Cover page

Non-ACT Voluntary Submission

This document contains the following IRB Approved documents:

Study Protocol & Statistical Plan (Date: Nov 29, 2021)
Protocol Amendment #1 (Dated: 13 Dec, 2021)

For study:

OVERNIGHT PANT SAFETY-IN-USE DIARY CLINICAL TRIAL FOR CHILDREN WITH NOCTURNAL ENURESIS

CSD2021096/ NCCI #12-2103

Date: Nov 29, 2021

NCT# 05178641

OVERNIGHT PANT SAFETY-IN-USE DIARY CLINICAL TRIAL FOR CHILDREN WITH NOCTURNAL ENURESIS

CSD2021096/ NCCI #12-2103

Date: Nov 29, 2021

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Clinical Trial Manager: [redacted]

Statistician: [redacted]

Clinical Data Manager: [redacted]

Regulatory: [redacted]

Toxicologist: [redacted]

BFF Clinical Director [redacted]

Clinical Trial Location: North Cliff Consultants
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Sponsor's Representatives Signatures

This protocol has been approved by the Sponsor and Sponsor's Representatives of the clinical trial.

[redacted]. Date
BFF Clinical Director

Susanna Brink, Ph.D. Date
Clinical Scientist

[redacted] Date
Clinical Trial Manager

[redacted] Date
Regulatory

[redacted] Date
Toxicologist

[redacted]
Statistician Date

[redacted]
Data Manager Date

Investigator's Signature

Protocol Number:	**CSD2021096**
Title of Protocol:	**OVERNIGHT PANT SAFETY-IN-USE DIARY CLINICAL TRIAL FOR CHILDREN WITH NOCTERNAL ENURESIS**

Investigator's Agreement Statement:

I have read and understand this protocol and concur with the clinical trial design. I agree to participate as an Investigator and to follow the protocol as outlined. I will submit a written report after completion of the clinical trial.

Principal Investigator _____ _____
Laura Huesing-Wray (Date)

Sub-Investigator

_____ _____
[redacted] M.D. (Date)
(Ped. Dermatologist)

Sub-Investigator

_____ _____
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List of Abbreviations:

AE	Adverse Event
ADE	Adverse Device Effect
AI	Adult Incontinence
CER	Clinical Evaluation Report
CRF	Case Report Form
eCRF	Electronic Case Report Form
GCP	Good Clinical Practices
H&P	Habits and Practices
ICH	International Conference on Harmonization
IRB	Institutional Review Board
MDR	Medical Device Regulation
ISO 14155	Clinical Investigation of Medical Devices for Human subjects GCPs
ISO 14971	Medical Devices - Application of Risk Management to Medical Devices
NJ EU	Ninjamas Europe Overnight Pant
[redacted]	[redacted]
pH	Potential Hydrogen
P&G	Procter & Gamble
QoL	Quality of Life
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
[redacted]	[redacted]
TMF	Trial Master File

Clinical Trial Protocol

1. Introduction

Ninjamas Europe (NJ EU) is an absorbent disposable single-use underwear pant developed for children suffering from nocturnal enuresis (nighttime bedwetting). The NJ EU absorbent underwear pant helps manage and contain urination gushes at night for up to 12 hours. It is not intended to treat or cure nocturnal enuresis. It is a non-invasive device and intended for external application on intact skin. It is a simple non-active device (without electronics or batteries) that is very easy to use. No specific training is required to use this product. It is available in 2 sizes: Size 7 for children aged 4-7 (17-29 kg) and Size 8 for children aged 8-12 years (27-43kg).

Since nocturnal enuresis in the age group 5 years and above is considered a medical condition in Europe, this absorbent underwear pant is regulated as a Class 1 medical device in the EU. This clinical trial will be part of the body of clinical evidence needed to support the Medical Device Report, which is required to market this absorbent product as a nocturnal enuresis management tool for children age 4-12 years in the EU.

There are several ways to manage nocturnal enuresis in children. This clinical trial will focus on the first option only:

- Absorbent underwear to manage urine loss without treating it.
- Bed mats absorb urine and prevent the mattress from getting wet but do not keep the child's clothing and bed sheets from getting wet.
- Fluid and diet restriction prior to bedtime.
- Waking the child at specific times during the night to go to the bathroom.
- Bladder training or retention control training, where the child is trained to hold the urine as long as possible in order to increase bladder capacity.
- Rewards and star charts to encourage nights without bedwetting.
- Wetness alarms (bells or vibrations that wake the child when urinating).
- Desmopressin (synthetic version of anti-diuretic hormone).
- Anticholinergic medicine (e.g., Oxybutynin) reduces the number of involuntary bladder contractions and has a relaxant effect on the smooth muscle of the bladder. This decreases the urge to pass urine and allows the bladder to hold more urine.
- Tricyclic drugs - work the same as Oxybutynin but are only used in cases where other drugs are not working. The need for close follow up and the potential for serious cardiac consequences with overdose mean they are considered for use in specialist centers only.
- Psychological treatment.

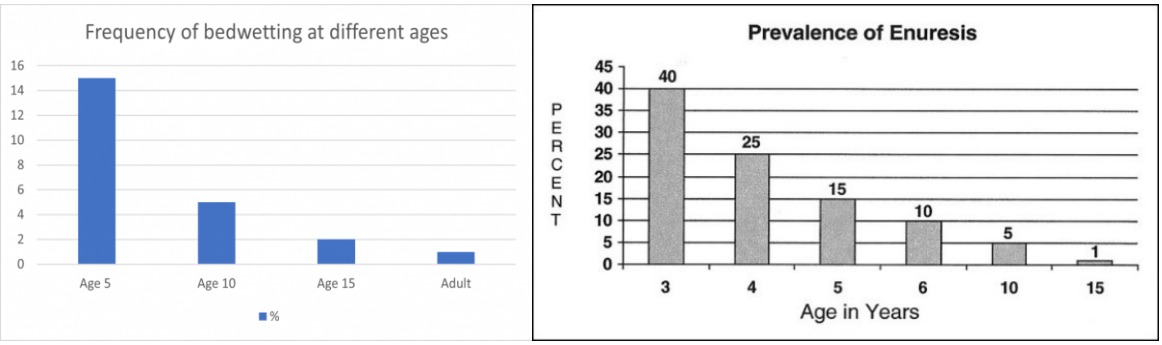
The P&G company has a 20+ year history of baby diaper clinical data (0-36 months) to show that our diaper and pant technology is safe to use and effective for managing urine gushes in a baby and toddler population. The P&G company also has adult (18+ years) female incontinence products in the EU market, including absorbent heavy incontinence pants, that are classified as Class 1 Medical Devices, which were demonstrated to be safe to use and effectively manages urine gushes of adults as seen in the statement of compliance from the CER report [1]. P&G markets a training pant (BabyDry Pants S7) in the EU. Based on the Post Market Safety Surveillance data of similar products in the EU und US market (BabyDry Pants, FemCare AI Pants,), we have reason to believe that the NJ EU product will have no safety

related issues when used as an overnight pant for children aged 4-12 years, based on skin and health related AEs. [2]

[redacted] the design of the P&G Adult Incontinence [redacted] pants and the [redacted] pants for babies and toddlers are comparable to that of the NJ EU [redacted] pant for bedwetting children, and there is a reason to believe that the NJ EU [redacted] pant meets all safety and product performance requirements [redacted]. This clinical trial provides helpful technical data to bridge to the existing body of evidence clinical data from adult and baby clinical trials and gather clinical safety in-use data for this specific population of children, with a different gush volume than adults and babies and using the products only during night.

