STUDY PROTOCOL

Study Number	**OBVIO-DAN-003**
Title	**A pilot study evaluating sleep, stress, and infant nutrition using a chatbot with parents of preterm and full-term infants**
Sponsor	**Danone**
Country	**Singapore**
Date	**31AUG2018**
Version Number	**3**

Table of Contents

1 Investigator Signature Page

PRINCIPAL INVESTIGATOR (PI)

Principal Investigator:

Dr. Chua Mei Chien

_____

Date

_____

Signature

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the conduct of the study.

I will only use the informed consent language approved by the sponsor or its representative and will fulfill all responsibilities for submitting pertinent information to the Independent Ethics Committee (IEC) and/or Institutional Review Board (IRB) responsible for this study.

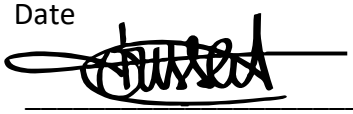
I agree that the sponsor or its representatives shall have access to any source documents from which case report form information may have been generated.

2 Sponsor Team Signature Page

CLINICAL PROGRAM LEADER

Agathe Foussat
Senior Digital Program Leader
Research and Innovation -
Early Life Nutrition
Danone Nutricia

12/11/2018
Date



Signature

PROJECT SCIENTIFIC DIRECTOR

Ruurd Van Elburg
Preterm Science and Program Director
Research and Innovation
Early Life Nutrition
Danone Nutricia

12 Nov 2018
Date

Signature

BIOSTATISTICIAN (CRO)

Jerrod Nelms, PhD, MPH
Director, Biostatistics
ObvioHealth

Date

Signature

OBVIOHEALTH PROGRAM LEADER

Camisha Harge

Senior Director, Clinical Operations

ObvioHealth

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Date

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Signature

3 Abbreviations

CDM	Clinical Data Manager
CPM	Clinical Project Manager
CRO	Contract Research Organization
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Council for Harmonisation
ICU	Intensive Care Unit
IEC	Independent Ethics Committee
IRB	Institutional Review Board
PI	Principal Investigator
SOP	Standard Operating Procedure
TMF	Trial Master File

4 Synopsis

Study Title	A pilot study evaluating sleep, stress and infant nutrition using a chatbot with parents of preterm and full-term infants
Study Objectives	**Primary Objective:** To generate real-life, in-home data from parents with infants (preterm and full-term) on sleep, stress, and infant nutrition via the study chatbot **Secondary Objective:** To investigate differences in data obtained from parents of preterm infants versus data obtained from parents of full-term infants on sleep, stress, and infant nutrition **Exploratory Objective:** To evaluate the usability of ClaimIt, the study chatbot, and chatbot tools in general, among this population
Study Design	An observational study of parents with infants (preterm and full-term)
Study Observation Duration	28 days per family
Country of Implementation	Singapore
Study Population	• 20 parents with healthy preterm infants (born at <37 weeks of gestation), age 0-6 months and discharged from the hospital at time of enrollment • 20 parents with healthy full-term infants (born at ≥37 weeks of gestation), age 0-6 months and discharged from the hospital at time of enrollment

Inclusion Criteria	**Subjects (parent and infant) must meet the following criteria:** • Healthy infants (preterm and full-term) must be 0-6 months of age at time of enrollment • Infants must be at home (discharged from the hospital) at time of enrollment • Informed consent from parent whose age is ≥21 years • Parent must be proficient in the English language • Parent must be able to comply with the required study tasks, as per PI's judgment • In-home access to reliable internet connections; a mobile device suitable for electronic communication
Exclusion Criteria	**Infant must not meet any of the following criteria:** • Known to have current or previous illnesses/conditions which could interfere with the study outcome (per PI's clinical judgment) • Must not be currently participating in any other clinical study **Parent must not meet any of the following criteria:** • Must not be known to have a significant medical condition that might interfere with the study (per PI's clinical judgment) that meets one of the following criteria: o Presence of current mental illness or history of mental illness o Any acute or chronic illness that makes the parent unsuitable for the study based on the PI's judgment • Must not be a single parent • Inability of the parent to comply with the study protocol or PI's uncertainty about the willingness or ability of the parent to comply with the protocol requirements
Endpoints	**Primary:** Obtaining records of sleep, stress, and infant nutrition from parents of infants (preterm and full-term) through interaction with the study chatbot

