# Data Management Plan – EDC

## Bristol-Myers Squibb

## Study Protocol CA209-655

Hodgkin Lymphoma Molecular Profiling and Clinical Outcomes in U.S. Community Oncology Practices

## Version Final 2.0

## Date: 09-Apr-2018

**Client:** Bristol-Myers Squibb **Protocol:** CA209-655 **Bill Code:** 16BMS-0021

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## 1. Overview

inVentiv Health Clinical will provide Data Management services for Bristol-Myers Squibb protocol CA209-655. This document details the Data Management processes to be followed based on the scope of work. This study will follow inVentiv Health Clinical SOPs unless otherwise indicated and agreed to with Bristol-Myers Squibb. The Clinical Data Management System for this study will be Medidata Rave®.

As of 4th January 2018, the name of the Company has changed to Syneos Health.

## 2. Scope of Work

The following detailed the roles, responsibilities and scope of work agreed between Bristol-Myers Squibb and inVentiv Health Clinical for this study.

| Parameter | SoW # of units |
|---|---|
| Unique eCRF pages | 29 |
| Total eCRF pages (unique + copy) | 43 (29 +14) |
| Total subjects (screened/randomised) | 500 |
| Total expected eCRF pages | 43 |
| Total edit checks | 295 |
| Total custom functions | 10 |
| Total data listings | 13 |
| Total SAEs | 210 |
| Total coded terms | 6000 |
| Total data exports | 9 |

## 3. Data Management Project Team Personnel

The Data Management project team contacts are:

Marie Pare, Sr. Clinical Data Manager
Lead Clinical Data Manager (LCDM)
Marie.Pare@inventivhealth.com Tel. No. +1-289-659-7058

Caroline Chapman, Principal Clinical Data Management Programmer
Lead Clinical Data Manager Programmer (LCDMP)
Caroline.Chapman@inventivhealth.com Tel. No. +44 (0) 1628 525154

Carmen Saylor Stiles, Sr. Data Services Project Manager
Data Services Project Management
Carmen.Stiles@inventivhealth.com Tel. No. 1-859-684-2048

## 4. DM Documentation

This Data Management Plan details the Data Management processes to be followed in processing the study data based on the scope of work. Additional Data Management documentation will be generated as follow:

| Document | Content |
|---|---|
| Annotated eCRF | Details the fields within the eCRF and their properties |
| Data Review Specifications / Data Validation Plan | Data cleaning specifications including programmed edit checks in the Data Validation Plan (DVP) and data listings |
| eCRF Completion Guidelines | Document to support completion of the eCRF by site users. This may be in the form of Help Text within the database, a pdf attached to specific eCRFs or a stand-alone document |
| Data Transfer Agreement(s) | Details of data to be transferred to inVentiv Health Clinical – Not Applicable for this study |
| Medical Coding Conventions | Describes how data will have appropriate medical codes assigned |
| Quality Control Plan | Scope of independent quality control to be conducted |

Version control of documents is performed after the initial approval. The first final version of a document is represented as 1.0. Subsequently, all drafted revisions to this version are numbered as Draft 1.1, 1.2 etc.; the revised final approved version is indicated as 2.0.

For the Data Management Plan and the Data Validation Plan all changes leading to a revised version will be detailed in the Document Revision History by the author(s) including a brief description of changes in reference to the respective revised section(s).

The Trial Master File for this study will be held electronically. Wet ink signatures will be scanned into the Electronic Trial Master File and the document stored. There will be no reconciliation of wet ink versus scanned images i.e. if a wet ink signature is not returned in addition to a scanned copy this will not be considered an audit finding with regard to Data Management. However if a signed approval form is missing from the Electronic Trial Master File this will be considered a SOP deviation.

## 5. Data Management Training

inVentiv Health Clinical Data Management team members will receive study specific training. Relevant team members will be trained on final Data Management documentation e.g. team members working on data cleaning will receive training on the Data Validation Plan. Should any document be updated the relevant team members will be trained on the updated final version.

## 6. Data Management Team Meetings

Internal Data Management team meetings will take place between the Lead Clinical Data Manager and the global Data Management team as needed to discuss study status, timelines, deliverables and any other relevant topics.

External Data Management meetings will take place as required between the Lead Clinical Data Manager and the Protocol Data Manager. These may cover the Data Management status reports, open and answered query metrics, outstanding eCRF pages, SAE reconciliation issues, coding status, upcoming deliverables and any other relevant topic.

## 7. CTMS/eCRF Security and User Accounts

User access to the clinical database is controlled through study level role based security. The process for granting, changing or revoking user access to the Clinical Data Management System is defined in SOP Data Management 015, User Account Management. Requests to grant, change or revoke user access to the study are documented on the User Account Request form. The User Account Request forms are saved to the Electronic Trial Master File for audit purposes.

All users of the Clinical Data Management System must be trained prior to being granted access to the study. Training is dictated by their role in the study. Access for site users is requested by the Data Management Team, Clinical Research Associate or Project Manager.

### 7.1. Specific Roles and Access Rights

If any specific rights are given during the study e.g. entry rights to enter a single field, this will be tested to ensure the restrictions are correct, any findings added to a Peer Review Log and tracked to resolution.