Looking at the prevalence of nocturnal enuresis, this condition is more likely among younger children (size 7, or S7, which is designed for children aged 4-7) than older children (size 8, or S8, which is designed for children aged 8-12). The graphs below show data from publications on nocturnal enuresis for UK [3] and USA [4] respectively.

Figure 1 & 2: Prevalence of Nocturnal Enuresis for UK [1] and USA [2].



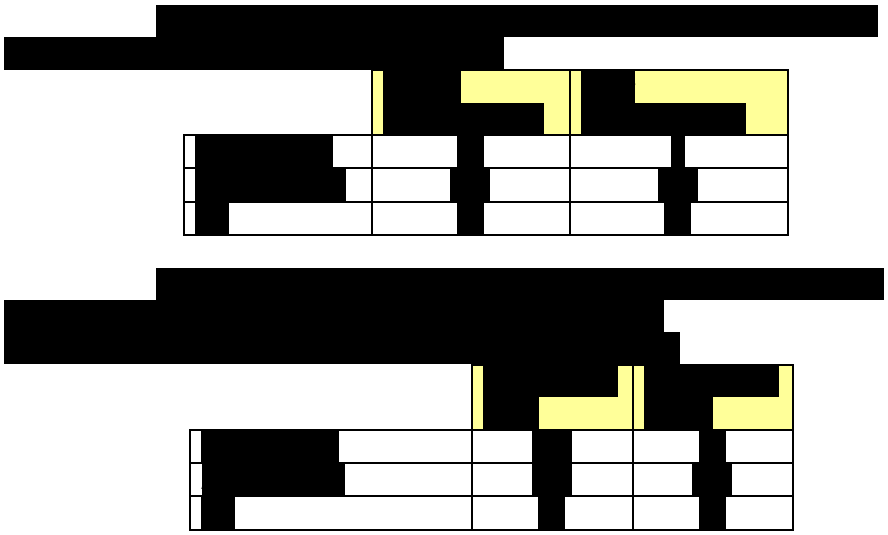
This clinical trial will therefore focus on the more representative S7 group. Reasons for choosing this group include:

1. This group will be easier to recruit with approximately 10-25% of the population suffering from nocturnal enuresis at age 4-7, compared to only 1-5% of the population at age 8-12. In addition, the willingness of younger children to participate in a bedwetting clinical trial where the parent needs to do measurements in the pant area will be higher than for older children, who may not want the parent in the room when they remove their pant.

2. Traditionally children are not considered for treatment of bedwetting until age 7. Over the age of 7 the child is usually treated with drug therapy to reduce urine production at night.

3. The S7 and S8 NJ EU pants have the same design, with S8 having a more absorbent capacity and a bigger fit.

[redacted]



5. Younger children are more likely to wait for a parent to assist with dressing and will therefore wear the wet pant longer than an older child, who is more likely to remove the pant themselves. Younger children also have a higher risk of feces on the skin (which is an irritant for the skin) as they are not well-practiced in wiping themselves clean after visiting the toilet. Therefore, the S7 group has more risk of developing rash from wet pants than the S8 group, because their skin is wet longer and any feces resting on the skin can result in compromised skin and rash in the pant area.

Our focus will be on children with monosymptomatic enuresis i.e., enuresis in children without any other lower urinary tract symptoms (e.g., increased frequency, daytime incontinence, urgency, genital, or lower urinary tract pain) and without a history of bladder dysfunction.

This clinical trial will accept children with both primary and secondary enuresis. Primary enuresis means the child has never had a dry period at night. Secondary enuresis means the child developed nocturnal enuresis after being dry for a period of at least six months.

This clinical trial will be a 6-week, in-home clinical trial to understand the safety, performance, and impact on skin of the NJ EU pant compared to the child's currently used absorbent pant or diaper product.

References:

1. CER-Adult Incontinence Devices- MDR 2017 745_Updated
2. Post Market Safety Surveillance report
3. /https://www.brollysheets.co.uk/blogs/night-training/bed-wetting-statistics-how-common-is-it
4. Kids Health Information: Bedwetting (rch.org.au)

2. Objectives

The primary objective of this clinical trial is to confirm the in-use tolerability of the Ninjama EU overnight pant product, in the target population of bedwetters aged 4-7 years, based on a body of evidence from clinical assessments of skin, adverse events and parent/child perception data. This data will be part of the clinical evidence in the Clinical Evaluation Report needed to market this product as a Class 1 Medical Device in the EU, confirming that the product is safe to use and performs within its intended purpose.

The secondary objective is to understand the clinical benefit of the NJ EU overnight pant product in a bedwetting population aged 4-7 years, based on [redacted] waking up in a dry bed, via collecting H&P and parent/child perception data in diaries and end-of-use questionnaires.

[redacted]

3. Investigational Plan

3.1 Clinical Trial Design

This will be a single center, single blinded (sponsor's team will be blinded to the product codes), randomized, cross-over, IRB-Approved, in-home clinical test design over 6 weeks, with two usage periods of 3 weeks each. During one period the child will maintain usage of their usual absorbent night pant/diaper and during the other usage period they will use the NJ EU absorbent pant. We will track habits and practices that may impact skin health and product performance as well as medication use and Adverse Events/ Adverse Device Effects (AEs /ADEs). Children will be asked to wear either their own pants or the test pants exclusively at night and parent/legal guardian will be asked to collect data in the evening before bed and in the mornings after getting up.

Parent/Legal Guardian will be trained to execute the measurements on their own child for the following reasons:

1. Children this age are usually told not to let strangers touch them in the genital and buttock area, so we want to avoid telling kids it is OK in this case. We will ensure that the child is comfortable to participate in this clinical trial and can at any time end their participation in this clinical trial should they feel uncomfortable.

2. Due to COVID restrictions, clinical trial personnel should minimize close contact with panelists as much as possible, especially with children under 5 years of age, who cannot be vaccinated. We will therefore ask the trained parent/legal guardian to do the measurements on his/her own child/ren. Children can stop the study procedures at any time if/when they feel uncomfortable.

This clinical trial is designed to track the following:

- general safety (AEs and ADEs),
- [redacted]
- assess fit and performance of the overnight pant products (fit images, leaks, [redacted])

[redacted]

The following table shows which endpoints will be measured at which time and where on the child:

Endpoint	When Measured	Where Measured
Leaking & Pant Fit	Before pant removal	Waist front and back, crotch area, leg cuffs
Child skin irritation [redacted] perception	Directly before removing pant	Entire pant area
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
AE, ADE, [redacted]	Observed all the time and reported twice a day	Observe child and pant

- [redacted]Leaking and Pant Fit: Mobile phone images of the pant on the child will be collected by the parent/legal guardian at home [redacted]

- Child Perception: Child will be asked simple yes/ no questions to determine if they feel irritation [redacted]. If yes, the parent/legal guardian will ask the child to point to location where they feel the irritation [redacted].