	Secondary: Comparison of the data obtained from parents of preterm infants and parents of full-term infants on sleep, stress, and infant nutrition **Exploratory:** An evaluation of the usability of ClaimIt, the study chatbot and chatbot tools in general, among this population
Study Implementation	**Prescreening** • Participants (parents and infants [preterm or full-term]) will be recruited by study team personnel in the Department of Neonatology at KK Women's and Children's Hospital • Upon successfully fitting the basic eligibility criteria, the parent will be provided: o Informed Consent Form (ICF) for review ▪ The parent will have the opportunity to ask questions and receive answers from study team personnel o Access to the ClaimIt app along with the following information: ▪ Overview of trial tasks and relevant notifications ▪ ClaimIt navigation instructions: How to interact with the ClaimIt app during the study period ▪ Additional study details & instructions ▪ All relevant contact information that may be required during the study

	Screening and Enrollment • Upon signing the ICF, the parent will be asked to respond to a detailed eQuestionnaire (Appendix I) to assess eligibility • If all the inclusion and none of the exclusion criteria are satisfied, the PI will enroll the subjects into the study • Upon enrollment, the parent will be provided full access to the study chatbot along with the following information: o How to connect to the study chatbot o Overview of trial requirements & parameters o The Chatbot navigation: How to interact with the study chatbot during the 28-day period o Overview of notifications related to trial activities o Additional study details & instructions **Data Collection Period** • The parent will be asked to regularly interact with the study chatbot on three (3) topics, three (3) days a week (suggested schedule: M, W, F) for 28 days • Through regular interaction with the study chatbot, records of parents' sleep, stress, and infant nutrition will be obtained **End of Study** • At the end of the 28-day data collection period, the parent will be asked to complete an eQuestionnaire about the usability of the study chatbot and ClaimIt (Appendix II)
Statistical Considerations	A sample size of 40 parents and their infants is estimated with the following considerations: • Descriptive summary statistics for the categorical and quantitative data will be reported

	• Expected dropout rate of ≤10 subjects (if the dropout threshold of 10 is reached, up to 10 additional subjects may be replaced at the sponsor's discretion) • A subject will be considered to have dropped out if they are determined to be non-compliant
Ethical Considerations	This study should be performed in accordance with the ethical principles based in the Declaration of Helsinki and its subsequent amendments, and in accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guideline (ICH E6(R1), 1996) and applicable regulatory requirements.

5 Introduction

An estimated 15 million infants, slightly more than 1 in 10, are born preterm each year worldwide.[1] Approximately 60% of those are born in South Asia and sub-Saharan Africa.[1] As the leading cause of death in children under the age of 5 years, about one million preterm infants die each year worldwide due to preterm birth complications, with a significantly greater mortality rate in low-income countries compared to high-income countries.[1] Consequently, given the significance of meticulous care required for the preterm infants, healthcare providers and parents play a central role in assuring proper care of these vulnerable children.

Parental involvement in caring for infants can lead to anxiety, worry, and psychological distress. In a follow-up clinic evaluation of parents and their premature infants, many reported parental concerns about medical and developmental outcomes were unsupported by their child's diagnosis.[2] In a study done with parents of late-preterm infants (≥34 to <37 weeks gestation), mothers reported significantly more stress than fathers on the Parent Stress Index (PSI-3), a tool designed for the early identification of parental and familial characteristics that fail to foster normal development and function in children.[3] An assessment of maternal psychological distress in singleton versus multiple-birth preterm infants found that mothers of multiples had greater posttraumatic stress symptoms, anxiety at discharge and depressive symptoms at six months as compared to mothers of singletons.[4] Among mothers of school-aged children who were born late preterm and admitted to an intensive care unit (ICU), there was a significant 18-fold increase in total stress compared to stress among mothers of full-term children.[5] In a parallel study group involving mothers of school-aged children who were born late preterm, but not admitted to the ICU, there was a 24-fold increase in total stress when compared to the mothers of full-term children.[5] Overall, multiple studies have demonstrated that parental stress, anxiety, and psychological distress are not only short-term problems when caring for a preterm infant, but may also have long-lasting effects.

