BIOSTYEMS, INC. Shield App by trained study personnel in the study’s database:

- Subject Study ID number
- Device ID
- Age, Gender, Height and Weight
- Date and time of tempshield™ application
- tempshield application (date and timestamp of tempshield temperature)
- Times of Handed entered temperature data
- Time of each tempshield reading and value.
- Times of temperature excursion based on agreed upon excursion.

Source documents will be coded with the study subject ID number. Only authorized research staff will have access to the source documents and study data. Source data retention requirements of the sponsor, AION BIOSTYEMS, INC., AION Biostyems, Inc. will keep all data for approximately two years. All data stored is de-identified data, and was not used for medical records.. All required data collected during the study must be collected by the investigator or designated research staff. Data should be entered as soon as possible after the information is collected. Data is collected electronically. Oral temperatures shall be entered when they are taken into the AION BIOSTYEMS, INC. application.

All hard copy data (consent/assent forms) will be stored in subject and regulatory binders in a secure location accessible only to authorized study personnel.

No PHI will be provided to the sponsor for this study. All PHI collected will remain in CNH research records. Research staff will collect name, date, MRN, and account numbers of screen subjects. This information will remain housed on CNH servers and will only be accessible by CNH research study staff.

All data is stored in the AION BIOSTYEMS, INC. Core and the Clinician Application. Post study the Clinician Application will be archived in a secure encrypted database that is HIPAA certified. The clinician data will remain for 7 years, and access to this data is only by certified AION BIOSTYEMS, INC. staff for the purpose of legal enquiries only.

AION Biostyems, Inc. cloud data (all de-identified will remain on the AION Biostyems, Inc. Server for minimally two years. The AION BIOSTYEMS, INC. cloud data is password protected, and the data on the data-base server is encrypted. AION Biostyems, Inc.'s strict password policy enforces complex passwords that must be change every 30 days.

Only AION Biostyems, Inc. personnel may access the AION Biostyems, Inc. cloud.

8.2 Confidentiality

Participants will be assigned a unique code or Participant ID. Any documents or files containing data collected for a specific participant will be identified only by the Participant ID. Any document that contains the link between a Participant ID and any personally identifiable information regarding that participant will be password protected, stored on a password protected computer or network, and will only be accessible by the Principal Investigator or Study Moderator on an as-needed basis.

8.3 Record Retention

The Principal Investigator shall arrange for the retention of all study documents and records, including subject records, device accountability log, and subject identification list for at least 3 years after the completion or discontinuation of the study.

Hence, the pseudonymized data collected by the AION BIOSTYEMS, INC. system are securely stored on the Cloud, where they will be archived for 2 years after FDA approval.

If the Principal Investigator moves or retires, they must nominate someone in writing to be responsible for archiving. Archived data may be held as electronic records as long as a backup exists, and a hard copy can be obtained if required. If the Principal Investigator cannot guarantee this archiving requirement at the study site for any of the documents, special arrangements must be made by the Sponsor to store these sealed containers outside of the site so they can be delivered to the site in case of a regulatory audit.

8.4 Clinical Quality Assurance and Quality Control

The Sponsor has integrated clinical quality assurance and quality control in the Sponsor's quality system. Quality assurance and quality control principles apply to the processes of the clinical investigation. The sponsor commits to:

- Implement and maintain written clinical quality procedures to ensure that the clinical investigation is designed, conducted and monitored, and that data are generated, documented, recorded and reported in compliance with ISO 14155:2020, the CIP, any subsequent amendment(s), and any other applicable standards and regulatory requirements,
- Maintain records to document the compliance of all parties involved in the clinical investigation,
- Ensure that the auditing requirements are met, and
- Justify and document significant exceptions to the requirements of ISO 14155:2020.

9 Amendments of the Clinical Investigation Plan

No change to the protocol may be made without the joint agreement of both the Principal Investigators and AION BIOSTYEMS, INC.. Any amendment to the original protocol will be made by AION BIOSTYEMS, INC.. The written amendment must be submitted to ECs/IRBs and the Principal Investigator must await for the approval before implementing the changes, as applicable per local law.

If in the judgment of the ECs/IRBs, the Principal Investigator, and/or AION BIOSTYEMS, INC., the amendment to the protocol substantially changes the study design and/or increases the potential risk to the subject and/or has an impact on the subject’s involvement as a study subject, enrolled study subjects will be informed of any changes.

10 Deviations from the Clinical Investigation Plan

Any changes made during the execution of the study will be evaluated by those conducting the study at the time to minimize deviation from the protocol and provide for the most beneficial data collection.