- [redacted].

- [redacted].

Up to 30 children (approximate split of 15 males and 15 females) who meet inclusion/exclusion criteria will be enrolled in the clinical trial. S7 children will be enrolled in this clinical trial because nocturnal enuresis is most prevalent in children aged 4-7 and the pant design for S7 and S8 products are similar. Therefore, the data generated for the S7 population can be used to support the S8 population. Children for this clinical trial will be enrolled by North Cliff Consultants in Cincinnati, USA. Eligible subjects will be bedwetters who have wet the bed at least once a week or more over the past 3 months. The children should be accustomed to wearing an absorbent pant product overnight. They will be asked to use their own overnight pant every night for 3 weeks of the clinical trial and will be asked to use the NJ EU test pant every night for the other 3 weeks of the clinical trial. The order of the NJ EU product and own product will be randomized. Parents will

be asked to refrain from using wet wipes to clean the child's skin for the duration of the clinical trial (no test wipes will be provided).
If a subject drops out of the clinical trial, they will not be replaced, due to the short duration of the clinical trial.

Once qualified, parent/legal guardian will be asked to pick up the equipment [redacted] from North Cliff Consultants. They will receive training on how to handle the equipment and how to complete the questionnaires. Parent/legal guardian will be required to begin with the clinical trial after the training session. They will be given 2 days to practice [redacted] before data is officially collected for the clinical trial.

Parent/legal guardian will be instructed to complete a digital questionnaire twice daily (once in the morning before removing the used pant and once in the evening when applying the fresh pant) [redacted]. This will include taking four photos of the child wearing the pant (front, back and both hips) [redacted]. It includes capturing adverse events and compliance questions. Subjects will also be asked to complete a H&P questionnaire at the clinical trial start and at the end of each 3-week period and they will also be asked to complete an after-use questionnaire.

This clinical trial will be submitted for IRB/ethics review.

3.2 Clinical Trial Procedures

3.2.1 Visit 1 – Enrollment and Training (on Site)

1. On the day of their appointment, a parent/legal guardian will be asked to come to the clinical site together with their participating child.

2. Parent/legal guardian will be instructed to read the Informed Consent document but not sign until they meet with clinical personnel. They will be given the opportunity to have any questions answered. They will be asked to sign two copies of the Informed Consent in the presence of clinical personnel. After verification of a legible signature, the parent/legal guardian will be instructed to keep one signed copy of the Informed Consent. The clinical site will keep the other copy.

3. Parent/legal guardian will be asked for demographic information and inclusion/ exclusion criteria to determine if their child is eligible to participate in the clinical trial. Children will be weighed on a bathroom scale and have their body length, waist circumference (lying down and standing), thigh circumference and hip circumference measured by the parent under the supervision of a clinical staff member. The participating child must be present, so clinical personnel can verify the age, weight, Fitzpatrick scale and general health of the child. The child will also be asked to try on one of the overnight test pants to ensure proper fit. If eligible, parent/legal guardian will be asked about the typical habits and practices of their child [redacted].

4. The subjects will be asked to bring along a packet of their currently used overnight pant product so the test site can verify that this product brand qualifies as one of the allowed "own product brands" (current marketed disposable or reusable absorbent overnight pants/diapers or training pants/diapers). The brand name and lot code of this product will be documented.

5. Subjects will be randomized to use either their current product, or, be distributed the NJ EU product, for the first 3-week test period of the study. If randomized to start with the NJ EU product, they will be asked to return any unused product at the end of the 3 weeks. If randomized to start with their own product, they will be instructed to use this brand exclusively for the 3-week test period. They will not be allowed to switch brands during this period.

6. Subjects will be instructed to use an overnight pant every night for the duration of the study.

7. The use of skin products like lotions, oils, powders, creams, sunscreens, wet wipes and moisturizing bubble baths will not be allowed to be used in the pant area and thighs, unless needed for medical reasons. Use of these skin preparations will be captured in the daily questionnaire [redacted].

8. After enrollment, parent/legal guardian will receive the following items:

[redacted]

- [redacted]
- Two coin-cell batteries as back-up
- [redacted])
- Kitchen scale (balance) with USB charging cable
- [redacted]
- Measuring tape
- [redacted]
- Written subject instructions

9. Parent/ legal guardian will participate in a training session on the following:

a. Review of [redacted] questionnaire
b. How to take photos using mobile phone [redacted]
c. How to assess rash, imprints/marks on the skin
d. [redacted])
e. [redacted]
f. [redacted]
g. [redacted]
h. How to weigh the pant

10. [redacted]

11. Parent/legal guardian will be asked to begin completing the questionnaire (2x/day) for 45 days. The first 2 days will be considered practice days and data from day 1 and 2 will be considered non-evaluable.

3.2.2 During the 6-Week at Home Clinical Trial

1. Parent/legal guardian will be asked to complete the questionnaire 2x daily for 45 days.
   - Once in the evening when applying the fresh night pant
   - Once in the morning when removing the used pant

2. In the evenings they will be asked to apply a fresh pant and wait ~15 minutes, before doing images, [redacted] and skin assessments. In the mornings, they will be asked to take the images before they remove the pant and then remove the pant to do skin assessments. [redacted].

3. [redacted] the questionnaire has several questions to check compliance and ADEs and AEs throughout the clinical trial [redacted].

4. Parent/ legal guardian will be asked to [redacted] assess skin [redacted] rash, [redacted], enter pant wear time and weight, assess leaking, and take images of the pant fit on the child in standing position. If the overnight pant did leak, they will be asked to take an image of the wet stain on the pajama pant in the crotch area as well as front, back or sides in a standing position, so we can see the location and size of the leak.

5. [redacted].

6. [redacted].

7. [redacted].

8. The parent/legal guardian will be called via phone or video chat after the 2 practice days to provide feedback after monitoring their data. Throughout the

clinical trial the submitted data will be monitored and subjects will be contacted at least once per week (either during planned study visits or remote phone/video calls) so the study site can give feedback, check on progress, track lot codes of new purchased products and answer questions throughout the clinical trial.

[redacted]

9. The following topics will be assessed by the site or sponsor based on the [redacted] responses and will be discussed during the weekly phone calls:

    1. Resolution/Tracking of any AEs or ADEs
    2. Resolution/Tracking of Medication Use
    3. Feedback on data quality and study progress
    4. Compliance (reasons for missed questionnaires or study instructions not being followed)
    5. [redacted]
    6. Track lot codes of new purchased own products
    7. Answer questions the subjects may have

3.2.3. Visit 2 – Return / Pick-up of Test Products After 3 Weeks (on Site)

1. Parent/legal guardian will be asked to return to the test site to either return the unused test product or to pick up the test product for the final 3 weeks of the clinical trial, depending on their randomization.