Any additional or change in roles will be tested and documented.

## 8. Tracking and Status Reports

inVentiv Health Clinical and Bristol-Myers Squibb will be using standard Medidata Rave® reports for the duration of the study which include:

- Enrollment Report
- 360 Data Cleaning Progress Report
- 360 Query Management Report
- Protocol Deviation
- Query Aging
- Query Detail
- Query Summary
- Page Status

- Data Listing
- SAS on Demand

## 9. eCRF Development

### 9.1. eCRF Design

inVentiv Health Clinical will design the eCRF based on protocol requirements using the inVentiv Health Clinical standards library where possible. For any assessment not available in the standards library a unique page will be designed.

The annotated eCRF and Design Specifications will be generated and circulated for review.

The annotations include:

- Data field names and type (character, numeric) and length
- Forms

The Design Specifications include:

- Fields, forms folders and matrices
- Derivations and custom functions
- Edit checks
- Dictionaries

A collaborative review meeting(s) will be arranged for review of the eCRF online. Changes may be made during the meeting. Updated annotated eCRF will be generated after each round of updates until the design process is completed.

### 9.2. User Acceptance Testing (UAT)

On finalization of the eCRF development UAT will be conducted. Pre-validated objects copied from the standards library unchanged do not require re-testing. Objects copied from the standards library but amended must have any amendments tested. All new unique eCRFs will undergo full testing. Any UAT findings are followed up to resolution.

All testing documentation will be maintained in the study files.

On conclusion of UAT the final annotated eCRF are generated and provided for Bristol-Myers Squibb approval.

### 9.3. Electronic Case Report Form Completion Guidelines (eCCG)

Study specific eCRF Completion Guidelines are drafted by the LCDM based on the approved draft annotated eCRF and reviewed as part of the database testing. The final approved eCCG will be sent to Medidata to upload into RAVE ® enabling each site to have access from within the database while performing data entry.

## 10. Data Validation Plan (DVP)

### 10.1. Data Validation Plan (DVP) Development

Where eCRF objects are copied from the standards library the associated embedded derivations, custom functions and edit checks will follow. For any assessment not available in the standards library new data validation specifications will be drafted.

The draft DVP is internally reviewed prior to Bristol-Myers Squibb review.

Once any Bristol-Myers Squibb comments are resolved the approved draft DVP will be used as the basis for programming.

### 10.2. DVP Programming and Testing

The draft DVP will be used for any new programming. Testing can take place in parallel and data will be entered to test scenarios that meet the specifications of the DVP.

Any findings are documented within the DVP and followed up to resolution.

Upon completion and prior to the release of the edit checks to production the final DVP will be sent for Bristol-Myers Squibb approval.

The Data Validation Plan is a living document that is updated by the Lead Clinical Data Manager as required during the project conduct.

## 11. Release to Production

On completion of all database development activities and on signed approval from Bristol-Myers Squibb, the eCRFs and final DVP will be moved to production.

If necessary, inVentiv Health Clinical will perform a split database release, where the clinical database will be released to production for entry followed by the edit checks at a later date.

## 12. Production Change Control

When a possible change is identified, the Lead Clinical Data Manager and/or Project Manager will determine the cost, process and programming implications of the change. Any changes to database specifications or edit check programming will be discussed with Bristol-Myers Squibb and will require Bristol-Myers Squibb approval to proceed.

Once it is determined that the change should be made and Bristol-Myers Squibb approval is received, the Lead Clinical Data Manager documents the request on a Production Change Request Form which includes an assessment of the impact on all aspects of data processing for the study and a change implementation plan. The form is reviewed and approved by a Peer Reviewer before proceeding.

Any change is tested prior to being implemented in the Production database.

## 13. Electronic Vendor Data

N/A – this section does not apply to this study.

### 13.1. Standard Procedures for Processing Electronically Imported Data

N/A – this section does not apply to this study.

### 13.2. Standard Procedures for Processing Local Laboratory Data

The local laboratory reference ranges will be entered in Medidata Rave® just once and the ranges will autopopulate on the Laboratory Blood Tests eCRF. All out of range values will trigger an online edit check programmatically.

Local laboratory normal ranges will be entered in the Laboratory Module screen of the Medidata Rave® EDC system by the InVentiv Health Clinical Data Manager and verified by a second Data Manager. Access is restricted for entry or update of lab ranges only to users assigned with Lab Range permission.

BMS Laboratory Reference Range template will be completed by site personnel with the normal ranges from the local laboratories whenever possible. In the event that site does not complete the template, the Data Manager will obtain the normal ranges from Local Laboratory document(s).

The name/address of the laboratory and corresponding Site ID Number, the Investigator name and signature of PI or designee, and the Date Effective will also be recorded on this template. Only normal ranges for parameters required by the protocol are included in the template.

In the event that the site cannot provide ranges for all tests, inVentiv will use the book value normal ranges as found on Stedman's online:

http://stedmansonline.com/webFiles/Dict-Stedmans28/APP17.pdf

During monitoring, the CRA will check if the ranges have changed and will send an updated Local Laboratory Normal Range Reference Sheet with the new ranges to the InVentiv Health Clinical Data Manager as required.