In this study, data will be collected comparing infant nutrition, stress, and sleep in parents of both preterm infants and full-term infants (after they have been discharged from the hospital), using a chatbot application. A chatbot is defined as, “an instant messaging account that is able to provide services using instant messaging frameworks with the aim of providing conversational services to users in an efficient manner.” In short, a chatbot can respond to a user as though they are communicating with another person via instant messenger, except there is a computer on the other end.[6] The chatbot application in this study is designed to provide an interactive tool for the parents to provide input on infant nutrition and parent stress and sleep.

6 Objectives of the Trial

6.1 Primary Objective

To generate real-life, in-home data from parents with infants (preterm and full-term) on sleep, stress, and infant nutrition via the study chatbot.

6.2 Secondary Objective

To investigate differences in data obtained from parents of preterm infants versus data obtained from parents of full-term infants on sleep, stress, and infant nutrition.

6.3 Exploratory Objective

To evaluate the usability of ClaimIt, the study chatbot, and chatbot tools in general, among this population.

7 Trial Design

7.1 Study Calendar

Schedule of Activities	Prescreening	Screening and Enrollment	Data Collection	End of Study
Basic study information provided to parents	X	-	-	-
Inclusion/exclusion criteria met	X	X	-	-
Review of Informed Consent Form (ICF) and consent provided by parent	-	X	-	-
Chatbot app and instructions provided	-	X	-	-
28-day data collection via study chatbot	-	-	X	-
Chatbot/ClaimIt usability eQuestionnaire	-	-	-	X

7.2 Type of Trial

This is an observational study of 40 parent and infant pairs (20 parents of preterm infants, 20 parents of full-term infants) residing in Singapore.

7.3 Endpoints

7.3.1 Primary Endpoint

Obtaining records of sleep, stress, and infant nutrition from parents of infants (preterm and full-term) through interaction with the study chatbot

7.3.2 Secondary Endpoint

Comparison of the data obtained from parents of preterm infants and parents of full-term infants on sleep, stress, and infant nutrition obtained via the study chatbot

7.3.3 Exploratory Endpoint

An evaluation of the usability of ClaimIt, the study chatbot and chatbot tools in general, among this population.

7.4 Participants and Location

7.4.1 Participants

Parents of healthy infants (preterm and full-term) residing in Singapore will be recruited through the prescreening process. Subjects will be identified by the site study staff and a brief explanation of the study will be provided to the parent.

7.4.2 Centers

Participants will be recruited through the Department of Neonatology at KK Women's and Children's Hospital. After the screening visit, infants and parents will not be required to visit a physical trial site (unless reconsent is required). Communication between parents and study personnel will be conducted via the ClaimIt platform and/or over the telephone or email messaging, as appropriate.

7.5 Study Duration

It is expected that the enrollment period will be four (4) months in total.

For each subject pair, the total study duration beginning with the initiation of recruitment and screening (approximately 3 weeks); 28 days of data collection; administration of a feedback eQuestionnaire; and follow-up monitoring, is expected to be approximately 7-8 weeks total.

8 Study Population

Subjects (parent and infant) must meet the following:

8.1 Subject Inclusion Criteria

- Healthy infants (preterm [born at <37 weeks of gestation] and full-term [born at ≥37 weeks of gestation]), 0-6 months of age at time of enrollment
- Infants must be at home (discharged from the hospital) at time of enrollment
- Informed consent from the parent (whose age is ≥21 years)
- Parent must be proficient in the English language
- Parent must be able to comply with the required study tasks, as per PI's judgment
- In-home access to reliable internet connections and a tablet and/or mobile device suitable for electronic communication

8.2 Subject Exclusion Criteria

To be considered for enrollment, the subjects must not meet any of the exclusion criteria listed below:

Infants:

- Known to have current or previous illnesses/conditions which could interfere with the study outcome, as per PI's clinical judgment
- Must not be currently participating in any other clinical study

Parent of infants:

