PREDICT Paediatric Research in Emergency Departments International Collaborative

Good Clinical Research Practice and related issues

Amanda Williams, Donna Franklin & Megan Bonisch

PREDICT Paediatric Research in Emergency Departments International Collaborative

Aims

To become familiar with…

- The key principles of good clinical practice (“GCP”)
- Adverse Event Reporting
- The practicality of obtaining informed consent

General notes

PREDICT Paediatric Research in Emergency Departments International Collaborative

What is Good Clinical Practice (GCP)?

- GCP provides a standard for good research practice
  - Often viewed as relevant only for drug & device clinical trials but the principles apply to all human research…
- Adhering to GCP provides assurance that in the design, conduct, recording and reporting of a study
  - Study participant rights are protected
  - Study data is accurate and valid (i.e. scientific integrity)

PREDICT Paediatric Research in Emergency Departments International Collaborative

Who is responsible for GCP compliance?

- **Research Team** (e.g. Principal Investigators, Study Coordinators, Data Entry person, Biostatisticians etc…)
- HRECs
- Institution where research is being conducted
- Sponsors

GCP compliance is a collaborative effort

PREDICT Paediatric Research in Emergency Departments International Collaborative

Applying GCP Principles – The 12 Golden Rules

1. Obtain **ethical approval**
2. Know & **follow your protocol**
3. Select, **train & log study personnel**
4. Ensure **participant consent is fully informed**
5. Ensure **quality data**
6. Ensure **study equipment is appropriate**
7. Document **drug/device accountability**
8. Ensure **quality of lab evaluations** (where applic)
9. Timely **safety assessment & reporting** (where applic)
10. Monitor **recruitment**
11. Maintain **comprehensive files & archives**
12. **Communicate** - keep everyone fully informed

PREDICT Paediatric Research in Emergency Departments International Collaborative

1. Obtain ethical approval

HREC and Governance approval

- BEFORE STUDY START obtain written HREC (ethics) approval for
  - the protocol& associated documents
  - participant information & consent form (PICF) and any other information to be viewed by participants

- DURING THE STUDY obtain written HREC approval prior to implementing:
  - Protocol amendments
  - Revised PICF and any other documents to be viewed by participants
    - If immediate safety need for revised PICF d/w HREC using prior to approval

PREDICT Paediatric Research in Emergency Departments International Collaborative

1. Obtain ethical approval

Multicentre Research

- NEAF: National Ethics Application Form
  - The lead site will submit the online NEAF
  - Ensures ETHICS approval for all sites listed on the NEAF
  - States included in NEAF: Queensland, New South Wales, Victoria, South Australia

- SSA: Site Specific Approval
  - Provides local governance approval
  - Must be completed by each site listed in the NEAF

  - Modifications
  - All sites listed on the NEAF must make appropriate modifications to their governance to reflect those of the lead site.

PREDICT Paediatric Research in Emergency Departments International Collaborative

2. Know & follow your protocol

Read
- Read & be familiar with the protocol

Agree
- Investigators must agree with all aspects of the study

Sign
- The protocol must be signed to indicate adherence to the protocol

Follow!!!
- Non-adherence to the protocol must be recorded
  - Deviation = any deviation from protocol
  - Violation = a protocol deviation which affects participant safety (must report to HREC)

Access
- The protocol must be available to the study team at all times

File
- All previous versions should be clearly marked as superseded (but file copy retained)

PREDICT Paediatric Research in Emergency Departments International Collaborative

3. Select, train & log study personnel

Adequate Training

- All staff must have training in GCP and the Protocol

Delegation & Training Logs

- Log of delegated duties signed by Principal Investigator
- Log of each person's signature (usually included on log above)
- Evidence of training

Investigators' CVs

- A signed and dated copy of each investigator's CVs in the site file

PREDICT Paediatric Research in Emergency Departments International Collaborative

Template Delegation of Duties Log

SIGNATURE LOG AND DELEGATION OF DUTIES (template)

	Protocol Name/No: Investigator Name: Sponsor:						
Start Date Of Involvement	**Print Name**	**Signature**	**Sample Initials**	**Function (e.g. sub-investigator, study nurse)**	**Task Delegated**	**Authorised by Investigator (initial+ date)**	**End date of Involvement**

a. Informed discussion
b. Informed consent sign off
c. CRF/Data query completion and correction
d. CRF/Data query sign-off
e. Subject Examination/evaluation
f. Investigational product dispensation
g. Investigational product accountability
h. Randomization (e.g. IVRS)
i. Essential / Regulatory documents handling
j. Study specific procedures – Specify:
k. Other

PREDICT Paediatric Research in Emergency Departments International Collaborative

3. Select, train & log study personnel

Hospital Staff

- All staff who recruit for your study, including all nurses and doctors, must have evidence of adequate training
- Keep a log of all education sessions- RN's and DR's to write their name and sign,

PREDICT Paediatric Research in Emergency Departments International Collaborative

4. Ensure participant consent is fully informed

Informed consent

- Must be voluntary & free of coercion
- All information for participants to make an informed decision must be provided
- Environmental factors

- NOTE: Update PICF if important new information becomes *available (e.g. risk-benefit ratio changes, new safety data, additional visits/procedures)*
  - Where re-consenting required, do this promptly

Appropriate storage

- Store all consent forms in locked cupboard
- Current version
- Uploading onto Database

PREDICT Paediatric Research in Emergency Departments International Collaborative

5. Ensure quality data

Collecting data

- ALCOA = Attributable, Legible, Contemporaneous, Original, Accurate plus EA = Enduring and Available
- Source document – is where the data is first recorded (e.g. medical record, questionnaire, participant diary, ECG)
  - Data on data collection forms/CRFs and database should = source

Data entry and corrections

- Case report forms (CRF) can be paper and/or electronic
  - Need clear & concise design and instructions
  - Paper – use permanent medium to record (no pencil). For corrections date & initial – do not obscure original entry
  - Electronic – strongly recommend auditable software (e.g. RED CAP)

Verify CRF data against source data

- Compare CRF data and database to check they match source data

PREDICT Paediatric Research in Emergency Departments International Collaborative

6. Ensure study equipment is appropriate

Suitable

- Check the correct equipment is being used (as per your protocol)

Available

- Ensure equipment will be available for the duration of the project

Calibrate and check

- If equipment requires regular calibration – ensure it is done!
- Calibration records should be kept & made available for audits

Maintain

- Maintenance - do regularly, and log (make available for audits)

PREDICT Paediatric Research in Emergency Departments International Collaborative

7. Document drug/device accountability (where applic)

Documentation – Accountability & Reconciliation

- Maintain detailed records of
  - Drug/device shipments
  - Storage conditions
  - Participant randomisation confirmations (where applic)
  - Dispensing
  - Returns
  - Destruction
- Monitor participant compliance

Standard Operating Procedures (SOPs)

- Create & adhere to department and study SOPs

Site Name: _____ Site Prefix: _____ Investigator: _____ Page ____ of ____

STUDY MEDICATION KITS*

*Each kit contains:
Bell Pic Study Drug (Prednisolone 5 mg/mL or Placebo) Oral Solution 4 x 30mL bottles, 2 x 10mL oral syringes, 2 x 3mL oral syringes and a Study Participant Card

DATE	STOCK Study Coordinator: Re-order stock when Number of Kits on Hand = 2			DISPENSING Refer to Dispensing Procedure				SIGN
	Number of Kits Received (+) or Dispensed (-)	Batch and Expiry	Number of Kits On Hand (Balance)	Patient Initials	Study Number	Number of Bottles Supplied Tick (✓)	Number of Bottles Returned Tick (✓)	
01/JAN/15	*+ 4*	*ZZ11/AA22 31/DEC/15*	*4*	*-*	*-*	☐ 2 ☐ 4	☐ 2 ☐ 0	*AB*
03/JAN/15	*- 1*	*ZZ11/AA22 31/DEC/15*	*3*	*AZ*	*ABC-001*	☑ 2 ☐ 4	☑ 2 ☐ 0	*Dr. CD*
						☐ 2 ☐ 4	☐ 2 ☐ 0	
						☐ 2 ☐ 4	☐ 2 ☐ 0	
						☐ 2 ☐ 4	☐ 2 ☐ 0	
						☐ 2 ☐ 4	☐ 2 ☐ 0	
						☐ 2 ☐ 4	☐ 2 ☐ 0	

DO NOT FILE THIS SHEET – RETURN TO RESEARCH BOX

PREDICT Paediatric Research in Emergency Departments International Collaborative

This participant is receiving the following:
Prednisolone (1mg/kg) or matching placebo for 10 days.

