Case Report Form and Data Management

From Case Report Forms to Final Analysis

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ICH GCP Workshop

Department of Medical Research, Yangon. **13-14 February, 2020**

Data Collection Tools/CRF Design

Most important step in ensuring data quality is appropriate form design

- CRF Content
- CRF Layout

Case Report Form

A printed, optical, or electronic document designed to record all of the protocol required information to be reported on each trial subject,

CRF Content

- CRF questions, prompts and instructions should be clear and concise
- Avoid open-ended questions
- Phrase questions in the positive in order to avoid confusion
- Use appropriate, mutually exclusive responses
- Include units of measurement (e.g. DLCO ml/min/mmHg)

CRF Content(Continue)

- Collect raw data versus derived data
- Explicitly identify data (e.g. first name, middle name, last name versus name
- Avoid referential and redundant data points
- Include an identifier for the protocol version
- Keep subject identifiers to minimum

DON'T

Q1. How much pain have you experienced lately?

Q2. Weight:_____kg/lbs

Q3. Current Medications:

1. _____
2. _____
3. _____

- **DO**

Q1. How much pain have you experienced lately?

none a little some a lot

Q2. Weight:_ _ _._ kg

Q3. Current Medications?

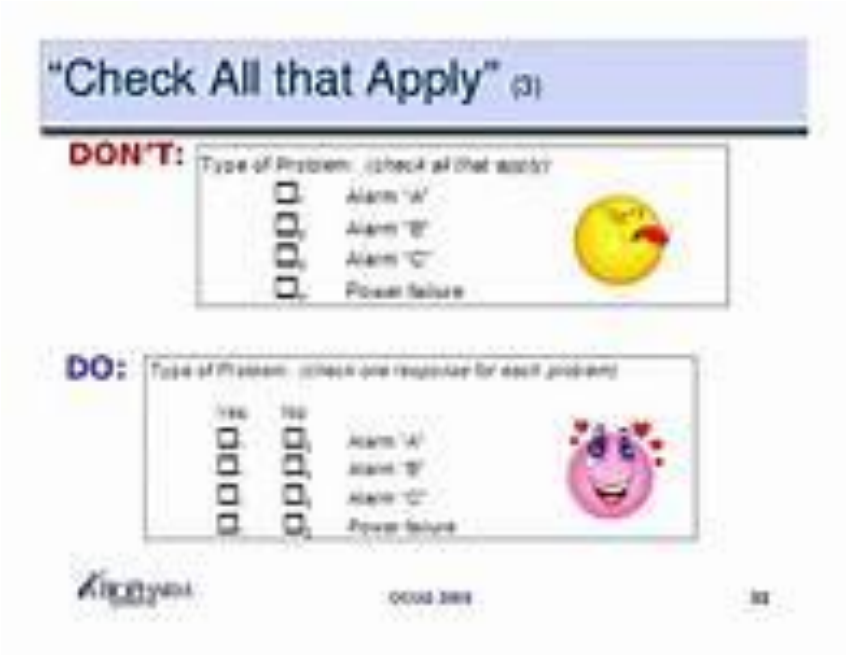
Tylenol • Yes No

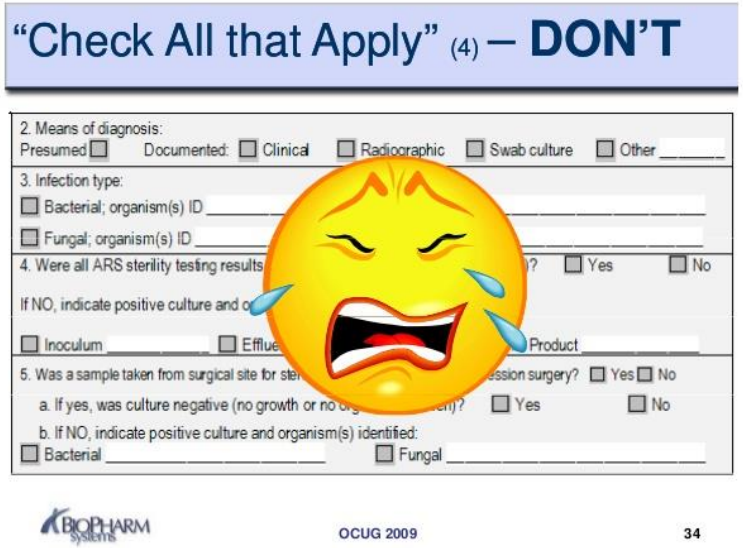
Advil • Yes No

Aleve • Yes No

CRF Layout

- Place key data used in the analysis prominently on the page
- Create well-ordered, structured , easy to follow CRFs
- Adopt consistent style for all the CRFs in the study
- Design the CRFs to follow the data flow from the perspective of the person completing the CRF
- Pilot the CRFs prior to study initiation





CRF Layout

Updated: 03/26/07

HIV-1 RNA RESULTS

IMAGING STUDY OF HIV CEREBRAL INJURY

MRHC 001 / Navia
VI8900

Patient Number ☐☐ ☐☐☐☐ ☐ Date of Specimen collected ☐☐ / ☐☐ / ☐☐☐☐

Form Week ☐☐☐ Completed By (Initials): ☐☐☐

*Sequence Number ☐ * Enter a "1" if this is the first of this form for this date. Designate subsequent forms on the same date with a 2, 3, etc.

Collection Site ☐ UCSD ☐ UCLA ☐ UCLA Harbor ☐ Rochester ☐ Pittsburgh ☐ Penn ☐ Colorado ☐ Stanford

INSTRUCTIONS: Key this form immediately upon receipt of the results from the laboratory.
Use the same header information that was used on the Virology Specimen Tracking Form (VI14688).

1. Was the HIV-1 RNA result obtained from testing lab?..... (1 - Yes, 2 - No) ☐

   If Yes, go to question 2.
   If No, complete (a.) and STOP.