- Must not be known to have a significant medical condition that might interfere with the study (per PI's clinical judgment) that meets one of the following criteria:
  - Presence of current mental illness or history of mental illness
  - Any acute or chronic illness that makes the parent (subject) unsuitable for the study based on the PI's judgment
- Must not be a single parent
- Inability of the parent to comply with the study protocol or PI's uncertainty about the willingness or ability of the subject to comply with the protocol requirements

8.3 Subject Withdrawal Criteria

Subjects may be withdrawn from the study at any time for any reason, including but not limited to:

1) At their request or the request of the legally authorized representative.
2) If, in the PI's opinion, continuation in the study would be detrimental to the parent or infant's well-being.
3) Non-compliance (failure to complete five [5] or more consecutive sessions), at the discretion of the PI (a situation where the parent consistently does not adhere to the study procedures).
4) Protocol deviation(s) which, in the opinion of Sponsor, warrant discontinuation from study (e.g., violation of inclusion and/or exclusion criteria).

A dropout of ≤10 families is built into the estimated total sample size. If the dropout threshold of 10 is reached, up to 10 additional participants may be replaced at the sponsor's discretion. The PI must make every effort to contact parents that are lost to follow-up. Attempts to contact the parent must be documented in the family's record (e.g., dates and times of attempted telephone/email contact).

The primary analysis will be an ITT (Intent-to-Treat) analysis; all enrolled families who engage with the study chatbot for at least one complete interaction (on all three topics) will be included in the final comparative analysis. The number and percentage of subjects who withdraw early and their reasons for withdrawal will be presented in a table and the equivalent of a CONSORT flow diagram.

The following information will be documented in the mother and infant/toddler's record in the event of a subject's withdrawal from the study:

I. Date of withdrawal
II. Reasons for withdrawal

Even if consent is withdrawn, all data that were acquired before consent was withdrawn will be maintained.

9 Assessment of Safety

As this is an observational study and the study procedures present no more than minimal risk, adverse events are not expected and therefore will not be collected or reported for this study.

10 Execution of the Trial

10.1 Screening and Enrollment

Prescreening:

1. Prescreening will be conducted through the Department of Neonatology at KK Women's and Children's Hospital with parents of healthy infants (preterm and full-term) residing in Singapore. Study personnel will assess alignment with the inclusion and exclusion criteria of the study and capability and willingness of the parent to comply with all aspects of the study design.

2. If the prescreening suggests that the infant and parent are appropriate for study inclusion, the parent will have an opportunity to review and ask questions about the ICF.

3. The decision to participate in the study is entirely voluntary by the parent. The PI and/or his/her designee(s) must emphasize to the parent that the consent to participate can be withdrawn at any time, without penalty or loss of benefits to which the subject is otherwise entitled.

4. The informed consent process will be managed on-site at the KK Hospital, supported as necessary by study personnel. If the parent agrees to participate, they will voluntarily sign the ICF prior to the conduct of any study related procedures.

   Note: During the study, any amendments to the ICF and/or protocol (outside of defined parameters) must be approved by the IRB prior to use/distribution. Based on the assessment of the IRB, the subjects may be required to review and re-sign the revised ICF to remain in the study.

Screening and Enrollment:

1. After the ICF is voluntarily signed, the parent will respond to a detailed eQuestionnaire (Appendix I). Their responses will be reviewed by the PI (or their designee) to further confirm that they and their infant appropriately meet all the inclusion and none of the exclusion criteria for the study before being formally enrolled.
2. If all the criteria are met, then the parent and infant will be enrolled in the study. Those who do not meet the screening criteria will be informed that they are not eligible for the study and dismissed.
3. Upon enrollment, the parent will be provided access to the study chatbot for regular interaction. Approximately 40 parent and infant pairs will be enrolled.

10.2 Study Period

The parent will be asked to interact with the study chatbot three times a week (e.g., Monday, Wednesday and Friday [suggested schedule]) over a maximum 28-day period. During each of those interactions, they will be asked to interact on all three topics: sleep, stress, and infant nutrition. Reminder notifications will be sent via ClaimIt for any parent that does not interact with the chatbot per protocol.

The maximum number of interactions per subject pair is 12 (in total).

