Data Management Plan

InstaTemp MD

Comparison of the InstaTemp MD™ Infrared Thermometer with Standard Thermometry in Canadian Routine Clinical Practice

FINAL 1.0
22-August-2017

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Abbreviations

ACR	Allphase Clinical Research Inc.
CDBL	Clinical Database Lock
CPS	Canadian Paediatric Society
(e)CRF	(electronic) Case Report Form
CSA	Clinical Study Associate
CRO	Contract Research Organization
CSM	Clinical Study Manager
eDC	electronic Data Capture
(e)DCF	(electronic) Data Clarification Form
EOS	End of Study
DE	Data Entry
DEM	Data Entry Manual
DBL	Database Lock
DBLF	Database Lock Final
DI	DataInsight
DM	Data Management
DMP	Data Management Plan
DMSMF	Data Management Study Master File
DVP	Data Validation Plan
FPFV	First Patient First Visit
FPLV	First Patient Last Visit
IS	Information Systems
LPFV	Last Patient First Visit
LPLV	Last Patient Last Visit
PD	Protocol Deviation
QA	Quality Assurance
SAS	Statistical Analysis System
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SEC	Self Evident Correction
SOP	Standard Operating Procedure
URS	User Requirement Specifications

1. Study Design and Timelines

Specification of study design	This study is a Comparison of the InstaTemp MD™ Infrared Thermometer with Standard Thermometry in Canadian Routine Clinical Practice. The InstaTempMD Study will be a Multicentre study comparing the InstaTemp MD™ to existing thermometers used in a routine clinical setting. Children in three different age cohorts will be evaluated. This study will involve collecting temperatures on patients using the InstaTemp MD™ device and the traditional method used in the clinical setting. Each of the cohorts will be analyzed by age and method of standard care as outlined by the CPS. In order to provide data on each method per cohort, subjects will be allocated to the definitive method (oral or rectal) for that cohort first followed by measurements by the InstaTemp MD™ device then the tympanic measurements where appropriate as per the CPS (2015) recommendations as indicated in section 2.0 above. Subjects therefore will be stratified by age group and standard of care as recommended by the CPS. Where three devices are used an attempt will be made to obtain measurements with all three devices but measurements with the first two devices are essential and the third device optional.
Number of patients planned	Subjects will consist of Male or female children from 1 month to 2 years, >2 years to 5 years and >5 to ≤10 years of age whose parent or legal guardian provides informed consent for participation. Each age cohort will have approximately 87 patients, 30-45 patients per cohort must be febrile. The total number of patients planned is 261.
Duration of the study for each patient	The Study period will be a single visit, 1 assessment session with up to 3 devices and up to 9 measurements performed sequentially.

Scheduled start of the study (First Patient First Visit, FPFV)	February 13 2017
First eCRF entered in DataInsight (DI)	February 13 2017
First DCFs available	March 11 2017
Scheduled end of the study (Last Patient Last Visit, LPLV)	October 31 2017
Last eCRF page entered in DataInsight	November 4 2017
Last resolved eDCF in DataInsight	November 7 2017
Database Lock (Soft)	November 7 2017
Transfer Data to Biostats (for testing)	November 7 2017
Tables and Listings sent to Sponsor	November 12 2017
Data Review Meeting	November 14 2017
Biostats Programs and Validation FINAL	November 18 2017
Data Resolution (if required)	November 19 2017
Database Final(DBLF) **	November 20 2017
Transfer Data to Biostats	November 20 2017
Tables and Listings (Biostats)	December 4 2017
Clinical Study Report	December 22 2017

** All timelines are dependent on a steady and continuous flow of eCRFs and DCFs to DM from Study Start.

2. Systems Used

Use of DataInsight	☒ Yes ☐ No
Database Hard-and Software	NA
Further Hard- and Software	NA
Query System	DataInsight and DM SOP 418 DCF process in DataInsight

3. Study Set-up

3.1 Database Set-up

Validation Requirement Asssessment Questionnaire (VRAQ)	07Dec2016	Constantin Rusan, IS
Validation Strategy Document (VSD) Final	14Dec2016	Constantin Rusan, IS
User Requirement Specifications (URS) Draft	07Dec2016	Lorraine Matthews, DM
Annotated CRF (aCRF) Final	02Dec2016	Information Systems, Data Management
e-CRFs Final	15Dec2016	Information Systems, Data Management
DMP Draft	07Jul2017	Lorraine Matthews, DM
DMP Final	30AUG2017	Lorraine Matthews, DM
Provide IS the Study Set-up	06Dec2016	Lorraine Matthews, DM
Set-up of Server and Study, provide DM Metadata Review	06Dec2016	Robert Podneau, IS
Approve initial Metadata	Dec2016	Lorraine Matthews, DM
Creation of the CRF Test Plan	07Dec2016	Robert Podneau, IS
Testing and Approval CRF Test Plan	13Dec2016	Lorraine Matthews, Cheryl Marron, DM
Creation of the SAS Transfer(s) Test Plan	09Dec2016	Lorraine Matthews, DM
Approval SAS Transfer(s) Test Plan	15Dec2016	Robert Podneau, IS