When changes are made during studies, the Principal Investigator will collect the necessary approvals and document the changes made including a rationale for the change(s). Reports generated for the study’s results will identify the changes that occurred during the study and any impact on the results they had.

Approvals for deviations will be obtained before the deviation occurs.

Type of Changes	Description	Approvals Required By:

Minor changes	Includes updates to introductory language. This would also include any re-ordering of tasks or repeating the set of tasks if conditions or timepoints are unable to be followed as outlined	Study Moderator
Major changes	Includes any changes to the study inclusion or exclusion criteria.	Principal Investigator Study Sponsor

10.1 Approvals

The approval designees listed are responsible for assessing the adequacy of this study protocol and changes to the protocol.

Role	Printed Name
Principal Investigator	Sephora Morrison
Chief Technology Officer	Thomas Blackadar
Director of Quality and Regulatory Affairs	Carl Shubitowski

11 Device Accountability

The Principal Investigator is obliged to establish a system to control study accountability, to ensure that an assigned person receives all supplies, and that the documentation of all deliveries and returns are signed for. Each use must be documented (including dates, subject ID and/or device serial numbers) at a level that enables full verification of the protocol specified procedures.

Study supplies shall be kept by the Principal Investigator in a secure place. All supplies will be used for this study only. Parents/Legal representatives of included subjects will be instructed to retain and return all AION BIOSTYEMS, INC. equipment to the Principal Investigator at the end of the study.

12 Statement of Compliance

The study will be conducted in accordance with all applicable FDA guidance and regulatory requirements, EN ISO 14155:2020, applicable sections of 21 CFR 812, and all applicable privacy requirements, and the ethical principles that are outlined in the Declaration of Helsinki, including:

- Belgian Law of 22 August 2002 on Patient's (and study subject's) Rights.
- Belgian Law of 7 May 2004 on experiments on human beings revised on June 5th, 2006.
- Belgian Law of 30 July 2018 on the protection of individuals with regard to the processing of personal data: The Parties shall comply with all applicable rules and legislation in relation to data protection and the processing of personal data (including the General Data Protection Regulation (EU) 2016/679 (GDPR), the Belgian law of 30 July 2018 on the protection of individuals with regard to the processing of personal data and other applicable Belgian or European regulations in relation to the processing of personal data)."
- HIPAA Privacy rule (45 CFR Part 160 and Subparts A and E of Part 164).

The clinical investigation shall be conducted in accordance with the protocol.

Prior to subject participation in this study, the Investigator will ensure obtaining written ECs/IRBs approval authorizations as appropriate for the protocol and HIPAA authorization.

Any additional requirements imposed by the ECs/IRBs or by the regulatory authority must be respected, if necessary.

In the event of project-related damage or injuries, the Sponsor will be liable, except for damages that are only slight and temporary; and for which the extent of the damage is no greater than would be expected in the current state of scientific knowledge.

13 Informed Consent Process

Provide the information sheet to the patient's caregiver. Documentation of informed consent is not required.

Inform the patient's caregiver of the purpose of the study (to test effectiveness of AION BIOSTYEMS, INC. tempshield in continuous monitoring of temperature in an ED setting) and what the study involves (wearing AION BIOSTYEMS, INC. tempshield on participant's chest for 7 hours and having oral temperature taken every 4 hours). Participation is voluntary and they are free to withdraw from participation at any time.

Due to age of participants (2-4years), no assent will be obtained for subjects. Documentation of assent is not required.

14 Adverse Events, Adverse Device Effects and Device Deficiencies

14.1 Safety Definitions

The following definitions are in accordance with the harmonized standard ISO 14155:2020 and with the FDA Code of Federal Regulations for Medical Devices (21 CFR 812.3(s)).

14.1.1 Device Deficiency

A **device deficiency** is defined as any inadequacy of a medical device related to its identity, quality, durability, reliability, safety, or effectiveness, such as malfunction, misuse or use error and inadequate labelling. Device Deficiency occurs in any case where the device does not perform in its intended function and when used in accordance with the device labelling.

A device failure has occurred when the device is used in compliance with the Instructions for Use but does not perform as described in the Instructions for Use and negatively impacts treatment of the study subject.

A device malfunction means the failure of a device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed.

Note that the subject and/or the subject's LAR are not responsible for the loss or damage of any devices and will not be held accountable by the study Sponsor AION BIOSTYEMS, INC..

14.1.2 Adverse Event

An **Adverse Event** (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users, or other persons whether or not related to the investigational medical device.