10.3 Data Collection

Chatbot transcripts will be created based on each interaction between the parent and study chatbot.

eCRFs will be completed by the parent for their infant based on data from:

- the Screening eQuestionnaire
- the end-of-study Usability eQuestionnaire

10.4 Compliance

Compliance with the study expectations will be monitored through the study chatbot's regular use and reported as follows:

- Compliant: Defined as having completed a total of 7 or more interactions with the study chatbot in the 4-week study period

  Note: If only seven (7) sessions are completed with the study chatbot, the five (5) missing interactions must not be consecutive

- Non-compliant: Defined as the failure to complete five (5) or more consecutive sessions in the 4-week study period

Subjects may be withdrawn from the study in the event of non-compliance.

10.5 End of Study

At the end of the study, the parent will be asked to complete an eQuestionnaire to assess and comment on the usability of ClaimIt, the study chatbot and chatbot tools in general (Appendix II). Access to the study chatbot will be discontinued, and the study team may contact the parent if there are any outstanding study related queries.

10.6 Application Description

The study chatbot is an interactive, conversational application where the parent can initiate a conversation with the chatbot, and it will respond appropriately. In certain instances, the study chatbot may also initiate a conversation with parent. The application converses with the user through the messaging platform. Transcripts of the chatbot conversations will be accessed and reviewed by the study team.

Completion of the Screening and Usability eQuestionnaires will occur via the ClaimIt app for each of the parents. The ClaimIt app is a mobile application available to subjects during their period of enrollment so they can perform specific study-related tasks and receive and transmit communications from and to the CRO staff.

10.7 Monitoring

The study will be monitored on an ongoing basis starting from the enrollment of the first parent and infant and continuing through the study exit of the last enrolled pair. Regular monitoring will be conducted by the designated ObvioHealth personnel during the study. The monitoring activities will be detailed in a monitoring plan. The following measures are in place to ensure consistent and regular engagement with the parent:

- Dedicated study personnel will be available for contact with the infant's parent to answer questions about the study, the study chatbot or the ClaimIt app, as necessary
    - KKH staff will manage all questions during the recruitment and enrollment process. After enrollment, subjects will have the ability to contact the KKH Study Coordinator/Study Nurse via the common e-mail provided for questions related to the study. Participants are encouraged to seek advice from their physician for their baby's health related issues.
    - ObvioHealth staff will be responsible for any ClaimIt, app-related questions and any other questions routed to them via the ClaimIt app. ObvioHealth staff will notify and/or redirect questions to KKH staff, as needed.
- Regular interactions with the study chatbot will determine compliance
- In some circumstances, the PI or study team personnel may initiate contact with the parent to determine compliance with chatbot use and study protocol
- Study team (Sponsor and CRO members) will review daily compliance with the study chatbot

As the parent and infant are not required to visit a physical site during the study period (unless reconsent is required), monitoring will be conducted throughout the study via

remote data reviews. The monitor will check the chatbot transcripts and eCRF data for completeness, consistency and any concerning text. If any errors are identified, they may be corrected consistent with the Data Handling Conventions (DHC) or may be addressed through direct contact with the parent. Concerning text will be communicated to the PI who will take appropriate action.

Protocol deviations will be reported in the monitoring report and a corrective action plan implemented, as necessary. The monitor will communicate any detected protocol deviations to the PI. These deviations will be recorded in a Protocol Deviation Log.

10.8 Computerized Data Entry - Security and Privacy of User Data

All data is hosted on Microsoft Azure service. All ObvioHealth employees and their affiliates are bound by strict confidentiality agreements. Transport Layer Security (TLS) is used to secure all data in transit.

10.9 Computerized Edit Checks

The database will incorporate the needed programmed edit checks to help ensure quality data. Messages to the parent may be generated automatically to alert him/her to any entry error or protocol non-compliance.

10.10 Audit Trail

All entries and alterations made in the database will be captured by an audit trail in which the individuals accessing the database and providing entries and/or making alterations are identified via their user IDs and passwords.