### 13.3. Conventions for Entry of Laboratory Normal Reference Ranges

**Age:**

| Age reported (example) | Lower limit of Age | Upper limit of Age |
|---|---|---|
| <= 70 | 1 | 70 |
| >= 20 | 20 | 99 |
| <65 | 1 | 64 |
| Up to 60 yrs | 1 | 59 |
| 21-51 | 21 | 50 |

| | | |
|---|---|---|
| 51- | 51 | 99 |
| 6M-adult<br>*see below | 1 | 99 |
| Adult | 18 | 99 |
| All | 1 | 99 |
| - | 1 | 99 |

*age provided as number of months will be entered as 1 year

If a range is provided for different ages however the ages overlap, we will round down by one on the earlier age e.g. age 21-51 is 16-40 u/L and age 51- is 17-45 u/L = this will be entered into RAVE as age 21-50 16-40 u/L and age 51-99 17-45 u/L.

If a set of ranges are received with only some tests having the age specified, the assumption will be that the other, non-specified ages are adult ranges and we will enter these into RAVE as 18-99 except where age is specifically noted.

**Analyte Test Value:**

| Range reported (example) | Lower limit of study range | Upper limit of study range |
|---|---|---|
| < 0.5 | 0 | 0.49 |
| <0.2 | 0 | 0.19 |
| < 13.6 | 0 | 13.5 |
| <79 | 0 | 78.9 |
| Negative | 0 | 0 |
| - to 10 | 0 | 10 |
| Below 37 | 0 | 36.9 |

**Effective Date:**

If effective date does not have a day provided, we will enter as first of the month eg. 00-Aug-2016 entered in RAVE as 01-Aug-2016.

## 14. Dictionary Coding

The following items are coded using the dictionary indicated:

| Medical Coding Dictionary | Dictionary Version | Dictionary Update Schedule | Dataset | Data Item |
|---|---|---|---|---|
| MedDRA | 19.0 | Twice a year per BMS Versioning Strategy | Treatment-related Adverse Event Term | Verbatim Term, Preferred Term, High Level Term (HLT), System Organ Class (SOC) |
| WHO Drug | Mar2016 DDE+HD | Twice a year per BMS Versioning Strategy | Concomitant Medications for Treatment-Related AEs | Verbatim Term, Preferred Term, ATC Classification |
| WHO Drug | Mar2016 DDE+HD | Twice a year per BMS Versioning Strategy | Steroid and Immunosuppressant Medications | Verbatim Term, Preferred Term, ATC Classification |

inVentiv Health Clinical licenses and maintains the most current version of the WHO Drug and MedDRA coding dictionaries.

inVentiv Health Clinical requires Bristol-Myers Squibb to have a current license and/or subscription agreement relating to the use of the WHO Drug Dictionary and MedDRA in order for inVentiv Health Clinical to forward WHO Drug Dictionary-coded medications and MedDRA-coded data to Bristol-Myers Squibb.

inVentiv Health Clinical utilizes the Oracle Thesaurus Management System (TMS) to process coding of study data on a monthly basis. Queries are issued during this cycle in the source database as needed per the Medical Coding Conventions. Answered queries will be reviewed, re-issued or closed in the study database during this monthly cycle. Upon completion of coding, the new coded datasets will be extracted from TMS and available for use as needed on study. This cycle is repeated prior to study deliverables that require current and complete coding for all or specific subject data.

Details of the Medical Coding process can be found in the attachment Medical Coding Conventions.

## 15. Data Entry by Investigative Sites

Data entry by the Principal Investigator or designated personnel is expected at a minimum frequency of two weeks following when new patient data becomes available.

The eCRF Completion Guidelines will instruct the Principal Investigator or designated personnel in performing data entry and discrepancy management. These instructions will contain study information and will explain how to enter uncommon data and/or how

to review/route/resolve specific discrepancies that may be generated during the data entry. These guidelines will be updated as necessary throughout the study.

Updates to saved data are made by the investigative site personnel and are saved in an electronic audit trail.

## 16. Data Cleaning

### 16.1. Source Data Verification

The Clinical Research Associate performs verification by comparing the entered data against the source documents. The Clinical Research Associate will flag any differences between initial data entry and verification through the creation of a manual discrepancy on that data point. For further details please refer to the Monitoring Plan.

### 16.2. Data Management Data Cleaning

The Data Management team reviews discrepancies created by the electronic validations on an ongoing basis. The paper QoL questionnaires are entered by site personnel and have limited data cleaning (as specified in the Data Validation Plan) as these are patient reported data and it is not possible to go back to the patient and verify the information provided.

Manual queries are generated by Data Management as a result of data cleaning, and may begin with a specific query text, depending on the query type:

- Queries generated for SAE reconciliation will begin with text: ‘Per SAE Reconciliation’.
- Queries generated for Coding will begin with text: ‘Per coding’.
- Queries generated based on protocol deviation edit checks will begin with text: ‘Protocol Deviation’.

Each query is identified by a unique query identification number for tracking purposes and the source will be noted via the Marking Group as follows:

- Queries generated electronically will have Marking Group noted as ‘Site from System’.
- Queries generated by Data Management will have Marking Group noted as ‘Site from Data Management ’.
- Queries generated by the CRA will have Marking Group noted as ‘Site from CRA’.
- Queries generated by the Medical Coder will have Marking Group noted as ‘Site from Coder’.