Any study related questions/concerns please contact:
Study Coordinator: <Name>
<number>
<Email>

2

Please tick off each day that your child receives their medication.

The next dose is due in the morning on ____/____/____

DAY	1	2	3	4	5	6	7	8	9	10
DOSE GIVEN (✓)	✓									

Do not throw out the bottles, please bring with you to your first appointment with the study team

3

PREDICT Paediatric Research in Emergency Departments International Collaborative

8. Ensure quality of lab evaluations (where applic)

Prior to starting

- Define & create reference ranges (as per protocol)
- Only use certification/accreditation laboratories

Collection of Samples

- Collection as per protocol
- Ensure quality – prompt handling, processing, transport
- Careful labelling

Review of Results

- Lab results/abnormal results should be reviewed by an investigator
- Document the review (signature & date) and any required actions.

PREDICT Paediatric Research in Emergency Departments International Collaborative

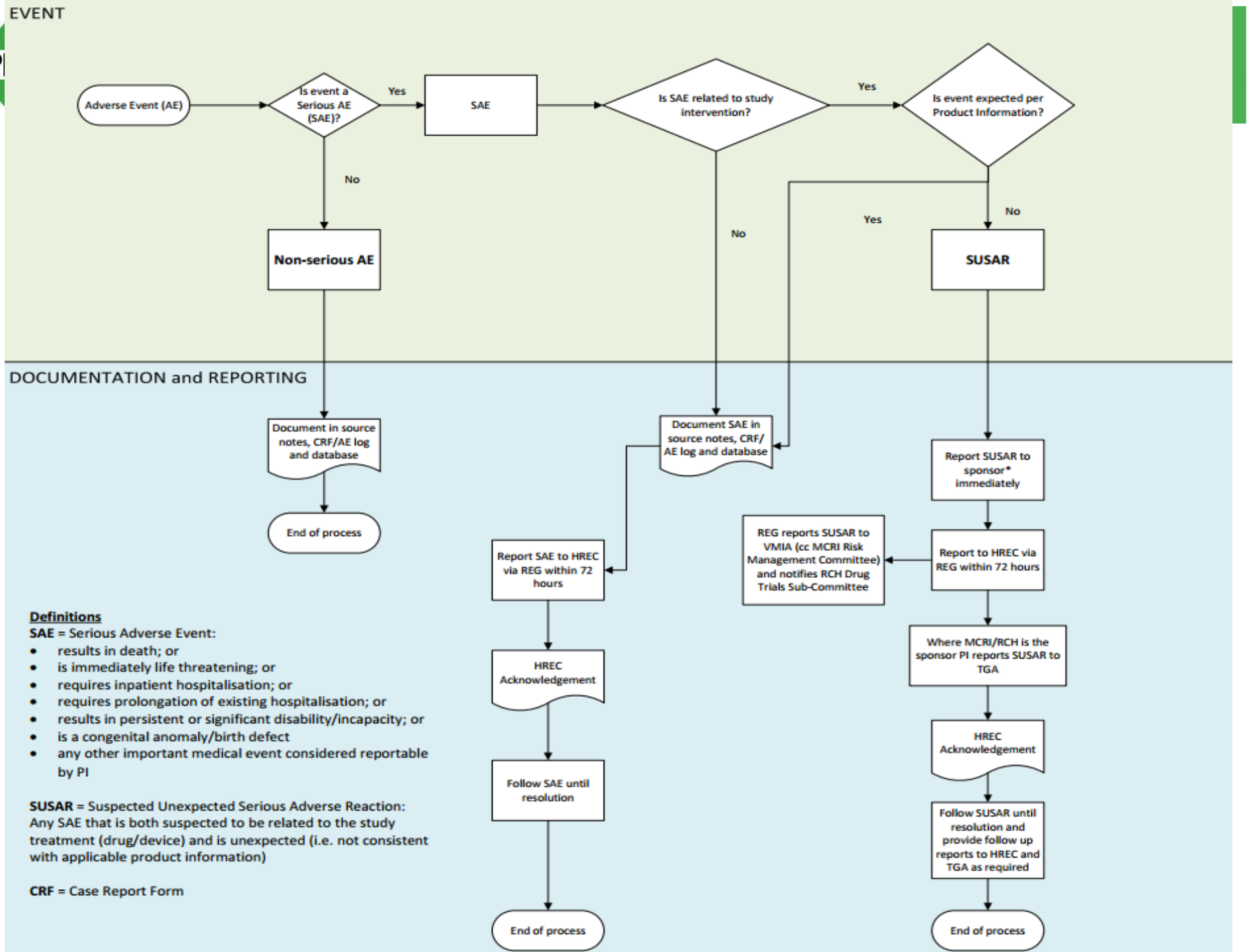
9. Timely safety assessment & reporting (where applic)

Definition

- **Adverse Event** (AE) - Any untoward medical occurrence to a participant which does not necessarily have a causal relationship with the treatment. Adverse events should be defined in the protocol & are protocol specific
- **Serious Adverse Event** (SAE) – Any untoward medical event related or unrelated to the study intervention/procedures which is life-threatening *or* results in death, hospitalisation (or its prolongation), disability/incapacity *or* is a congenital anomaly/birth defect *or* is a medically important event.
- **Suspected Unexpected Serious Adverse Reaction** (SUSAR) - An SAE that is (i) at least possibly related to the study intervention AND (ii) is unexpected (i.e. outside known safety profile of drug/intervention)

Reporting Requirements

- **AE** – will be defined in your protocol
- **SAE & SUSAR** - Report within 24 - 72 hours to HREC, Report to Sponsor within their required timeline (usually 24 hours)
- **External SUSUARs** - report promptly to HREC where has an impact on study conduct, otherwise submit as periodic listing


EVENT
Adverse Event (AE)
Is event a Serious AE (SAE)?
Yes
SAE
Is SAE related to study intervention?
Yes
Is event expected per Product Information?
No
Non-serious AE
No
Yes
No
SUSAR
DOCUMENTATION and REPORTING
Document in source notes, CRF/AE log and database
End of process
Document SAE in source notes, CRF/ AE log and database
Report SAE to HREC via REG within 72 hours
HREC Acknowledgement
Follow SAE until resolution
End of process
Report SUSAR to sponsor* immediately
REG reports SUSAR to VMIA (cc MCRI Risk Management Committee) and notifies RCH Drug Trials Sub-Committee
Report to HREC via REG within 72 hours
Where MCRI/RCH is the sponsor PI reports SUSAR to TGA
HREC Acknowledgement
Follow SUSAR until resolution and provide follow up reports to HREC and TGA as required
End of process
Definitions
SAE = Serious Adverse Event:
results in death; or
is immediately life threatening; or
requires inpatient hospitalisation; or
requires prolongation of existing hospitalisation; or
results in persistent or significant disability/incapacity; or
is a congenital anomaly/birth defect
any other important medical event considered reportable by PI
SUSAR = Suspected Unexpected Serious Adverse Reaction: Any SAE that is both suspected to be related to the study treatment (drug/device) and is unexpected (i.e. not consistent with applicable product information)
CRF = Case Report Form

PREDICT Paediatric Research in Emergency Departments International Collaborative

10. Monitor recruitment

Predict Accurately

- Refer to appropriate data source (e.g. hospital records)
  - Consider inclusion criteria
  - Allow contingency for non-adherence

Participant Recruitment

- Adhere to inclusion/exclusion criteria
- Maintain log of (pre)screened & enrolled participants
  - Take note of reasons for non-enrolment (ineligibility, refusal etc)

PREDICT Paediatric Research in Emergency Departments International Collaborative

11. Maintain comprehensive files & archives

Trial Master Files/Study Binders

- Prepare files using Trial Master File (TMF) template
- this is a central repository for all project level documents (not participant data or documents)
- set up separate files for each participant (signed consent form/s, completed CRFs/questionnaires, SAE reports etc.)