AE includes non-routine inpatient hospitalizations (>48 hours by Medicare criteria) and events related to the investigational device. This includes events related to the procedures involved (any procedure in the clinical investigation plan). For users or other persons this is restricted to events related to the investigational medical device. Routine pre-operative and post-operative hospitalizations are not considered adverse events.

AE does not include conditions pre-existing to the subject's enrollment. Pre-existing conditions will not be reported as AEs unless the condition has an increased occurrence or intensity.

14.1.3 Adverse Device Effect

An **Adverse Device Effect** (ADE) is defined as any adverse event related to the use of an investigational medical device.

ADEs include any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. This includes any event that is a result of a use error or intentional misuse.

For the purposes of this study, the patient will only be monitored for any newly diagnosed skin condition (e.g., dermatitis, abrasion) at the site of the study device use throughout the duration of subjects' participation in the study.

14.1.4 Serious Adverse Event

A **Serious Adverse Event** (SAE) is defined as any adverse event (AE) that led to:

- Death.
- A serious deterioration in the health of the participant that either:
    a. resulted in a life-threatening illness or injury (i.e., the subject is at risk of death at the time of the event; it does not refer to an AE that might hypothetically have caused death had it been more severe), or
    b. resulted in a permanent impairment of a body structure or a body function (i.e., the subject is unable to function, such as swallowing dysfunction that limits the ability to eat with ongoing weight loss or speech dysfunction that leaves unintelligible articulation; it does not refer simply to a noticeable disturbance in function, such as a globus sensation with swallowing or subtle articulation change), or
    c. required in-patient hospitalization or prolongation of existing hospitalization (i.e., hospitalization > 48 hours consistent with Medicare definition of in-patient for medical reasons; it does not refer to prolonged hospitalization for social reasons such as inadequate transportation home or routine pre-operative or post-operative hospitalization), or
    d. resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function (i.e., medical or surgical intervention alone does not meet this criterion for serious; it must be to prevent a life-threatening illness or injury or permanent impairment consistent with criteria 2a and 2b).
- Fetal distress, fetal death or a congenital abnormality or birth defect.

A planned hospitalization for pre-existing condition without a serious deterioration in health or to prevent life threatening illness or injury or permanent impairment to a body structure or a body function, is not considered to be a SAE.

SAE includes device deficiencies that might have led to a serious adverse event if (a) suitable action had not been taken or (b) intervention had not been made or (c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

14.1.5 Serious Adverse Device Effect

A **Serious Adverse Device Effect** (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

14.1.6 Unanticipated Serious Adverse Device Effect

An **Unanticipated Serious Adverse Device Effect** (USADE) is a SADE which by its nature, incidence, severity or outcome has not been identified in the protocol or in the investigational device manuals.

Per 812.3(s) this includes any SAE caused by, or associated with, a device, if that SAE was not previously identified in nature, severity, or degree of incidence in the investigational, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

14.2 Classification and Documentation of Adverse Events

14.2.1 Assessment of Intensity/Severity

The clinical "intensity" of an AE will be assessed by the Investigator, using the following categories:

- **Mild** – Events require minimal or no treatment and do not interfere with the subject's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate "serious".

14.2.2 Relationship to Investigational Device/Procedure

The Investigator will assess if the AE (or SAE) is related to the AION BIOSTYEMS, INC. system. The probability that a particular AE is related to the device shall be coded on the AE CRF as *not related, unlikely, possibly, probably,* or *definitely* as defined below.

- **Not related**: The Principal Investigator (PI) has determined that the complication is not related to the study device.
- **Unlikely**: The PI indicates that a relationship to the use of investigational device is unlikely; Other causes provide plausible explanations for the event.
- **Possibly**: The PI has determined that the event has a possible relationship to the use of the investigational device; There is some evidence to suggest a causal relationship. However, other factors may have contributed to the event.
- **Probably**: The PI has determined that the event has a probable relationship to the use of the investigational device; there is evidence to suggest a causal relationship,

influence of other factors is unlikely. There is a clinically reasonable response on withdrawal of study intervention.

- **Definite**: The PI has determined that the complication is related to the investigational device. There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. There is a clear clinical response to withdrawal of study intervention.

Probability ratings are based on the temporal relationship to intervention, the likelihood that the symptom could have been produced by the participant's clinical state, the environment, or other interventions, whether the participant's symptom course follows a known pattern of response to the intervention, and the experience and judgment of the investigators.

14.2.3 Assessment of Outcomes

The clinical outcome of the event at the time of last observation will be characterized as follows:

- Not Recovered/Not Resolved
- Recovered/Resolved
- Recovered/Resolved with Sequelae
- Recovering/Resolving
- Fatal
- Unknown

14.2.4 Expectedness

There are no anticipated adverse events related to the use of the study device.

