OFFICE OF HUMAN RESEARCH PROTECTION PROGRAMME

(OHRPP)

11. POST DSRB APPROVAL MONITORING & REPORTING REQUIREMENTS

BIOMEDICAL DOMAINS A-E

&

POPULATION HEALTH – DOMAIN F

Reference:

NHG Investigator Manual

NHG Group Research

Version November 2022

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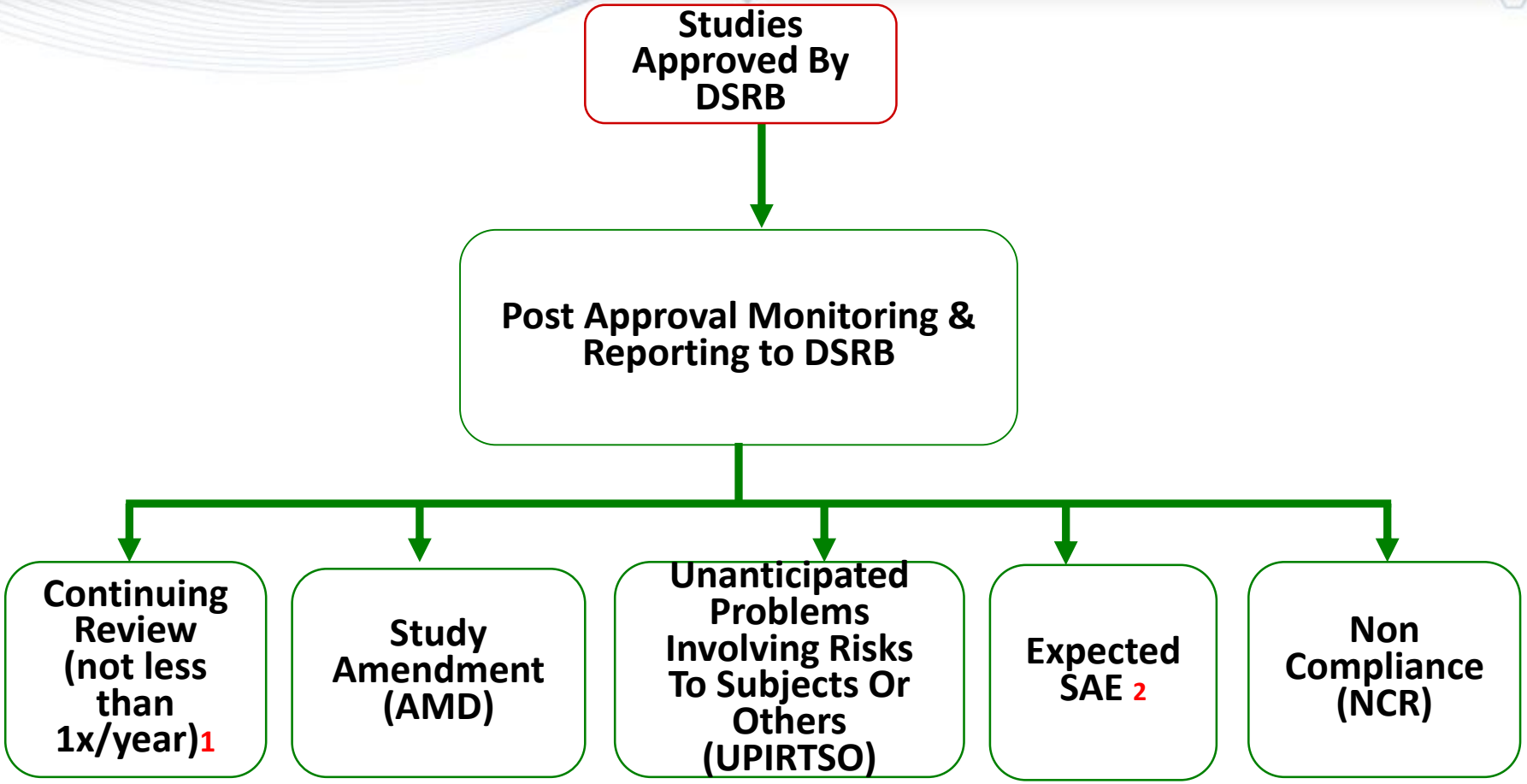
Post-Approval Reporting Requirements