Electronic filing

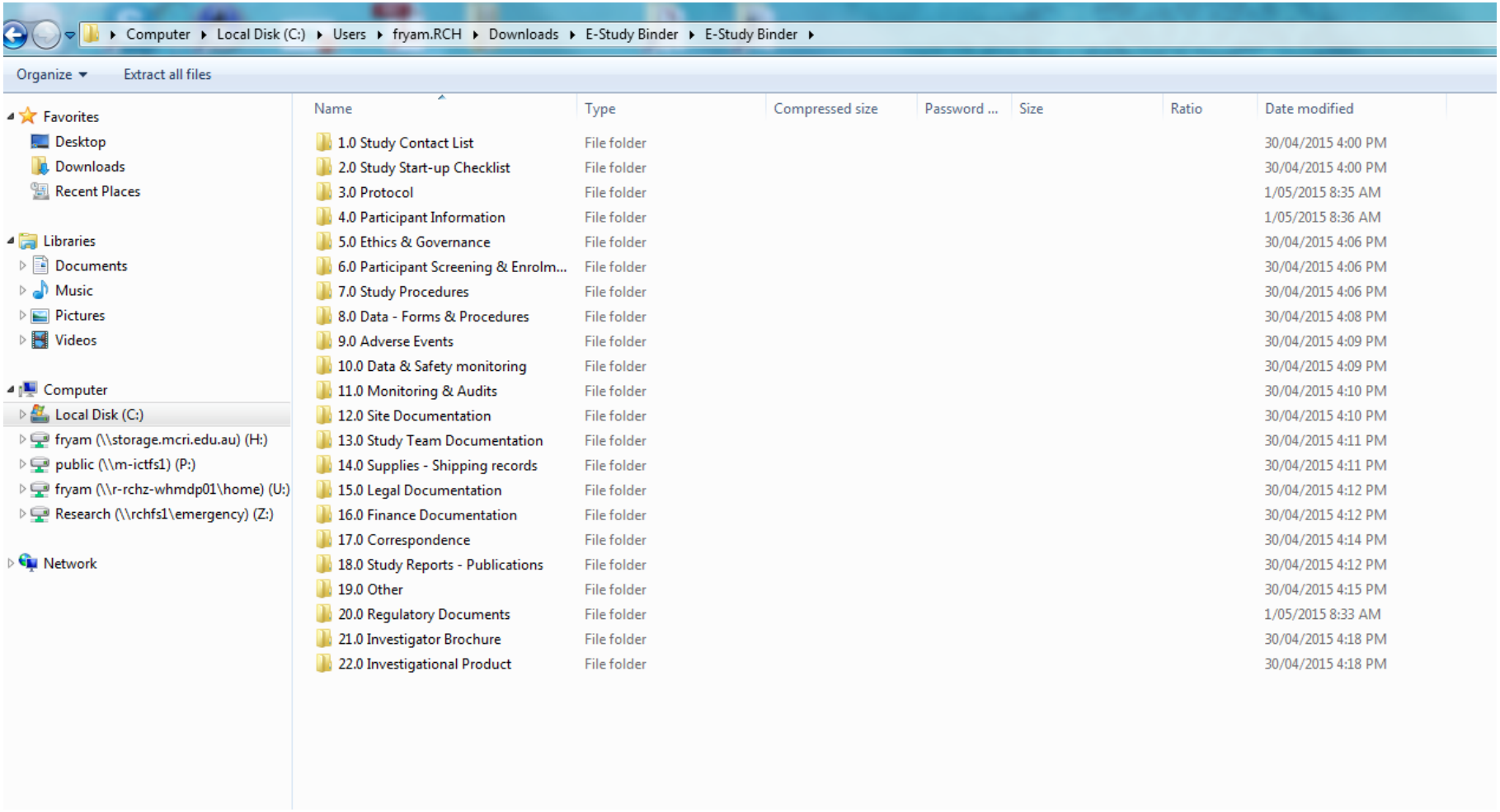
- Password protection
- Version control
- Standard nomenclature

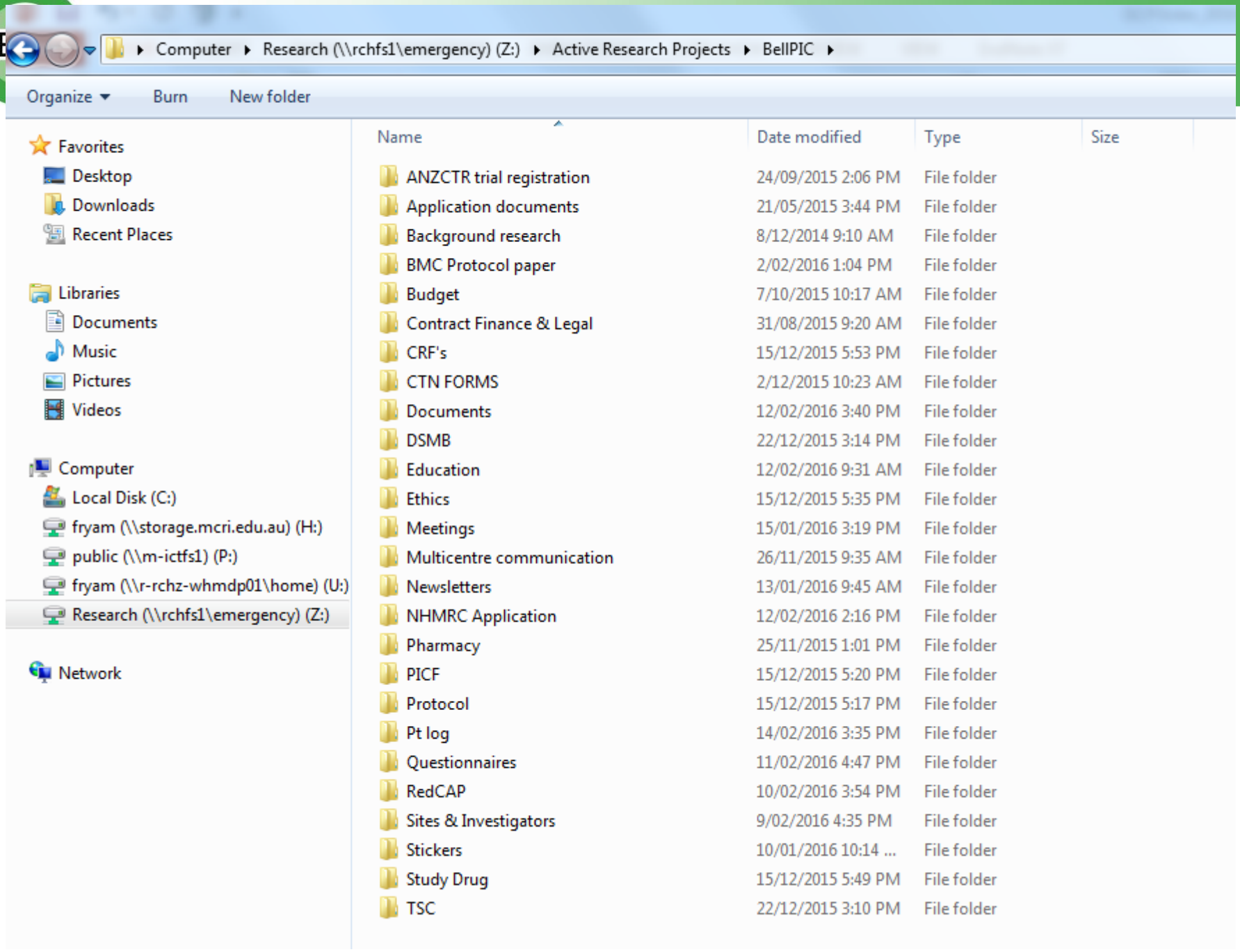
Archiving

- Duration - check national / state requirements
- Format for electronic documents – save as pdf-A or print and store as hardcopy
- Method of disposal – confidential