CRF Guidelines Final	16Mar2017	Lorraine Matthews, DM
Draft SAP	March 2017	BIO
Final SAP	TBD	BIO
Data Validation Plan Final	07July2017	Lorraine Matthews, DM
Programming and Testing of Edit Checks	07Sep2017	Information Systems
URS Final	15Dec2016	Lorraine Matthews, DM
System Release Memo	19Dec2016	Information Systems

****Dates are estimated and dependant on review of documents by the required timelines.**

3.2 Data Handling

Work-flow of CRFs	Site personnel will be provided a Study Specific Data Entry Manual and trained on all aspects of DataInsight (DI), data entry, as well as the Data Clarification (DCF) process in DI. Once the site training is completed and the site has been qualified for eDC, access will be granted and user accounts set-up by the IS department. SOP DM406 will be followed to assign User Access once all training and documentation has been completed for the Study Protocol by the site. Workflow management of the eCRFs is as assigned within DI and within each study specific role in the system. Data will be entered at the site by authorized site staff using DI. Validation Checks will be written in SAS and implemented along with manual checks and failed validation checks as outlined in the DVP. The Data Validation checks and listings will be used in e-CRF Review by the Data Manager or Designee. There will be DM manual review of the CRFs on an ongoing basis and DCFs will be generated as a result if required.
Work-flow of SAE-Forms	Not Applicable
Protocol Deviations	Not Applicable

CRF Tracking	CRFs will be tracked by DM at ACR using DI. Reports will be generated as defined by the Sponsor. Specific list of Reports and Frequency of the reports can be found in Appendix 2. DCFs will be added to DI and will be tracked within DI. There will be one monitoring visit per Site during the study.

3.3 Data Entry

Type of Data Capture	All Data Entry will be performed using eDC in DI and data will be entered by each site directly into DI.
Location of Data Entry (DE)	DE will be done by the Study Coordinator/site personnel at the clinical site once they have completed the Study Specific eDC Training and associated Training Logs & User Access

	forms have been completed.
Data Entry Schedule	The main person responsible for DM will be Lorraine Matthews. The peak of workload is expected between the months of October to December 2017. eCRF Data Entry by site personnel should be completed as soon as possible from FPFV.

3.4 Query Process

Work-flow of DCFs	DCFs will be generated by DM at ACR. All DM personnel will be trained on all aspects of Data Clarification as per the protocol and the DVP. A Report on all NEW and Updated Queries (DCFs) will be run in batches bi-weekly. The Report from "Notes and Discrepancies" will be exported in Excel and sent to the CSM/CSA to review and follow-up with the sites to complete. Data Management will contact sites on all outstanding queries. The Data Manager/DM personnel will identify any discrepancies on the eCRFs and look for any information that is missing or needs to be queried. SOP DM418 DCF Process in DataInsight will be followed. DCFs will be added as either a Manual DCF, Failed Validation Check and/or via a SAS program. All DCFs will be handled as per the workflow of the eCRF completion at the site. Once the Site completes an eCRF (status is marked completed in DI) the Data Manager will review the DCFs and assign to site personnel on an ongoing basis. All site personnel with DI access can review all DCFs at that site. **MANUAL DCFS (will be created as follows):** • Data Manger/DM personnel will find the specific variable that needs to be queried (e.g. Date of Birth) and click on the Discrepancy Note icon (flag) that is beside that variable. • An "Add Discrepancy Note" window will pop up and the Data Manager/DM personnel will complete all information required: ➢ Under Type, **select Query.** ➢ Under Description, Consult the Study's DVP and copy and paste the exact