### 16.3. Medical Review

N/A - this section does not apply to this study.

### 16.4. Protocol Deviation Review

During the development of the DVP any edit checks that identify protocol deviations will be listed in a separate tab. The query message will be prefixed with 'Protocol Deviation'. All confirmed protocol deviators will be removed from the study database after confirmation by the clinical team.

### 16.5. Query Management

The Principal Investigator or designated personnel is responsible for responding to the queries by updating the eCRF or indicating no change is necessary in the response section of the query within 10 working days of receipt of the query. If queries are not answered within the timeframe then the Lead Clinical Data Manager will escalate to the Lead Clinical Research Associate and Project Manager.

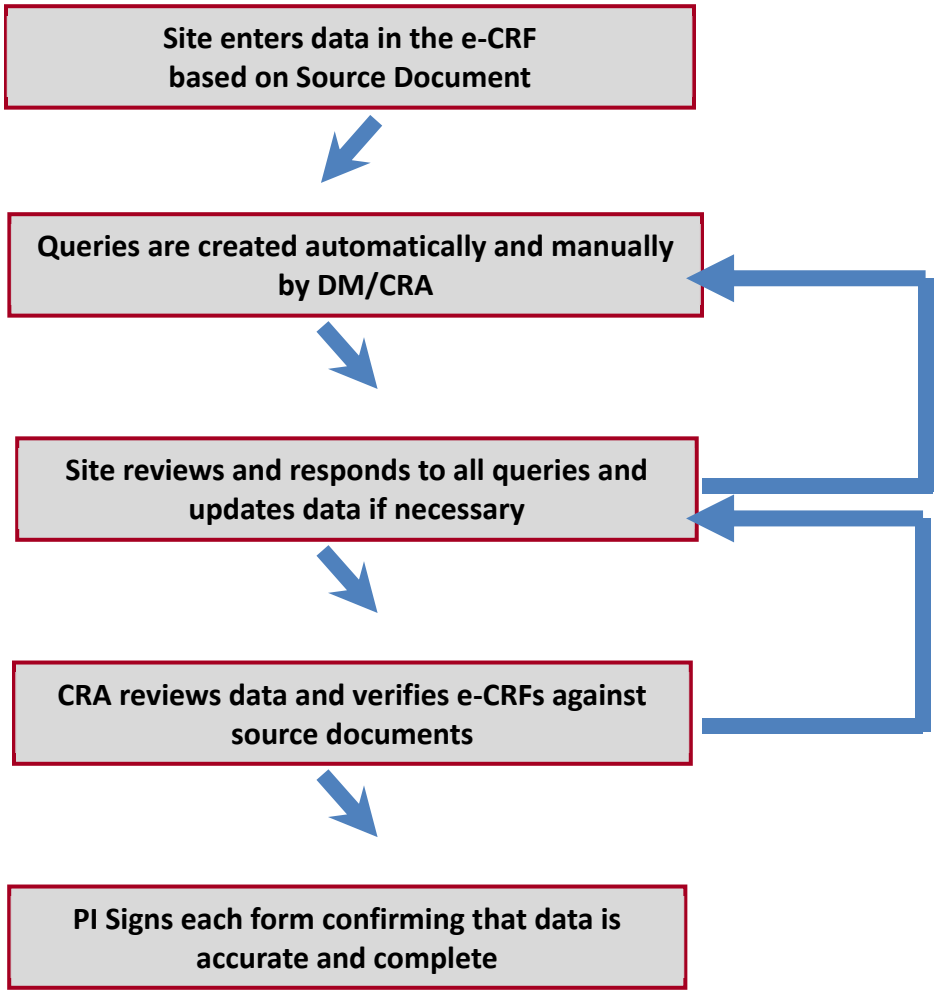
The Data Management Team, Clinical Research Associate and the Medical Coding Specialist will review query responses to ensure the queries have been resolved appropriately. Should further clarification be required, then a re-query will be issued. This process will continue until the data has been updated or sufficiently addressed within the comments section of the query.

If a query has confirmed that a page or log line was not needed and was saved blank in error however the site has not performed the steps of inactivating the blank page or log line, inVentiv Data Management may inactivate it. This can always be reversed and reactivated by the site if the page or log line is needed at a later date.

### 16.6. Ongoing Review

Data trends, including outstanding queries, will be identified on a routine basis and reported to the project team at the regularly scheduled project management team meetings.

On completion of all data cleaning activities the Investigator may sign the eCRF upon notification from the CRA.




## 17. Quality Control Activities

Quality control procedures will be conducted internally on an ongoing basis during study processing. Procedures relating to data quality and discrepancy management are detailed in the Quality Control Plan.

## 18. Independent Data Meeting Committees

N/A - this section does not apply to this study.

## 19. Serious Adverse Event Management

The Lead Clinical Data Manager and the Safety Associate will liaise during study start-up activities to ensure that the clinical database and the SAE Report Form are designed according to the protocol to capture commonly collected data in a similar format.