11 Statistics

11.1 Sample size calculations

A sample size of 40 subjects is estimated under the following considerations:

- Descriptive summary statistics for the categorical and quantitative data will be reported
- Expected dropout rate of ≤10 subjects (if the dropout threshold of 10 is reached, up to 10 additional participants may be replaced at the sponsor's discretion)
- A subject will be considered to have dropped out if they are determined to be non-compliant; however, qualifying chatbot interactions will be included in ITT

11.2 Datasets to be analyzed

11.2.1 Intent-to-treat (ITT) analysis dataset

All parents participating in at least one-day chatbot interactions (on all three topics) will be included in the collected data and safety analyses, in accordance with the Intent-to-treat (ITT) principle.

11.2.2 Per Protocol (PP) analysis dataset

All subjects who have no protocol violations (protocol deviations are permitted and reportable) and remained in the study for the full data collection period will be included.

Protocol violations and deviations and study completion data will be evaluated through statistical analysis.

11.3 Statistical Analysis

Free text qualitative data will be generated from transcripts recorded through daily interactions with the study chatbot. The resulting datasets will be analyzed and appropriately categorized to sleep, stress, and infant nutrition as primary endpoints using the RDQA package in R version 3.4.3. All patterns will be categorized and tabulated as appropriate.

Descriptive statistical analysis will be performed on data generated from the study's two surveys (Screening, and Usability). Data points from the Screening questionnaire will be categorized with like questions in each questionnaire being compared to each other as a simple test for within subject consistency. All other variables will be presented as univariate and bivariate distributions as appropriate.

Likert scale data from the Usability Questionnaire will be analyzed using univariate descriptive statistics (mean, median, standard deviation) and bi/multivariate categorizations as appropriate. As the number of responses will likely be low, open-ended questions will be reviewed manually for patterns and described in either paragraph or tabular form.

12 Legal and Ethical Prerequisites

12.1 Legal Requirements

The study will be conducted after approval from SingHealth Centralised Institutional Review Board (CIRB), which follows the guidance of Singapore regulatory bodies and general GCP/ICH regulations.

12.2 Ethical Aspects

12.2.1 Protection of the Subject's Confidentiality

Confidentiality of all study participants will be maintained; codes for subject identification will be utilized. Subjects will review and consent to the SingHealth Data Protection Policy during the informed consent process.

12.2.2 Informed Consent

A signed ICF by the parent indicating consent to his/her and his/her infant's participation in the study is required. This will be completed prior to conducting any study-related activities and will be done in accordance with all applicable regulatory requirements.

The ICF will inform the parent about all aspects of the parent and infant's study participation. Dedicated study personnel will be available to the parent to answer questions about the study or the informed consent. The IRB/EC will approve the ICF. Any amendments to these documents must be approved by the IRB/EC.

The parent must sign the ICF prior to the initiation of any study-related activities beyond prescreening. Parents must be ≥21 years of age.

The decision to participate in the study is entirely voluntary. The PI and/or his/her designee must emphasize to the parent that the consent to participate can be withdrawn at any time without penalty or loss of benefits to which the subject is otherwise entitled.

12.2.3 Ethics Committee Approval

The study protocol will be submitted by the PI for examination by the SingHealth Centralised Institutional Review Board (CIRB)/EC. Commencement of the clinical trial is not permitted without written approval of the IRB/EC.

The IRB/EC must be notified of all subsequent additions or changes in the study protocol. If a protocol amendment and revisions to the consent form are made and approved by IRB/EC, subjects may be required to re-sign the ICF after review to remain in the trial.

12.2.4 Declaration of Helsinki

This trial will be conducted according to the principles and rules detailed in the Declaration of Helsinki and its subsequent amendments.

13 Quality Control and Quality Assurance

13.1 Monitoring

As the parent and infant are not required to visit a physical site during the study period (unless reconsent is required), monitoring will be conducted throughout the study via remote data reviews. The monitor will check the chatbot transcripts and eCRF data for completeness, consistency and any concerning text. If any errors are identified, they may be corrected consistent with the Data Handling Conventions (DHC) or may be addressed through direct contact with the parent. Concerning text will be communicated to the PI who will take appropriate action.