   Reason from testing lab that results were not obtained: [70]

   a. _____

2. Enter the specimen ID number [15]:..... ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

CRF Layout, continued

3. Enter the name of the testing lab..... _____

4. Date assay performed:..... ☐☐ / ☐☐ / ☐☐☐☐

5. Type of assay:..... ☐

1 - Roche RT-PCR (Amplicor™) HIV-1 Monitor
2 - Roche Ultra-sensitive ™
3 - Chiron 1 Generation bDNA
4 - Chiron 2 Generation bDNA (ultra-sensitive)
5 - Organon (Teknika™) NASBA
6 - Organon (Teknika™) Nuclisens
7 - Roche RT-PCR (Amplicor™) HIV-1 Monitor V.1.5
8 - Roche Ultra-sensitive V.1.5

9 - Other, specify [30]: _____

6. Enter the plasma HIV-1 RNA result in copies/mL and the quantifier code:

Plasma RNA Results (copies/mL) ☐☐☐☐☐☐☐☐ **Quantifier Code 1 (=), 2 (>), 3 (<)** ☐

7. Enter the CSF HIV-1 RNA result in copies/mL and the quantifier code:

a. Date CSF RNA performed ☐☐ / ☐☐ / ☐☐☐☐

b. CSF RNA Results (copies/mL) ☐☐☐☐☐☐☐☐ **Quantifier Code 1 (=), 2 (>), 3 (<)** ☐

8. Were there any additional comments, (i.e. censor codes) from the testing lab?..... (1 - Yes, 2 - No) ☐

If No, STOP.
If Yes, complete (a.)

a. Comments [70]: _____

Delaware Adult HIV Confidential Case Report Form

(Patients ≥ 13 years of age at time of diagnosis

DATE ENTERED:

I. HEALTH DEPT USE ONLY

Document ID	Soundex Code	Report Status	Date Rec'd at DPH	State Number
DE00-		New Update	_____/_____/_____	
Document Source	**New Investigation**	**Report Medium**	**Surveillance Method**	
A_____-_____-_____-_____	Y N U		A F P R U	

II. PATIENT IDENTIFIER INFORMATION – *data not transmitted to CDC*

Patient Name: _____ Patient Alias: _____ SS#: _____-_____-_____
(last first middle)

Current Address: _____

City: _____ County: _____ State: _____ Zip: _____ Phone: ( ) _____-_____

III. FORM INFORMATION

Date form completed: ____/____/_____ Person completing form: _____ Phone: ( ) _____-_____

IV. CURRENT PROVIDER INFORMATION

Physician: _____ Facility: _____
(last first middle)

City: _____ State: _____ Phone: ( )_____-_____

Med Rec No: _____ Date of Most Recent Visit: ____/_____/_____

V. DEMOGRAPHIC INFORMATION – *complete ALL fields*

Diagnostic Status:
☐ Adult HIV
☐ Adult AIDS

Sex at Birth:
☐ Male
☐ Female

Date of Birth:
____/____/_____

Country of Birth:
☐ U.S. ☐ U.S. Territory
☐ Unk ☐ Other_____

Status:
☐ Alive
☐ Dead
☐ Unk

Death Date: ___/_____/_____
State/Terr of Death: _____

Marital Status:
S M W D Oth Unk

Ethnicity:
Hispanic ☐ Yes ☐ No ☐ Unk
Arabic ☐ Yes ☐ No ☐ Unk

Race (check all that apply):
☐ Black/AA ☐ White ☐ Asian ☐ Native American or Alaskan
☐ Hawaiian/PI ☐ Unk ☐ Other_____

Residence at HIV Diagnosis: ☐ Same as Current Street Address: _____
City: _____ County: _____ State/Country: _____ Zip: _____

Residence at AIDS Diagnosis: ☐ Same as Current Street Address: _____
City: _____ County: _____ State/Country: _____ Zip: _____

VI. FACILITY OF DIAGNOSIS

HIV Facility:
Address:
City, State/Country

AIDS Facility:
Address:
City, State/Country

HIV	Facility Type	AIDS
	Private Physician	
	Hospital Inpatient	
	Outpatient	
	Emergency Department	
	Other:_____	

VII. PATIENT HISTORY – COMPLETE ALL FIELDS

Before the 1st positive HIV test/Stage 3 HIV diagnosis, patient had:	Y	N	U
Sex with male			
Sex with female			
Injected drugs			
Received clotting factor			
Heterosexual relations with the following:			
• Injecting Drug User (IDU)			
• Bisexual male **(applies to females only)**			
• Person with hemophilia/ coagulation disorder			
• Transfusion recipient w/ documented HIV infection			
• Person with AIDS or documented HIV infection, risk unspecified			
Received transfusion Date 1st: / Date last: /			
Received organ transplant, tissue or artificial insemination			
Worked in healthcare/clinical laboratory **OCCUPATION:**			
Perinatally Infected			
Other:			

VIII. DUPLICATE REVIEW AND ADDITIONAL PATIENT OR DEMOGRAPHIC INFORMATION:

_____
_____
_____
_____
_____

COMPLETE REVERSE SIDE OF FORM

MISSOURI DEPARTMENT OF HEALTH AND SENIOR SERVICES
Section for Disease Prevention
930 Wildwood Drive, P.O. Box 570, Jefferson City, MO 65102-0570
Telephone: (573) 751-6113 FAX: (573) 526-0235

DISEASE CASE REPORT

IF THE CONDITION REQUIRES IMMEDIATE PUBLIC HEALTH INTERVENTION, OR IS SUSPECTED OF BEING A DELIBERATE ACT, OR PART OF AN OUTBREAK, CALL THE DEPT OF HEALTH AND SENIOR SERVICES 24 HOURS A DAY, 7 DAYS A WEEK AT 1-800-392-0272

FOR PUBLIC HEALTH AGENCY USE ONLY	
CONDITION I.D.	PART Y I.D.
OUTBREAK I.D.	DATE RECEIVED BY LPHA
JURISDICTION	

NAME (LAST, FIRST, M.I.)	PATIENT IDENTIFIER	DATE OF BIRTH	AGE	MARITAL STATUS	SEX
					☐ Male ☐ Female

PATIENT'S COUNTRY OF ORIGIN	DATE ARRIVED IN USA	OCCUPATION	RACE/ETHNICITY (CHECK ALL THAT APPLY):
			☐ AMERICAN INDIAN ☐ PACIFIC ISLANDER ☐ UNKNOWN ☐ ASIAN ☐ WHITE ☐ BLACK ☐ OTHER RACE – Specify:
HOME TELEPHONE	WORK TELEPHONE	PARENT OR GUARDIAN	HISPANIC: ☐ YES ☐ NO ☐ UNK