DM will perform a reconciliation of the Adverse Events marked as “Serious” in the clinical database versus a CARES listing of the SAE’s provided by the Bristol-Myers Squibb Pharmacovigilance from their safety database. A Serious Adverse Event reconciliation programmatic report will be created by the Lead Clinical Data Management Programmer and the reconciliation will be performed quarterly and prior to database finalization activities. It will include the following SAE reconciliation variables:

| Serious Adverse Event Reconciliation Variables | Type of Match (Exact / Logical) |
|---|---|
| Protocol Number | Exact |
| Patient Identifier (site and subject number) | Exact |
| Verbatim Term | Logical |
| Serious Adverse Event Onset Date | Logical |
| Outcome (if Fatal - Safety DB / Death - Clinical DB) | Logical |

Any information concerning SAEs will be sent to the Safety Associate immediately upon being noted, regardless of whether the safety database requires updating.

Queries generated for SAE reconciliation will begin with text: ‘Per SAE reconciliation’.

Data Management will review the output of the SAE reconciliation program and identify any reconciliation discrepancy between the two sets of data. All actions will be annotated onto the reconciliation listing.

The Lead Clinical Data Manager and the Safety Associate will discuss and review any queries that are outside the agreed plan of action provided in this Data Management Plan and work to resolve issues.

If updates are required to the safety database, the Data Manger will send screenshots of data entered in the clinical database, along with the audit trail showing changes to the data field to the Safety Associate. Additionally the Data Manager will send a list of SAEs that are entered in the clinical database but are missing in the safety database, to the Safety Associate.

Prior to database lock, when all queries have been resolved and SAE reconciliation is finalised, the Lead Clinical Data Manager will obtain the appropriate signatures on the Serious Adverse Event /Serious Adverse Drug Reaction/Serious Adverse Device Effect Reconciliation Form, including Bristol-Myers Squibb signature. When all signatures have been obtained, the LCDM will forward the form for inclusion in the eTMF.

# 20. Database Finalization and Approval

## 20.1. Principal Investigator Approval

Before soft lock, the Principal Investigator is required to approve all pages for each subject when the following criteria have been met:

- Subject has completed or discontinued from the study
- All eCRF pages have been entered into the clinical database
- All key eCRF pages have been source verified by the CRA
- All outstanding discrepancies have been resolved

This process requires the investigator to enter an electronic signature, consisting of a User ID and a password, for each screen/book that has been entered. This electronic signature is the equivalent of a handwritten signature and is legally binding. The Principal Investigator may create manual discrepancies on any data thought to be inaccurate. If the resolution of the discrepancy requires a modification to the data then that screen will have to be re-verified prior to being approved.

## 20.2. Finalisation of Data Cleaning

A subject is considered to be 'clean' when the following criteria have been met:

- All Source Data Verification is complete as per the Monitoring Plan.
- All eCRF data have been entered and accounted for and Investigator signature has been applied.
- All patient QoL data has been entered.
- All queries have been issued and resolved to terminal status.
- All relevant data has been manually reviewed via listings
- Medical Coding is complete
- Serious Adverse Event reconciliation is complete.
- All eCRFs are locked.(if locking or freezing on an ongoing basis)

## 20.3. Final Documentation

The Lead Clinical Data Manager ensures that all data management documentation is at final approved status prior to Soft Lock:

- Data Management Plan and attachments
- Signed approval forms
- All other Data Management documents as required by inVentiv Health Clinical SOPs

## 20.4. Soft Lock

Once all data cleaning is complete the data will be extracted from the clinical database. The Lead Clinical Data Manager will run the final status reports and confirm that all required activities are completed and all eCRFs are locked.

A new data extract will be taken and compared to the earlier extract to ensure there are no late changes after all data is deemed clean. Any issues are resolved by the Lead Clinical Data Manager and peer reviewed.

The Lead Clinical Data Manager circulates the Soft Lock Approval Form for signature and once completed will declare Soft Lock. The Lead Clinical Data Management Programmer transfers the data to Bristol-Myers Squibb and the inVentiv Health Clinical Statistician.

In the event that data corrections are needed between Soft Lock and Hard Lock the relevant eCRFs must be unlocked for changes to be made. The Lead Clinical Data Manager will then repeat the comparison process and declare re-lock.

### 20.5. Hard Lock

The Clinical Data Manager Programmer extracts the SAS datasets from the eCRF for comparison with the previous data extract to ensure that no undocumented data changes have occurred.

Once the compare process is complete, the Lead Clinical Data Manager will notify the team of Hard Lock.

Hard Lock is declared and the SAS datasets are transferred to Bristol-Myers Squibb and the inVentiv Health Clinical Statistician.

Post Hard Lock data corrections require Bristol-Myers Squibb approval via the Post Hard Lock Modification Approval form.

## 21. Data Management Deliverables

These are listed below.

