STATISTICAL ANALYSIS PLAN

BASICC
- PMCF study -

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Version number	Date	Author	Changes compared to the previous version	
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A: Addition, C: Creation, D: Deletion, M: Modification

APPROVAL OF THE STATISTICAL ANALYSIS PLAN

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LIST OF ABBREVIATIONS

AE:	Adverse Event
ANCOVA:	Analysis of covariance
ARSSQ:	Acute Rhinitis Symptoms Severity Questionnaire
ATC:	Anatomical Therapeutic Chemical Classification
AUC:	Area Under the Curve
CI:	Confidence Interval
CRF:	Case Report Form
CRO:	Contract Research Organisation
Dx:	Day x
[E]:	Number of events
FAS:	Full Analysis Set
ICH:	International Conference on Harmonisation
LOCF:	Last Observation Carried Forward
MedDRA:	Medical Dictionary for Regulatory Activities
NSAID:	Non-Steroidal Anti-Inflammatory Drugs
PMCF:	Post-Market Clinical Follow-up
PP:	Per Protocol
PT:	Preferred Term
Q1 / Q3:	First / Third Quartile
QoL:	Quality-of-Life
SAS®:	Statistical Analysis System
SD:	Standard deviation
SOC:	System Organ Class
TEAE:	Treatment-Emergent Adverse Event
Vy:	Visit y
WHO-DRUG:	World Health Organization Drug Dictionary

TABLE OF CONTENTS

1. INTRODUCTION

This statistical analysis plan is based on protocol LPH-2202 – version 1.1, dated on February 2nd, 2023. It defines populations of analysis and the evaluation methods of the principal and secondary criteria.

2. STUDY OBJECTIVES

2.1. Primary objective

The primary objective is to assess the efficacy of **Healsea® Babykids** on the overall health status score of the Acute Rhinitis Symptoms Severity Questionnaire (ARSSQ) in 2-6 years old children during a treatment period of 7 to 10 days as compared to Placebo.

2.2. Secondary objectives

The secondary objectives are:

- To assess the impact of **Healsea® Babykids** on the duration of each infectious rhinitis symptom and on quality of life as compared to Placebo;
- To assess the impact of **Healsea® Babykids** on the intake of conventional common cold medications (antibiotics, antipyretics, mucolytics, decongestants, antitussives, systemic and topical corticosteroids) as compared to Placebo;
- Safety: to assess systemic and local tolerance of **Healsea® Babykids** over the study period.

3. STUDY DESIGN

This is a prospective, interventional, double-blinded, placebo controlled, randomized, national (Bulgaria), multicentre PMCF study.

The study comprises two parts:

- Part 1 (D1-D11): treatment of the acute phase, with **Healsea® Babykids** or with **isotonic nasal spray (Placebo)**, 2 puffs in each nostril 2 times per day with a minimum of 7-day-treatment period (14 intakes of the investigational device) up to 10 days (20 intakes of the investigational device);
- Part 2 (up to D15/D18): follow-up phase.

Investigational plan description (see Figure 1):

- **Visit 1 (V1) – (Day 1): Screening/Inclusion/Randomization**

Information and provision of the information sheet to legal guardians/parents of participants, consent signature, demographic data and medical history, ongoing medication, inclusion/non-inclusion criteria, physical and clinical examination, baseline assessment of the ARSSQ, randomization, diary presentation, treatment dispensation of **Healsea® Babykids** Nasal Spray or **Placebo (Isotonic nasal spray)** (according to randomization list).

- **D1-D8 up to D1-D11 (at home):**

Daily completion of the paper diary (questionnaire, adverse events/incidents and concomitant medications), **Healsea® Babykids / Placebo** nasal spray treatment daily administration.

- **Between D8 and D11 (at home):**

End of **Healsea® Babykids / Placebo** nasal spray treatment.

- **Up to D15/D18 (at home):**

Daily completion of the diary (adverse events/incidents, concomitant medications, ARSSQ if applicable, until the patient feels not sick for two consecutive days).

- **Visit 2 (V2) – (Day 15-18): end of study**

Diary review, reporting of the adverse events/incidents, compliance, ARSSQ completion if "not sick" is not ticked for two consecutive days in the previous days.

The maximal study duration for each patient is 18 days.

	Acute phase		Follow-up phase	
Visit name	Screening/Inclusion	At home	At home	End of study
Visit Number	V1			V2
Days	D1	D1 to D11	D12 to End of study	D15-D18
Informed consent	X			
Eligibility criteria	X			
Demography and Medical history ***	X			
Physical and clinical examination	X			X
Baseline assessment of the Acute Rhinitis Symptoms Severity Questionnaire	X			
Ongoing medication	X			
Randomization	X			
Treatment (Healsea® Babykids or Placebo)	X*	X#		
Subject paper diary (Acute Rhinitis Symptoms Severity Questionnaire**)	———	———	- - - - - -	- - - - - -
Adverse events/incidents and concomitant medication reporting	———	———	———	———
Compliance				X

* Treatment dispensation
** ARSSQ to be completed with the investigator on site at screening and at the end of the study if the patient still has symptoms ("not sick" not ticked for 2 consecutive days in the previous days). After day 8, until complete resolution of symptoms for 2 consecutive days (question 1 of the questionnaire).
# Treatment from D1 to D8 and up to D11.
*** Medical History - Relevant medical history in connection to infectious acute rhinitis, allergic rhinitis, nasal disorders and asthma back to 2 years

Figure 1 : Flow chart of the study

4. SAMPLE SIZE

This is a PMCF study. The primary endpoint is a customized symptom and quality of life questionnaire. An arbitrary cohort of 200 children has been chosen. A cohort of 100 children in the Healsea® Babykids arm and 100 children in the Placebo arm is anticipated to allow to demonstrate the interest of using Healsea® Babykids in the acute infectious rhinitis. Indeed, 100 patients by arm are enough to detect a Cohen's effect size of 0.4 with a power of 80% and a type I error of 5%. Cohen's effect size is defined as the standardized difference between area under the curve (AUC) in groups. According to Cohen's methodology, 0.4 is an intermediate size between a small effect (0.2) and a medium effect (0.5) and is coherent with the expected result. The Placebo arm will be used as the reference group.
The recruitment will be performed using a 1:1 randomization ratio.

5. DEFINITION OF THE ANALYSIS SETS

Enrolled patients: all patients whose parents/legal guardians signed an informed consent.

Included patients: all the enrolled patients who participated in the study.

Randomised patients: all the included patients who were assigned a treatment number.

Safety population: all the randomised patients who used the nasal spray at least once.

Full Analysis Set (FAS): all the patients from the Safety population and with at least one post-baseline efficacy data.

Any patient not satisfying major entry criteria or for whom post randomisation data are not available will be identified by the Validation Committee during the data review, and could be excluded from the FAS in agreement with circumstances exposed in the ICH-E9 §5.2.1.

Per Protocol (PP) Set: Efficacy population based on the FAS without patients with major protocol deviations.

The status of protocol deviations (minor or major) will be validated during the data review meeting.

Safety endpoint will be performed on the Safety Set.

The analyses of primary and secondary endpoints will be performed on the FAS.
The primary and one secondary (modelling of AUC on global ARSSQ score by multivariate ANCOVA) endpoints will also be analysed on the PP set, analyses on the PP set being supportive in superiority trials.

6. STATISTICAL METHODS

6.1. Data processing

The analyses will be computed with SAS Version 9.4 TS Level 1M6 Copyright (c) 2016 by SAS Institute Inc., Cary, NC, USA.

6.2. Description

The number of available data and the number of missing data will be given and the following descriptive statistics will be provided:

- For quantitative parameters: mean, standard deviation, median, Q1, Q3, extreme values (min and max).

  In this case, calculated statistics (mean, standard deviation, median, Q1, Q3) will generally be displayed with one more significant figure than the observed data, unless the described variable necessitates less precision.

- For qualitative parameters: number and percentage of each modality.

  Usually, one decimal digit will be given. A second decimal digit could be provided to improve the display, if required.

6.3. Statistical/Analytical issues

6.3.1. Significance level

All statistical analyses will be performed at the 0.05 global significance level (type I error rate), using two-sided tests.

The statistical results will only allow to conclude on the primary efficacy criterion. All other statistical results have to be considered within a descriptive perspective and not as inferential issues. No adjustment for Type I error will be done. P-values of statistical tests on secondary criteria will be provided for information only.

