Clinical Research Seminar: Case Report Form Design

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Learning Objectives

- The necessity of incorporating data sharing requirements
- **Key design elements and inclusion of standard measures**
- Importance of pilot testing, change management and optimization of data architecture

Good News: Every one can create a Case Report Form (CRF)!

Bad News: Not everyone can create a “reliable and valid” CRF?

Case Report Form (CRF)

- A printed, optical or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject (ICH E6 GCP Guidelines)
- **An informative and well-structured CRF simplifies database design and data validation processes as well as manipulation of data during statistical analysis**[1]

CRF Design

- Collect data specified by the protocol. Ideally CRFs should be developed concordantly with the protocol (and statistical analysis plan if available)
  - Assemble multidisciplinary team to provide input (investigators, biostatistician, data manager)
  - Focus on primarily on safety and efficacy endpoints
  - Implement standards where possible (more on this later)
  - Ensure questions, prompts, instructions are clear and concise
  - CRF questions flow in logical order and are culturally and individual/condition sensitive
  - Instruments created by independent source (validated measures), licensed for use (e.g,Beck Depression Inventory) and follow prescribed formatting/copyright requirements
- Ensure the process for design, development, approval and version control documented

Schedule Evaluation and Events (SOEE)

Construct/Domain	Measures	Visit (Days from Hospital Discharge Date)				
		SCRN	BASE (1:14)	1 Mo (28:55)	2 Mo (56:83)	3 Mo (84:168)
Participant Characteristics						
Consent/Eligibility	Date of Consent, Inclusion/Exclusion Criteria including toxicology (urine) and safety (blood)	X				
Demographics & SES	Age, Sex, Race, Marital/Partner Status, Health Insurance and Living Situation (homeless)	X	X			X
Health Characteristics						
Co-Morbidities	Charleson Index (EMR)	X	X	X	X	X
Mental Health	Depression (PHQ)	X	X			X
Substance Use, Motives, Consequences, Cravings, Readiness and Biomarkers						
Alcohol Severity	AUDADIS	X				X
Alcohol Use	Timeline Follow-back (TLFB)		X			X
Consequences	Short Inventory of Problems – Revised (SIP-2R)		X			X
Intervention						
NTX Route	Randomization Group (XR-NTX – PO-NTX)		X			
Compliance						
Medications	# of RW-MM visits with nurse or PO med mailing		X	X	X	X
Visit	Research Visits		X			X
Safety						
Adverse Events	Patient reported side effects, problems during RW-MM visits –opioid meds	X	X	X	X	X
Labs	Liver Tests (ALT, AST, GGT*), Pregnancy Test (SCRN as indicated)*	X		X	X	X

Modified from the NIAAA Alcohol Disorder hospital Treatment (ADOPT) Study

SOEE

- What is the difference between an assessment and an unscheduled event?
- Why does it matter?

Data Management Minimum Requirements

CRFs are not developed in a silo, majority of data is typically captured using CRFs or Forms and is integral to study success and part of the data management plan. Minimum requirements for data management:

- Traceability
- Data Quality

Risk Assessment – how good is good enough – what rigor is required[2]?

- Consider:
  - Ethics
  - Regulations
  - Institutional policies
  - Sponsor requirements
  - **Plans for data use and reuse**
- Ensure three tenets:
  - the rights and well-being of human subjects are protected,
  - the reported data are accurate, complete and verifiable from source,
  - the conduct of the trial is in compliance with the protocol, Good Clinical Practice guidelines and the applicable regulatory requirements

Proactively Determine Plans for Data use and Reuse/Data Sharing

- Data sent to FDA likely using CDISC standards
- Mandated for NIH sponsored research awards (>$500,000)
- In RFA/RFP often will state use of standards (PhenX) or CDISC
- Data sent to sponsor or regulatory agency should require minimal data manipulation
- Using standards will save time (data build and analysis) and improve data quality and traceability since it will minimize harmonization and documentation required

Sample Annotated Demographics Case Report Form - CDISC

Sponsor EAP-001	SITEID Site Number	SUBJID (Assigned by System) Patient Number	SUBJINT F M L Patient Initials	VISITNUM (Assigned by System) Visit Number
Demographics				