## 22. Data Transfers

### 22.1. Type of Data Transfers and Transfer Schedule

| **Data to be Transferred** *(Test, Interim, Final)* | **Data Status** *(Clean/ Not Clean)* | **Recipient** | **File format** *(SAS XPT, password protected zip file)* | **Transfer Method** *(sFTP, email, CD)* | **# Transfers** *(1, 2, 3, etc.)* | **Timing/ Frequency** *(Study start-up, prior to draft database, specified intervals)* |
|---|---|---|---|---|---|---|
| Interim | Not clean | BMS | SAS XPT | sFTP | 8 | Interim data cut – date TBD |
| Final Database (raw datasets) | Clean | Bristol-Myers Squibb | SAS XPT | sFTP | 1 | Final Database |

SAS On Demand will be utilized to extract raw datasets from the clinical database, which will be sent to Bristol-Myers Squibb and the inVentiv Health Clinical Statistician.

The final transfer will be generated after all user access has been removed and the clinical database is declared final.

## 23. Study Archiving

### 23.1. Archiving electronic Case Report Forms

Archive files of the eCRFs and associated audit trail will be created as follows:

- All subjects for shipment to Bristol-Myers Squibb
- All subjects by site to be stored in site folders

The archive PDF files will be saved as password protected ZIP files, copied to optical storage disc (e.g. DVD) and files for each site will be stored in site folders. A separate disc containing all subjects will be forwarded to Bristol-Myers Squibb.

### 23.2. Archiving Paper Documentation

The Lead Clinical Data Manager sends the final study documentation to the eTMF.

## 24. Document Revision History

| Version # | Plan Section Affected by Change | Change Made to Plan | Author |
|---|---|---|---|
| Draft 0.1 | NA | Initial Draft | Kiran Potdar |
| Draft 0.2 | NA | Updated per internal review | Marie Paré |
| Final 1.0 | NA | Initial Release | Marie Paré |
| Draft 1.1 | 13.2, 13.3, 16.5 | inVentiv DM took over the responsibility of entering lab normal reference ranges from the sites therefore section 13.2 was revised and 13.3 added. Also Appendix A and B added to clarify the process of entering lab normal ranges. One comment was added to Query Management section 16.5. | Marie Paré |
| Draft 1.2 | 1, 13.2 | Added note regarding change in company name; updated the online reference for standard lab ranges | Marie Paré |
| Final 2.0 | NA | Second Release | Marie Paré |
| | | | |

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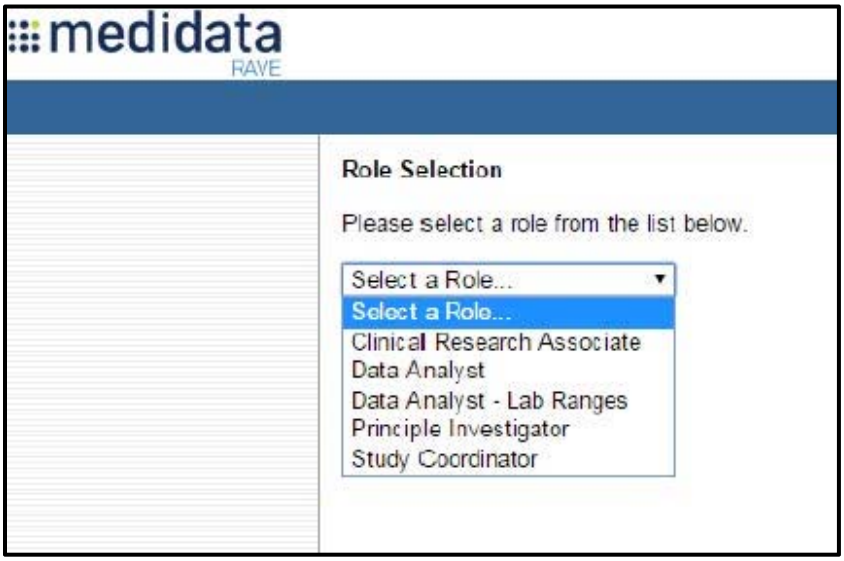
## APPENDIX A – Laboratory Reference Range Entry

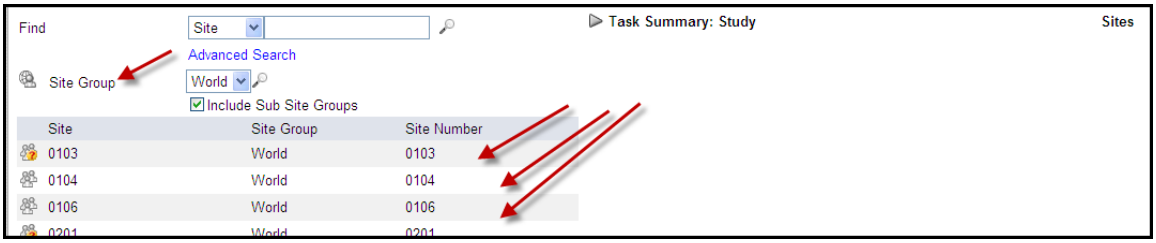
## How to enter lab reference ranges in Medidata Rave®