2. [redacted]

3. [redacted].

4. Parent/legal guardian will be instructed on use of the test product or own product for the next 3 weeks.

5. Parent/legal guardian will be asked to complete [redacted] an after-product use feedback questionnaire after the first 3 weeks of the trial. Part of the questions is to be completed by the parent/legal guardian and part of the questions is to be completed by the child with the help of the parent/legal guardian.

3.2.4. Visit 3 – Return of Study Supplies and Close Out Visit

1. Parent/legal guardian will be asked to return to the test site for the final visit.

2. The following will be resolved and recorded by clinical personnel:

    1. Subject Accountability
    2. Resolution/Tracking of any ADEs and AEs

3. Resolution/Tracking of any Medications Used
   Document lot codes of any new purchased own products
4. Return of instruments (balance, [redacted])
5. Return of unused test pants (if applicable)

3. Parent/legal guardian will be asked to complete [redacted] an after-product use feedback questionnaire after the last 3 weeks of the trial. Part of the questions is to be completed by the parent/legal guardian and part of the questions is to be completed by the child with the help of the parent/legal guardian.

4. Subjects will be released from clinical trial and be allowed to go back to their normal habits.

5. Compensation details will be provided to parent/legal guardian. Payment will occur after all equipment is returned and verified by clinical personnel. Any damaged equipment should be returned to the site for safe disposal. Subjects will not be charged for equipment that was unintentionally broken or lost. At the completion of this visit, the subject will have completed the clinical trial.

3.2.5. Clinical Trial Schedule of Events

Procedure	**Visit 1:** Enrollment and Training	**Visit 2:** Product pick up and instrument check (3 weeks after visit 1)	**AT HOME:** Clinical Trial Mode Days 1 – 45	**Weekly Phone Calls** (after 2 days and then weekly, if no study visits planned for that week)	**Visit 3:** Final Visit
Informed Consent	X				
Demographics	X				
Inclusion/Exclusin	X				
Anthropometry	X				
Subject Instructions (training session)	X				
H&P Questionnaire [redacted]	X				
Randomization	X				
Product Distribution (per randomization)	X	X			
Compliance/ AE Resolution		X	X	X	X
Twice Daily Questionnaire [redacted] (photos and measurements)			X		
[redacted]		X			X
Subject Accountability					X

3.3. Selection of Clinical Trial Population

North Cliff Consultants will recruit children meeting the inclusion/exclusion criteria from their Cincinnati database.

3.3.1 Inclusion Criteria

Inclusion and Exclusion criteria will be assessed at the Enrollment visit in an individual conversation with parent/legal guardian (with child present).

Subjects are eligible for enrollment if the parent/legal guardian responds positively ("Yes") to the following questions:

INCL01: Have you read and understood the Informed Consent document?

INCL02: Is your child generally healthy? [excluding acute conditions such as flu/cold symptoms, diarrhea, fever, ear infection, etc.]

INCL03: Is your child 4-7 years of age?

INCL04: Does your child weigh approximately 37–63 pounds and fit into the test pant [Clinical trial personal to confirm fit]?

INCL05: Thinking of the past 3 months, does your child wet the bed at night at least once per week?

INCL06: Is your child currently using overnight pants or diapers?

INCL07: Is your child willing to use their usual and/or supplied overnight pant products every night for the duration of the study?

INCL08: Are you and your child willing to refrain from using wet wipes in the pant area for the duration of the clinical trial?

I**NCL09**: Are you willing to refrain from enrolling your child in other clinical or consumer studies for the duration of this clinical trial?

INCL10: Are you and your child willing to refrain from using lotions, creams, ointments, oils, moisturizing bubble baths, powders, sunscreen and/or skin preparations in the child's pant area and on thighs for the duration of this clinical trial, unless required for medical reasons?

I**NCL11**: Are you and your child willing and able to comply with all study instructions?

INCL12: Do you have an iPhone 7 (or higher) with iOS 13.0 operating system (or higher) or do you have an Android smartphone with operating system Android 9 (or higher) installed?

INCL13: [redacted]

INCL14: Are you able to fill in the required questionnaires in English?

INCL15: Are you willing to complete the [redacted] questionnaires twice daily for 6 weeks, once in the morning when removing the pant and once more in the evening when applying the pant?

3.3.2 Exclusion Criteria

Subjects are <u>ineligible</u> for enrollment if the parent/legal guardian responds positively ("Yes") to any of the following questions:

EXCL01: Does your child have any acute or chronic skin conditions (excluding skin rash) in or around the pant area?

EXCL02: Does your child currently have (or have a history of) any significant illness or chronic medical condition (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results, for example medications to treat nocturnal enuresis,antibiotics, antihistamines, anti-inflammatory medications, corticosteroids, mediations to treat yeast infection or similar)?

EXCL03: Is your child currently using any medications? (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results)?

EXCL04: Does your child currently wear absorbent products during the day?

EXCL05: Does your child suffer from any other lower urinary tract symptoms (e.g., increased frequency, daytime incontinence, urgency, genital, or lower urinary tract pain) or a history of bladder dysfunction?

3.3.3 Compliance and Habits & Practice Questions

The following questions will be asked twice daily (am/pm) [redacted]:

1. Did your child experience any of the following health conditions since you last completed the questionnaire: diarrhea, fever, other illness, injury, or none of the above?
2. Has your child taken, or did you apply any of the following since you last completed the questionnaire: vaccination, medication, or none of the above?
3. Did your child bathe since you last completed the questionnaire?
4. Did your child swim since you last completed the questionnaire?
5. Did you or your child use cosmetics in the pant area since you last completed the questionnaire (lotion, oil, cream, powders, sunscreen, moisturizing bath additives, wet wipes, etc.)?
6. Which pants did you use since you last completed the questionnaire?

3.3.4 Data Measurement Collection

The following information will be collected twice daily (am/pm) [redacted]:

1. Leaks (If yes, parent/legal guardian will be asked to take an image of the wet stain on the pant and send the image to the site) [redacted]
2. [redacted]
3. [redacted]
4. [redacted]
5. Photos of pant on child [left hip, right hip, front, back] [redacted]
6. Parent/child assessment of rash [hips, genital, buttock, perianal] [redacted]
7. [redacted]
8. Pant weight (loaded pant mornings / fresh pant evenings)
9. Hours of pant wear
10. Pant contents [urine, both urine & BM, parent removed solid BM, nothing]
11. Number of pants used since last questionnaire
12. Observations during pant removal: [redacted]

3.4 Subject Identification

The 4-digit unique panelist number in addition to their 3-letter code will identify subjects throughout the clinical trial. Boy subjects start with 1001 and girl subjects start with 2001. Each panelist will also get a 3-letter code to help identify them in case they accidentally enter a wrong subject number.

3.5 Subject Accountability

A Subject Accountability form will be completed at visit 3 for all subjects enrolled into the clinical trial.