The main protocol deviations that will be targeted are:

- Informed consent process not adequately performed
- Violation of inclusion and/or exclusion criteria
- Non-compliance with study-related daily requirements (interactions with the study chatbot)
- Any other GCP non-compliance

Protocol deviations will be tracked and logged in the Protocol Deviation Log.

At the end of the trial, the monitor and/or Clinical Data Manager (CDM) will ensure that all documentation and the Trial Master File (TMF) are complete. In all cases, it is the responsibility of the CPM, CDM and other study team members to maintain subject confidentiality.

13.2 Quality Control of Essential Documents

ObvioHealth will implement and maintain quality assurance, and quality control systems with Standard Operating Procedures (SOPs) to ensure that this clinical trial is conducted, and data are generated, documented (recorded) and reported in

compliance with the protocol, GCP/ICH standards, and other applicable local regulations.

13.3 Responsibilities of the PI

The PI is responsible for the following:

- Obtaining the written and dated approval of the applicable IRB/EC and other regulatory agency, if any, prior to the conduct of the study
- Address any concerning text with the parent, as communicated via the monitor
- Selection of participants/subjects in accordance with the inclusion and exclusion criteria after obtaining written informed consent of the parent
- Maintain confidentiality and safety of subjects in accordance with the Declaration of Helsinki
- Adherence to the study protocol and the spirit of GCP
- If modification becomes necessary, the rationale will be provided in a protocol amendment signed by the PI and Sponsor for submission to the IRB/EC
    - After the protocol amendment approval, subjects may be required to re-sign an amended ICF to remain in the trial
- During the trial, provide subjects with any newly available information regarding the study or its components that may be relevant to them
- Cooperation in the case of an audit and/or a regulatory inspection, providing direct access to source data and/or documents

14 Study End Procedures

14.1 Premature Termination of Study

Should it prove necessary to discontinue the study permanently prior to completion, the Sponsor will notify ObvioHealth, the subjects, and the IRB/EC of the rationale. All relevant study documents and data will then be sent to the Sponsor.

14.2 Termination of Study

After the completion or termination of the study, all relevant study documents and data will then be sent to the Sponsor. The PI will inform the IRB/EC of the end of the study, and a certificate of study closure will be issued.

15 References

1. World Health Organization. (2017). *Preterm birth.* 2017 November [Accessed February 2, 2018]; Fact Sheet. Available from: http://www.who.int/mediacentre/factsheets/fs363/en/.

2. Fletcher, L., et al. (2017). *Parental Perception of Risk Associated With Their Premature Infant.* Adv Neonatal Care, 2017. **17**(4): p. 306-312.

3. Mughal, M.K., et al. (2017). *Parenting stress and development of late preterm infants at 4 months corrected age*. Res Nurs Health, 2017. **40**(5): p. 414-423.

4. Gondwe, K.W., et al. (2017). *Maternal Psychological Distress and Mother-Infant Relationship: Multiple-Birth Versus Singleton Preterm Infants*. Neonatal Netw, 2017. **36**(2): p. 77-88.

5. Polic, B., et al. (2016). *Late preterm birth is a strong predictor of maternal stress later in life: Retrospective cohort study in school-aged children.* J Paediatr Child Health, 2016. **52**(6): p. 608-13.

6. Rahman, A. M., Al Mamun, A., & Islam, A. (2017). Programming challenges of chatbot: Current and future prospective. *Humanitarian Technology Conference* (R10-HTC), 2017 IEEE Region 10: p. 75-78.

16 Appendices

APPENDIX I: Chatbot Study Screening eQuestionnaire

Date: _____

Parent

Relationship to Infant: ___Father ____Mother

Date of Birth: _____ *(excluded if not in ≥21 years of age)*

Infant

Gender: ___Boy ___ Girl

Date of Birth: _____ (*excluded if not in age group 0-6 months at time of enrollment)*

*The following is a questionnaire to help us better understand you and your baby; this will allow us to determine if this study is right for you. Please pick the **best** answer.*

1. Was your baby from a singleton pregnancy?
   a. Yes
   b. No *(exclusion)*

2. Was your baby born after 37 weeks of gestation? (i.e., how many weeks pregnant were you at delivery?)
   a. Yes
   b. No
   c. Don't Know/Not sure *(exclusion)*