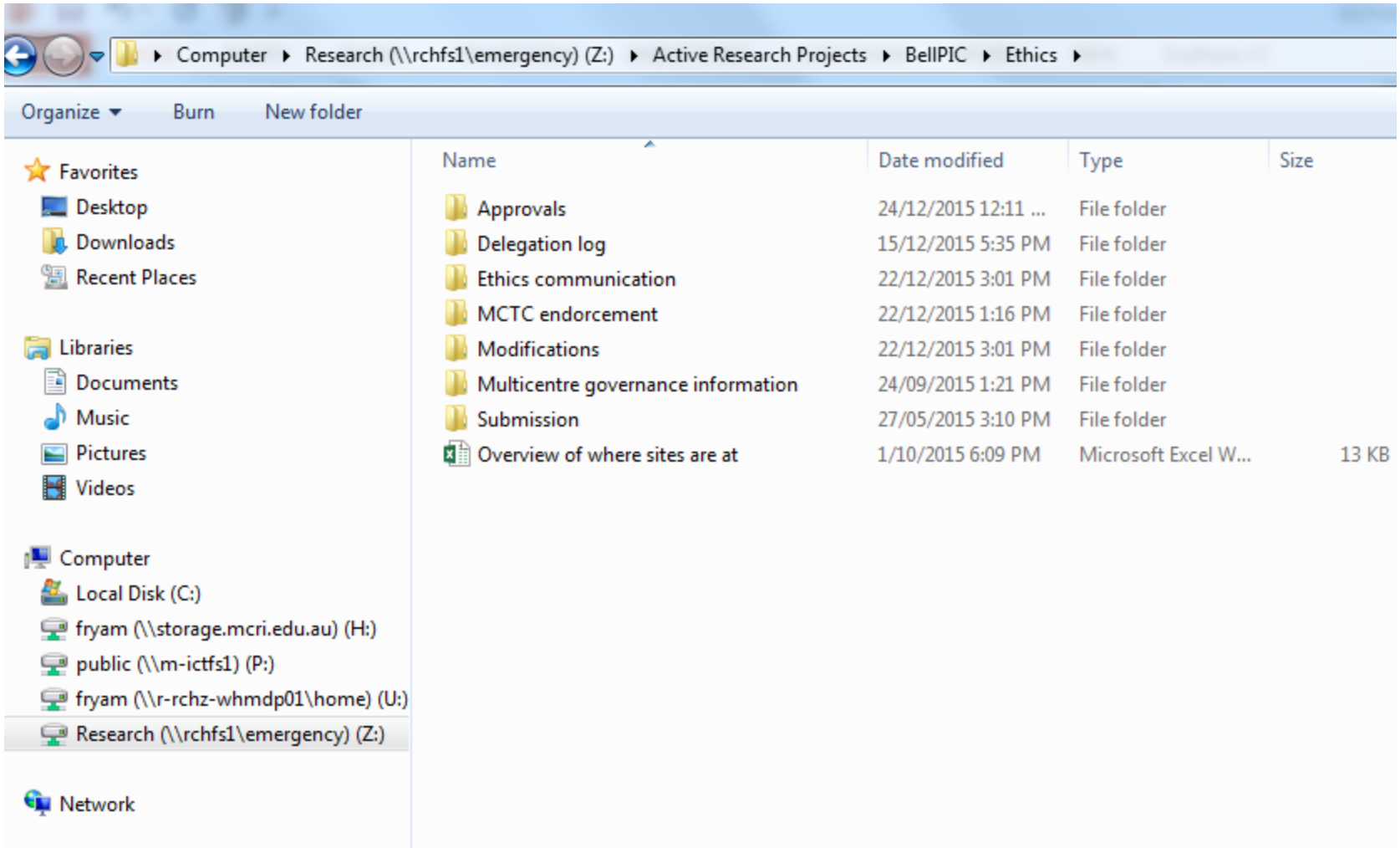
PREDICT Paediatric Research in Emergency Departments International Collaborative