1. Date of Birth: BRTHDAT ____ ____ ____ (DD MON YYYY)

2. Biological Sex at Birth: SEX ☐ Male ☐ Female

   If Female, is the patient of child-bearing potential? CHILDNY ☐ No ☐ Yes

3. Ethnicity: ETHNIC ☐ Hispanic or Latino ☐ Not Hispanic or Latino

4. Race: RACE
   - ☐ American Indian or Alaska Native
   - ☐ Asian
   - ☐ Black or African American
   - ☐ Native Hawaiian / Pacific Islander
   - ☐ White
   - ☐ Other: RACESP _____ (*specify*)

CDISC - Demographics Example (Data Dictionary)

Variable Name	Variable Label	Type	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char	Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	Identifier	Two-character abbreviation for the domain.	Req
SUBJID	Subject Identifier for the Study	Char	Topic	Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF.	Req
USUBJID	Unique Subject Identifier	Char	Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product. This must be a unique number, and could be a compound identifier formed by concatenating STUDYID-SITEID-SUBJID.	Req
DMGRPID	Group ID	Char	Identifier	Used to tie together a block of related records for a subject within a domain.	Perm
RFSTDTC	Subject Reference Start Date/Time	Char	Record Qualifier	Reference Start Date/time for the subject in ISO 8601 character format. Usually equivalent to date/time when subject was first exposed to study treatment. Required for all randomized subjects; will be null for all subjects who did not meet the milestone the date requires, such as screen failures or unassigned subjects.	Exp
RFENDTC	Subject Reference End Date/Time	Char	Record Qualifier	Reference End Date/time for the subject in ISO 8601 character format. Usually equivalent to the date/time when subject was determined to have ended the trial, and often equivalent to date/time of last exposure to study treatment. Required for all randomized subjects; null for screen failures or unassigned subjects	Exp
SITEID	Study Site Identifier	Char	Record Qualifier	Unique identifier for a site within a study.	Req
INVID	Investigator Identifier	Char	Record Qualifier	An identifier to describe the Investigator for the study. May be used in addition to SITEID. Not needed if SITEID is equivalent to INVID.	Perm
INVNAM	Investigator Name	Char	Synonym Qualifier	Name of the investigator for a site.	Perm
BRTHDTC	Date/Time of Birth	Char	Record Qualifier	Date/time of birth of the subject.	Perm
AGE	Age	Num	Record Qualifier	Age expressed in AGEU. May be derived from RFSTDTC and BRTHDTC, but BRTHDTC may not be available in all cases (due to subject privacy concerns).	Exp
AGEU	Age Units	Char	Variable Qualifier	Units associated with AGE.	Exp

Primary Data Collection - Consent CRF

- What information is required?
- Who is answering the questions?
- How do we collect and store this information?
- How do we check that this information is accurate (reliable) and valid?
- What information is protected or confidential?
- What information can be shared and under what circumstances?
- What would a “data collection” form or screen shot look like to collect this information?
- How do we account for changes in the consent form versioning changes

Sample Patient Enrollment Case Report

Sponsor EAP-001	__ __ __ Site Number	01 (Assigned by System) Visit Number
Patient Enrollment		

1. **Patient Number:** ____ ____ ____

2. **Patient Initials:** ____ ____ ____
   F M L

3. **Date Informed Consent Signed:** ____ / ____ / _____
   DD MON YYYY

4. **If child < 18, Date Assent Signed:** ____ / ____ / _____
   DD MON YYYY

5. **Protocol Version Number of Executed Informed Consent:** _____

THE SAFE PASSAGE STUDY

MAIN STUDY CONSENT TRACKING FORM

Participant ID _____

[BISH and RAPD ONLY]
Recruitment Location: _____ _____ *(use codes)*

BISH Location Codes
01=Belhar Antenatal Clinic
02=Bishop Lavis Midwife Obstetric Unit
03=Tygerberg Hospital

RAPD Location Codes
06=Native Women's Health Center
14=Black Hills OB/GYN
15=Midland Office