IS PERSON HOMELESS? ☐ YES	ADDRESS	CITY, STATE, ZIP CODE	COUNTY OF RESIDENCE

WAS PATIENT HOSPITALIZED? ☐ YES ☐ NO	IF YES, NAME OF HOSPITAL	HOSPITAL ADDRESS	CITY, STATE, ZIP CODE	HOSPITAL TELEPHONE

REPORTER NAME (Form Completed By)	REPORTING FACILITY	REPORTER ADDRESS	CITY, STATE, ZIP CODE	REPORTER TELEPHONE

TYPE OF REPORTING FACILITY	DATE OF REPORT	PHYSICIAN/CLINIC NAME	PHYSICIAN/CLINIC TELEPHONE	HAS PATIENT BEEN NOTIFIED OF DIAGNOSIS/LAB RESULTS?
☐ PHYSICIAN ☐ OUTPATIENT CLINIC ☐ HOSPITAL ☐ LABORATORY ☐ SCHOOL ☐ OTHER:		PHYSICIAN/CLINIC ADDRESS	CITY, STATE, ZIP CODE	☐ YES ☐ NO ☐ UNK

PREGNANT	OTHER ASSOCIATED CASES?	RECENT TRAVEL OUTSIDE OF IMMEDIATE AREA?			
☐ YES - DUE DATE: ☐ NO ☐ UNK	☐ YES ☐ NO ☐ UNK	☐ YES ☐ NO ☐ UNK	DATE OF DEPARTURE	DATE OF RETURN	TRAVEL LOCATION

CHECK BELOW IF PATIENT OR MEMBER OF PATIENT'S HOUSEHOLD (HH/LD):	PATIENT			HH/LD MEMBER			IF YES, PROVIDE BUSINESS NAME, ADDRESS AND TELEPHONE NUMBER
	YES	NO	UNK	YES	NO	UNK	
IS A FOOD HANDLER?	☐	☐	☐	☐	☐	☐	
ASSOCIATED WITH OR ATTENDS CHILD/ ADULT CARE CENTER?	☐	☐	☐	☐	☐	☐	
ASSOCIATED WITH OR RESIDENT OF NURSING HOME?	☐	☐	☐	☐	☐	☐	
ASSOCIATED WITH OR INMATE OF CORRECTIONAL FACILITY?	☐	☐	☐	☐	☐	☐	
ASSOCIATED WITH HOMELESS SHELTER?	☐	☐	☐	☐	☐	☐	
IS A STUDENT OR FACULTY/STAFF OF A SCHOOL?	☐	☐	☐	☐	☐	☐	
IS A HEALTH CARE WORKER?	☐	☐	☐	☐	☐	☐	
OTHER (specify):	☐	☐	☐	☐	☐	☐	
HAS PATIENT DONATED OR RECEIVED BLOOD OR TISSUE?	☐	☐	☐	DATE DONATED		DATE RECEIVED	SPECIFY TYPE OF BLOOD OR TISSUE AND FACILITY NAME/ADDRESS

DISEASE (CONDITION NAME(S))	ONSET DATE(S)	DIAGNOSIS DATE(S)	SEVERITY OF VARICELLA	VACCINATION HISTORY FOR REPORTED CONDITION/DATES ☐ UNKNOWN
			☐ <50 lesions ☐ 50-249 lesions ☐ 250-500 lesions ☐ >500 lesions	

SYMPTOM	SYMPTOM SITE	ONSET DATE (MO/DAY/YR)	DURATION (DAYS)

DID PATIENT DIE OF THIS ILLNESS? ☐ YES ☐ NO - IF YES, GIVE DATE:

COMMENTS:

DO NOT COMPLETE DIAGNOSTICS IF LAB SLIP IS ATTACHED

RESULT DATE (MO/DAY/YR)	TYPE OF TEST	SPECIMEN TYPE/SOURCE	SPECIMEN DATE (MO/DAY/YR)	QUALITATIVE/QUANTITATIVE RESULTS	REFERENCE RANGE	LABORATORY NAME/ADDRESS (STREET, or RFD, CITY, STATE, ZIP CODE)	LIVER FUNCTION RESULTS
							ALT
							AST

For Section of EPI use only:
AKSTARS #_____
Fax to ASVL
(Fax: 907-474-4036)

Confidential Influenza-Associated Mortality Case Report Form
State of Alaska, Section of Epidemiology

PATIENT INFORMATION

Last name	*First name*	*Date of birth* / /
Street address	*City*	*Zip code*

Gender · Female · Male

Ethnicity · Hispanic · Non-Hispanic · Unknown

Race · White · Black · Native American · Asian/Pacific Islander · Other · Unknown

ONSET, HOSPITALIZATION AND DEATH INFORMATION

Date of onset of symptoms / /	*Hospitalized?* · Yes · No · Unknown	*If hospitalized, hospital name and location*
Date of hospital admission / /	*Date of hospital discharge* / /	
Date of death / /	*Location of death (i.e. home, ED-name of hospital ED, etc.)*	*If died, autopsy performed?* · Yes · No · Unknown

INFLUENZA LABORATORY TESTING INFORMATION (Please attach a copy of the test result, if available)

Date of specimen collection / /	*Specimen type (e.g. nasopharyngeal swabs, endotracheal aspirate, bronchoalveolar lavage)*

Influenza type and/or subtype _____ *Where was testing performed?*

*Rapid test*_____ *PCR*_____

INFLUENZA VACCINATION HISTORY

Received seasonal influenza vaccine during the current season?
Yes · No · Unknown

If yes, date vaccinated:
/ / *Please specify the type of influenza vaccine received:* _____

CLINICAL COURSE

Received antiviral treatment? · Yes · No · Unknown	*Type of antiviral* · Oseltamivir · Zanamivir · Other *Specify other*: _____	
Date antiviral treatment started / /	*Date antiviral treatment ended* / /	*Intubated?* · Yes · No · Unknown

Complications
· Pneumonia · ARDS · Sepsis · Acute renal failure · Encephalitis/encephalopathy · Required vasopressor · Required hemodialysis
· Pulmonary embolus · Secondary bacterial infection *If yes, specify organism*: _____
· Other *Specify other*: _____

SIGNIFICANT PAST MEDICAL HISTORY

· Cardiac disease · Chronic pulmonary disorder · Immunosuppression (e.g. cancer) · Immunosuppressive medications (e.g. chemotherapy, steroids)
· Metabolic disorder (e.g. diabetes mellitus, renal) · Neurological disorder (e.g. cerebral palsy) · Hemoglobinopathy (e.g. sickle cell disease)
· Genetic disorder (e.g. Down syndrome) · Obesity *If obese*, BMI (if known):_____ Height:_____Weight: _____
· Pregnant *If pregnant*, estimated delivery date:_____/_____/_____
· Postpartum *If postpartum*, delivery date:_____/_____/_____ · Other conditions (e.g. hypertension, hyperlipidemia)

Reported By:_____ **Date Reported:**_____/_____/_____

Phone Number: _____

Fax reports to (907) 563-7868. This form is also available online at:
http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.aspx

Rev
3/31/16

To report Public Health Emergencies ***call (907) 269-8000 or after hours (800) 478-0084***

Zika Virus Case Report Form

WANIDD ID: .....