Study Binder- electronic or hard copy

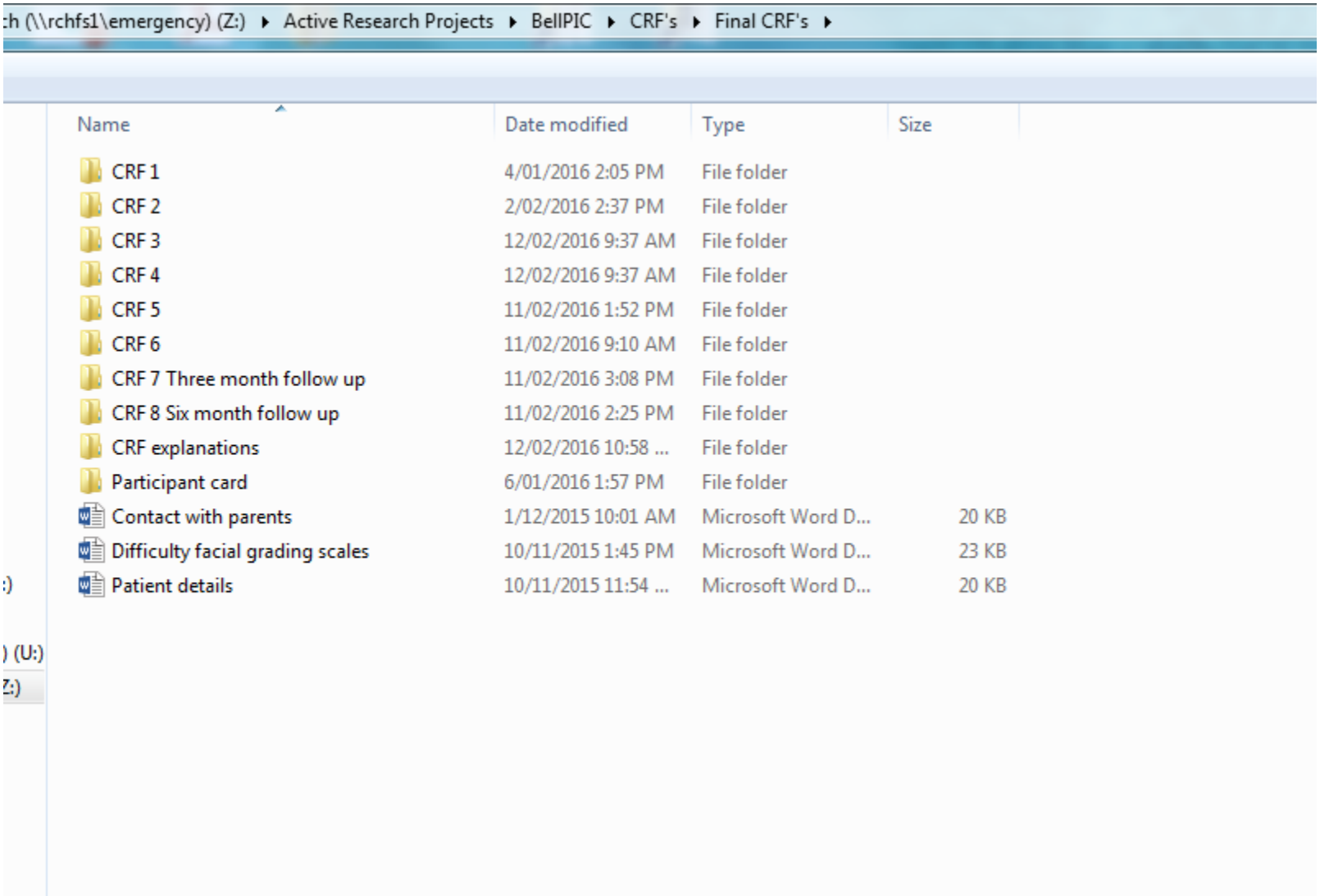



Computer ▸ Research (\\rchfs1\emergency) (Z:) ▸ Active Research Projects ▸ BellPIC ▸
Organize
Burn
New folder
Favorites
Desktop
Downloads
Recent Places
Libraries
Documents
Music
Pictures
Videos
Computer
Local Disk (C:)
fryam (\\storage.mcri.edu.au) (H:)
public (\\m-ictfs1) (P:)
fryam (\\r-rchz-whmdp01\home) (U:)
Research (\\rchfs1\emergency) (Z:)
Network
Name
Date modified
Type
Size
ANZCTR trial registration 24/09/2015 2:06 PM File folder
Application documents 21/05/2015 3:44 PM File folder
Background research 8/12/2014 9:10 AM File folder
BMC Protocol paper 2/02/2016 1:04 PM File folder
Budget 7/10/2015 10:17 AM File folder
Contract Finance & Legal 31/08/2015 9:20 AM File folder
CRF's 15/12/2015 5:53 PM File folder
CTN FORMS 2/12/2015 10:23 AM File folder
Documents 12/02/2016 3:40 PM File folder
DSMB 22/12/2015 3:14 PM File folder
Education 12/02/2016 9:31 AM File folder
Ethics 15/12/2015 5:35 PM File folder
Meetings 15/01/2016 3:19 PM File folder
Multicentre communication 26/11/2015 9:35 AM File folder
Newsletters 13/01/2016 9:45 AM File folder
NHMRC Application 12/02/2016 2:16 PM File folder
Pharmacy 25/11/2015 1:01 PM File folder
PICF 15/12/2015 5:20 PM File folder
Protocol 15/12/2015 5:17 PM File folder
Pt log 14/02/2016 3:35 PM File folder
Questionnaires 11/02/2016 4:47 PM File folder
RedCAP 10/02/2016 3:54 PM File folder
Sites & Investigators 9/02/2016 4:35 PM File folder
Stickers 10/01/2016 10:14 ... File folder
Study Drug 15/12/2015 5:49 PM File folder
TSC 22/12/2015 3:10 PM File folder

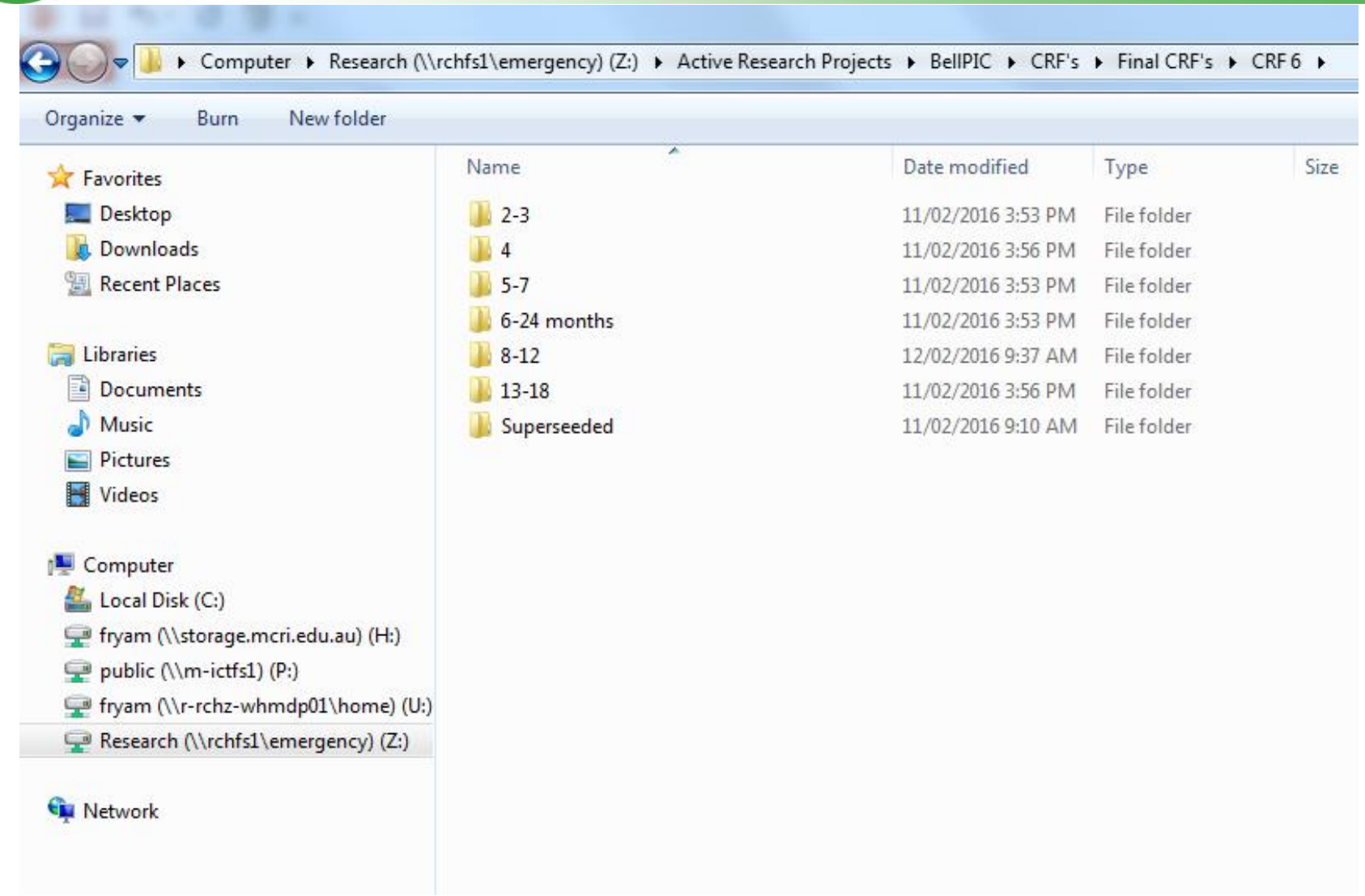
PREDICT Paediatric Research in Emergency Departments International Collaborative



PREDICT Paediatric Research in Emergency Departments International Collaborative



PREDICT Paediatric Research in Emergency Departments International Collaborative



Archiving duration - Australia

Original data must be retained (archived) post-study – the time will vary:

- **At least 5 years** post-publication (the "Australian Code for the Responsible Conduct of Research"
- For **15 following completion of a clinical trial** (TGA's adaptation of ICH-GCP)

And for Victoria:

- For **7 years after age 18 years (Vic Health Records Act)** for any information on health collected as part of research (unless already recorded in a document subject to the Act).

PREDICT Paediatric Research in Emergency Departments International Collaborative

12. Keep everyone fully informed

Communication is the key

- Systems in place to facilitate clear, open & timely communication
- Know what and whom to communicate with (e.g., stakeholders, participants & research team)

Reporting

- Annual and final reports
- Adverse event reporting
- Reporting to funding bodies (e.g., NHMRC & Sponsors)

PREDICT Paediatric Research in Emergency Departments International Collaborative

The most vital points....

If it is not written down, it did not happen

If it is not documented, it does not exist

And if it was supposed to happen and didn't - document and explain!

"Adhering to GCP is one thing, but proving that this has been done is another. For a trial to be credible in the eyes of the authorities, investigators must be able to show that the study is in compliance with GCP guidelines. This means documenting every study-related action"

(Hutchinson 2009 – 12 Golden GCP Rules for Investigators. Canary Publications, London)

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Event Reporting

Definition

- **Adverse Event** (AE) - Any untoward medical occurrence to a participant which does not necessarily have a causal relationship with the treatment. Adverse events should be defined in the protocol & are protocol specific
- **Serious Adverse Event** (SAE) – Any untoward medical event related or unrelated to the study intervention/procedures which is life-threatening *or* results in death, hospitalisation (or its prolongation), disability/incapacity *or* is a congenital anomaly/birth defect *or* is a medically important event.
- **Suspected Unexpected Serious Adverse Reaction** (SUSAR) - An SAE that is (i) at least possibly related to the study intervention AND (ii) is unexpected (i.e. outside known safety profile of drug/intervention)

Reporting Requirements

- **AE** – will be defined in your protocol
- **SAE & SUSAR** - Report within 24 - 72 hours to HREC, Report to Sponsor within their required timeline (usually 24 hours)
- **External SUSUARs** - report promptly to HREC where has an impact on study conduct, otherwise submit as periodic listing

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Event Reporting:

BellPIC Study

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Events (As defined in protocol)

- Any untoward medical occurrence in a patient enrolled into this study regardless of its causal relationship to study treatment.
  - Conditions that are present at screening and do not deteriorate will not be considered AEs.