1.	**Consent signed**	*(check one)* ☐ NO ☐ YES
	a. Date Consent signed or refused	__ __ / __ __ / __ __ __ __ *(month) (day) (year)*
	b. If not signed, please specify reason for refusal	Code: __ __ *(use codes below)* Other: _____ *(If code 99, specify other reason)*
2.	**Addendum signed for Embedded Study**	*(check one)* ☐ NO ☐ YES ☐ N/A
	a. Date Addendum signed or refused	__ __ / __ __ / __ __ __ __ *(month) (day) (year)*
	b. If not signed, please specify reason for refusal	Code: *(use codes below)* Other: _____ *(If code 99, specify other reason)*
		(check one for each)
3.	**May collect maternal saliva**	☐ NO ☐ YES
4.	**May collect maternal blood**	☐ NO ☐ YES
5.	**May review maternal medical records**	☐ NO ☐ YES
6.	**May collect placental tissue**	☐ NO ☐ YES
7.	**May collect cord or infant blood sample** *(Guthrie card)*	☐ NO ☐ YES
8.	**May collect baby's stool**	☐ NO ☐ YES
9.	**May collect brain tissue**	**N/A**
10.	**May take photo of infant**	☐ NO ☐ YES
11.	**May take video recordings of baby's movement**	☐ NO ☐ YES
12.	**May review baby's medical records**	☐ NO ☐ YES
13.	**Willing to participate in genetics studies**	☐ NO ☐ YES
14.	**May use specimens for future studies**	☐ NO ☐ YES
15.	**May measure baby's brain activity and hearing**	☐ NO ☐ YES ☐ N/A
16.	**May contact for future studies**	☐ NO ☐ YES ☐ N/A
17.	**May take 3D photo of infant**	☐ NO ☐ YES ☐ N/A

CRF Design

- Gather relevant reference documents (e.g., protocol, CRF reference library, Statistical Analysis Plan (SAP), data requirements from Sponsor or regulatory agency, review standards (C-DASH, PhenX), most recent versions of measures (don't modify an independent or validated scale)
- Develop CRFs, CRF form completion guidelines concurrently
- Cross-check information from CRF, protocol and consent form and SAP
- Visually appealing (uncluttered, organized by construct of measurement)
- Written at 5-8th grade reading level, clear instructions provided, clear and unambiguous questions and response options (limit text responses)
- Parsimony (questions asked once and required for research)
- Traceability (map origin)
- Language translation and back-translation (reliability and validity)

Response Options: Simplistic View[2]

- Structured
  - Name (categorical)
  - Categorical (dichotomous, categories order doesn't matter)
  - Ordinal (order matters, Likert scales)
  - Interval (quantative)

- Unstructured
  - Open text
    - Qualitative

Design and Development Process

All data attributable to a subject with sufficient identifiers to link data with page numbers and if applicable provides provision for signature

Catalyst EAP-001	___ ___ ___ Site Number	___ ___ ___ (Assigned by System) Patient Number	___ ___ ___ F M L Patient Initials
Adverse Event Log			

List all Serious Adverse Events (SAEs) the patient experiences after signing the Informed Consent Form. List all other Adverse Events (AEs) the patient experiences after the first administration of amifampridine phosphate. Follow each SAE/AE through 4 weeks after last dose, until each SAE/AE is resolved or stabilized, the patient becomes lost to follow-up, or it has been determined that amifampridine phosphate is not the cause of the event. Use the Adverse Event Log within the Clinical Data Management System (CDMS) to monitor and follow-up on existing events, and to determine the Adverse Event Number. Check the box for "Not an Adverse Event" if the event automatically generated from the CDMS is subsequently determined to be not adverse. If the adverse event is serious, complete the BioMarin SAE Form. Print additional pages, as needed.

Description: ❑ Not an Adverse Event

Adverse Event Number	*Visit Number*	*Date Onset*	*Serious Event*	*CTCAE Grade*	*Attribution to Amifampridine*	*Action Taken*	*Outcome of Event*	*Date Resolved*
____	____	____ / ____ / ____ DD / MON / YYYY	❑ No ❑ Yes If Yes, Criteria : _____ (separate by comma) If 99, Specify: _____	____	____	Amifampridine: _____ Other Action: _____ (separate by comma) If 99, Specify: _____	____ If 99, Specify: _____	____ / ____ / ____ DD / MON / YYYY OR ❑ Ongoing

Comments:

Serious Criteria Codes:	CTCAE Grade Codes:	Attribution Codes:	Action Taken with Amifampridine Codes:	Other Action Taken Codes:	Outcome Codes:
1 = Death 2 = Life Threatening 3 = Hospitalization 4 = Disability/Incapacity 5 = Congenital Anomaly 6 = Involves Cancer 7 = Overdose 99 = Other Important Medical Event	1 = Mild 2 = Moderate 3 = Severe or medically significant but not immediately life-threatening; hospitalization or prolonged hospitalization; disabling 4 = Life-threatening consequences 5 = Death related to AE	1 = Not Related 2 = Possibly Related 3 = Probably Related	1 = Dose Not Changed 2 = Drug Interrupted 3 = Drug Withdrawn Permanently 4 = Dose Reduced 5 = Dose Increased 6 = Unknown 7 = Not Applicable	1 = None 2 = Concomitant Medication 3 = Hospitalization 4 = Surgical/Diagnostic Procedure 5 = Patient Withdrawn 99 = Other	1 = Recovered/Resolved 2 = Recovering/Resolving 3 = Not Recovered/Not Resolved 4 = Recovered/Resolved with Sequelae 5 = Patient Withdrawn 6 = Death 99 = Other