3.5.1 Removal of Subjects from the Clinical Trial

Participation in this clinical trial is completely voluntary. After admission to the clinical trial, the subject may withdraw at any time for any reason and will be asked to report such reason fairly and accurately. The Principal Investigator or clinical trial representative may elect to discontinue a subject's participation at any time if they deem it necessary or if it is in the subject's best interest. Reasons for subject withdrawal or discontinuation will be documented in Subject Accountability.

3.5.2 Replacement of Subjects

If a subject drops out of the clinical trial, they will not be replaced, due to the short duration of the clinical trial.

3.6 Products

All participants will be asked to use either their current night pant product or the NJ EU pant product during the clinical trial (order based upon randomization).

Test product: Ninjama S7 [redacted] product produced in Targowek plant in Poland [redacted]

Own product: Any disposable overnight pant/diaper, disposable training pant/diaper or reusable cotton pant/diaper available on the market for children age 4-7. Parent/legal guardian will purchase and use their own overnight pant as agreed upon in the enrollment visit. They will be asked not to switch brands during the 3 weeks they use their own product. Lot codes of own product will be documented.

3.7 Assessment and Collection Details

3.7.1 Skin Rash [redacted] Grading [redacted]

The parent/legal guardian will use the following multi-level grading scale to assess rash [redacted] in the following regions of the pant area: hips, genital area, buttock area, perianal area (only rash grading):

- None
- Mild
- Moderate
- Severe

3.7.2 [redacted]

3.7.3 [redacted]

[redacted]

3.7.4 Pant Weight/Wear Time [redacted]

Pant weight will be measured on a kitchen scale after pant removal. Pant wear time will be recorded in the mornings. Both measurements will be recorded [redacted].

3.7.5 [redacted]

[redacted]

3.7.6 Photos [redacted]

Photo images will be taken by parent/legal guardian to collect images of the pant fit [redacted]

Parent/legal guardian will also be asked to take an image of wet stains in the pajama pant, so we can determine where the leak happened and how big the stain was. Images should be taken of the pant on the child in the crotch area, front, back or sides, depending on where the stain is.

Photos will be stored without personally identifiable information and in such a manner as to restrict access through password protection. [redacted]

Images will be assessed by an expert grader to look for potential incorrect use of the product (e.g., worn the wrong way)[redacted].

3.7.7 Twice Daily Questionnaire [redacted]

Parent/legal guardian will be asked questions twice daily (once in the morning when removing the night pant and once in the evening when applying the fresh night pant) regarding [redacted] their perception of skin rash[redacted]. They will be asked to take photos, [redacted] and answer questions about the child's H&P and overall health. [redacted]

3.7.8 Skin Irritation Perception

Child will be asked their perception of skin irritation by picking one of the following options. If they pick an option, they will be asked where they feel the irritation.

- Nothing
- Skin is burning/stinging
- Skin is itching/tingling
- Skin is feeling warm/hot

4. Statistical Methods

4.1 Statistical Analysis

All statistical analyses will be the responsibility of the Sponsor. A separate statistical analysis plan is in Attachment B.

4.2 Determination of Sample Size

This data will be used to bridge to a wealth of existing P&G Baby and FemCare AI clinical trial data, therefore sample size was based on practical limitation, not on statistical considerations.

5. Risk Assessment- See Attachment A

6. Conduct of the Clinical Trial

6.1 Protocol Amendment(s)

No amendments to the protocol will be permitted without approval from both the Sponsor and Principal Investigator and where applicable, the Ethics Commission. Such changes and the reasons for those changes will be documented in writing and signed by the Principal Investigator if required. Approval by the Ethics Commission (if applicable) must be obtained prior to initiation of the amendment.

The Principal Investigator, the project manager or their designee will communicate any deviations from the protocol to the Sponsor as soon as possible. The Principal Investigator is responsible for documenting any deviation in the clinical trial file and in the final report.

7. Obligation of the Investigator

This clinical trial will be conducted in accordance with the applicable ISO 14155 Clinical Investigation of Medical Devices for Human subjects – Good Clinical Practices (GCPs) and GCPs according to the International Conference on Harmonization (ICH). The Principal Investigator will perform or directly supervise the performance of all the services described herein, or incidental to those described herein, in accordance with the highest standards of medical and clinical research practice. Delegation of any clinical trial responsibility will be documented in writing. The Investigator will also be required to submit a report documenting clinical trial execution.

7.1 Adherence to Protocol

The Investigator will have responsibility for all aspects of the clinical trial, including but not limited to ensuring the signed/approved protocol is followed exactly.

Any deviations from this protocol will be discussed with the Sponsor and appropriately documented. No modifications of the protocol will be permitted without the approval from the Sponsor and the Investigator. Such changes must be documented in writing as soon as possible.

7.2 Advertising

If an Investigator chooses to advertise for subjects, whether in professional or consumer publications, radio, television, or any other means, all advertising must be approved by the Sponsor prior to initiation.

7.3 Subject Consent

Each subject's parent/legal guardian must sign and date an Informed Consent to allow their child to participate in the clinical trial. Each parent/legal guardian will be given the opportunity to have his/her questions answered to their satisfaction. Without this signed document, a child will be ineligible to participate in this clinical trial.

This consent form will comply with all applicable regulations governing the protection of human subjects. The elements of Informed Consent and the documentation of Informed Consent are specified in ICH GCPs chapter 4. A signed copy of the Informed Consent will be kept by the parent/legal guardian of the child and the Investigator will retain a signed copy

Subjects may withdraw from participation in the clinical trial at any time. Additionally, the Investigator may remove subjects from the clinical trial if it is in the best interest of the subjects. The reason for all Investigator removals from the clinical trial will be documented.

7.4 Data Collection

The Principal Investigator is responsible for ensuring that data are collected and reported according to the clinical trial protocol.

Data Collection System

A [redacted] will be the primary tool used for data collection. [redacted]

Additionally, the Electronic Case Report Forms (ECRF) data capture system, a database developed through a validated, Electronic Records/Electronic Signatures (ERES)-compliant

platform (21 CFR Part 11) will be utilized to collect data by the site (e.g., Demographics, Inclusion/Exclusion, Anthropometry, Adverse Events, Medications, General Comments, and Subject Accountability).

All protocol specified data included in the clinical trial database will be collected as e-source.

7.4.1 Source Documents

Direct data entry will be used via the [redacted] and ECRF. The electronic records are considered to be source documents.

There will be periodic monitoring of the site on the critical enrollment days and the study conduct via remote data reviews. Data entered by the parents [redacted] will be monitored periodically to check for compliance via remote monitoring.

7.5 Adverse Events or Adverse Device Effects

An Adverse Event (AE) is defined as any unfavorable and unexpected medical occurrence in a subject. An Adverse Device Effect (ADE) is defined as any AE related to the use of the investigational medical device. This definition includes AEs resulting from insufficient or inadequate instructions for use, any malfunction, use error or intentional misuse of the medical device. Each day (following the initial visit), the parent/legal guardian will be asked if there has been any change in the child's health (illness or injury) since the previous visit or the previous time the questionnaire was filled in. Changes in health will be documented as an AE or ADE as appropriate, regardless of the causality relationship with product use. All AEs and ADEs will be followed to resolution.