Eliciting Adverse Event Information

- The parent/guardian/participant will be asked to report AE when contacted at 10 days and at the 1 month follow up visit.
- In addition, AEs noted during the visit or noted from any other documentation (e.g. hospital unit record and correspondence) will be documented in the source documents and on the CRF by the investigator team.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Serious Adverse Events (SAE)

A serious adverse event is an adverse event that:

- results in death
- or is immediately life threatening
- or requires prolongation of existing hospitalisation
- or results in persistent or significant disability/incapacity
- or is a congenital anomaly/birth defect.
- In addition, an important medical event which, in the opinion of the investigator, may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition may be reported as an SAE.
- Hospitalisation due to progression of Bell's palsy will not be considered an SAE for the purposes of this study.

SERIOUS ADVERSE EVENT REPORTING (SAE)

The site PI is responsible for recording and reporting all SAEs for the period from the first dose until the 1 month visit. The following exceptions apply:

- Conditions that are present at screening and do not deteriorate will not be considered AEs.

Any SAE occurring in a study participant will be reported to the approving Human Research and Ethics Committee (HREC) in accordance with the safety reporting policy of the HREC (this timeframe is usually between 24 and 72 hours). The report to HREC will be completed, signed and submitted by an investigator. ***SAE reports will also be submitted to the study coordinating centre at RCH.***

PREDICT Paediatric Research in Emergency Departments International Collaborative

Suspected Unexpected Serious Adverse Events (SUSAR)

A SUSAR is an SAE that is both suspected to be related to the study treatment and is unexpected (i.e. not consistent with applicable product information).

The site PI is responsible for recording and reporting all SUSARs for the period from the first dose until the 1 month visit.

All SUSARs occurring in a study participant will be reported to:

- The CPI within 24 hours of investigator team awareness of the event.
- The approving HREC within the required HREC-specified timeframe.
- The national government regulatory body within the required timelines.

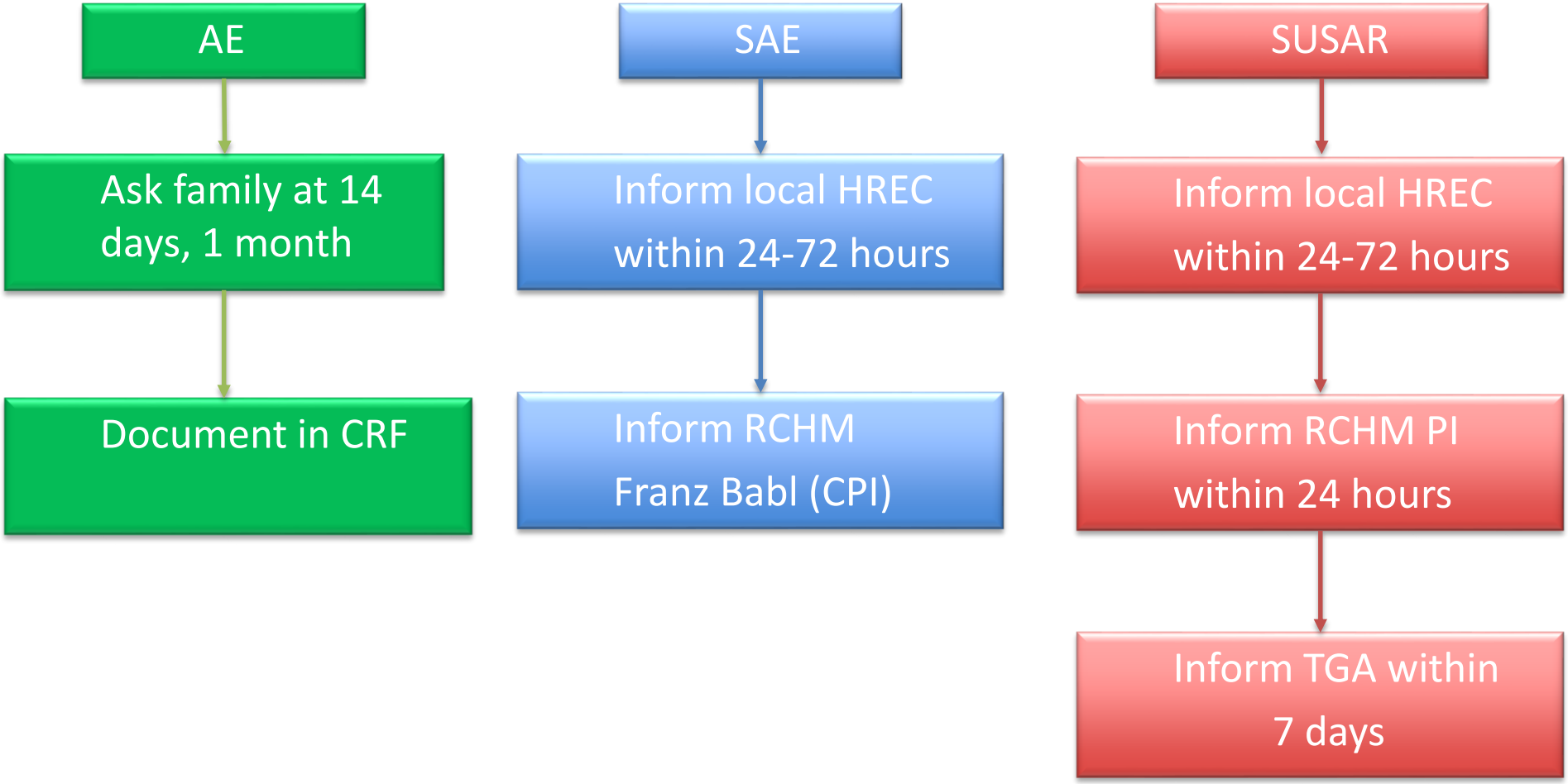
The site sponsor will report the SUSAR to the national government regulatory agency/ies.

- In Australia, reports should be submitted to the TGA in an expedited fashion (i.e. within 15 calendar days of first knowledge), or for fatal or life threatening events, an initial or full report within 7 calendar days and a follow-up report if necessary within the 15 calendar day timeframe.
- In New Zealand, reports must be sent to Medsafe within 7 days of the sponsor receiving an investigator's report of a SUSAR.

The Principal Investigator at each participating site will be notified of any SUSAR in the study population.

Adverse Event Reporting - BellPIC

PREDICT Paediatric Research in Emergency Departments International Collaborative



** each site is responsible for their own TGA reporting but Franz and Amanda will assist

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Event Reporting:

ConSEPT Study

Adverse Events

- Event which is an expected and measured outcome.
- (eg. Admission to ICU is an AE in this trial as this is expected to occur in approx 22%)
- AEs /Clinical events for ConSEPT are calculated from data supplied through routine CRF's.
- Reported to the DMC blinded by study intervention group.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Events

- **As per CRF 1**

- **Clinical events occurring in hospital at any time <u>PRIOR</u> to starting Study Drug 1 (Levetiracetam)** (tick):

a.	**Airway repositioning:**	**Yes ☐ No ☐**
b.	**Oral or nasal airway placement**	**Yes ☐ No ☐**
	Arrived in situ via ambulance service/other medical carers	**Yes ☐ No ☐**
c.	**Application of positive pressure or ventilation with bag mask:**	**Yes ☐ No ☐**
d.	**Tracheal intubation:**	**Yes ☐ No ☐**
	Arrived in situ via ambulance service/other medical carers	**Yes ☐ No ☐**
e.	**Fluid bolus started:**	**Yes ☐ No ☐**
f.	**Chest compression:**	**Yes ☐ No ☐**
g.	**Cardiac defibrillation:**	**Yes ☐ No**