Coding Key:
(-7) = Unknown

Investigator Signature: _____ Date: ____ / ____ / _____
DD MON YYYY

Clarity of Use[1]

- CRF Layout
- Wording
- Coding
- Use of minimal referential questions (e.g., skip logic)
- Minimize redundancies (collect data once unless for validation purposes)
- Distinction between paper-based CRFs, eCRFs and Patient Reported Outcomes (PRO)

CRF Layout

THE SAFE PASSAGE STUDY

EDINBURGH DEPRESSION SCALE | **Participant ID**

Date of Interview: ____ / ____ / ____ (month) (day) (year)	**Interviewer Name:** ____ (Last) ____ (First) ____ (MI)
Language of Interview: ____ (use codes below)	**Location of Interview:** ____ (use codes below)
Contact: (circle one) 20-24 Weeks; 28-32 Weeks; 34+ Weeks; 1Mth Maternal; 12Mth Maternal	
Time Interview Began: ____ : ____ (military time in your local time zone)	**Time Interview Ended:** ____ : ____ (military time in your local time zone)

Instructions for the Clinical Coordinator

Complete this questionnaire by reading each statement to the participant. Be sure to read each response option to the participant and have the participant follow along using the response cards. After completing the questionnaire, add the numbers that are circled and fill in the total score at the end of the questionnaire.

Interviewer's Script

Please indicate the closest to how you have felt to the following statements in the past seven days.

1. **I have been able to laugh and see the funny side of things:** *(circle one)*
   - As much as I always could 0
   - Not quite as much now 1
   - Definitely not so much now 2
   - Not at all 3

2. **I have looked forward with enjoyment to things:** *(circle one)*
   - As much as I ever did 0
   - Rather less than I used to 1
   - Definitely less than I used to 2
   - Hardly at all 3

3. **I have blamed myself unnecessarily when things went wrong:** *(circle one)*
   - Yes, most of the time 3
   - Yes, some of the time 2
   - Not very often 1
   - No, never 0

Language of Interview:
01=English
02=Afrikaans
03=Afrikaans and English

Location of Interview:
01=Belhar Antenatal Clinic
02=Bishop Lavis Midwife Obstetric Unit
03=Tygerberg Hospital
04=Pine Ridge Indian Health Services
05=Oglala Lakota College, Department of Nursing
06=Native Women's Health Center
07=Rapid City Regional Hospital
08=Sanford Health
09=Altru Clinic
10=The Johnson House
11=Mercy Hospital
12=Spirit Lake Native American Maternal Health Child Program
13=Karl Bremer
14=Black Hills OB/GYN
15=Midland Office

Coding Key:
-7 = Don't Know
-8 = Refused to Answer
-9 = Does Not Apply

THE SAFE PASSAGE STUDY

RECRUITMENT INTERVIEW | **Participant ID**

Date of Interview: ____ / ____ / ____ (month) (day) (year)	**Interviewer Name:** ____ (Last) ____ (First) ____ (MI)
Language of Interview: ____ (use codes below)	**Location of Interview:** ____ (use codes below)
Time Interview Began: ____ : ____ (military time in your local time zone)	**Time Interview Ended:** ____ : ____ (military time in your local time zone)

Background Information

1. **What is your marital status now (in the last month):** *(circle one)*
   - Married 1
   - Partnered *(boyfriend or girlfriend)*, living together 2
   - Partnered *(boyfriend or girlfriend)*, not living together 3
   - Separated 4
   - Divorced 5
   - Single 6
   - Widowed 7
   - Other ____ (please specify) 8

   a. How long have you been in this relationship:
   ____ ____ years ____ ____ months ____ ____ weeks
   (specify number) (specify number) (specify number)
   (If married be sure to include the length of the entire relationship)