	wording of the desired query from the DVP into DI (if the desired query cannot be found in the Study's DVP, create a text for the DCF and add it to the DVP or modify the text that is copied from the DVP). CSM may use their choice of query text, and it does not have to follow, or be added to the DVP. ➢ Select the "Set to Status" box as **New** from the drop down list when first creating new query. ➢ Assign to Site personnel. ➢ Once a discrepancy note has been created, the flag icon changes to red. ➢ Do NOT select the "email assigned user" option. **Resolving the DCF(s)** • Within the DI Home page, the Site personnel will see "Notes and Discrepancies assigned to me: "X", where "X" is the number of DCFs assigned to that person. All site personnel will have access to All DCFs. • Site personnel will respond to the DCFs by completing a 'Description' response and updating the Status to '**Resolution Proposed'.** • If the eCRF requires updating, the site will complete the Data Entry changes as per the Reason for Change (if CRF marked completed). • DM personnel will verify all changes have been completed in the DB by the site before any DCF is reviewed. DM personnel will close only DM generated DCFs and the CSMs will be responsible to verify and close all DCFs generated by the CSM. • <u>Do not check the box for 'Email Assigned User'.</u> • Submit the data. **Closing the DCF(s)** • Data Manager/DM personnel/CSM will review the changes made to the database by the Site. • Once an answer is provided the receiver/creator may change the status to 'Closed' if the response is acceptable or request more feedback or action by re-submitting the form to the original

	assignee. • The DCF will be set to UPDATED if the response is incorrect or requires clarification and assigned back to the original personnel at the site. **Administrative FAILED VALIDATION CHECK** **DM Personnel** • The Administrative Failed Validation Check is handled only by DM personnel and is automatic within DI. • The overall process is identical to Manual DCFs with the exception that the Failed Validation Check is initially created by the system (through programmed edit checks run by DM personnel) and NOT ASSIGNED. • Once the discrepancy note has been created, the flag icon changes to red. • Data Manager reviews the Failed Validation Checks and decides on validity. • If valid, Data Manager will select the person to whom the Failed Validation Check should be assigned to (Site). • If not valid, the Failed Validation Check will be closed by the Data Manager. • If required, a self-evident correction can be used to answer the DCF (sponsor approval required). **SAS PROGRAMS** **DM Personnel** • Export the required datasets as per SOP DM422 Export Data. • Run the Rules to be used for the eCRF Review. • Review the eCRF along with the study specific DVP found on the ACR Sponsor Drive, the rule results and any applicable line listings to determine what needs to be queried. The DVP outlines those aspects of the eCRF that need to be manually checked and those which are checked by the rules and line listings. • Find the specific variable that needs to be queried (e.g. Date of Birth). Click on the Discrepancy Note Icon (the blue flag) that

	is beside that variable. • An Add Discrepancy Note window will pop up and the Data Manager/DM personnel will be required to fill out all information required: ➢ Under Type, **select Query**. ➢ Under Description, consult the Study's DVP and copy and paste the exact wording of the desired query from the DVP into DI (if the desired query cannot be found in the Study's DVP, create a text for the DCF and add it to the DVP or modify the text that is copied from the DVP). ➢ Select a Resolution Status of **NEW** from the drop down list when first creating a query. • Once a discrepancy note has been created, the flag icon changes to red. • Select the person to whom the DCF should be assigned to (by default the system pre-selects the person whom performed the DE on the variable being queried), Site Personnel.
Study Specific Self Evident Corrections (SEC)	Self-Evident Corrections (SEC) will be identified as they occur during the course of the Study and added to the 'working copy' of the DVP. Once the Data Manager identifies a self-evident correction, an email will be sent to Mark Khachaturian for approval within the DVP section for Self-Evident Corrections. Once approved, the Data Manager will update the DVP with a section on Self-Evident corrections and create a NTF and this will continue during the course of the study. The Self-Evident Correction and this will be updated as a 'Reason for Change' in the Database.

3.5 Coding

Coding Specifications	Not Applicable
Location of Coding	Not Applicable
Coding Frequency	Not Applicable

3.6 External Data

3.6.1 Specification of external data

Data Transfer Activities	No transfers applicable
Frequency of Data Transfers	Data Transfers will follow SOP DM422 and will be set-up as a SAS dataset per each unique CRF. No regular data transfers are required unless requested by the Sponsor.

3.7 SAE/AE Reconciliation

Use of DataInsight	☒ Yes ☐ No
Process of SAE Reconciliation	Not Applicable

3.8 Quality Check

QA (patients)	The QA of the eCRF data will be done on an ongoing basis and prior to Database Lock and the listings will be reviewed for data trends. The QA will be completed by trained DM personnel on the study protocol and DVP. The trends will be for common data inconsistencies within CRFs (i.e. Year is not logical, same questions for a site or site(s) are always missing or not done, common errors on the same forms etc.) If DM notices trends, the CSM will be contacted by email to investigate the issue with the site.
Error rate (Data Management)	Error rate cannot be calculated for eCRFs. Data Manager will ensure that the Data Transfers are completed as specified in the Study Specific DMP. The Data Extracts set-up at the beginning of the Study will be extracted as per SOP DM422 Export Data. An initial transfer will be sent to the Biostatistician. The Biostatistician will determine if there are any discrepancies and/or issues that need further clarification before Database Final. A Data Review Meeting will occur between Allphase, the Sponsor and Biostatistician prior to Final DB lock. During the meeting, the Sponsor and the Allphase Team will discuss the results of the data transfer and determine next steps (if applicable), if changes to the database are required or if clarification is required from a Site(s). Once all discrepancies are resolved, the Final

	DB Lock occurs and the final transfer will be sent to the Biostatistician.