PREDICT

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Events

- 24 **Clinical events occurring at any time in the first two hours <u>AFTER</u> starting Study Drug 1 (Levetiracetam)** (tick)**:**
-
- **a. Airway repositioning: Yes ☐ No ☐**
- **b. Oral or nasal airway placement: Yes ☐ No ☐**
- **c. Application of positive pressure or ventilation with bag mask: Yes ☐ No ☐**
- **d. Tracheal intubation: Yes ☐ No ☐**
- **e. Fluid bolus started: Yes ☐ No ☐**
- **f. Chest compression: Yes ☐ No ☐**
- **g. Cardiac defibrillation: Yes ☐ No ☐**
- **h. Allergic reaction: Yes ☐ No ☐**
- **i. IV access tissued: Yes ☐ No ☐ *no* IV ☐**
- **j. IO access tissued: Yes ☐ No ☐ *no* IO ☐**
- **k. Extravasation of IV/IO infusions: Yes ☐ No ☐**
- **l. Purple glove syndrome: Yes ☐ No ☐**
- **m. Other: (explain) _____**

PREDICT

Serious Adverse Events

- Definition: Any event that is fatal, life-threatening, permanently disabling, incapacitating or results in hospitalisation, prolongs a hospital stay or is associated with congenital abnormality, carcinoma or overdose.

SAE's ConSEPT Study

- Death
- Serious Airway Complications in first 24 hrs
- Cardiovascular instability
- Any other event that is life-threatening or jeopardises the patient or requires medical or surgical intervention

PREDICT Paediatric Research in Emergency Departments International Collaborative

SAE's ConSEPT Study cont.

- Reported within 24 hours to local site investigator.
- Site investigator must report the SAE to their local ethics committee within 48 hours if required (or as per local governance)
- Site Investigator should complete a SAE report form and detailed report and sent to the PI.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Suspected Unexpected Serious Adverse Events (SUSAR)

A SUSAR is an SAE that is both suspected to be related to the study treatment and is unexpected (i.e. not consistent with applicable product information).

The site PI is responsible for recording and reporting all SUSARs for the period from the first dose until the 1 month visit.

All SUSARs occurring in a study participant will be reported to:

- The CPI within 24 hours of investigator team awareness of the event.
- The approving HREC within the required HREC-specified timeframe.
- The national government regulatory body within the required timelines.

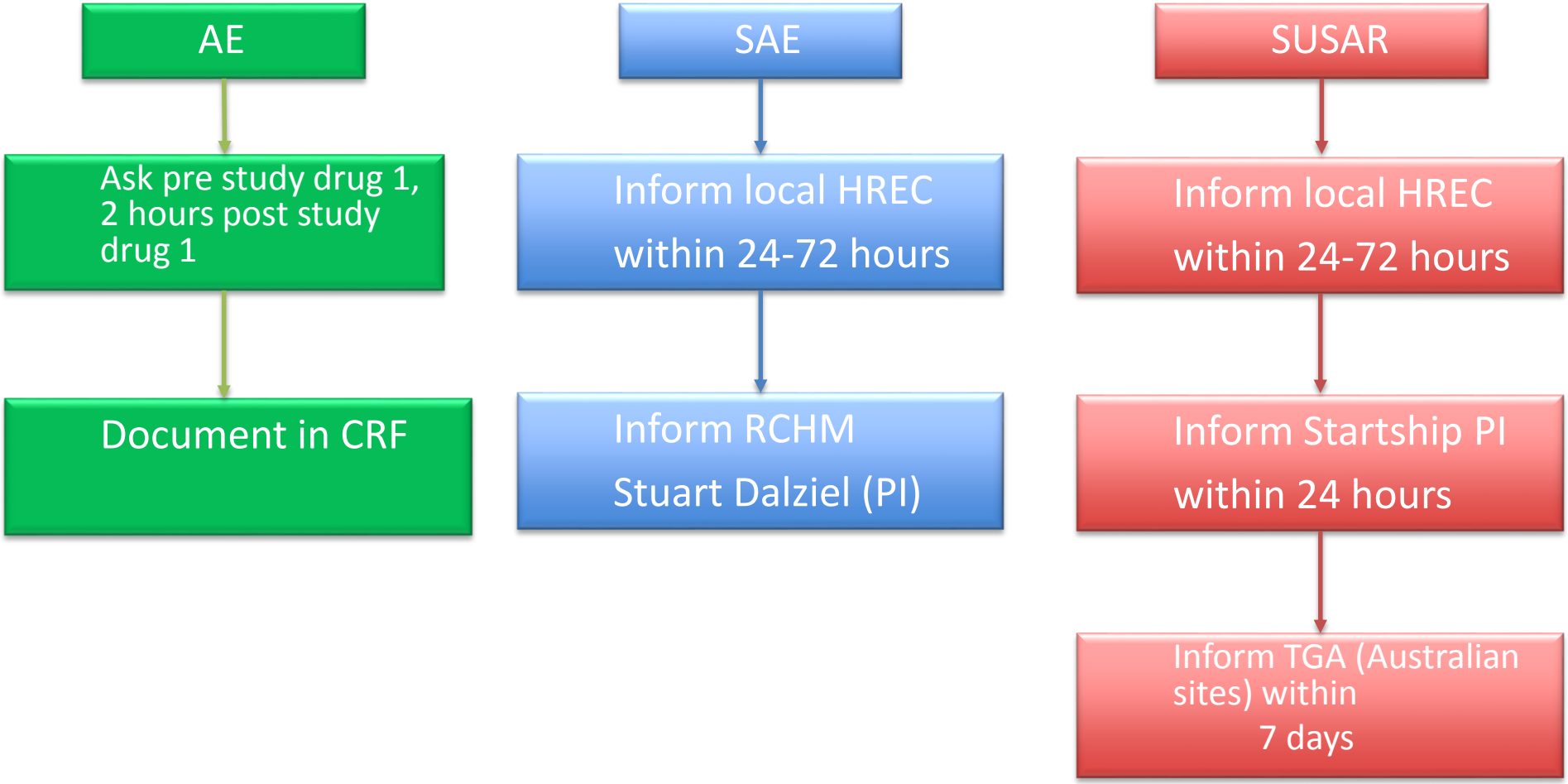
The site sponsor will report the SUSAR to the national government regulatory agency/ies.

- In Australia, reports should be submitted to the TGA in an expedited fashion (i.e. within 15 calendar days of first knowledge), or for fatal or life threatening events, an initial or full report within 7 calendar days and a follow-up report if necessary within the 15 calendar day timeframe.
- In New Zealand, reports must be sent to Medsafe within 7 days of the sponsor receiving an investigator's report of a SUSAR.

The Principal Investigator at each participating site will be notified of any SUSAR in the study population.

Adverse Event Reporting - ConSEPT

PREDICT Paediatric Research in Emergency Departments International Collaborative



** each site is responsible for their own TGA reporting but Stuart and Megan will assist

ConSEPT SAE's

- 1 year old child presented in CSE, received both levetiracetam and phenytoin and required RSI and ICU admission. Then diagnosed with HHV6 Necrotising Encephalitis requiring palliative care untill death within a few weeks.