2. **How many years of formal education have you completed:** *(circle one)*

(Northern Plains)			(South Africa)
Grade School	Kindergarten	0	Primary School
	Grade 1	1	
	Grade 2	2	
	Grade 3	3	
	Grade 4	4	
	Grade 5	5	
	Grade 6	6	
	Grade 7	7	
	Grade 8	8	
High School	Grade 9	9	High School
	Grade 10	10	
	Grade 11	11	
	Grade 12 or GED	12	
College	Grade 13	13	College or University
	Grade 14	14	N/A
	Grade 15	15	
	Grade 16	16	
Graduate or Professional School	Grade 17+	17	

3. **When did you find out you were pregnant:** ____ / ____ / ____ (month) (day) (year) *(check all that apply)*
   - Unsure of month ☐
   - Unsure of day ☐

Language of Interview:
01=English
02=Afrikaans
03=Afrikaans and English

Location of Interview:
01=Belhar Antenatal Clinic
02=Bishop Lavis Midwife Obstetric Unit
03=Tygerberg Hospital
04=Pine Ridge Indian Health Services
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Coding Key:
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Wording, Coded Responses and Redundancy (minimize)

13. How is your medical care paid for during this current pregnancy:

		(circle one for each item) NO	YES
(Northern Plains only)			
a.	Statewide Medicaid Program	0	1
b.	Other Statewide Option	0	1
c.	Veteran's (VA) Benefits	0	1
d.	Indian Health Services	0	1
e.	Commercial Health Insurance/Commercial HMO	0	1
f.	Self Pay	0	1
g.	Other_____ (please specify)	0	1
(South Africa only)		NO	YES
h.	Free Government Health Care	0	1
i.	Self Pay	0	1
j.	Other_____ (please specify)	0	1

6. Do you currently have:

		(circle one for each item) NO	YES
a.	Electricity	0	1
b.	Working phone service or cell phone service	0	1
c.	Running water (inside house)	0	1
d.	Toilet (inside house)	0	1

7. Including yourself, how many people currently live in your home: ___ ___ (specify number)

8. How many times have you moved within the past 12 months: ___ ___ (specify number)

Reproductive History

Instructions for the Clinical Coordinator

This information must be obtained directly from the mother. Do not obtain any of this information from the medical record. Use as many additional sheets (page 6) as needed to record the participant's complete Reproductive History.

Interviewer's Script

Now, I would like to ask you a few questions about each of your previous pregnancies. Please begin with your first pregnancy:

1. On what date did your first [second, etc.] pregnancy end?
2. Did this pregnancy end in a live birth, stillbirth, spontaneous abortion (miscarriage), therapeutic abortion, ectopic pregnancy, or molar pregnancy?
3. How many weeks were you pregnant? *(if precise weeks and days unknown, approximate using Gestational Age Code)*
4. How much did your baby weigh? *(most likely only completed for live birth and the occasional stillbirth)*
5. Did you experience any complications during your pregnancy or delivery? *(SHOW CARD 2)*
6. Did the baby experience any complications during this pregnancy or delivery? *(SHOW CARD 3)*
7. If live birth and the child is not living: *(SHOW CARD 4)*
   a. What was the date of your child's demise?
   b. What was the reason for your child's demise?
   c. Was an autopsy performed?

15. Check if this is the participant's first pregnancy: ❑ *(Questionnaire is complete – enter Time Interview Ended on page 1)*

OR

Please list your past pregnancy history, starting with your first pregnancy:

Pregnancy Outcome	3. Gestational Age	4. Birth Weight	Complications *(REFER TO CARD 2 and 3)* 5. Maternal Code (Only specify if Other (code 99))	6. Fetal/Infant Code (Only specify if Other (code 99))	*(REFER TO CARD 4)* 7. If LB & Child NOT Living
Pregnancy # 01					a. Date of Demise: __/__/__ __ __ __ (mm / dd / yyyy)
1. Date: __/__/__ __ __ __ (mm / dd / yyyy)	GA: |__|__| / |__|__| (wks / days)	__ __/__ __ (lbs / oz)	a. |__|__| a._____	a. |__|__| a._____	b. Reason(s) for Demise Code: |__|__|, |__|__|, |__|__| _____ (Only specify if Other (code 99))
	OR	OR	b. |__|__| b._____	b. |__|__| b._____	
2. Outcome: |__|__|	GA Code: |__|__| (If GA is unknown use code)	|__|__|__|__|__| (grams)	c. |__|__| c._____	c. |__|__| c._____	c. Check if Autopsy performed: ❑