14.3 Safety Documentation and Reporting

14.3.1 Documentation of and Reporting Adverse Events

AEs are identified, assessed, and documented by the Investigation Site staff. All AEs are to be recorded, starting with the informed consent through the final visit required of the subject. AEs documented at a previous visit/contact and designated as not resolved or ongoing will be reviewed at subsequent visits/contacts until the end of the study.

For the purposes of this study, the patient will only be monitored for any newly diagnosed skin condition (e.g., dermatitis, abrasion) at the site of the study device use throughout the duration of subjects' participation in the study.

All AEs (including SAEs) must be reported in a timely manner to the Sponsor by completing a Note-to-Files. All AEs should also be documented in the site's source documents.

Any medical condition existing at the time of inclusion must be reported as baseline data, and do not need to be reported as AEs unless it increases in severity during the course of the study. AEs, which resolve and recur, should be reported as separate AEs. AEs which have not resolved at the time of the initial report, and which increase in severity or subsequently resolve, should be reported as AE follow-up information rather than as new events. The duration for each severity level is to be reported.

Information to be collected includes event description, time of onset, Investigator's assessment of severity, relationship to study device/procedure, outcome, and time of resolution/stabilization of the event, treatment/action taken. All AEs occurring while on study must be documented appropriately regardless of relationship.

Treatment of AEs is at the sole discretion of the Investigator and according to current good medical practice. It should be documented in the source documentation.

14.3.2 Documentation and Reporting of SAE/UADE

Once an investigator becomes aware that a SAE has occurred in a study subject, the investigator (or designate) must complete the SAE information via the AE form WITHIN 24 HOURS after the investigator first learns of the event. The report will always be completed as thoroughly as possible with all available details of the event. Even if the investigator does not have all information regarding a SAE, the report should still be completed within 24 hours. Once additional relevant information is received, the report should be updated WITHIN 24 HOURS.

The investigator will always provide an assessment of causality at the time of the initial report.

Investigators are responsible for submission of SAEs occurring at their site to their local IRB/EC in accordance with institutional requirements. Documentation of submission will be retained by the site.

In case of UADE, the investigator (or designate) shall complete the UADE information and submit to the Sponsor within 24 hours after the investigator first learns of the effect. The study sponsor is responsible for conducting an evaluation of a UADE and shall report the results of such evaluation to the IRBs/ECs and Investigators within 10 working days after the Sponsor first receives notice of the effect. Also, the investigator (or designate) is responsible to report the UADE to the IRB/EC as soon as possible, but no later than 10 working days after the investigator first learns of the effect. All UADEs are to be reported throughout the study.

The Sponsor will review significant new information, including unanticipated adverse events and ensure that such information is provided to the investigators and to all reviewing IRBs/ECs within the required timelines.

14.3.3 Documentation and Reporting of Device Deficiencies

All device deficiencies shall be documented throughout the clinical investigation in the source documents and appropriately reported to the Sponsor on Note-to-Files.

14.3.4 Death Reporting

Each subject death shall be reported using the AE form. Any other source documents relied upon to decide of death classification and cause of death will also be filed with the subject's study documents.

14.3.5 Investigator Reports

The relevant form should always be completed as thoroughly as possible with all available details of the event. Even if the investigator does not have all information regarding an event, the report should still

be completed within the defined timeframes. When additional relevant event information is received, the relevant report should be updated within the designated timeframe.

Prompt notification of any UADE, SAE, device deficiency by the Investigator to the Sponsor is essential so that legal obligations and ethical responsibilities towards the safety of other subjects are met. The Sponsor has a legal responsibility to promptly notify, within the required time period, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation.

Non-emergent protocol deviations shall first be approved by sponsor and if deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of subject, a protocol amendment may have first to be submitted and approved by IRB/EC.

The following reports should be prepared by the Investigator (or designate) within the timeframes described in Table 2.