Completed by: .....

NOTIFIER DETAILS

Notifier: ..... Organisation: .....

Telephone: ..... Fax: ..... Email: .....

CASE DETAILS

Name: .....
First name *Surname*

Address: ..... **Post code:** .....

Telephone: ..... **Mobile :** ..... **Email:** .....

Date of birth: ...../...../..... **Age:** ..... Years **Sex:** □ Male □ Female

Country of birth: ..... **English preferred language:** □ Yes □ No – *specify* .....

Ethnicity: □ Aboriginal / Torres Strait Islander □ Other □ Unknown **Occupation:** .....

CLINICAL DETAILS

Symptoms: □ No □ Yes → Date of onset: ...../...../..... **Date of first consultation:** ...../...../.....

- Fever : □ Yes (>38C) □ Yes (self-report) □ No
- Rash: □ Yes □ No
- Arthralgia: □ Yes □ No
- Myalgia: □ Yes □ No
- Headache: □ Yes □ No
- Retro-orbital pain: □ Yes □ No
- Conjunctivitis (non-purulent): □ Yes □ No
- Other: – *specify* .....

Hospitalised: □ No □ Yes → Hospital: ..... Date: ...../...../..... Days: .....

Complications: □ No □ Unknown □ Yes – *specify* .....

Is the case pregnant? □ No □ Unsure □ Yes → .. .. weeks gestation EDD: ...../...../.....

Vaccination history

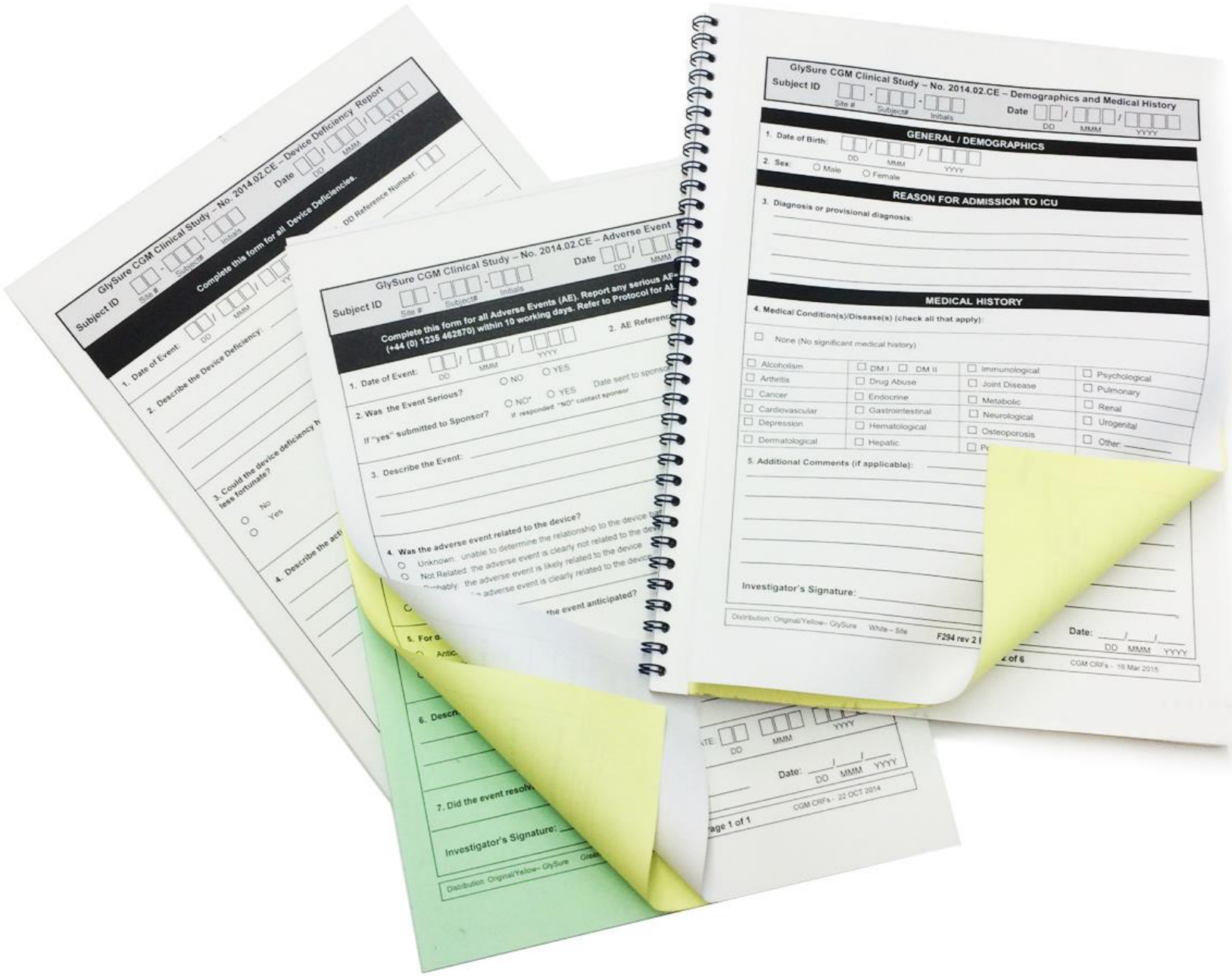
- Japanese encephalitis: □ No □ Unsure □ Yes – Date: ...../...../.....
- Yellow fever: □ No □ Unsure □ Yes – Date: ...../...../.....

LABORATORY DETAILS

Date of first specimen: ...../...../..... **Lab:** .....