7.5.1 Adverse Event and Adverse Device Effect Reporting

[redacted] the parent/legal guardian will be asked twice daily about their child's health and medication intake. Based on the information provided, Sponsor and PI will determine if it is appropriate to record as an Adverse Event or Adverse Device Effect and will contact the parent/legal guardian for more information. Such an occurrence does not necessarily have to have a causal relationship with product use. Due to the nature of this clinical trial, skin irritation in the pant area (diaper rash) will not be documented as an Adverse Event or Adverse Device Effect given it is one of the end points of interest for the clinical trial. However, if a skin reaction occurs in the pant area which causes the parent/legal guardian to seek medical attention, outside the normal follow-up given to the child within the clinical trial, this will be documented and followed in the same manner as other Adverse Events or Adverse Device Effects.

The Investigator or designee will review each Adverse Event Report and complete the form based on the following decision charts:

Chart 1: Categories of ADE and AEs

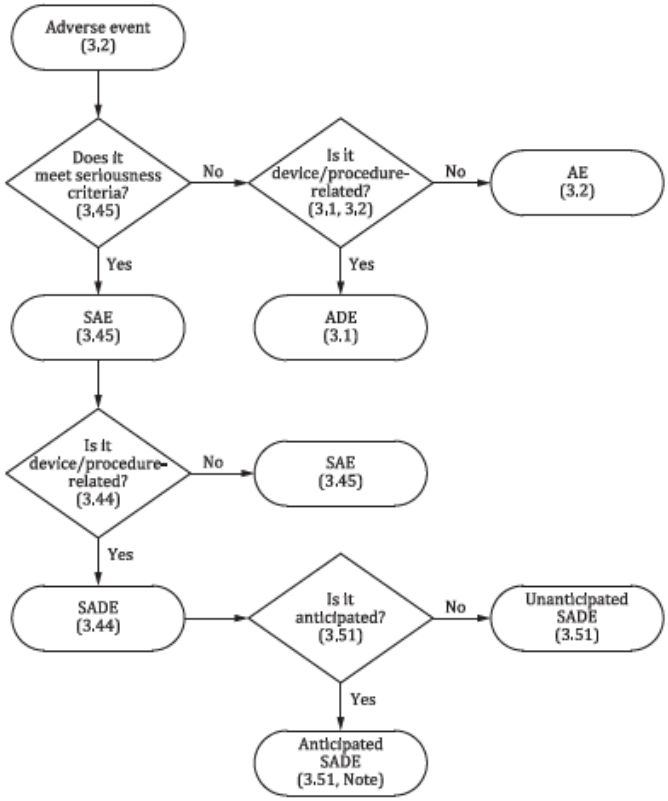
Adverse events	Non-device-related	Device- or investigational procedure-related	
Non-serious	Adverse event (AE)[a] (3.2)	Adverse device effect (ADE)[c] (3.1)	
Serious	Serious adverse event (SAE)[b] (3.45)	Serious adverse device effect (SADE) (3.44)	
		Anticipated	**Unanticipated**
		Anticipated serious adverse device effect (ASADE)[c] (3.1, Note 1 to entry)	Unanticipated serious adverse device effect (USADE) (3.51)

[a] Includes all categories.

[b] Includes all categories that are serious.

[c] Includes all categories that are related to the device or the investigational procedure.

Chart 2: AE categorization flow chart



The Investigator or designee will review each Adverse Event Report and complete the form based on the following definitions:

Severity:

- Mild - normal activities unaltered, AE or ADE is annoying, but tolerable
- Moderate - normal activities altered or AE or ADE requires intervention
- Severe - unable to undertake normal activities or is incapacitated

Investigator's Opinion of Causality:

- Not Related - there is no medical evidence to suggest that the AE or ADE may be related to product usage
- Doubtful – there is no medical evidence to suggest that the AE or ADE may be related to product usage, or there is another more probable medical explanation

- Possible - there is possible evidence to suggest that the AE or ADE could possibly be related to product usage
- Probable - there is probable evidence to suggest that the AE or ADE is probably related to product usage

Action Taken by Investigator:

- None - no change in product usage
- Reduced/Interrupted - product usage reduced or temporarily interrupted
- Discontinued - product usage discontinued.

Note: Actions taken by parent/guardian may be documented in General Comments.

The Investigator will decide on a case-by-case basis as to whether any subject should be dropped from the clinical trial. If the Investigator(s) or subject decides to discontinue clinical trial participation, this should be documented and filed with the Sponsor within 72 hours. All adverse events and adverse device effects will be followed until resolution or until the Investigator deems it safe to discharge the subject.

7.5.2 Serious or Unexpected Adverse Events or Adverse Device Effects Reporting

A Serious Adverse Event (SAE) or Serious Adverse Device Effect (SADE) is defined as any unexpected medical occurrence that at any exposure:

1. Results in death
2. Is life-threatening
3. Requires in-patient hospitalization or prolongation of existing hospitalization
4. Results in persistent or significant disability/incapacity
5. Results in a congenital anomaly/birth defect
6. Requires medical or surgical intervention (devices)
7. Is medically significant

All SAEs and SADEs will be recorded on the written and/or electronic SAE or SADE form and tracked in this clinical trial.

The Investigator/Designee must contact the Sponsor within 24 hours to discuss potentially serious or unexpected AEs. During normal business hours: [redacted]

7.6 Device Deficiency Reporting

Device deficiency is defined as the inadequacy of a medical device with respect to its identity, quality, durability, reliability, suability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. In this clinical trial we will document any product or material defects, potential wrong application (via pant fit images), leaking/failure of overnight absorbent pants and all AEs /ADEs.

All device deficiencies of the investigational products will be documented throughout the clinical trial and managed by the sponsor in accordance with written procedures for the control of a non-conforming product. The sponsor shall take, where applicable, and appropriate, and corrective actions to protect the safety of subjects, users, and other persons. Device deficiencies of the comparator, if applicable, shall be documented.

Device deficiencies that did not lead to an adverse event, but could have led to a serious adverse device effect:

1. if either suitable action had not been taken
2. if intervention had not been made, or
3. if circumstances had been less fortunate

shall be reported to the sponsor, who will prepare the needed Clinical Evaluation Report documentation and report the potential risk to the EC/IRB and national authorities as applicable. The sponsor will decide whether the risk analysis needs to be updated and assess whether preventative or corrective action is required.

7.7 Investigator's Final Report

The Investigator will provide a Final Report within approximately 30 days from the completion of the in-life phase of the clinical trial. The report will consist of a description of the conduct of the clinical trial including subject enrollment, subject demographics, protocol deviations, subject dropouts, and a discussion of AEs. Data analyses or data interpretation, if any, may be included in a separate document.

7.8 Records Retention

The Investigator(s) must retain the subject identification codes, Informed Consent documentation, CRFs, medical records, and other source data for a minimum of 2 years after clinical trial completion. The Investigator(s) must receive written authorization from the Sponsor before destroying any clinical trial document.