6.3.2. Interim analysis

No interim analysis will be performed.

6.3.3. Multiplicity

There is only one main efficacy criterion and no comparative testing will be performed, then multiplicity adjustments are not needed.

6.3.4. Multicentre studies and Adjustment for covariates

No adjustment on centre will be performed.

6.3.5. Handling of dropouts and missing data

a) Repositioning of visits

Not applicable.

b) Partially filled scales and missing data (other than ARSSQ and dates)

Concerning dates and ARSSQ, see §6.4.

No imputation will be done. Missing data will not be estimated and will be treated as missing data for the statistical analysis.

c) Dropouts

Patients from FAS who prematurely discontinued the study will be included in the analysis.

Except for ARSSQ and dates, no method will be applied to replace missing data.

6.4. General conventions and/or calculated variables

6.4.1. Patient reference start/end dates

For each patient, the reference dates will be the following:
- The reference start date is the date of inclusion visit.
- The reference end date is the date when patient was determined to have ended the trial.

6.4.2. Computation of a duration

The formula below will be generally used:
- Duration (in days) = Date#2 – Date#1 + 1 day

6.4.3. Missing dates of inclusion visit or end of study

Missing dates of inclusion visit and of end of study will be reviewed by the members of the Validation Committee and extrapolated using all information recorded.

6.4.4. Missing start/end dates of adverse events / incidents

In the following paragraphs, adverse events and incidents will be referred to as "adverse events" for ease of reading.

a) Start date

Completely missing date: it will be estimated by the reference start date.

If the day and the month are missing:
- If the year = year of reference start date, it will be estimated by the reference start date
- If the year < year of reference start date, it will be estimated by the 31st December
- If the year > year of reference start date, it will be estimated by the 1st January

If only the day is missing:
- If the month/year = month/year of reference start date, it will be estimated by the date of reference start date
- If the month/year < month/year of reference start date, it will be estimated by the last day of the month
- If the month/year > month/year of reference start date, it will be estimated by the first day of the month

If after imputation, the estimated start date is after the end date of the adverse event, it will be replaced by the end date of the adverse event.

b) End date

Note: the following rules concern events that are not "ongoing" at the end of the study.

Completely missing date: it will be estimated by the reference end date

If the day and the month are missing:
- If the year = year of reference end date, it will be estimated by the reference end date
- If the year < year of reference end date, it will be estimated by the 31st December
- If the year > year of reference end date, it will be estimated by the 1st January

If only the day is missing:
- If the month/year = month/year of reference end date, it will be estimated by the reference end date
- If the month/year < month/year of reference end date, it will be estimated by the last day of the month
- If the month/year > month/year of reference end date, it will be estimated by the first day of the month

If after imputation, the estimated end date is before the start date of the adverse event, it will be replaced by the start date of the adverse event.

6.4.5. Missing start/end dates of concomitant medications

Same rules as for adverse events.

6.4.6. Scores of ARSSQ

To compute any score of ARSSQ, if the questionnaire has been completed at a given time point except some items, these missing answers will be imputed by the last observation carried forward (LOCF).

At time points the questionnaire has not been completed at all, no imputation will be done and the score will be missing.

6.4.7. AUC on global score of ARSSQ

The computation of the AUC on global score of the questionnaire will be made for patients with non-missing value at D1 and at least another non-missing time point between D2 and D11. Otherwise, the AUC will be missing.

The AUC will be computed by the trapezoidal rule from D1 to D11 (Acute Phase).

If the value at D11 is missing, then it will be estimated by the value at the last non-missing time point before D11.

7. STUDY PATIENTS

7.1. Disposition of patients

Enrolled patients as well as included and randomised patients will be summarised using frequencies and percentages.

The number and percentage of patients who withdrew prematurely after inclusion, are lost to follow-up as well as the number of completers will be described by treatment group and overall. All withdrawn patients after their inclusion will be described regarding their main reason for withdrawal.

7.2. Protocol deviations

Protocol deviations will be discussed during the data review meeting and the status (minor or major) of these deviations will be validated in order to identify the patients to be excluded from the Per Protocol Set.

Major deviations are defined by:

- Non-compliance with the inclusion or exclusion criteria;
- No assessment of the primary efficacy criterion (ARSSQ) at D1, D5±1 and D8-1 during the treatment period;
- Intake of forbidden medication: saline irrigation;
- Intake of wrong treatment, i.e. wrong treatment given to the patient after randomization;
- A compliance to study product intake below 80% or greater than 120%;
- More than 23 intakes of Babykids nasal spray.

All other deviations will a priori be considered as minor, e.g.:

- V2's date that does not conform with the flow chart of the study;
- V2 not performed;
- Treatment stopped before D8 morning or after D11 morning (less than 14 intakes of the investigational device or more than 20 intakes);
- ARSSQ data missing (but data available at D1, D5±1 and D8-1) until patient's recovery (two consecutive and negative – "not sick" – answers to the first item) or D18/patient's end of study, whichever occurs first.

Major and minor deviations and their types will be described by treatment group and overall.
They will be summarised with frequencies and percentages.
Patients will be counted only once within each type of deviation and within each category (major/minor).
A listing of all deviations will be provided for all included patients, including the category.

7.3. Data Sets Analysed

The number and percentage of patients in each analysis data set, as described in §5, will be provided.

8. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

All demographic and baseline characteristics will be described on the Safety Set and on the FAS, by treatment group and overall.

8.1. Demographic characteristics

Age (years) and sex will be summarised using descriptive statistics already mentioned in §6.2. Age will be computed using the formula below:

Age (years) = Collected Age (years) + [Age precision in months] / 12 *(rounded at 1 digit)*

8.2. Previous medications

Previous and concomitant medications (taken at least once before reference start date) are coded by ATC class and substance name using the WHO-DRUG dictionary version 2022 Q1.

They will be summarised with frequencies and percentages.

Patients will be counted only once within these ATC categories.

Moreover, answers to questions about past or concomitant forbidden medications and about concomitant treatments for first symptoms of infectious rhinitis will be summarised.

8.3. Medical and surgical past history

Medical and surgical past history is coded using the MedDRA dictionary version 25.0. Events are classified by System Organ Class and Preferred Term.

The number and percentage of patients with at least one medical and surgical past history of each category (SOC/PT) will be given.

Patients will be counted only once within these categories.

8.4. Acute Rhinitis Symptoms Severity Questionnaire

The scores to each of the ten items of the ARSSQ, the score of cold symptoms (the sum of the scores to the items 2 to 7), the score of impact on Quality-of-Life (the sum of the scores to the items 8 to 10) and the global score (the sum of the scores to all the ten items) will be described at baseline.
A Student (or Wilcoxon if the normality assumption is not acceptable) between-groups test will be performed for each score.

8.5. Other baseline variables

The presence of fever in the patient and the reported body temperature will be summarised.
The presence of fever in each group will be compared by means of chi-square or exact Fisher test.
A Student (or Wilcoxon if the normality assumption is not acceptable) between-groups test will be performed for the reported body temperature.

9. COMPLIANCE

Compliance will be calculated according to the following formula and analysed on the Safety set, by treatment group and overall.

The compliance will be calculated as follows:

Compliance (%) = [Initial weight of the container (g) – Real weight of the container at the end of the study (g)] × 100 / [Initial weight of the container (g) – Theoretical weight of the container at the end of complete study (g)]

with:

- Initial weight of the container = 32.615 g;
- Theoretical weight of the container at the end of complete study is a function of treatment duration and is noted $weight_{theo}$;

i.e.:

$$\boldsymbol{Compliance}\ (\%) = \mathbf{100} \times \frac{\mathbf{32.615} - \boldsymbol{weight_{end}}}{\mathbf{32.615} - \boldsymbol{weight_{theo}}}$$

with $weight_{end}$ the real weight of the container at the end of the study in g.

The table below gives the value of $weight_{theo}$ by last day of treatment:

Table 1 : Theoretical weight of the container at the end of complete study by last day of treatment

Patient stopped treatment	$weight_{theo}$ (g)
Before D8	27.55875
At D8 morning	27.55875
At D8 evening	27.21750
At D9 morning	26.85750
At D9 evening	26.53750
At D10 morning	26.21500
At D10 evening	25.87125
At D11 morning	25.52500
At D11 evening	25.20250
At D12 morning	24.86500
At D12 evening	24.51000
After D12	24.51000

Compliance will be also described according to the following categories: <80%, [80%; 120%] and >120%.