Table 2: List of Investigator reports

Type of Event	Document	Report prepared for	Reporting Timeframe
Serious Adverse Event (SAE)	Relevant eCRF page (or scanned relevant form to email in case of technical issue)	Sponsor/IRB/EC*	Immediately, but no later than 24 hours after investigator is first notified of the event.
Adverse Events (AE)	Relevant eCRF page (or scanned relevant form to email in case of technical issue)	Sponsor	Within 3 business days after investigator is first notified of the event
Unanticipated Adverse Device Effect (UADE)	Relevant eCRF page (or scanned relevant form to email in case of technical issue)	Sponsor and IRB/EC*	Immediately, but no later than 24 hours after investigator is first notified of the effect.
Withdrawal of IRB/EC Approval or other action on part of the IRB/EC that affects the study	Any written document	Sponsor	Within 5 working days of notice of IRB/EC decision.
Deviations from CIP	Relevant eCRF page (or scanned relevant form to email in case of technical issue)	Sponsor and IRB/EC*	• Emergency use (i.e., if to protect the life or physical wellbeing of a subject in an emergency): as early as possible but not later than 5 working days

Type of Event	Document	Report prepared for	Reporting Timeframe
			after protocol deviation. • Otherwise: within 10 working days
Device deficiency that might have led to SAE	Relevant eCRF page (or scanned relevant form to email in case of technical issue)	Sponsor	Immediately, but no later than 24 hours after investigator is first notified of the deficiency.
Use of an Investigational Device without Informed Consent	Any written document	Sponsor and IRB/EC*	Within 5 working days after the use occurs.
Study Progress information	Any written document	Sponsor and IRB/EC*	At regular intervals, but no less than yearly
Termination or completion of study or investigator's participation	Any written document	Sponsor and IRB/EC*	Within 3 months after termination or completion of study or investigator's participation.
Other	As required	As required	Upon request by the IRB/EC or FDA or national Competent Authority, provide accurate, complete, and current information about any aspect of the study.

* Reporting to the IRB/ECs will be according to applicable national/local regulations and institution requirements.

14.3.6 Sponsor Reports

The following reports should be prepared by the Sponsor within the timeframes described in Table 3 below.

Table 3: List of Sponsor Reports

Event	Document	Report Prepared for	Reporting Timeframe
Serious Adverse Event	MEDDEV Report	IRB/ECs*, and Competent Authorities**	Within 2 calendar days from sponsor awareness (MEDDEV 2.7/3)
Unanticipated Adverse Device Effect	UADE Report	IRB/ECs*, Investigators	Within 10 working days from the time the sponsor first learns of the effect
Serious Breach from Clinical Investigational Plan	Written report/notification, or interim progress report or final report	IRB/ECs*	• Emergency use (i.e., if to protect the life or physical wellbeing of a subject in an emergency): as early as possible but not later than 5 working days after protocol deviation. • Otherwise: as part of the progress and final reports
Use of an Investigational Device or Treatment without Informed Consent	Any written document	IRB/ECs*	Within 5 working days after the use occurs.
Withdrawal of IRB/EC Approval	Written report/notification	IRB/ECs*, Investigators	Within 5 workings days of notification of such notification
Device Recall and disposition	Written report/notification	IRB/ECs*	Within 30 days after device recall or withdrawal request is made to an investigator
Study Progress information	Interim Progress Report	IRB/ECs*	Annually, on the anniversary of the IDE approval date
Termination or completion of study	Final Report	IRB/ECs*	Within 6 months of completion or termination of the study
Final Report	Final study report	Investigators, IRB/ECs*	Within 6 months of study closure
Other	Written report/notification	IRB/ECs*	Upon request by the IRB/EC, provide accurate, complete

Event	Document	Report Prepared for	Reporting Timeframe
			and current information about any aspect of the study

* Reporting to the IRB/ECs will be according to applicable national/local regulations and institution requirements.

** Reporting to the Competent Authorities will be according to applicable national/local regulations and institution requirements.

15 Vulnerable Population

As the study device is intended for children < 4 years old, the study population is made of vulnerable participants.

Subjects will be recruited during the course of a hospitalization, hospital visit or visit to the emergency department. If the HCP assesses that the subject may be eligible for this study, parent(s)/legal representative(s) will be presented with the project and all relevant documents.

If the parent(s)/legal representative(s) are interested in their child's participating in this trial, at least of the child's parents/legal representatives will be provided with provide verbal consent and be given an information sheet discussing study procedures and involvement.

16 Early Termination or Suspension of the Clinical Investigation

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause (e.g., technical problem with the study design, unexpected significant concerns about safety for the subjects, lack of compliance to protocol requirements or lack of sufficient data, primary endpoint met, or futility) by Sponsor or IRB/EC. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to Investigators, IRB/EC and sponsor. Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the Sponsor and IRBs/ECs.

17 Final Report and Policy Publication

The Sponsor, in cooperation with the Coordinating Investigator, will prepare the final study report, which will be signed by the Coordinating Investigator and the Sponsor.

The results of the clinical investigation will be published YES ☐ NO ☒

If yes, conditions of publication:

Literature review

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