The Investigator(s) will make the records available for inspection and copying upon the request of an authorized employee of a government authority or the Sponsor, at reasonable times.

In the event the Investigator(s) retires, relocates, or for any other reason withdraws from the responsibility for maintaining records for the period of time required, custody of the records may be transferred to another person who will accept responsibility for the records. Notice of such a transfer must be given in writing to the Sponsor.

The sponsor will maintain clinical records according to P&G Records Management Guidelines.

7.9 Publications

All data collected during this clinical trial is the sole responsibility of the Sponsor. No publication by the site or any of the non-employees of the sponsor is allowed from the results of this clinical trial. The Sponsor reserves the right to withhold consent for publications due to the confidential nature of the data. Subjects will be identified only by the assigned four-digit code and no identifiable personal information will be included.

8. Sponsor Clinical Trial Management

8.1 Data Quality Assurance

The following steps will be taken to ensure the accuracy, consistency, completeness, and reliability of the data:

- Source/CRF review,

- Data management quality control checks, and
- Statistical quality control checks.

In addition, a representative from the Sponsor may conduct periodic audits of clinical trial processes, including, but not limited to, a review of the Investigator's Trial Master File (TMF), Standard Operating Procedures (SOPs) pertaining to the clinical trial, and training records of staff involved.

8.1.1 Monitoring

Prior to the commencement of the clinical trial, an initiation meeting will be held with the appropriate clinical trial site personnel to review the objectives and procedures of the clinical trial and any other training needs associated with the clinical trial and protocol execution.

This clinical trial will be monitored by Sponsor representatives at all stages of conduct from inception to conclusion in accordance with and ICH GCPs chapter 5.

8.2 Clinical Trial Termination

The clinical trial will be terminated upon completion of all subject treatments and evaluation. The Sponsor may discontinue the clinical trial at any time. In any case where this happens, the Principal Investigator and/or designee will return all clinical trial supplies, and equipment to the Sponsor. In addition, all data which has been collected up to that point will be turned over to the Sponsor at that time.

8.3 Sponsor's Final Report

A final report will be prepared by the Sponsor at the conclusion of this clinical trial. The Sponsor's final clinical trial report will summarize the method, data, and conclusions. Source data may be retained by the testing facility. The original source data will be maintained according to the Principal Investigator's standard operating procedure. A copy of the source documents may be obtained upon request of the clinical trial Sponsor.

Attachment A

Risk Assessment

Product Safety

No safety issues are anticipated with this clinical trial as outlined. Children participating in this clinical trial are using marketed products or products that are close to being marketed. From products purchased on the market, we can assume that they have been tested and evaluated for their safety in daily use. Children will be asked to use these products as intended.

For the NJ EU test products, a full risk assessment according to the ISO 14971 standard is being conducted and will be summarized in a separate document before the start of the clinical trial.

The P&G company has a 20+ year history of baby diaper clinical data (0-36 months) to show that our diaper and pant technology is safe to use and effective for managing urine gushes in a baby and toddler population. The P&G company also has adult (18+ years) female incontinence products in the EU market, including absorbent heavy incontinence pants, that are classified as Class 1 Medical Devices, which were demonstrated to be safe to use and effectively manages urine gushes of adults as seen in the statement of compliance from the CER report dated Feb 2020 [1]. [redacted] P&G markets a training pant (BabyDry Pants S7) in the EU. Based on the Post Market Safety Surveillance data of similar products in the EU und US market (BabyDry Pants, FemCare AI Pants, [redacted]), we have reason to believe that the NJ EU product will have no safety related issues when used as an overnight pant for children aged 4-12 years, based on skin and health related AEs. [2]

Based on our current knowledge about this product and similar marketed products, we conclude the following statement, which will be updated based on the outcome of this clinical trial:

> *Statement of Compliance for Children's Nocturnal Enuresis Devices*
> *It is understood that similarity between intended use and indications for use exists between the Procter & Gamble Children's Nocturnal Enuresis Devices and competitor products. Such devices serve as morphotypes. Procter & Gamble Children's Nocturnal Enuresis Devices when used under the conditions and for the purposes intended, will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable other persons. The benefit of* Procter & Gamble *Children's Nocturnal Enuresis* Devices outweighs the risks associated with the product.
>
> *Clinical risk identified in risk management has been adequately addressed for use in this clinical trial. This risk associated with the product is very minimal compared to the benefits of the product. Clinical investigation performed on similar Procter & Gamble* [redacted] *pants identified no serious adverse events and no withdrawals due to adverse events. Procter and Gamble* [redacted] *pants were well tolerated by the subjects with no product-related adverse events.*
>
> *Procter & Gamble Children's Nocturnal Enuresis Devices are very simple devices and easy to use. No specific training is required to use this product. There is full consistency between current knowledge/ the state of the art, the available clinical data, the information materials supplied by the manufacturer, and the risk management documentation for Procter & Gamble Adult Children's Nocturnal Enuresis Devices.*

As with any absorbent pant or diaper, it is possible in exceptional cases that these products may cause skin reactions like redness, blisters, or sores. These skin reactions are usually temporary and usually need no medical treatment, nor are they dangerous to the health. The risk of allergies cannot be totally excluded but can be considered very unlikely for these products. For subjects in this clinical trial, we do not expect any further risks apart from potential skin reactions (like redness). In case your child has some skin reactions (redness, swelling or blisters) during this test that concerns you, please contact the clinical trial personnel.

Study Safety:

For the twice daily questionnaire, the parent/legal guardian will be asked to touch the child's skin in the pant area. Parent/legal guardian will be instructed to wash their hands before and after for hygienic reasons.

[redacted]

Parent/legal guardian will be asked to use a pH meter to measure skin pH and a gpskin device to measure skin hydration. The pH meter is made of glass and can break. Parent/legal guardian will be asked to take precautions when using the instrument to avoid the risk of glass breakage and not to use a broken device.

Parent/legal guardian will receive training on how to use these measuring devices correctly. They will be asked to ensure all instruments are switched off when not in use. These devices are not toys and should only be handled by an adult. Parent/legal guardian will be reminded to keep these devices out of the reach of children and pets. In addition, the associated chemicals (storage solution and buffer solutions) should be kept in a safe place. These solutions are not dangerous when swallowed.

In case the instruments get contaminated or dirty, parent should wipe with a provided alcohol wipe. They should not immerse any devices in water or rinse under running water. Parent/legal guardian will be instructed to disinfect all devices after use with an alcohol wipe to prevent bacterial growth.

Attachment B

Statistical Analysis Plan

Study Populations

The Intent-to-treat (ITT) population is defined as all subjects who experienced the application of the assigned study product. The Per Protocol (PP) population includes subjects in the ITT population who have no serious inclusion/exclusion violations, no serious continuance criteria violations, no serious concomitant medication violations, and high study product compliance. The ITT population will be used for the safety analysis. Analyses of the Per Protocol population will be done to better understand the data.