Laboratory tests *Please mark as +, – or equivocal and provide titres where relevant*

Virus	Specimen date	IgM	HI	Neutral-isation	NS1	PCR	Virus isolated	Comment
Zika virus								
Dengue								
Flavivirus								
Other								


GlySure CGM Clinical Study – No. 2014.02.CE – Demographics and Medical History
Subject ID
Site #
Subject#
Initials
Date
DD
MMM
YYYY
GENERAL / DEMOGRAPHICS
1. Date of Birth:
2. Sex:
Male
Female
REASON FOR ADMISSION TO ICU
3. Diagnosis or provisional diagnosis:
MEDICAL HISTORY
4. Medical Condition(s)/Disease(s) (check all that apply):
None (No significant medical history)
Alcoholism
DM I
DM II
Immunological
Psychological
Arthritis
Drug Abuse
Joint Disease
Pulmonary
Cancer
Endocrine
Metabolic
Renal
Cardiovascular
Gastrointestinal
Neurological
Urogenital
Depression
Hematological
Osteoporosis
Other:
Dermatological
Hepatic
5. Additional Comments (if applicable):
Investigator's Signature:
Date:
Distribution: Original/Yellow– GlySure White – Site
F294 rev 2
CGM CRFs - 16 Mar 2015
GlySure CGM Clinical Study – No. 2014.02.CE – Adverse Event
Complete this form for all Adverse Events (AE). Report any serious AE
(+44 (0) 1235 462870) within 10 working days. Refer to Protocol for AE
1. Date of Event:
2. Was the Event Serious?
NO
YES
If "yes" submitted to Sponsor?
NO*
YES
Date sent to sponsor
if responded "NO" contact sponsor
3. Describe the Event:
4. Was the adverse event related to the device?
Unknown: unable to determine the relationship to the device
Not Related: the adverse event is clearly not related to the device
Probably: the adverse event is likely related to the device
Definitely: the adverse event is clearly related to the device
the event anticipated?
5. For a
Antic
6. Descri
7. Did the event resolv
Investigator's Signature:
Distribution: Original/Yellow– GlySure
CGM CRFs - 22 OCT 2014
GlySure CGM Clinical Study – No. 2014.02.CE – Device Deficiency Report
Complete this form for all Device Deficiencies.
DD Reference Number:
1. Date of Event:
2. Describe the Device Deficiency:
3. Could the device deficiency h
less fortunate?
No
Yes
4. Describe the acti

Data Management

- Estimate of the data management budget
- Data Management Plan
- Data Collection Tools/ CRF design
- Data Management System planning and implementation
- Interim Analysis datasets
- Reports
- Final Analysis datasets
- Study Closure

Principles

- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification.
- The confidentiality of records that could identified subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements.
- The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
- The sponsor should utilized appropriately qualified individuals to supervise the overall conduct of the trial, to handle the data, to verify the data, to conduct the statistical analyses, and to prepare the trial reports.

Principles

- Maintain SOPs
- Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e., maintain an audit trail, data trail ,edit trail).
- Maintain a security system that prevents unauthorized access to the data
- Maintain a list of the individuals who are authorized to make data changes.
- Maintain adequate backup of the data.
- Safeguard the blinding, if any, during data entry and processing.

Data Management Plan (DMP)

- DMP – a document which describes and defines all data management activities
- DMP - helps an organization develop and standardize data management procedures

Association for Clinical Data Management

- Data Entry Procedures
- Specification for Clinical Laboratories
- Electronic Data Transfer
- Query Handling
- Backup and Recovery Procedures
- Archiving and Security
- Contract Research Organizations

Data Management System

- Selection of hardware and Software
- Database Management System (DBMS)
- Data Dictionary
- Database Development
- Data Entry System
- Reporting System
- System Documentation
- System Maintenance and Support
- Security and Data Confidentiality

Spreadsheet vs. Database

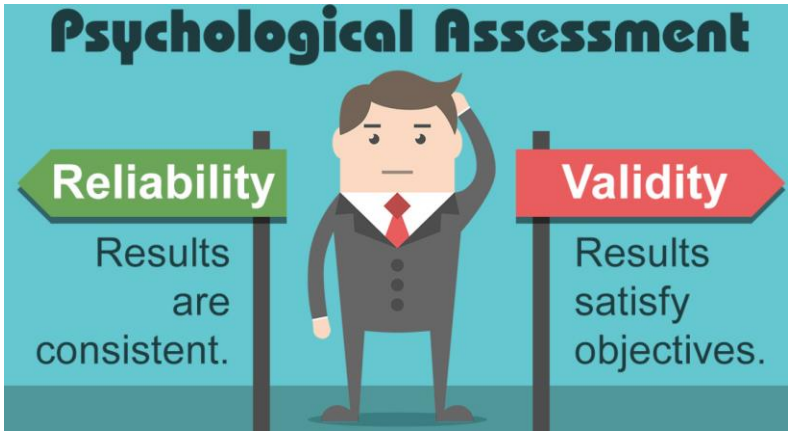
Property	Spreadsheet	Relational Database
Structure	Cells, Sheets	Tables, Rows, Columns Queries, Reports
Usage	Short Term	Long Term
Data Integrity	Possible, not	Enforced
Multiple	Common easily	More difficult
Copies	Duplicated Fewer	Multiple Uses
Flexibility	Uses	Multiple
Concurrency	One user	users

Database Design

- Identify key fields on the CRF
- Select appropriate data types
- Choose meaningful field names
- Maintain consistency of names and data types for key fields
- Prepare for missing data
- Coding for missing data
- Database tables
- Data dictionary

Database Validation

- Test data entry screens to ensure data are mapped to the correct fields
- Validate the data field definitions in terms of length and type
- Verify that out-of-range data are flagged and error messages trigger properly
- Verify that primary key fields are assigned correctly, no duplicates
- Validate edit, range and logic checks



Data Analysis and Reporting

- IRB Continuing review
- Data Safety Monitoring Boards (DSMB)
- Interim analyses for safety or efficacy
  - Interim analyses for abstracts
- Final analyses