Note that in case of spray not returned, compliance will be considered unknown and missing.

10. EFFICACY

10.1. Analysis of the primary efficacy criterion

The primary objective will be analysed by performing a t-test (or a Wilcoxon test if the normality assumption is not acceptable) on the means of AUC on global score of ARSSQ during the first eleven days of the study between treatment groups.

The answers of the ten items of ARSSQ are scored **from 0 to 3** (0: negative answer; from 1 to 3: positive answer with an increasing severity level). See the daily report in appendix (§13.3). The global ARSSQ score at each time point is the sum of the scores to the ten items of the ARSSQ:

$$\text{At each time point t: } \mathbf{ARSSQ_{TOT}(t)} = \sum_{j \text{ in } \{1;\ ...;\ 10\}} \mathbf{ARSSQ_j(t)}$$

AUC of global ARSSQ score will be computed by the method described in §6.4.7.

Patients will be analysed on the FAS and the PP Set. In each case, boxplots of the AUC on global score will be realized by treatment group. The number of available data and the p-value will be printed on the figure.

10.2. Analysis of the secondary efficacy criteria

The analysis of the secondary efficacy criteria will involve multivariate analysis.

The selection of variables in multivariate analysis will be performed using a 0.20 significance level and a stepwise method. Covariates considered as potential confounding factors to be initially tested with the treatment in the multivariate models are:

- Body temperature at baseline (°C);
- Scores to each of the items 2 to 7 of the ARSSQ at baseline.

All multivariate analyses below will follow this logic.

10.2.1. Modelling of AUC on global score by multivariate ANCOVA

A multivariate ANCOVA model of the AUC on global score of ARSSQ during the first eleven days of the study will be performed.

Patients will be analysed on the FAS and the PP Set.

10.2.2. Durations of cold symptoms and of impacts on Quality-of-Life

Hereinafter, the "recovery date" is the first day of the **two** first **consecutive** days the patient gave a negative answer to the question 1 ("not sick") without giving a positive answer to the same question (other than "not sick") later. Otherwise, there is no "recovery date" for the patient.

The scores of cold symptoms and of impact on Quality-of-Life (QoL) will be computed at each time-point the patient completed the questionnaire (see §6.4.6), using the following formulae:

At each time point t: $\mathbf{ARSSQ_{SYMP}(t) = \sum_{j \text{ in } \{2;\ ...;\ 7\}} ARSSQ_j(t)}$

$\mathbf{ARSSQ_{QOL}(t) = \sum_{j \text{ in } \{8;\ ...;\ 10\}} ARSSQ_j(t)}$

- The duration of common cold is defined as the duration between the reference start date and the recovery date.

  Common cold's duration (days) = Recovery date – Reference start date

  The origin date will be the reference start date.

  The considered event is the end of common cold, i.e. the recovery of the patient. The event date will be the last day before the recovery date.

  Patients without recovery date will be censored at D18 or at the end of the study, and the censoring date will be the date of D18 or the reference end date, whichever occurs first.

- The duration of the cold symptoms is defined as the duration between first symptomatic day and last symptomatic day.

Cold symptom's duration (days) = Last symptomatic day – first symptomatic day + 1

The first symptomatic day is the first day the patient had a non-zero and non-missing score of cold symptoms. It will be the origin date.

The last symptomatic day is defined as the day before the **two** first **consecutive** days the patient had a zero score of cold symptoms without having a non-zero and non-missing score of cold symptoms later. The considered event is the end of cold

symptoms, i.e. the definitive nullification of the corresponding score during at least two consecutive days.

The considered symptomatic days are between D1 and either D18, or the end of the study, or the day before the recovery date, whichever occurs first. Symptomatic days from the recovery date will not be taken into account.

For patients who definitely nullified the score of cold symptoms, or for patients with a recovery date, the event date will be the last day before the definitive nullification of the score of cold symptoms, or before the recovery date if it exists.

Patients who did not definitely nullify the score of cold symptoms, and without recovery date, will be censored at D18 or at the end of the study, and the censoring date will be the date of D18 or the reference end date, whichever occurs first.

For patients who never had a non-zero score of cold symptoms (never ticked "mild", "moderate" or "severe" for any symptom) and having completed the questionnaire at D1, the origin date for the symptom will be D1, the cold symptoms will be censored at D1 and the duration will be zero. If patients who never reported the presence of any symptom did not complete the questionnaire at D1, neither origin date nor censoring date will be defined for cold symptoms and the duration will be missing.

- The duration of impact on QoL is defined as the duration between first impacted day and last impacted day.

Impact on QoL's duration (days) = Last impacted day – first impacted day + 1

The first impacted day is the first day the patient had a non-zero and non-missing score of impact on QoL. It will be the origin date.

The considered event is the end of impact on QoL, i.e. the definitive nullification of the corresponding score during at least two consecutive days. The last impacted day is defined as the day before this definitive nullification, and the duration is computed by the same way as for cold symptoms' duration.

A Cox survival regression model will be used to analyse each of the durations of common cold, of cold symptoms and of impact on QoL.

Since the computed duration in the three cases is a recovery time and not a survival time, unlike the usual case of application of Cox survival regression, the provided hazard ratios will measure the likeliness of the recovery.
Consequently, and particularly for the treatment (with Placebo as reference), a hazard ratio greater than 1 will have to be considered under a positive aspect, because it will significate that the recovery is more likely under Healsea® Babykids treatment than under Placebo. On the contrary, a hazard ratio lower than 1 will have to be considered under a negative aspect.

For the three durations, a forest plot of the hazard ratios and their 95% CIs from the final multivariate Cox survival regression model will be provided.

In addition, for the three durations, a Kaplan-Meier graph will be provided. Survival curves will be drawn by treatment group. Number of sick / symptomatic / impacted patients, number of events (recoveries) and number of censors in each arm will be displayed on the same graph, as well as the log-rank p-value.
For the same reason as above and unlike the usual case of application of Kaplan-Meier graph, if the log-rank p-value is under 5%, a survival curve for Healsea® Babykids group under the curve for Placebo group will have to be considered under a positive aspect, and the contrary under a negative aspect.

Patients will be analysed on the FAS.

10.2.3. Use and number of days of use of conventional common cold medications

A multivariate logistic regression model will be used to analyse use (yes/no) of conventional common cold medications (overall and by therapeutic class: antibiotics, antipyretics, mucolytics, decongestants, antitussives, systemic and topical corticosteroids).

A multivariate Poisson regression model will be used to analyse the number of days of use of conventional common cold medications (overall and by therapeutic class).

The number of days of use of these medications is defined as follows:

- A day is counted when the patient used at least one of these medications this day;
- Each day is counted once, whatever the number of these medications used this day;
- The total number is the sum of all distinct days of use of these medications, from D1 to D18.

Patients will be analysed on the FAS.

10.3. Concomitant treatments

Concomitant treatments are coded using the WHO-DRUG dictionary version 2022 Q1.

All treatments taken at least once from reference start date or appeared during the study will be summarised by Anatomical Therapeutic Class (ATC) and substance name. The number and percentage of patients in each category will be computed.

Patients will be counted only once within these ATC categories. They will be analysed on the FAS, by treatment group and overall.

Note: A medication which began strictly before reference start date and is on-going after reference start date is counted only in “previous medications” (see §8.2) and not in “concomitant medications”.

10.4. Non-related adverse events

In the following paragraph, for a smoother reading:

- adverse events will be referred as AE;
- treatment-emergent adverse events will be referred as TEAE.

Adverse events are coded using the MedDRA dictionary version 25.0. They are classified by System Organ Class and Preferred Term.

For efficacy analyses, only non-related AEs are considered, i.e. adverse events with a relationship to study device equal to "not related". These analyses will be performed on the Safety Set and on the FAS, by treatment group and overall.

An adverse event will be considered as a treatment-emergent adverse event (TEAE) if:

- it was reported at least one day after screening;
- it was not present prior to the reference start date;
- it was present prior to the reference start date and worsened during the study (increase of intensity);
- it reappears after the reference start date (finished before the reference start date).