Outcome Code	GA (Gestational Age) Code	Maternal Complications Code *(CARD 2)*	Fetal/Infant Complications Code *(CARD 3)*	Reason for Demise Code *(CARD 4)*
LB=Live Birth SB=Stillbirth SA=Spontaneous Abortion TA=Therapeutic Abortion EP=Ectopic Pregnancy MP=Molar Pregnancy *Note: If the participant reports "termination of pregnancy," document this as TA (Therapeutic Abortion)*	FT=Full Term(≥ 37+ weeks) NT=Near Term (32-36 weeks) PT=Early Preterm (20-31 weeks) ET=Early Termination (<20 weeks)	00=None 01=Anemia 02=CHTN 03=Infection 04=PAH, Preeclampsia 05=Placenta Previa 06=Placental Abruption 07=Pre-gestational Diabetes – Type I 08=Pre-gestational Diabetes – Type II 09=Gestational Diabetes 10=PPH, requiring blood transfusion 11=PTL, requiring treatment 12=PPROM 99=Other (specify)	00=None 01=Cleft Lip or Palate 02=Down Syndrome 03=Fetal Alcohol Syndrome 04=Potential Fetal Alcohol Syndrome 05=Heart Defects 06=Hypoxia/Encephalopathy 07=IUGR/SGA 08=Jaundice 09=Mental Retardation 10=NICU Admission 11=Neural Tube Defects 12=Poor Weight Gain 13=Shoulder Dystocia 99=Other (specify e.g., congenital defect, genetic abnormality or disease, aneuploides)	01=Accident / Unintentional Injury 02=Cardiovascular 03=Congenital Defect 04=Gastrointestinal 05=Prematurity 06=Respiratory 07=SIDS 08=SUID 09=Assault / Homicide 10=Infection 99=Other (specify)

Coding Key:
(-7) = Don't Know
(-8) = Refused to Answer
(-9) = Does Not Apply

Referential Questions

Interviewer's Script

Now, I am going to ask you some questions about smoking. Because these questions are personal, any information you share with me will be kept confidential. You will be identified by a number only, not by name. Your name will not be placed on this form. Here is a calendar for you to refer to. *(SHOW CALENDAR)*

Smoking and Tobacco Use History – *Section A (Cigarettes)*

10A. If you ever smoked, when was your last cigarette: ___ ___ / ___ ___ / ___ ___ ___ ___
(month) (day) (year)

(check all that apply)
Unsure of month ❑
Unsure of day ❑

OR

NEVER SMOKED CIGARETTES: ❑ ⟶ ***If checked, SKIP TO (Section B – top of page 4)***

Instructions for the Clinical Coordinator

Determine the following date range: ___ ___ / ___ ___ / ___ ___ ___ ___ *to* ___ ___ / ___ ___ / ___ ___ ___ ___
(1 year before the LMP date, mm/dd/yyyy) *(LMP date from Eligibility Form, mm/dd/yyyy)*

Based on the participant's response to Question 10A, check here if the date of the last cigarette was more than one year before the LMP date: ❑ ⟶ ***If checked, SKIP TO Section B – top of page 4***

11A. In the year before you became pregnant, how often did you smoke a cigarette: *(SHOW CARD A)*

(circle one)

None	0	⟶ *SKIP TO (Interviewer's Script A)*
Monthly or less	1	
2 to 4 days a month (approx. once a week)	2	
2 to 3 days a week	3	
4 to 6 days a week	4	
7 days a week	5	

12A. How many cigarettes did you smoke on a typical day when you were smoking in the year before you became pregnant:

Number of cigarettes: _____ - _____
(specify number OR range)

A few notes about Modality and Patient-Reported Outcomes

Paper: Greater potential for missing data, particularly if poorly designed and not administered. Use common format (date fields, headers, response options, shading), page numbering (e.g., 1 of 5), large font, avoid referential questions

EDC: Build in edit checks, picture fields, calendar pop-up, better for referential questions (dependent on whether CRF is paper or electronic) source or paper)

PRO: Content should be clear and understandable to the subject population

Review and Quality Control Process

- Before finalized - all CRFs should be reviewed by multi-disciplinary team, new forms pilot-tested
- CRFs translated into multiple languages should be translated and back translated
- Paper-based CRFs should be carefully reviewed prior to release using version control
- Electronic CRFs must undergo user acceptance testing