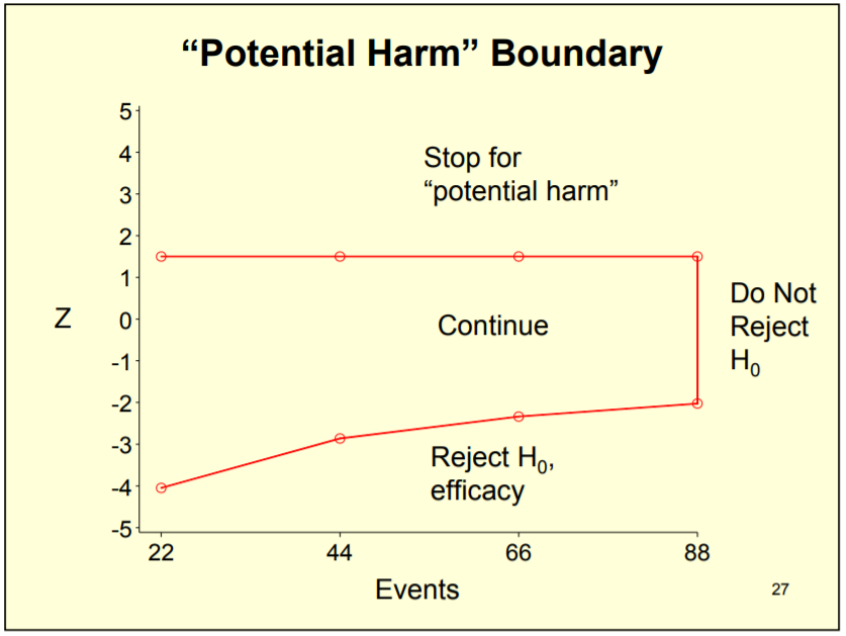
Plan for Early Stopping

- Desire to stop the trial early in the event of:

1. clear early evidence of efficacy
2. clear early evidence of harm (wrt HIV)
3. early evidence of harm based on additional safety data (AEs, labs, vital signs, etc.)

- Also might decide to stop for futility
  - What is "futility"? Pointlessness/uselessness
- Could also stop for poor trial quality, slow enrollment, high loss, etc.

4



Reference: Interim analyses and early stopping in clinical trials : classical and adaptive methods Christopher Jennison Dept of Mathematical Sciences, University of Bath, UK, 2006

Analysis

- Delineate the research question with the statistician and investigator
- Determine critical data required to evaluate the research question
- Prepare statistical analysis datasets and QC listings
- Work with statisticians to complete the analysis
- Participate in the review of the analysis with the statistician and investigator

    - List and description of investigators and other important participants in the study, including brief (1 page) CVs or equivalent summaries of training and experience relevant to the performance of the clinical study

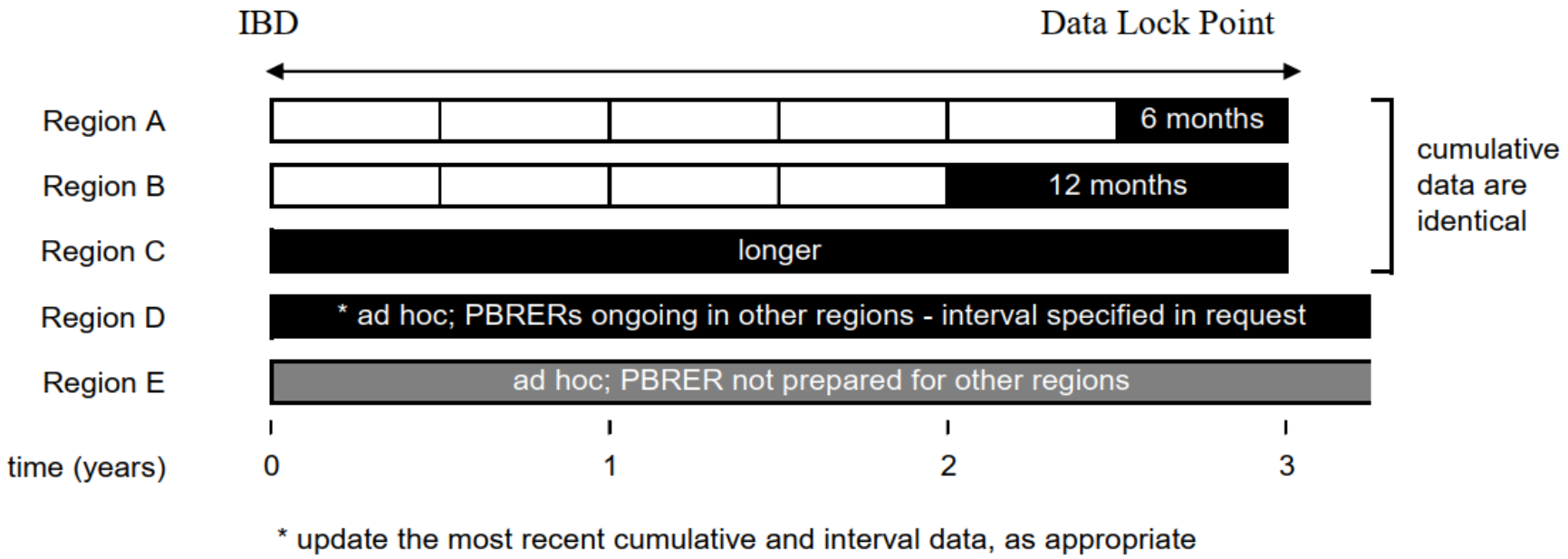
Conclusions

- Data quality is the most important aspect of clinical data management
- Data quality must support the evaluation of study objectives
- Data quality is a multidisciplinary effort
- Data quality requires sufficient resources and expertise

PBER and Data Lock Point (Periodic Benefit Risk Evaluation Report)

Figure 1: Submission of PBRERs Based on the Same Data Lock Point, with Various Reporting Periods.

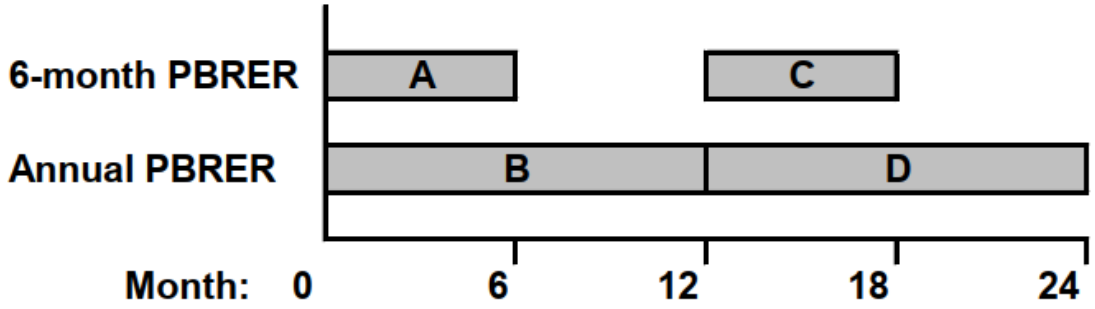
Shading indicates period of interval data.
For all reports, the cumulative data reflect all data from the IBD/DIBD**.