Missing or incomplete dates will be estimated as described in §6.4.4 in order to determine the TEAEs, but they will be presented as reported in CRF in the data listings. Generally, an adverse event for which the onset date is missing or incomplete and does not permit to identify the onset according to the date of the reference start date (i.e. missing onset day and month/year corresponding to the reference start date) will be considered as treatment-emergent.

Note: if the intensity/severity is missing, a conservative approach will be adopted and the intensity/severity will be considered as severe.

A given treatment-emergent adverse event (according to the MedDRA terminology) will be counted only once per patient. If a patient experienced several AEs in the same SOC/PT, the most severe intensity will be retained for this SOC/PT.

- Summary of non-related adverse events

A summary table will be produced:

- number and percentage of patients with at least one non-related adverse event (AE);
- number and percentage of patients with at least one non-related AE leading to definitive study device discontinuation;
- number and percentage of patients with at least one non-related AE leading to definitive study discontinuation;
- number and percentage of patients with at least one serious non-related AE;
- number and percentage of patients with at least one non-related TEAE;
- number and percentage of patients with at least one serious non-related TEAE.

The number of non-related AEs of each category will also be provided in this table.

- Analysis of non-related treatment-emergent adverse event

The number and percentage of patients with non-related TEAEs will be summarised by System Organ Class and Preferred term.

The number of non-related TEAEs of each category will also be provided in this table.

A listing of serious non-related AEs will be provided.

All non-related AEs leading to definitive discontinuation of the trial device or to definitive discontinuation of the study will be listed.

11. SAFETY

The following analyses will be performed on the Safety Set, by treatment group and overall.

11.1. Treatment and study duration

Study duration will be calculated according to the formula below:

Study duration (days) = Reference End Date – Reference Start Date + 1

Treatment duration will be calculated according to the formula below:

Treatment duration (days) = Device Stop Date – Reference Start Date + 1

Both will be described (see §6.2) on the Safety Set.

In addition, number and percentages of patients who stopped treatment before D8, at D8 morning, at D8 evening, …, at D12 morning, at D12 evening and after D12 will be provided.

11.2. Incidents

For safety analyses, only incidents are considered, i.e. adverse events with a relationship to study device other than "not related".

- Summary of incidents

A summary table will be produced:
- number and percentage of patients with at least one incident;
- number and percentage of patients with at least one incident leading to definitive study device discontinuation;
- number and percentage of patients with at least one incident leading to definitive study discontinuation;
- number and percentage of patients with at least one serious incident.

The number of incidents of each category will also be provided in this table.

- Analysis of incident

The number and percentage of patients with incidents will be summarised by System Organ Class (SOC) and Preferred term (PT).

The number of incidents of each category will also be provided in this table.

A listing of serious incidents will be provided.

All incidents leading to definitive discontinuation of the trial device or to definitive discontinuation of the study will be listed.

12. CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

The planned analysis in the protocol to assess the primary objective (multivariate ANCOVA model of the AUC on global score of ARSSQ during the first eleven days of the study) has been replaced by the comparison of the means of the AUC on global score of ARSSQ during the first eleven days of the study between treatment groups. The multivariate ANCOVA has been put among secondary analyses.

This change has no impact on the relevance of the sample size calculation since the primary endpoint is the same as planned in the protocol.

Moreover, since several patients still reported having symptoms while they reported they did not feel sick anymore at the question 1 during at least the two last days of completion of the ARSSQ, their positive answers to the cold symptoms' items have been considered as non-significant. Consequently, the question 1 has been taken into account in addition to the corresponding items to determine the end of the cold symptoms' duration, however only on the condition that the last days of completion were consecutive.

If the last days of completion were not consecutive, positive answers to cold symptoms' items are still considered as symptomatic, even if the two last answers to the question 1 are negative. The symptom ends at the last symptomatic day if the patient reported the absence of this symptom at least twice and consecutively after this day. Otherwise, the duration of the symptom is censored at D18 or at the end of the study, whichever occurs first.

The same change has been applied to compute the duration of impact on QoL.

13. APPENDICES

13.1. List of statistical tables, figures and listings

File (BASICC_...)	Type	Number	Title	Mock
STUDY PATIENTS				
T_14_1_1_1_ds_enrl.rtf	Table	14.1.1.1	Patients' disposition – Enrolled patients	T1
F_14_1_1_1_ds_enrl.rtf	Figure	14.1.1.1	Patients' disposition – Enrolled patients	F1
T_14_1_1_2_1_dv_incl.rtf	Table	14.1.1.2.1	Summary of protocol deviations by category and type – Included patients	T2
L_14_1_1_2_1_dv_incl.rtf	Listing	14.1.1.2.1	Patients with at least one protocol deviation – Included patients	L1
T_14_1_1_2_2_disc_incl.rtf	Table	14.1.1.2.2	Premature withdrawal – Reason of withdrawal	T3
L_14_1_1_2_2_disc_incl.rtf	Listing	14.1.1.2.2	Patients prematurely withdrawn – Included patients	L2
DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS, COMPLIANCE, STUDY DURATION				
T_14_1_2_1_1_dm_saf.rtf	Table	14.1.2.1.1	Demographic characteristics – Safety Set	T4
T_14_1_2_1_2_dm_fas.rtf	Table	14.1.2.1.2	Demographic characteristics – Full Analysis Set	T4
T_14_1_2_2_1_1_prevm_saf.rtf	Table	14.1.2.2.1.1	Summary of previous medications – Safety Set	T5
T_14_1_2_2_1_2_prevm_fas.rtf	Table	14.1.2.2.1.2	Summary of previous medications – Full Analysis Set	T5
T_14_1_2_2_2_1_forbidm_saf.rtf	Table	14.1.2.2.2.1	Past or concomitant forbidden medications at baseline – Safety Set	T6
T_14_1_2_2_2_2_forbidm_fas.rtf	Table	14.1.2.2.2.2	Past or concomitant forbidden medications at baseline – Full Analysis Set	T6
T_14_1_2_2_3_1_cmbl_saf.rtf	Table	14.1.2.2.3.1	Concomitant treatments for first symptoms of infectious rhinitis at baseline – Safety Set	T7
T_14_1_2_2_3_2_cmbl_fas.rtf	Table	14.1.2.2.3.2	Concomitant treatments for first symptoms of infectious rhinitis at baseline – Full Analysis Set	T7
T_14_1_2_3_1_mh_saf.rtf	Table	14.1.2.3.1	Medical and surgical past history – Safety Set	T8

File (BASICC_...)	Type	Number	Title	Mock
T_14_1_2_3_2_mh_fas.rtf	Table	14.1.2.3.2	Medical and surgical past history – Full Analysis Set	T8
T_14_1_2_4_1_arssqbl_saf.rtf	Table	14.1.2.4.1	Acute Rhinitis Symptoms Severity Questionnaire at baseline – Safety Set	T9
T_14_1_2_4_2_arssqbl_fas.rtf	Table	14.1.2.4.2	Acute Rhinitis Symptoms Severity Questionnaire at baseline – Full Analysis Set	T9
T_14_1_2_5_1_fever_saf.rtf	Table	14.1.2.5.1	Fever and body temperature at baseline – Safety Set	T10
T_14_1_2_5_2_fever_fas.rtf	Table	14.1.2.5.2	Fever and body temperature at baseline – Full Analysis Set	T10
T_14_1_3_compl_saf.rtf	Table	14.1.3	Summary of compliance per treatment group – Safety Set	T11
T_14_1_4_stdur_saf.rtf	Table	14.1.4	Treatment and study durations by patient – Safety Set	T12
EFFICACY				
T_14_2_1_1_aucarssq_fas.rtf	Table	14.2.1.1	AUC on global score of ARSSQ per treatment group – Full Analysis Set	T13
T_14_2_1_2_aucarssq_pp.rtf	Table	14.2.1.2	AUC on global score of ARSSQ per treatment group – Per Protocol Set	T13
F_14_2_1_1_aucarssq_fas.rtf	Figure	14.2.1.1	Boxplots of AUC on global score of ARSSQ by treatment group – Full Analysis Set	F2
F_14_2_1_2_aucarssq_pp.rtf	Figure	14.2.1.2	Boxplots of AUC on global score of ARSSQ by treatment group – Per Protocol Set	F2
T_14_2_2_1_1_ancovarssq_fas.rtf	Table	14.2.2.1.1	Multivariate ANCOVA model for the AUC on global score of ARSSQ – Full Analysis Set	T14
T_14_2_2_1_2_ancovarssq_pp.rtf	Table	14.2.2.1.2	Multivariate ANCOVA model for the AUC on global score of ARSSQ – Per Protocol Set	T14
T_14_2_2_2_1_coxcc_fas.rtf	Table	14.2.2.2.1	Cox survival regression model for the duration of common cold – Full Analysis Set	T15
F_14_2_2_2_1_1_hrcc_fas.rtf	Figure	14.2.2.2.1.1	Forest plot of Hazard Ratios from final multivariate Cox survival regression model for the duration of common cold – Full Analysis Set	F3
F_14_2_2_2_1_2_kmcc_fas.rtf	Figure	14.2.2.2.1.2	Kaplan-Meier graph for the duration of common cold by treatment group – Full Analysis Set	F4
T_14_2_2_2_2_coxcs_fas.rtf	Table	14.2.2.2.2	Cox survival regression model for the duration of cold symptoms – Full Analysis Set	T15