ConSEPT SAE's

- 14 year old with severe disabilities and complex medical history. Enrolled on study, seizure ceased, no adverse events, discharged home.
- 4 weeks later (just before phone follow-up) patient contracted pneumonia and died.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Adverse Event Reporting:

PARIS Study

PREDICT Paediatric Research in Emergency Departments International Collaborative

Serious Adverse event:

- any unfavourable or unintended sign, symptom or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

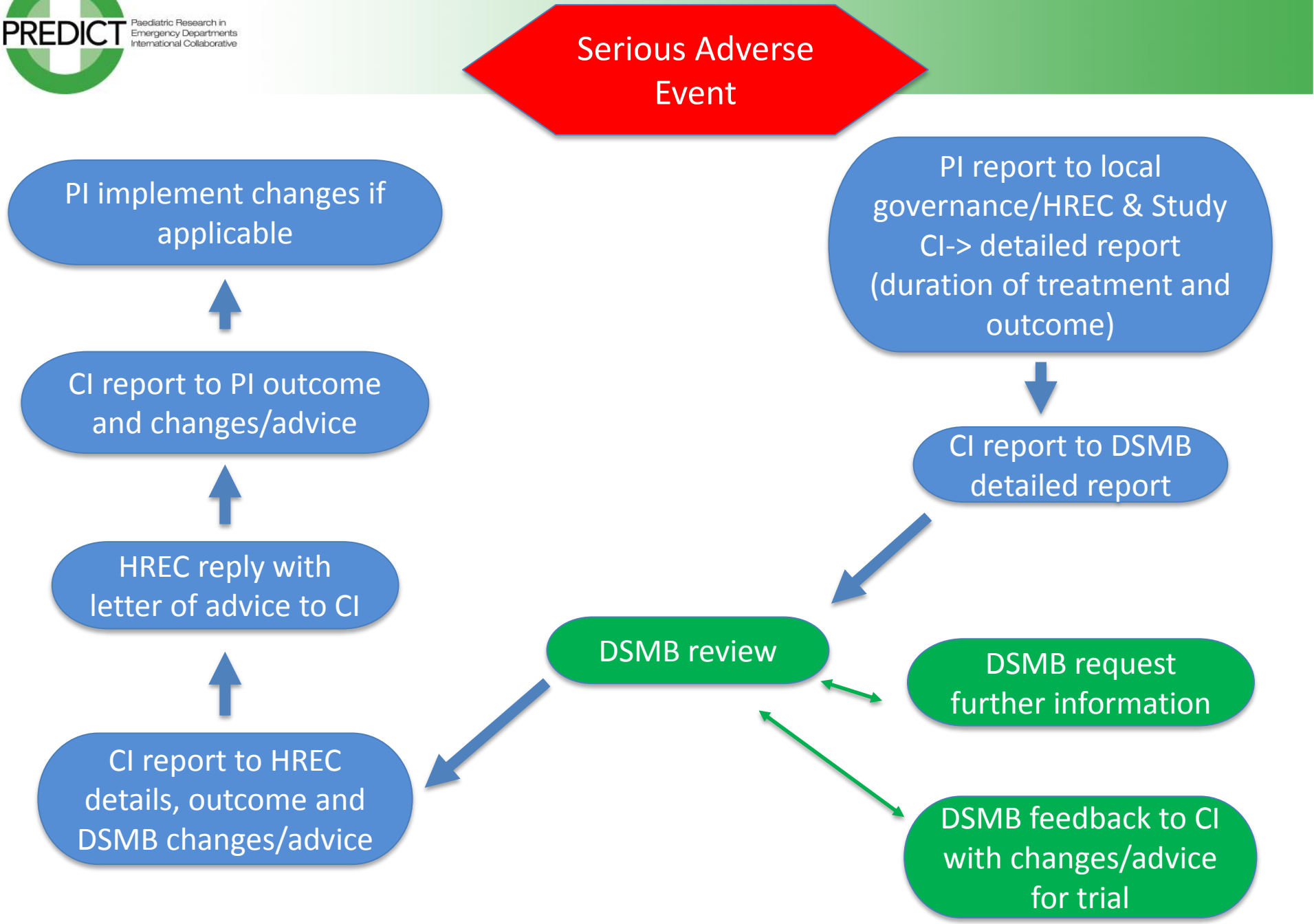
- All serious adverse events must be notified to the Committee as soon as possible.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Serious Adverse events reporting

- Timely manner (within 24-72hrs) to:
  - DSMB (2 independent members)
  - Report to governance/HREC (local & central)
  - Feedback to relevant team involved with advice/changes
  - Action changes required if outlined

PREDICT Paediatric Research in Emergency Departments International Collaborative



PREDICT Paediatric Research in Emergency Departments International Collaborative

Informed Consent:

BellPIC Study

BellPIC study Consent Process

Prospective consent

- Written informed consent required before participant is enrolled in the study
- Two consent forms
  - Parent/Guardian Consent
  - Participant Consent (12 years above)
- Optional consent for photos and videos.
- ***Witness sections

PREDICT Paediatric Research in Emergency Departments International Collaborative

Informed Consent:

ConSEPT Study

PREDICT Paediatric Research in Emergency Departments International Collaborative

ConSEPT study Consent Process

Retrospective

- Written informed consent to remain in the study sought at the earliest possible time after emergency stabilisation of the CSE
- To be performed by most senior clinician (often site investigator)

PREDICT

PREDICT Paediatric Research in Emergency Departments International Collaborative

ConSEPT study Consent Process

USA Wavier of Informed Consent if

- Study is of a life threatening condition
- Current standard of treatment is unproven or unsatisfactory
- There is prospect of direct benefit to the patient
- Informed consent is not possible within the therapeutic window
- The research cannot practicably be conducted without utilising the guidelines for Waiver of Informed Consent

PREDICT

PREDICT Paediatric Research in Emergency Departments International Collaborative

ConSEPT study Consent Process

UK

- Similar regulations exist

Declaration of Helsinki

- “If the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee.”

PREDICT

ConSEPT study Consent Process

In New Zealand consent can occur following interventions if it is (National Ethics Advisory Committee)

- Impractical (e.g. for studies in emergency care)
- Undesirable (e.g. when the delay of the intervention would harm the patient)

Australia (National Statement on Ethical Conduct in Human Research)

- Consent prior is impractical
- Potential benefit
- Research has merit

PREDICT Paediatric Research in Emergency Departments International Collaborative

ConSEPT study Consent Process

- Not possible to gain informed consent prior to randomisation and treatment in this study
- The study has received ethical approval for the consent process from the 4 ethics review committees responsible for reviewing the study in NZ and Australia
- Additional ethical safe guard
  - Independent DMC will also have role in monitoring consent
  - Includes experts in both EM and ethics

PREDICT

PREDICT Paediatric Research in Emergency Departments International Collaborative

Informed Consent:

PARIS Study

PREDICT Paediatric Research in Emergency Departments International Collaborative

Consent - PARIS

- Delayed Consent ALL participating sites except:
  - NSW – Informed Consent (legislation)
  - New Zealand
    - Delayed consent - children presenting with O2 requirement
    - Prospective Consent – children admitted without an O2 requirement

Delayed Consent

Refer to the **The National Statement Section 4.4.6**

Which recognises that in emergency care research, recruitment into a research project often has to be achieved rapidly and that a waiver of consent may be granted provided the conditions of the **N.S paragraph 4.4.1 and N.S. paragraph 2.3.6 are satisfied.**

4.4.1 relates to research merit and integrity – for research involving people who are highly dependent on medical care where:

a. It is likely that the research will lead to increased understanding about, or improvements in, the care of this population

b. The requirements of relevant jurisdictional laws are taken into account; and

c. Either (i) any risk or burden of the proposed research to this participant is justified by the potential benefits to him/her (ii) where participants have capacity to consent, any risk or burden is acceptable to them and justified by the potential benefits of the research.

2.3.6 states that before deciding to waive the requirement for consent the HREC must be satisfied that:

a. Involvement in the research carries no more than low risk

b. The benefits from the research justify any risks of harm associated with not seeking consent

c. It is impracticable to obtain consent (eg. Age)

d. There is no known or likely reason for thinking that participants would not have consented if they had been asked.

PREDICT Paediatric Research in Emergency Departments International Collaborative

Delayed Consent Benefits

- Parent/child stressed on presentation
- Low risk disease (mild to moderate) and have time
- Nursing staff (regional centres) well practiced at consenting with greater experience
- PREDICT centres mix of medical/nursing consenting
- Likely higher enrolment rate achieved
- Delivers a real world study (as all patients presenting enrolled)

PREDICT Paediatric Research in Emergency Departments International Collaborative

Delayed Consent Challenges

- ‘Creep in effect’ & previous bias already formed (not enough scientific evidence)
- Forgotten and requires follow up (letter with PICF/phone call)
- Parent sign revocation form instead of consent