1. Log into Medidata Rave® and select your study.

2. Select the 'Data Analyst – Lab Ranges' role.




3. Select the site for which you wish to add 'Lab Ranges'.



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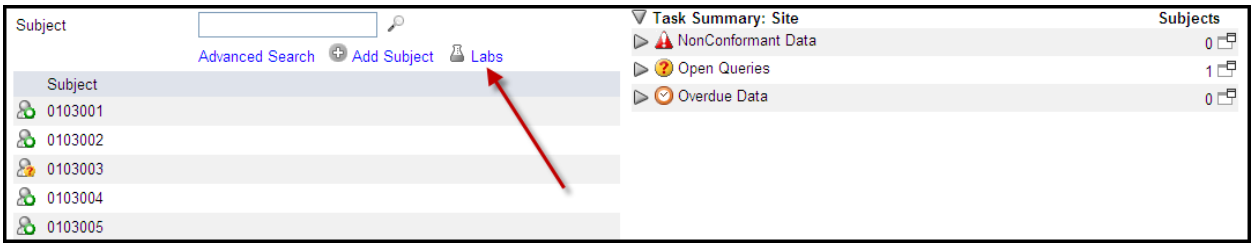
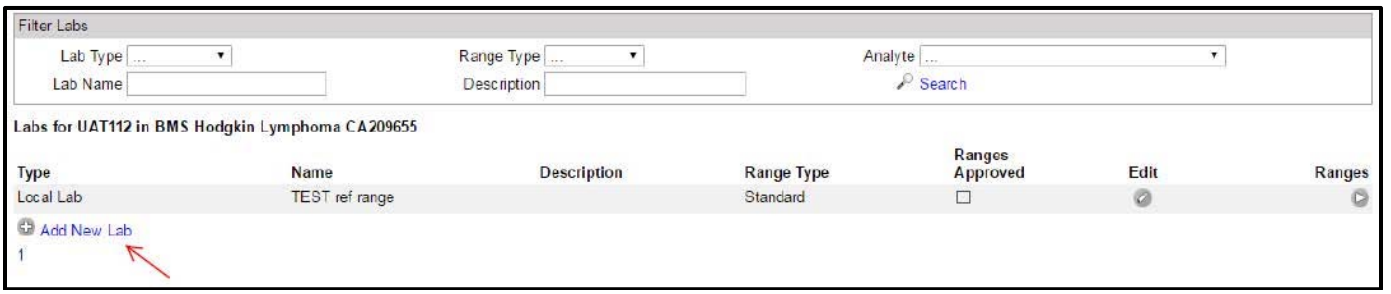


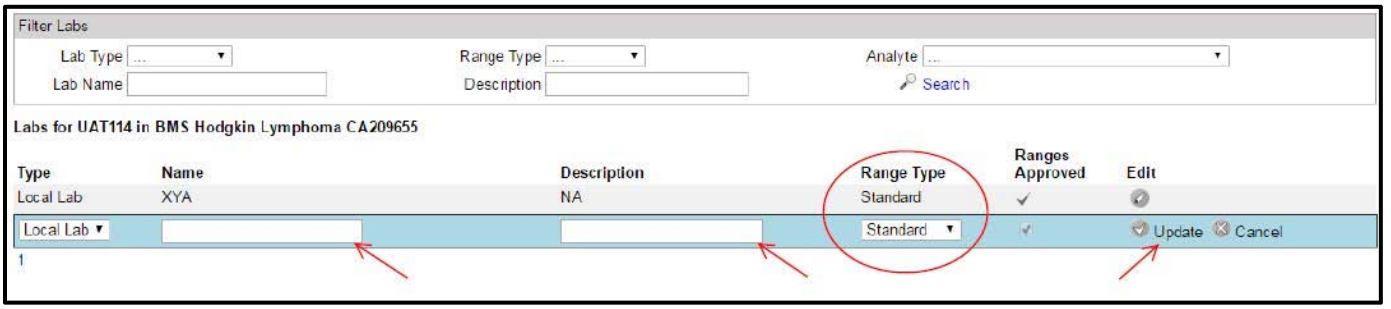

4. On the screen as shown above, click on the 'Labs' icon at the top of the screen.
5. Then click on 'Add New Lab'.



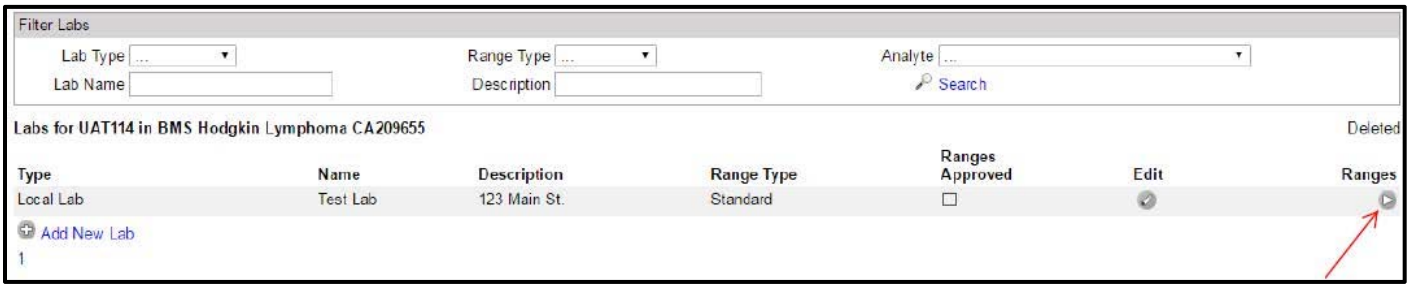

- 

6. Enter new 'Lab Name', 'Description', 'Range Type', then click 'Update'.

- (Note: since both genders are eligible to participate in this study, **always select 'Range Type' as 'Standard'** when entering lab reference ranges. This 'Standard' type will enable you to choose specific genders when entering analyte ranges that are not the same for both male and female).