- All should ensure participant confidentiality and change control/versioning

CRF Completion Guidelines and Edit Checks

CRF Completion Guidelines designed from user perspective, written when creating CRFs and Edit Checks

Edit Check Categories[1]:

- Manual: CRF review prior to entry
- Programmed in Database: majority of checks where possible
- Endpoint: missing, out of range
- Safety: ensure timely reporting of SAE and PV
- Protocol Compliance: adherence to visit schedule
- Listings: discrepancies in redundant data, free text
- External: data transferred from outside source

CRF	Field Name (Number)	Check Name	Edit Check	Edit Check Message
ENROLL	Subject ID (2)	DUP_REC	Duplicate subject ID number	This subject ID number has already been assigned for this site. Please confirm correct ID number.
DEMOG	Subject ID (2)	NO_SUBJ_ID	Missing subject ID number	A subject ID number has not been entered for this record.
DEMOG	Subject DoB (6)	INVLD_AGE	Subject age is out of range	The date of birth value entered may be invalid. Please confirm correct date of birth.

Good Data Reporting Practices[2]

- Foundation for using research data to support research decisions
- Applies to manual, instrument and computer systems
- FDA took lead with respect to aspects to recording of data (ALCOA) to represent the principles for data quality[2]
  - Attributable: Data values associated with individual or device which observed, recorded and changed (audit trail) information (traceability)
  - Legible: Readable/Legible, long term storage mechanism
  - Contemporaneous: Data recorded at time of observation or measurement*
  - Original: Data traceable back to origin
  - Accurate: reflects truth; data errors - inaccuracy, Data discrepancies - suspected or possible data errors

*one ten – one hundred rule: Costs $1 to identify and resolve discrepant data at origin, $10 to resolve during processing, $100 at later stages[2]

Sample Patient Enrollment Case Report

Sponsor EAP-001	__ __ __ Site Number	01 (Assigned by System) Visit Number
Patient Enrollment		

1. **Patient Number:** ____ ____ ____

2. **Patient Initials:** ____ ____ ____
   F M L

3. **Date Informed Consent Signed:** ____ / ____ / _____
   DD MON YYYY

4. **If child < 18, Date Assent Signed:** ____ / ____ / _____
   DD MON YYYY

5. **Protocol Version Number of Executed Informed Consent:** _____

THE SAFE PASSAGE STUDY

MAIN STUDY CONSENT TRACKING FORM

Participant ID _____

[BISH and RAPD ONLY]
Recruitment Location: _____ _____ *(use codes)*

BISH Location Codes
01=Belhar Antenatal Clinic
02=Bishop Lavis Midwife Obstetric Unit
03=Tygerberg Hospital