File (BASICC_...)	Type	Number	Title	Mock
F_14_2_2_2_2_1_hrcs_fas.rtf	Figure	14.2.2.2.2.1	Forest plot of Hazard Ratios from final multivariate Cox survival regression model for the duration of cold symptoms – Full Analysis Set	F3
F_14_2_2_2_2_2_kmcs_fas.rtf	Figure	14.2.2.2.2.2	Kaplan-Meier graph for the duration of cold symptoms by treatment group – Full Analysis Set	F4
T_14_2_2_2_3_coxqol_fas.rtf	Table	14.2.2.2.3	Cox survival regression model for the duration of impact on Quality-of-Life – Full Analysis Set	T15
F_14_2_2_2_3_1_hrqol_fas.rtf	Figure	14.2.2.2.3.1	Forest plot of Hazard Ratios from final multivariate Cox survival regression model for the duration of impact on Quality-of-Life – Full Analysis Set	F3
F_14_2_2_2_3_2_kmqol_fas.rtf	Figure	14.2.2.2.3.2	Kaplan-Meier graph for the duration of impact on Quality-of-Life by treatment group – Full Analysis Set	F4
T_14_2_2_3_1_cccmed_fas.rtf	Table	14.2.2.3.1	Impact of the treatment on the intake of conventional common cold medications – Full Analysis Set	T16
T_14_2_2_3_2_antibio_fas.rtf	Table	14.2.2.3.2	Impact of the treatment on the intake of antibiotics – Full Analysis Set	T16
T_14_2_2_3_3_antipyr_fas.rtf	Table	14.2.2.3.3	Impact of the treatment on the intake of antipyretics – Full Analysis Set	T16
T_14_2_2_3_4_mucol_fas.rtf	Table	14.2.2.3.4	Impact of the treatment on the intake of mucolytics – Full Analysis Set	T16
T_14_2_2_3_5_decong_fas.rtf	Table	14.2.2.3.5	Impact of the treatment on the intake of decongestants – Full Analysis Set	T16
T_14_2_2_3_6_antitus_fas.rtf	Table	14.2.2.3.6	Impact of the treatment on the intake of antitussives – Full Analysis Set	T16
T_14_2_2_3_7_cortico_fas.rtf	Table	14.2.2.3.7	Impact of the treatment on the intake of systemic and topical corticosteroids – Full Analysis Set	T16
T_14_2_3_cm_fas.rtf	Table	14.2.3	Concomitant treatments – Full Analysis Set	T5
T_14_2_4_1_1_1_ae_saf.rtf	Table	14.2.4.1.1.1	Summary of non-related adverse events – Safety Set	T17
T_14_2_4_1_1_2_ae_fas.rtf	Table	14.2.4.1.1.2	Summary of non-related adverse events – Full Analysis Set	T17

File (BASICC_...)	Type	Number	Title	Mock
T_14_2_4_1_2_1_trtae_saf.rtf	Table	14.2.4.1.2.1	Non-related treatment-emergent adverse events by System Organ Class and Preferred Term – Safety Set	T18
T_14_2_4_1_2_2_trtae_fas.rtf	Table	14.2.4.1.2.2	Non-related treatment-emergent adverse events by System Organ Class and Preferred Term – Full Analysis Set	T18
L_14_2_4_2_1_1_sae_saf.rtf	Listing	14.2.4.2.1.1	Serious non-related adverse events – Safety Set	L3
L_14_2_4_2_1_2_sae_fas.rtf	Listing	14.2.4.2.1.2	Serious non-related adverse events – Full Analysis Set	L3
L_14_2_4_2_2_1_aedisct_saf.rtf	Listing	14.2.4.2.2.1	Non-related adverse events leading to definitive discontinuation of the trial device – Safety Set	L3
L_14_2_4_2_2_2_aedisct_fas.rtf	Listing	14.2.4.2.2.2	Non-related adverse events leading to definitive discontinuation of the trial device – Full Analysis Set	L3
L_14_2_4_2_3_1_aediscs_saf.rtf	Listing	14.2.4.2.3.1	Non-related adverse events leading to definitive discontinuation of the study – Safety Set	L3
L_14_2_4_2_3_2_aediscs_fas.rtf	Listing	14.2.4.2.3.2	Non-related adverse events leading to definitive discontinuation of the study – Full Analysis Set	L3
SAFETY – INCIDENTS				
T_14_3_1_1_incsum_saf.rtf	Table	14.3.1.1	Summary of incidents – Safety Set	T17
T_14_3_1_2_incsocpt_saf.rtf	Table	14.3.1.2	Incidents by System Organ Class and Preferred Term – Safety Set	T18
L_14_3_2_1_sinc_saf.rtf	Listing	14.3.2.1	Serious incidents – Safety Set	L3
L_14_3_2_2_incdisct_saf.rtf	Listing	14.3.2.2	Incidents leading to definitive discontinuation of the trial device – Safety Set	L3
L_14_3_2_3_incdiscs_saf.rtf	Listing	14.3.2.3	Incidents leading to definitive discontinuation of the study – Safety Set	L3
PATIENTS DATA LISTINGS				
L_16_2_1_disc.rtf	Listing	16.2.1	Discontinued patients	NA
L_16_2_2_dv.rtf	Listing	16.2.2	Protocol deviations	NA