3. How many weeks pregnant were you at delivery?
   _____ *(Open-ended question)*

4. What type of food does your baby typically eat? *(check all that apply)*

   ____ Breastmilk _____ Formula _____ Solid-food _____ Other *[Open-ended question]*

   (if breastmilk)

   a. At what approximate age (in weeks) do you plan to stop feeding your baby breastmilk? *[Open-ended question]*
   b. Do you know when you are planning on introducing solid food?
      i. Yes
      ii. No

      (if yes) When do you plan on introducing solid food? *[Open-ended question]*

5. Is your baby currently in the hospital?
   a. Yes *(exclusion)*
   b. No

6. Are you a single parent?
   a. Yes *(exclusion)*
   b. No

7. Are you proficient in the English language?
   a. Yes
   b. No *(exclusion)*

8. Do you or your baby have a significant limitation (including medical or physical concerns, etc.), which may interfere with daily study participation for 30 days in a row?
   a. Yes *(exclusion)*
   b. No
   c. Don't Know/Not Sure

9. Do you live in a household where you have reliable, easy access to the internet and electronic devices such as a computer, laptop, smartphone or tablet?
   a. Yes
   b. No *(exclusion)*

10. Has your baby been diagnosed with a current or previous illness or medical condition (other than prematurity)?
    a. Yes
    b. No

    (if yes) What illness or medical condition? *(open-ended response; PI to follow up)*

11. Have you been diagnosed with any of the following (please check all that apply; check "not applicable" if you have not been diagnosed with any of those listed below):

    ☐ Current or history of mental illness

    ☐ Recent or new illness/medical condition

    ☐ Ongoing illness/medical condition

    ☐ Not applicable *(if not applicable checked, participant is eligible to proceed)*

    If any responses (except not applicable) are checked:

    What specifically have you been diagnosed with? *(Open-ended response; PI to follow up)*

APPENDIX II: Usability of Chatbot and ClaimIt eQuestionnaire

The following is a questionnaire is for you to provide feedback on your interactions with the chatbot. Please pick the best answer.

1. Please rate the study chatbot's overall ease of use on a scale of 1 to 5:

   (Very Difficult) 1 2 3 4 5 (Very Easy)

2. Please rate the ClaimIt application's overall ease of use on a scale of 1 to 5:

   (Very Difficult) 1 2 3 4 5 (Very Easy)

3. How satisfied were you with your interactions with the study chatbot?

   (Very Dissatisfied) 1 2 3 4 5 (Very Satisfied)

4. How satisfied were you with your interactions with ClaimIt?

   (Very Dissatisfied) 1 2 3 4 5 (Very Satisfied)

5. Did the study chatbot malfunction?

   a. Yes (will be asked a follow-up question)
   b. No

   (If Yes) How did the study chatbot malfunction? *[Open-ended question]*

6. Did ClaimIt malfunction?

   a. Yes (will be asked a follow-up question)

   b. No

   (If Yes) How did ClaimIt malfunction? [Open-ended question]

7. How likely are you to consider using a chatbot application as an interactive tool to provide input on similar topics?

   (Not at all Likely) 1 2 3 4 5 (Very Likely)

8. How would you rate the length of interactions you had with the study chatbot?

   (Too Long) 1 2 3 4 5 (Easily Manageable)

9. What did you like the least about the study chatbot? _____ *[Open-ended question]*

10. What did you like the most about the study chatbot? _____ *[Open-ended question]*

11. Do you have any other comments about the study chatbot that you would like the investigators to know? _____ *[Open-ended question]*

12. What did you like the least about the ClaimIt app? _____ *[Open-ended question]*

13. What did you like the most about the ClaimIt app? _____ *[Open-ended question]*

14. Do you have any other comments about the ClaimIt app that you would like the investigators to know? _____ *[Open-ended question]*

15. How worried were you about sharing your data with the study chatbot?

    (Not at all worried) 1 2 3 4 5 (Very worried)

16. How likely would you be to use a chatbot tool like this in real life to get access to information and reassurance if you could?

    (Not at all likely) 1 2 3 4 5 (Very likely)

    Why or why not? *[Open-ended question]*