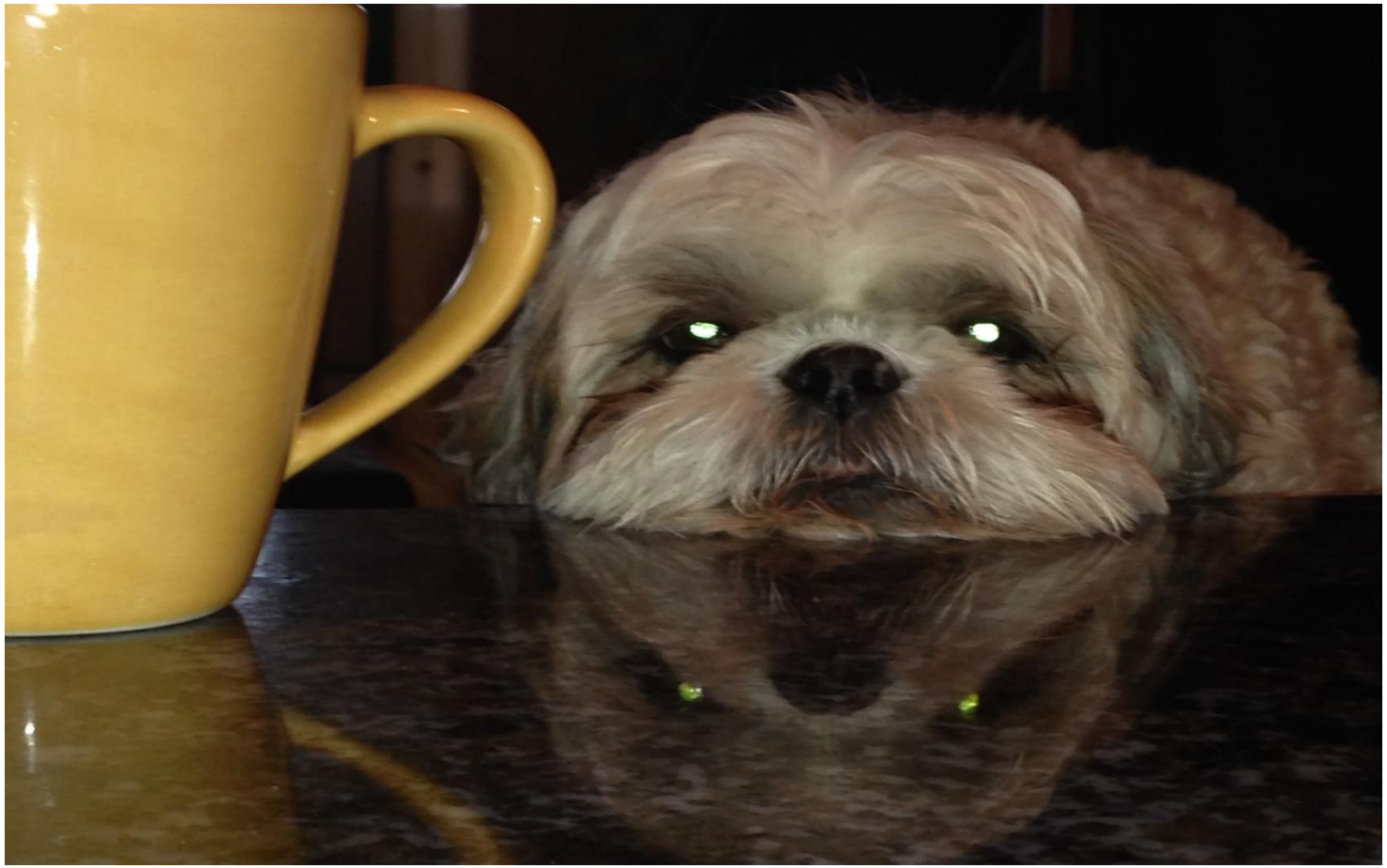
RAPD Location Codes
06=Native Women's Health Center
14=Black Hills OB/GYN
15=Midland Office

1.	**Consent signed**	*(check one)* ☐ NO ☐ YES
	a. Date Consent signed or refused	__ __ / __ __ / __ __ __ __ *(month) (day) (year)*
	b. If not signed, please specify reason for refusal	Code: __ __ *(use codes below)* Other: _____ *(If code 99, specify other reason)*
2.	**Addendum signed for Embedded Study**	*(check one)* ☐ NO ☐ YES ☐ N/A
	a. Date Addendum signed or refused	__ __ / __ __ / __ __ __ __ *(month) (day) (year)*
	b. If not signed, please specify reason for refusal	Code: *(use codes below)* Other: _____ *(If code 99, specify other reason)*
		(check one for each)
3.	**May collect maternal saliva**	☐ NO ☐ YES
4.	**May collect maternal blood**	☐ NO ☐ YES
5.	**May review maternal medical records**	☐ NO ☐ YES
6.	**May collect placental tissue**	☐ NO ☐ YES
7.	**May collect cord or infant blood sample** *(Guthrie card)*	☐ NO ☐ YES
8.	**May collect baby's stool**	☐ NO ☐ YES
9.	**May collect brain tissue**	**N/A**
10.	**May take photo of infant**	☐ NO ☐ YES
11.	**May take video recordings of baby's movement**	☐ NO ☐ YES
12.	**May review baby's medical records**	☐ NO ☐ YES
13.	**Willing to participate in genetics studies**	☐ NO ☐ YES
14.	**May use specimens for future studies**	☐ NO ☐ YES
15.	**May measure baby's brain activity and hearing**	☐ NO ☐ YES ☐ N/A
16.	**May contact for future studies**	☐ NO ☐ YES ☐ N/A
17.	**May take 3D photo of infant**	☐ NO ☐ YES ☐ N/A

Learning Objectives

- The necessity of incorporating data sharing requirements
- Key design elements and inclusion of standard measures
- Importance of pilot testing, change management and optimization of data architecture

Thank you!!!!



References:

[1]Good Clinical Data Management Practices, Society for Clinical Data Management, Oct 2013

[2]The *Data Book Collection and Management of Research Data, by Meredith Zozus.* CRC Press, 2017