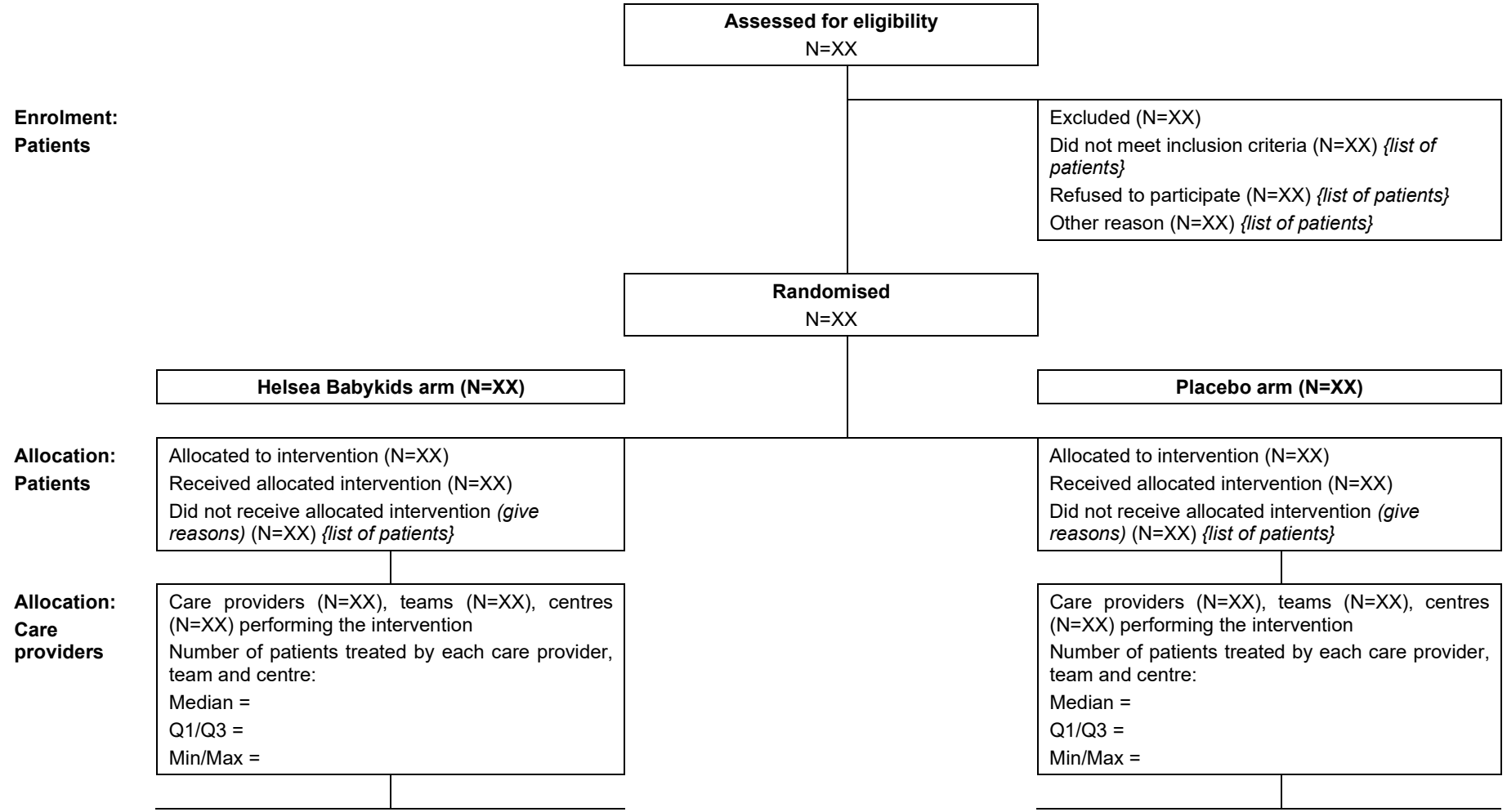
File (BASICC_...)	Type	Number	Title	Mock
L_16_2_3_excl_eff.rtf	Listing	16.2.3	Patients excluded from the efficacy analysis	NA
L_16_2_4_1_dm.rtf	Listing	16.2.4.1	Demographic characteristics by patient	NA
L_16_2_4_2_1_mh.rtf	Listing	16.2.4.2.1	Medical history by patient	NA
L_16_2_4_2_2_mh_coded.rtf	Listing	16.2.4.2.2	Medical history events (MedDRA V25.0)	NA
L_16_2_4_3_ie.rtf	Listing	16.2.4.3	Inclusion/Exclusion criteria	NA
L_16_2_4_4_forbidm.rtf	Listing	16.2.4.4	Past or concomitant forbidden medications and concomitant treatments for first symptoms of infectious rhinitis at enrolment / inclusion	NA
L_16_2_4_5_fever.rtf	Listing	16.2.4.5	Fever and body temperature	NA
L_16_2_5_1_sv.rtf	Listing	16.2.5.1	Dates of visits	NA
L_16_2_5_2_rand.rtf	Listing	16.2.5.2	Randomization and product unblinding	NA
L_16_2_5_3_compl.rtf	Listing	16.2.5.3	Compliance to treatment intake	NA
L_16_2_6_1_1_arssq.xml	Listing	16.2.6.1.1	Acute Rhinitis Symptoms Severity Questionnaire	NA
L_16_2_6_1_2_tte.rtf	Listing	16.2.6.1.2	Durations of common cold, of cold symptoms and of impacts on Quality-of-Life	NA
L_16_2_6_2_1_1_cm.rtf	Listing	16.2.6.2.1.1	Previous and concomitant medications by patient	NA
L_16_2_6_2_1_2_cm_coded.rtf	Listing	16.2.6.2.1.2	Coded medications (WHO-DRUG 2022 Q1)	NA
L_16_2_6_2_2_intak.rtf	Listing	16.2.6.2.2	Intakes of common cold medications	NA
L_16_2_6_2_3_cm_end.rtf	Listing	16.2.6.2.3	Concomitant treatments at end of study / premature termination	NA
L_16_2_6_3_symp_end.rtf	Listing	16.2.6.3	Symptoms of acute rhinitis at end of study / premature termination	NA
L_16_2_7_1_ae.rtf	Listing	16.2.7.1	Adverse events and incidents	NA
L_16_2_7_2_ae_coded.rtf	Listing	16.2.7.2	Coded adverse events and incidents (MedDRA V25.0)	NA
L_16_2_7_3_ae_end.rtf	Listing	16.2.7.3	Adverse events and incidents at end of study / premature termination	NA

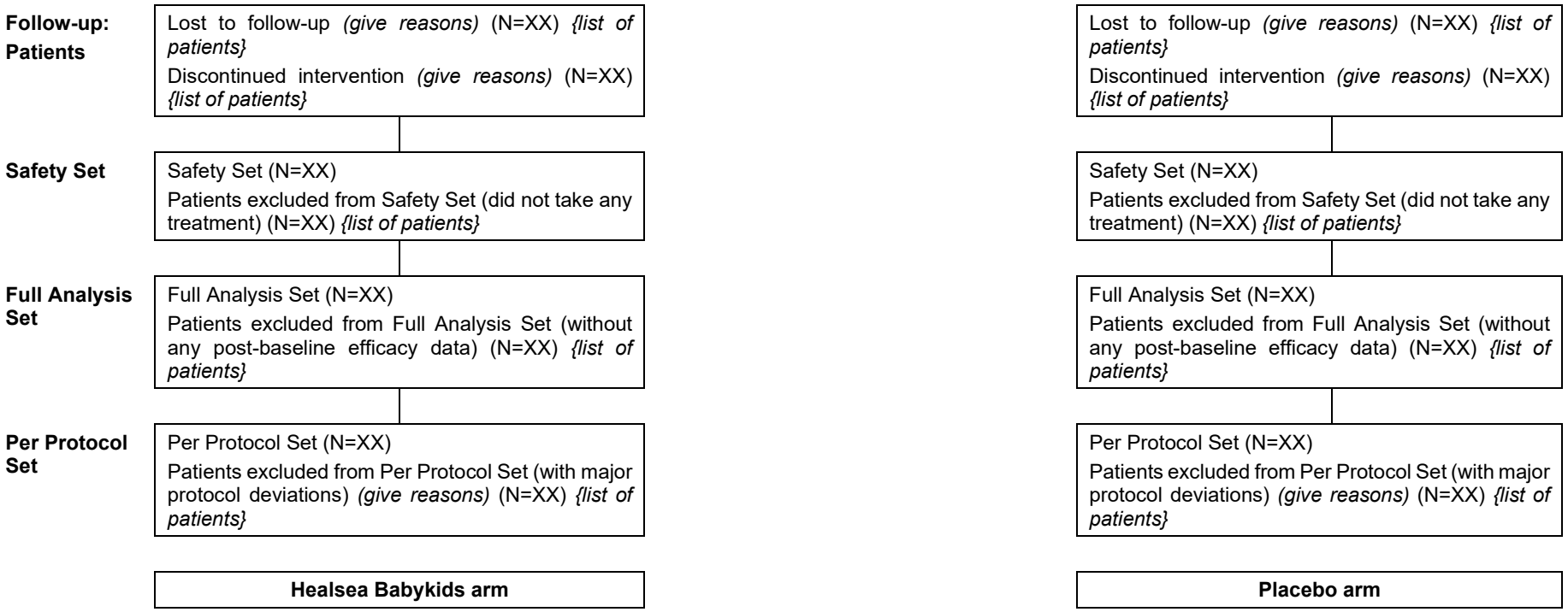
13.2. Mock tables

Mock T1

	Healsea Babykids N=XX	**Placebo N=XX**	**Total N=XX**
Analysis Sets			
Enrolled patients	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Included patients	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Randomised patients	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Safety Set	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Full Analysis Set	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Per Protocol Set	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock F1


Assessed for eligibility
N=XX
Enrolment: Patients
Excluded (N=XX)
Did not meet inclusion criteria (N=XX) {list of patients}
Refused to participate (N=XX) {list of patients}
Other reason (N=XX) {list of patients}
Randomised
N=XX
Helsea Babykids arm (N=XX)
Placebo arm (N=XX)
Allocation: Patients
Allocated to intervention (N=XX)
Received allocated intervention (N=XX)
Did not receive allocated intervention (give reasons) (N=XX) {list of patients}
Allocated to intervention (N=XX)
Received allocated intervention (N=XX)
Did not receive allocated intervention (give reasons) (N=XX) {list of patients}
Allocation: Care providers
Care providers (N=XX), teams (N=XX), centres (N=XX) performing the intervention
Number of patients treated by each care provider, team and centre:
Median =
Q1/Q3 =
Min/Max =
Care providers (N=XX), teams (N=XX), centres (N=XX) performing the intervention
Number of patients treated by each care provider, team and centre:
Median =
Q1/Q3 =
Min/Max =