3.9 Status Reports

Data Entry Status	Data Entry Status Reports will be generated by DM.
Query Status	Query Status Reports will be generated using DI. The reports on Outstanding Queries by Site and by Type of Query will be run by the IS Department and sent to the CSA on a monthly basis.

4. Analysis

Analysis	Details of data handling procedures and statistical methodology will be defined in the Statistical Analysis Plan (SAP) prior to database lock. All deviations and discrepancies will be final prior to database lock and the Data Manager will complete the Final Checklist for Database Lock as per Allphase SOP DM414. DM personnel will ensure the following: • All expected CRF data has been entered in the Clinical Study Database as per the Study specific Data Entry Manual (DEM). • All Edit Checks as outlined in the Study specific DVP have been completed and resulting queries have been issued regarding any patient data. • All queries have been resolved, the Database has been updated with the resolution (if applicable) or a Note to File has been granted as per the Data Manager or Sponsor for any deviation(s). The Data Manager then will ensure the Quality Check is completed (if applicable) as follows: • Run all of the Study Specific Edit checks on the Clinical Study Database to ensure all queries have been resolved and no discrepancies exist. • Remove all User Access to the Database with the exception of the Data Manager. • Provide in writing to the CSM or Sponsor that the Database has been locked.

	This is the process to be followed for any interim database locks that may also occur during the course of the study. Any discrepancies noted after database lock and resulting in a database change will follow the Allphase SOP DM413 Post Database Lock Change Requests. The DM personnel will initiate the post database change process as follows: 1. Inform the Data Manager that a database change is required by completing the Post Database Change Request Form DM414Frm001 and provide the following information: • Sponsor, Protocol # and Study Title • Work Order # and DB Platform • Reason for the Database Change • Include the CRF(s): Variable Name(s) and Annotations to be modified with the DB change description • If applicable, the current data term (to be replaced) and updated data term with rationale for change. 2. Attach a copy of the CRF(s), Annotated CRF and any other applicable supporting documentation. 3. Submit to the Data Manager for Approval. **The Data Manager will then:** 4. Review the DM414Frm001 against the CRF(s) to ensure the information on the DM414Frm001 is correct. 5. Review the request to ensure the change in the data suggested has no impact on other Tables/Variables in the Database. If this does, the change must be discussed with IS personnel. 6. Export the data from the table(s) to be modified. 7. Sign and date the DM413Frm01 as approved or declined. 8. If approved, submit a User Access Form (DM406Frm01) as per DM SOP 406 to IS to allow DE to make the change. 9. Return to the completed DM413Frm01 to the Author to execute the changes. If the change is not approved the Study Team will meet to discuss the next steps.

	The DM personnel will then update the database as per the changes authorized in DM413Frm001 and select 'DB Modified' to verify the DB was updated. The Data Manager will then export the raw data from the tables that were modified and ensure no other patient data was modified. Once confirmed, the Data Manager will request IS to remove all User Access and sign off on the DM413Frm001 and file the fully execute DM413Frm01 in the DMSMF.
Interim Analysis	There is no Interim Analysis planned at this time, but may be defined at a later date if required for the Study.
Personnel, Biostats	TBD

5. Sites and Personnel – see InstaTemp MD Site List

Signature Page v 0.1 22Aug2017

Mark Haig Khachaturian
Chief Technology Officer
ARC .

8/29/2017
Date


Signature

Clinical Study Manager
Jenny Tortorici
Allphase Clinical Research Inc.

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Date

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Signature

Biostatistician
TBD

_____
Date

_____
Signature

Sr. Manager, Data Management
Lorraine Matthews
Allphase Clinical Research Inc.

_____
Date

_____
Signature

Appendix 1: Study Contact List

Name	Function	Location	Phone/fax/e-mail address
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Appendix 2: Study Specific Reports

- Full listing of open queries (by site), run monthly beginning August 2017
- DCF Status report, run monthly beginning August 2017