Prior to the statistical analysis, all data will be checked for accuracy, completeness, and compliance to the study protocol. Subject evaluations will be checked for compliance to the study protocol regimen and subjects will be assessed for compliance to the protocol inclusion/exclusion criteria. Additionally, investigator comments will be assessed for extraneous factors that could affect the usefulness of the subject's data. Non-evaluable observations and the rationale, along with the method for handling the observations will be documented by the sponsor prior to analysis of the data.

Period and carryover effects will be evaluated for potential influence on the results. Means will be plotted by periods to understand these effects.

Summary descriptive statistics will be provided for all parameters. Ninety-five percent confidence intervals (CIs) will be constructed for all clinical assessments for each treatment code. Any data reported as 'unable to evaluate' will be treated as missing and excluded from the analysis.

The methods used for the analysis will include but not be limited to a variety of parametric and non-parametric statistical methods based on the distribution/characterization of the data.

The following endpoints will be investigated.

General Safety:

1. ADE (adverse device effect) and AE (adverse event) tracking twice daily via a safety in-use diary. We will list a summary of the product related ADE and AEs for both treatment periods and the PI, Sub-PI, Statistician and Clinical Scientist will make a recommendation whether the product safety of Ninjamas is comparable to current product based on the medical and clinical evidence of the reported AE and ADE data.

Product Fit and Performance:

2. Product performance in terms of urine leaking (yes/no). We will calculate the percentage of leaks from loaded pants only. When comparing both products, Ninjama EU option should not be [redacted] worse than current product).

3. [redacted].

4. Pant fit images will be investigated by an expert grader to identify any application errors (e.g., applied wrong way) [redacted]

[redacted]

5. Images of the wet stain on the overnight pajama pant will help identify the size of the stain and where the pant was leaking. This will be compared with the pant fit images.

Skin Health

6. Parental skin rash perception (none/mild/moderate/severe). We will calculate the cumulative number of [redacted] scores [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

10. Skin irritation perception from child (burning/itching/ stinging/tingling/feeling of heat). We will calculate the cumulative number of skin irritation scores [redacted]

[redacted]

[redacted]

[redacted]

Protocol Amendment I

CSD2021096/ NCCI #12-2103

OVERNIGHT PANT SAFETY-IN-USE DIARY CLINICAL TRIAL FOR CHILDREN WITH NOCTERNAL ENURESIS

Rationale for amendment:

1. Correction of mistake in exclusion criteria. List of medication examples are mentioned in EXCL 2, but should be listed in EXCL 3.
2. Clarification of blinding of sponsor. Blinding of the sponsor representatives will be very difficult, due to the diary question about what product they used and the photos. Therefore the CTMs and DM cannot be fully blinded when they download the data, but all attempts will be made to blind the statistician and clinical scientist until after the database was locked. Also data for the evaluability meeting will be blinded by coding the options Own product and test product.
3. Include stratification criteria into the protocol.
4. Update the number of subjects enrolled to 32 instead of 30.

Amended Protocol Sections for #1:

3.5.3 Exclusion Criteria

Original Wording:

EXCL02: Does your child currently have (or have a history of) any significant illness or chronic medical condition (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results, f**or example medications to treat nocturnal enuresis,antibiotics, antihistamines, anti-inflammatory medications, corticosteroids, mediations to treat yeast infection or similar**)?

EXCL03: Is your child currently using any medications? (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results)?

Revised Wording:

EXCL02: Does your child currently have (or have a history of) any significant illness or chronic medical condition (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results)?

EXCL03: Is your child currently using any medications? (SITE: that in the opinion of the investigator may negatively impact child's health and/or clinical trial results), f**or example medications to treat nocturnal enuresis, antibiotics, antihistamines, anti-inflammatory medications, corticosteroids, mediations to treat yeast infection or similar**).

Amended Protocol Sections for #2:

3.1 **Clinical Trial Design**

Original Wording:

This will be a single center, single blinded (sponsor's team will be blinded to the product codes), randomized, cross-over, IRB-Approved, in-home clinical test design over 6 weeks, with two usage periods of 3 weeks each.

Revised Wording:

This will be a single center, single blinded (sponsor's statistician and substitute clinical scientist for the evaluability meeting will be blinded to the product codes), randomized, cross-over, IRB-Approved, in-home clinical test design over 6 weeks, with two usage periods of 3 weeks each.

Amended Protocol Sections for #3:

3.1 **Clinical Trial Design**

Original Wording:

The order of the NJ EU product and own product will be randomized.

Revised Wording:

The order of the NJ EU product and own product will be randomized. At the end of visit 1, subjects will be randomized according to the strata as follows: gender (M or F) and age (4-5 or 6-7).

3.2.1 Visit 1 – Enrollment and Training (on Site)

Original Wording:

5. Subjects will be randomized to one of two usage periods, either starting with their own current product or starting with test product.

Revised Wording:

5. Subjects will be randomly assigned to begin with either their own product or the test product per a stratified randomization plan that utilizes randomization strata based on child's sex (male or female) and age group (4-5 years or 6-7 years). Randomization will be done so approximately 50% (n=16) of subjects will begin with their own product and approximately 50% (n=16) of subjects will begin with the test product. Product sequence will be assigned from a computer-generated randomization program provided by the Sponsor. The sequence of numbers used for the randomization will be 3-digit consecutive numbers whose first digit will not be the same as the 4-digit sequence used for subject identification (e.g., 301).

Attachment R: COVID or Weather Impact to Clinical Trial Procedures

3.2.1 **Visit 1A – Enrollment (Virtual for Covid)**

Original Wording:

5. Subjects will be randomized to one of two usage periods, either starting with their own current product or starting with test product.

Revised Wording:

5. Subjects will be randomly assigned to begin with either their own product or the test product per a stratified randomization plan that utilizes randomization strata based on child's sex (male or female) and age group (4-5 years or 6-7 years). Randomization will be done so approximately 50% (n=16) of subjects will begin with their own product and approximately 50% (n=16) of subjects will begin with the test product. Product sequence will be assigned from a computer-generated randomization program provided by the Sponsor. The sequence of numbers used for the randomization will be 3-digit consecutive numbers whose first digit will not be the same as the 4-digit sequence used for subject identification (e.g., 301).

Amended Protocol Sections for #4:

3.1 **Clinical Trial Design**

Original Wording:

Up to 30 children (approximate split of 15 males and 15 females) who meet inclusion/exclusion criteria will be enrolled in the clinical trial.

Revised Wording:

Approximately 32 children (approximate split of 16 males and 16 females) who meet inclusion/exclusion criteria will be enrolled in the clinical trial.

Attachment A : Informed Consent: Procedures

Original Wording:

Approximately 30 children with nocturnal enuresis (bedwetting) at least once per week will participate in this clinical trial.

Revised wording:

Approximately 32 children with nocturnal enuresis (bedwetting) at least once per week will participate in this clinical trial.

I am in agreement with the Amendment as described:

_____

Laura Huesing Wray (Principal Investigator) Date

_____

Dr. Susanna Brink (Clinical Scientist & Sponsor Representative) Date