Follow-up: Patients
Lost to follow-up (give reasons) (N=XX) {list of patients}
Discontinued intervention (give reasons) (N=XX) {list of patients}
Safety Set
Safety Set (N=XX)
Patients excluded from Safety Set (did not take any treatment) (N=XX) {list of patients}
Full Analysis Set
Full Analysis Set (N=XX)
Patients excluded from Full Analysis Set (without any post-baseline efficacy data) (N=XX) {list of patients}
Per Protocol Set
Per Protocol Set (N=XX)
Patients excluded from Per Protocol Set (with major protocol deviations) (give reasons) (N=XX) {list of patients}
Healsea Babykids arm
Lost to follow-up (give reasons) (N=XX) {list of patients}
Discontinued intervention (give reasons) (N=XX) {list of patients}
Safety Set (N=XX)
Patients excluded from Safety Set (did not take any treatment) (N=XX) {list of patients}
Full Analysis Set (N=XX)
Patients excluded from Full Analysis Set (without any post-baseline efficacy data) (N=XX) {list of patients}
Per Protocol Set (N=XX)
Patients excluded from Per Protocol Set (with major protocol deviations) (give reasons) (N=XX) {list of patients}
Placebo arm

Mock T2

Category of deviation – Type of deviation	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Patients with at least one protocol deviation			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Major deviations			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Minor deviations			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock L1

ID – Sex – Age	Treatment	Safety Set	Full Analysis Set	Per Protocol Set	Protocol deviation	Classification of deviation

Mock T3

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Reason of premature withdrawal			
XXXXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock L2

ID – Sex – Age	Treatment	Safety Set	Full Analysis Set	Per Protocol Set	Reason of withdrawal

Mock T4

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Age (years)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Sex			
N	XX	XX	XX
Missing	XX	XX	XX
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T5

ATC1 - ATC2	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Patients with at least one previous / concomitant medication			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T6

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Is the patient currently taking antibiotics or has the patient taken antibiotics within 2 weeks before screening?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Is the patient currently taking systemic corticosteroids or has the patient taken systemic corticosteroids within 4 weeks before screening?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Has the patient a chronic use of decongestant?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Has the patient taken any medicine (in the previous 48 hours) that could modify the ARSSQ assessment?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T7

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Has the patient taken / has the patient been prescribed any treatment for first symptoms of infectious rhinitis?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T8

SOC - Preferred Term	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Patients with at least one medical history			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX			
All	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXXXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T9

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
How sick does your child feel today?			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Runny nose			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Stuffy nose / Blocked nose			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Yellow / Green discharge			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Nasal crust (dry mucus)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Sore throat (hurts to swallow)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Sneezing / Cough			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Cold symptoms			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Impact on Sleeping			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Impact on Breathing			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Impact on Playing / Going to the nursery or to school			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Impact on Quality-of-Life			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		
Global score			

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		

Mock T10

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Has the patient fever?			
N	XX	XX	XX
Missing	XX	XX	XX
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Between-groups test	XXX (Chi-2/Fisher)		
Body temperature (°C)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		

Mock T11

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Compliance (%)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Compliance category			
N	XX	XX	XX
Missing	XX	XX	XX
<80%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
[80%; 120%]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>120%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

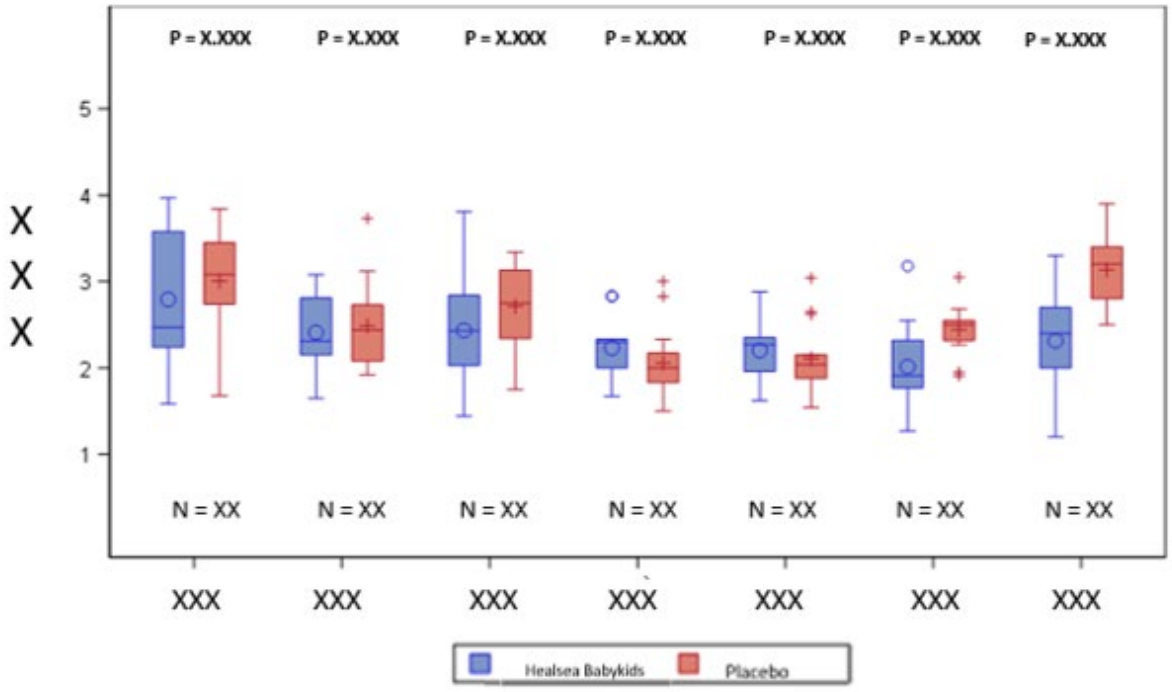
Mock T12

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
Study duration (days)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Treatment duration (days)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Patients who stopped treatment			
N	XX	XX	XX
Missing	XX	XX	XX
Before D8	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D8 morning	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D8 evening	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D9 morning	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D9 evening	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D10 morning	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D10 evening	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D11 morning	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D11 evening	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D12 morning	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At D12 evening	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
After D12	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Mock T13

	Healsea Babykids N=XX	Placebo N=XX	Total N=XX
AUC on global score of ARSSQ			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX	XX
Q1/Q3	XX / XX	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX	XX / XX
Between-groups test	XXX (Student/Wilcoxon)		