** Cumulative Clinical Trial Summary Tabulation of Serious Adverse Events & Clinical Trial Exposure data only

Ref: Periodic Benefit-Risk Evaluation Report (PBRER)
IDB Injury DataBase; DSUR = Development Safety Update Report

Figure 2: Submission of 6-Month and Annual PBRERs



Region 1 requires 6-monthly PBRER, and receives PBRER A, B, C, and D (assuming agreement has been reached with pertinent regulatory authority[ies]).

Region 2 requires annual PBRER, and receives PBRER B and D.

Ref: Periodic Benefit-Risk Evaluation Report (PBRER)

Table 1 – Estimated Cumulative Subject Exposure from Clinical Trials

Estimates of cumulative subject exposure, based upon actual exposure data from completed clinical trials and the enrolment/randomisation schemes for ongoing trials.

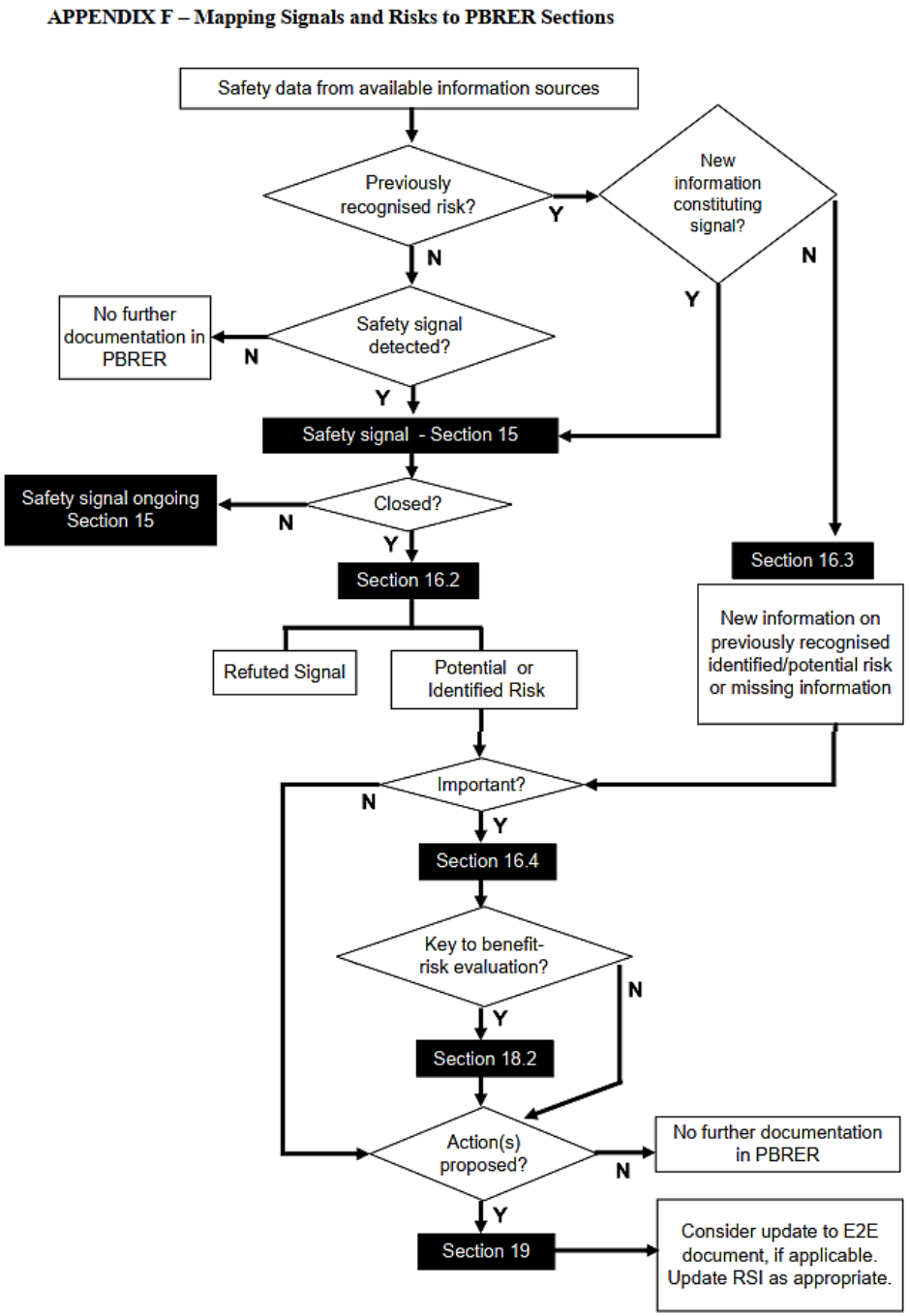
Treatment	Number of subjects
Medicinal product	
Comparator	
Placebo	

Table 2 – Cumulative Subject Exposure to Investigational Drug from Completed Clinical Trials by Age and Sex*