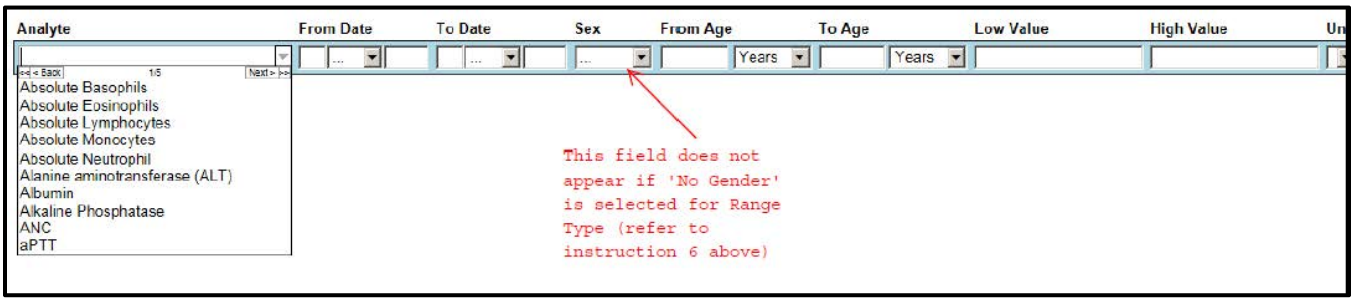


7. You will then see a screen as shown in the image below. Click on 'Ranges'.

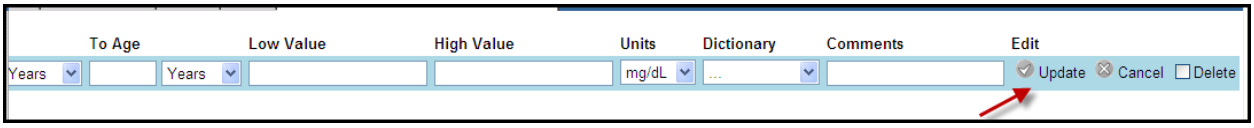



8. You will now see the screen shown below. Click Add New Range.

9. Select the required analyte from the drop down list and enter all information requested across each field.
    - *Mandatory fields include: Analyte name, From Age, To Age, Low Value, High Value and Units.*
    - **Sex: If you are entering a range that is specific for one gender, select either 'Male' or 'Female' from the drop down box. If you are entering a range that is the same for both male and female subjects, leave the 'Sex' box blank and the Medidata RAVE® system will automatically apply the range to both genders.**
    - If To Dates are not entered, that means the range will be valid until otherwise specified. From Date must be entered.
    - The Dictionary Column can be left blank and Comments are optional.




10. Click on 'Update' once all fields for each lab test have been entered and ADD additional lab analyte ranges as required until ALL laboratory results captured on the eCRF page have corresponding normal range information applied.




The above process of entering and updating Laboratory Normal Ranges is required for the Laboratory Blood Tests page in the study.

**Client:** Bristol-Myers Squibb **Protocol:** CA209-655 **Bill Code:** 16BMS-0021

## APPENDIX B – Laboratory Reference Range Template

Bristol-Myers Squibb

inVentiv Health clinical

| Study: BMS Hodgkin Lymphoma CA209655 | | Site Number: |
|---|---|---|
| Investigator Name: | | Name & Address of Laboratory: |
| Investigator Signature (*or approved designee*): | | |
| Signature Date: | _____ / _____ / _____ | |

**Effective Date of Ranges** (dd/MMM/yyyy): _____ / _____ / _____

| Analyte Name | Age Lower | Age Upper | Gender: Male or Female or Both | Unit | Lower Limit of Range (≥) | Upper Limit of Range (≤) |
|---|---|---|---|---|---|---|
| *e.g. 1* | *19* | *-* | *Both* | *g/dL* | *-* | *400* |
| *e.g. 2* | *all* | *all* | *M*<br>*F* | *%* | *11.5*<br>*13* | *17*<br>*21* |
| Hematocrit | | | | | | |
| Hemoglobin | | | | | | |
| Platelet Count | | | | | | |
| Red Blood Cell Count (RBC) | | | | | | |
| White Blood Cell count (WBC) | | | | | | |
| Absolute Neutrophil Count (ANC) | | | | | | |
| Absolute Lymphocytes | | | | | | |
| Absolute Monocytes | | | | | | |
| Absolute Eosinophils | | | | | | |
| Absolute Basophils | | | | | | |
| Lactate dehydrogenase (LDH) | | | | | | |
| Erythrocyte sedimentation rate (ESR) | | | | | | |
| Red Blood Cell Distribution Width (RDW) | | | | | | |
| Aspartate aminotransferase (AST) | | | | | | |
| Alanine aminotransferase (ALT) | | | | | | |
| Albumin | | | | | | |