Mock F2



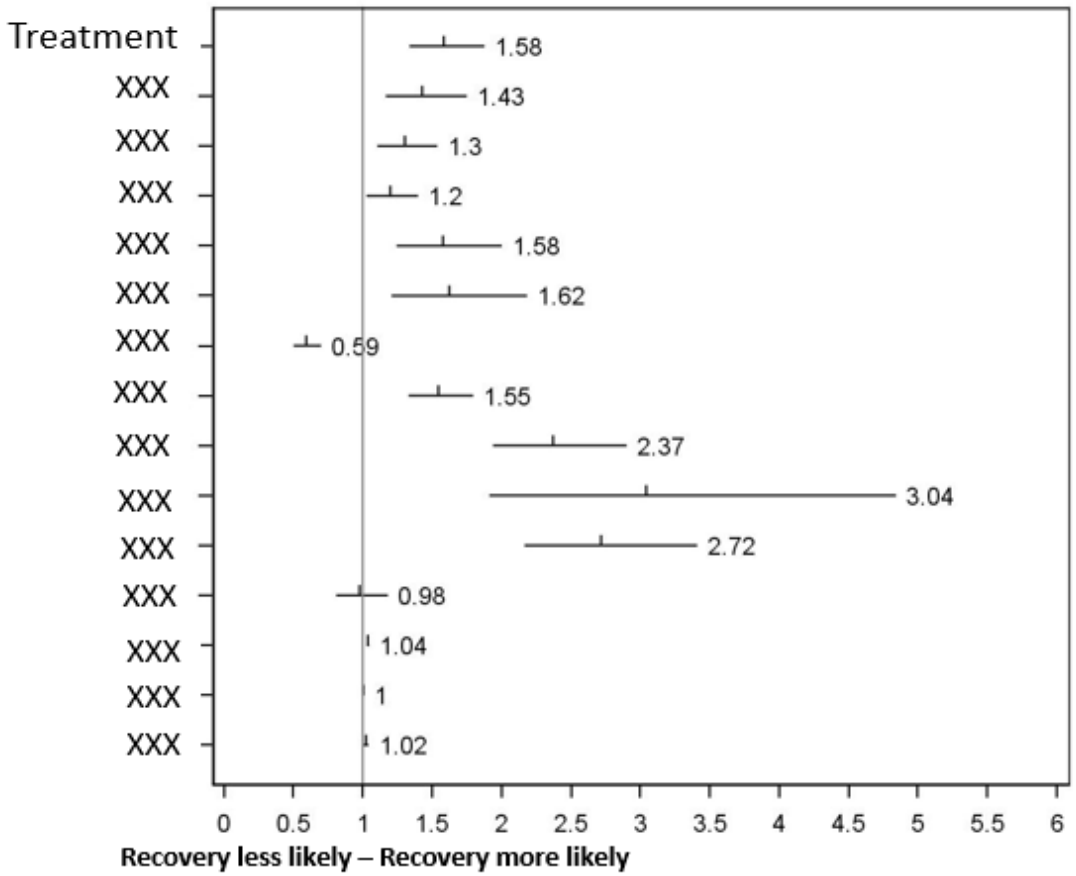
Mock T14

	Healsea Babykids N=XX	Placebo N=XX
AUC on global score of ARSSQ		
ANCOVA model :		
AUC = Treatment + …		
Type 3 Tests of Fixed Effects		
Treatment	XXX	
…	XXX	
Adjusted mean		
LSMeans (SE)	XX.X (XX.X)	XX.X (XX.X)
[LSM 95%CI]	[XX.X; XX.X]	[XX.X; XX.X]
Adjusted mean (diff. vs Placebo)		
LSMeans (SE)	XX.X (XX.X)	
[LSM 95%CI]	[XX.X; XX.X]	
Contrast vs Placebo, p=	XXX	

Mock T15

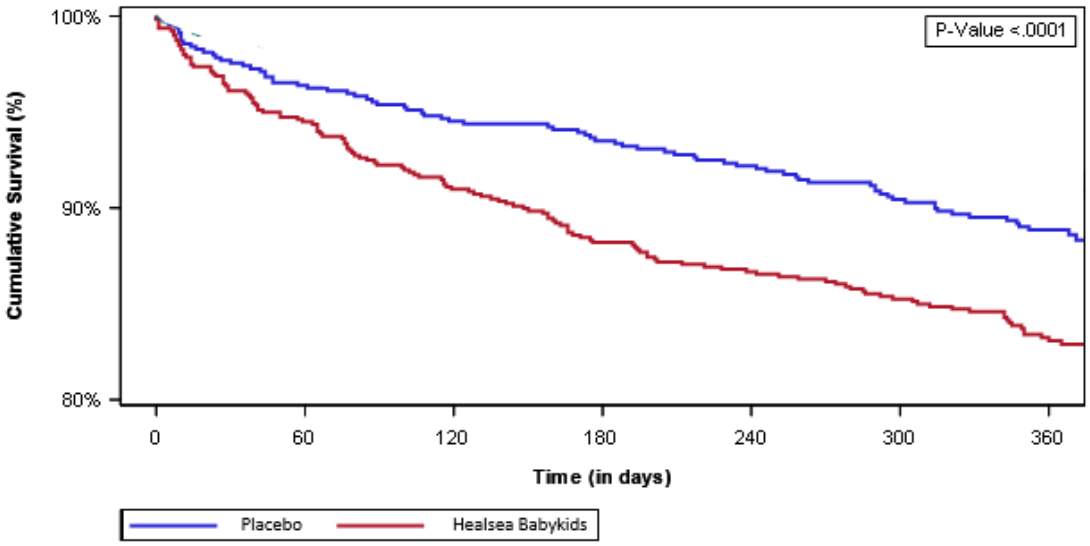
	Healsea Babykids N=XX	Placebo N=XX
Duration of common cold / cold symptoms / impact on Quality-of-Life		
N	XX	XX
Missing	XX	XX
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)
Median	XX	XX
Q1/Q3	XX / XX	XX / XX
Min/Max	XX / XX	XX / XX
Cox survival regression model :		
Hazard Ratios [95%CI]		
Treatment	XX.X [XX.X; XX.X]	
…	XX.X [XX.X; XX.X]	
p-values (Wald)		
Treatment	XXX	
…	XXX	

Mock F3



For Treatment: the reference is Placebo

Mock F4



	Number of symptomatic / impacted patients						
Healsea Babykids	XX	XX	XX	XX	XX	XX	XX
Placebo	XX	XX	XX	XX	XX	XX	XX
	Number of recoveries						
Healsea Babykids	XX	XX	XX	XX	XX	XX	XX
Placebo	XX	XX	XX	XX	XX	XX	XX
	Number of censors						
Healsea Babykids	XX	XX	XX	XX	XX	XX	XX
Placebo	XX	XX	XX	XX	XX	XX	XX

Mock T16

	Healsea Babykids N=XX	Placebo N=XX
Use of XXX		
N	XX	XX
Missing	XX	XX
No	XX.X (XX.X%)	XX.X (XX.X%)
Yes	XX.X (XX.X%)	XX.X (XX.X%)
Logistic model :		
Odds Ratios [95%CI]		
Treatment	XX.X [XX.X; XX.X]	
…	XX.X [XX.X; XX.X]	
p-values (Wald)		
Treatment	XXX	
…	XXX	
Number of days of intakes of XXX		
N	XX	XX
Missing	XX	XX
0	XX.X (XX.X%)	XX.X (XX.X%)
1	XX.X (XX.X%)	XX.X (XX.X%)
2	XX.X (XX.X%)	XX.X (XX.X%)
…	XX.X (XX.X%)	XX.X (XX.X%)
Poisson regression :		
Type 3 Tests of Fixed Effects		
Treatment	XXX	
…	XXX	

Mock T17

	Healsea Babykids N=XX		Placebo N=XX		Total N=XX	
	n (%)	[E]	n (%)	[E]	n (%)	[E]
Number and percentage of patients with / Number of *(non-related)*						
Incident *(Adverse event)*	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
Incident *(Adverse event)* leading to definitive study device discontinuation	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
Incident *(Adverse event)* leading to definitive study discontinuation	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
Serious incident *(adverse event)*	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
(Treatment-emergent adverse event)	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
(Serious treatment-emergent adverse event)	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX

Mock T18

	Healsea Babykids N=XX		Placebo N=XX		Total N=XX	
SOC - Preferred Term	n (%)	[E]	n (%)	[E]	n (%)	[E]
Incidents *(Non-related treatment-emergent adverse events)*						
All	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
XXXXX						
All	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
XXXXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
XXXXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX

Mock L3

ID – Sex – Age	Treatment	Incident *(Adverse event)*	Start date / end date	Ongoing at the end of the study	Intensity	Serious	Action taken	Causality

13.3. Acute Rhinitis Symptoms Severity Questionnaire – Daily report

Q1: How sick does your child feel today:

Not sick ☐	A little sick ☐	Sick ☐	Very sick ☐

Q2-Q7: How do you evaluate the intensity of the following symptoms of your child?

Symptoms	Not present	mild	moderate	severe
Runny nose	☐	☐	☐	☐
Stuffy nose/blocked nose	☐	☐	☐	☐
Yellow/green discharge	☐	☐	☐	☐
Nasal crust (dry mucus)	☐	☐	☐	☐
Sore throat (hurts to swallow)	☐	☐	☐	☐
Sneezing/cough	☐	☐	☐	☐

Q8-Q10: How do you evaluate the impact of the common cold on your child's activities?

Activity	No impact	Mild impact	Moderate impact	Severe impact
Sleeping	☐	☐	☐	☐
Breathing	☐	☐	☐	☐
Playing/going to the nursery or to school	☐	☐	☐	☐