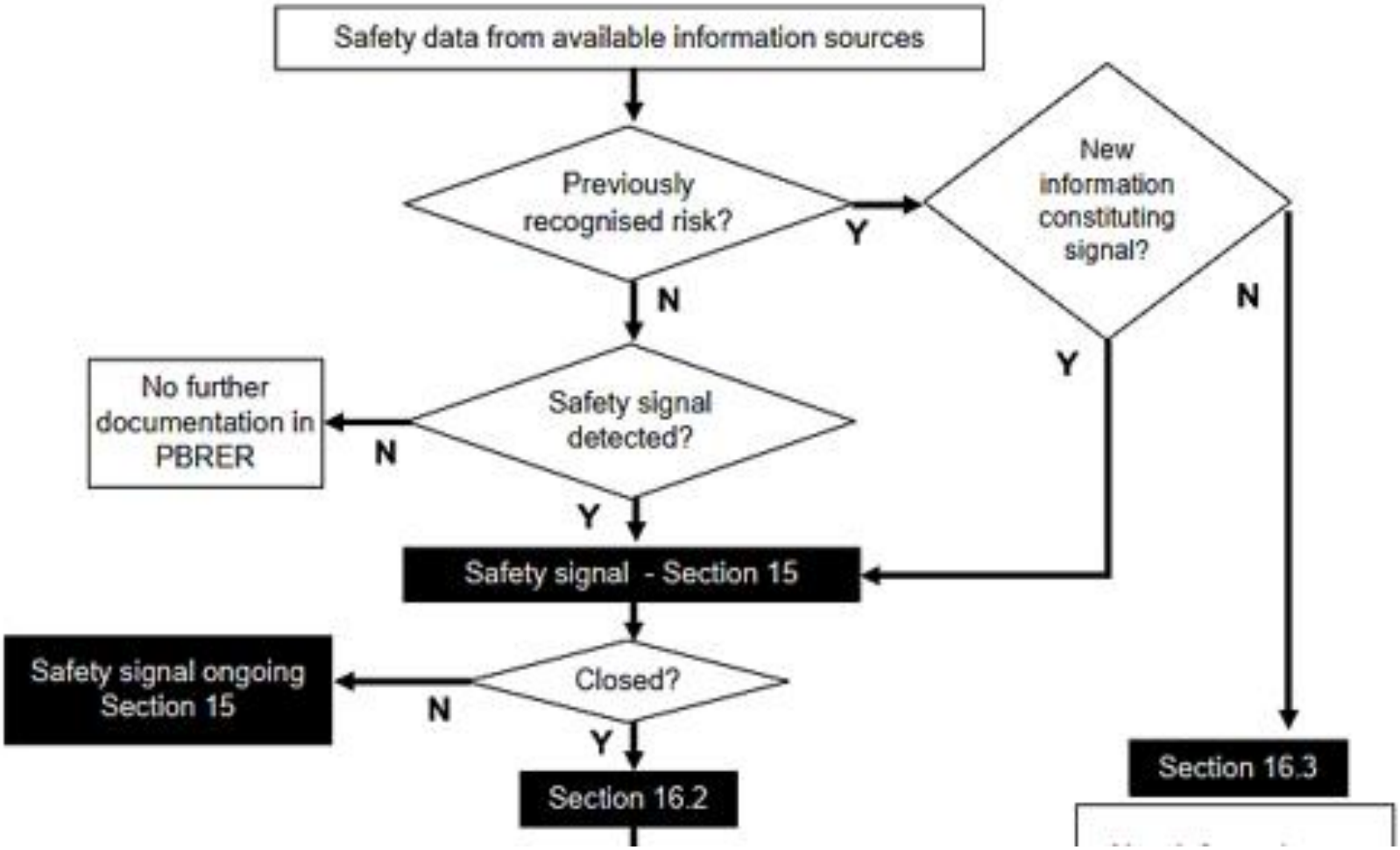
	Number of subjects		
Age range	Male	Female	Total

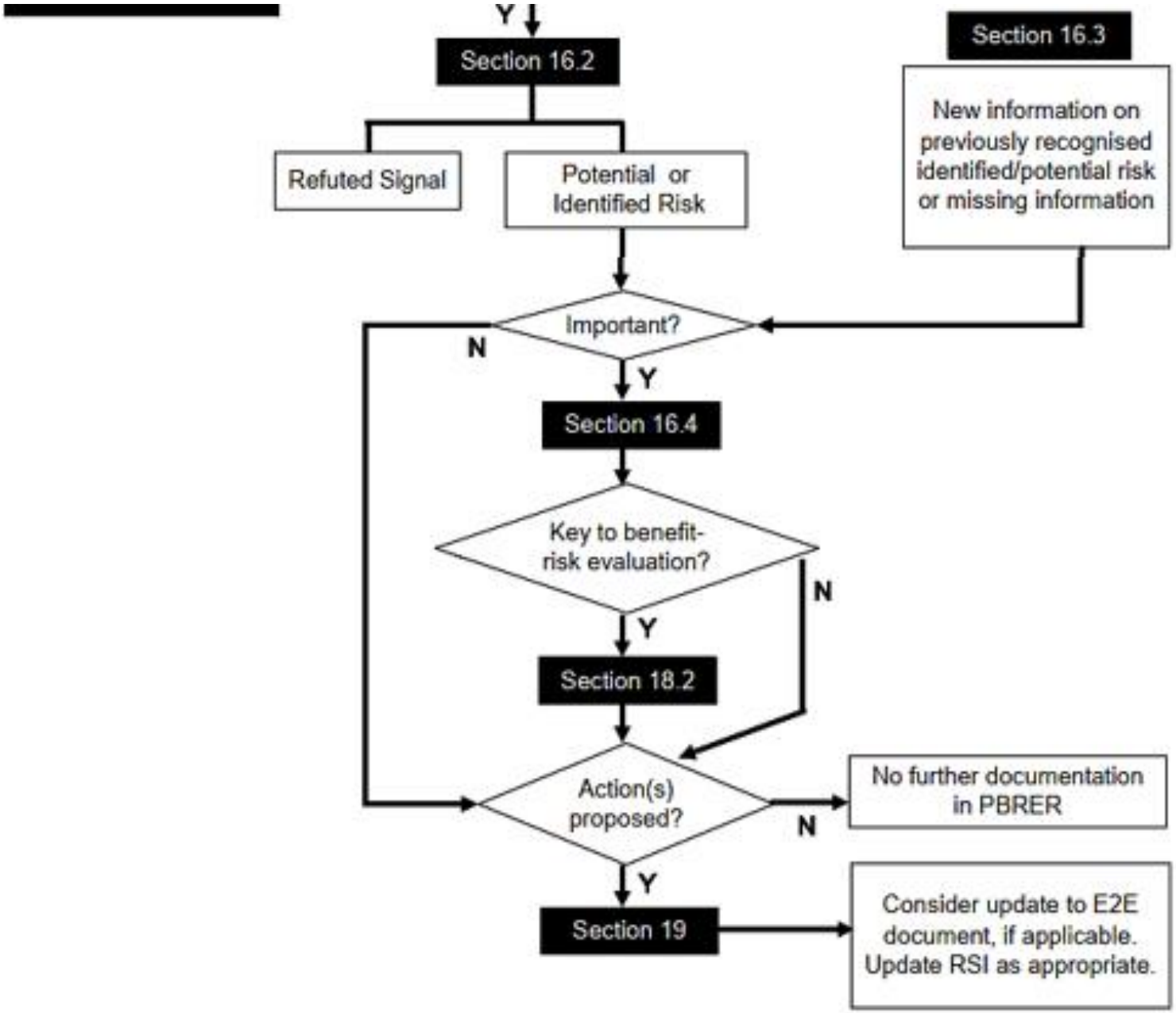
* Data from completed trials as of [date]

Mapping Signals and Risk to Periodic Benefit Risk Evaluation



APPENDIX F – Mapping Signals and Risks to PBRER Sections





RSI = Reference Safety Information; E2E = End to End

Thank You