1. *Not required for Exempt Studies and studies that have reported to be in data analysis only stage*
2. *Only applicable to Human Biomedical Research (HBR) studies*

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Continuing Review

Continuing Review (not less than 1x/year)[1]

It is a **monitoring mechanism** that assures continuing safeguards are in place to protect rights and welfare of subjects

Allows DSRB to determine whether **risks and benefits** of study have changed as the study progresses

Period of approval and **category** of continuing review is determined by the DSRB at the time of initial review

Prior to expiry of the approval period, a continuing review is to be performed for renewal of DSRB approval

1.Not required for Exempt Studies and studies that have reported to be in data analysis only stage

What should Principal Investigators do?

- ✓ The PI should submit a completed **Study Status Report Form** at least 4-6 weeks before expiry.
- ✓ If approval expires, no research activities can be conducted on/after the expiry date, including:
  - Screening
  - Enrollment
  - Interventions, interactions
  - Collection of identifiable data

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Continuing Review – For Studies in Data Analysis Stage

Unless otherwise determined by the DSRB, studies that have submitted a Status Report Form (SRF) indicating the study status as "***Ongoing, Last Participant, Last Visit Over & Only Data Analysis Ongoing***" can enjoy a waiver from continuing review.

The study team:

- will only need to submit the SRF when the study is completed
- must submit a SRF when there is change to the study status, e.g. resume the recruitment/data collection.

The PI **must** continue to submit other reports (AMD, UPIRTSO, Expected SAE and NCR) to DSRB.

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Study Amendments (AMD)

Types of Amendments

- **Administrative Amendments** – E.g. change in addresses, contacts, correction of typographical and grammatical errors.
- **Minor Amendments** – Changes that pose any increase in risk which are no more than minimal risk.
- **Major Amendments** – Changes that significantly affect the risk-benefit ratio will be reviewed by the full board.

- No changes to the approved study should be implemented without documented DSRB approval except where necessary to eliminate apparent intermediate hazard to the study subjects.
- Any deviation from the protocol to eliminate an immediate hazard should be documented and promptly reported to the DSRB within 7 calendar days.

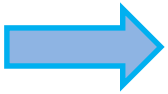
What to submit?

- ROAM online DSRB Study Amendment Cover Note (including summary and rationale of amendments)
- Amended documents (both tracked and clean versions)
- Any other documentation that the DSRB may specifically request/ other relevant documentation to be given to subjects to add meaningfully to the protection of the rights, safety and/or well-being of subjects.

UPIRTSOs

***U**nanticipated **P**roblems **I**nvolving **R**isks **T**o **S**ubjects or **O**thers*

Definition: A problem that is:
1) unexpected,
2) related or possibly related and
3) suggests that the research places subject or others at greater risk of harm.



✓ **Reportable to DSRB**

A problem that is
1) unexpected,
2) related or possibly related and
3) suggests that the research places subject or others at greater risk of harm.

The PI is responsible for the accurate documentation, investigation, follow-up and timely reporting of UPIRTSOs.

IMPORTANT NOTE: There are events that are NOT associated with the use of drugs, but qualify for UPIRTSO reporting as well e.g.:

- Loss of sensitive data (a breach of confidentiality)
- Change in protocol taken without prior DSRB review to eliminate an apparent immediate hazard to a research participant.

For more information, refer to:
- *NHG Proper Conduct of Research_501-C05 UPIRTSO and Expected SAE*

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UPIRTSOs – Reporting Timeline

UPIRTSO & Local Deaths Reporting Criteria – Based on Risk Profile of the Study

Risk Profile of study	More than Minimal Risk (Reviewed via Full Board)	No more than Minimal Risk (Reviewed via Expedited/ Exempt)	Regardless of Risk Profile	Regardless of Risk Profile
Event/ Problem	*Local Death	*Local Death	Life-threatening Problems not resulting in Death	All other Problems
When to Report	Regardless of expectedness and causality	Must be related/ possibly related to the study and regardless of expectedness	Related/ Possibly related to the study and unexpected	Related/ Possibly related to the study and unexpected
Initial Report Timeline	Soonest possible but Not later than 7 calendar days after first knowledge by the investigator	Soonest possible but Not later than 7 calendar days after first knowledge by the investigator	Not later than 7 calendar days after first knowledge by the investigator	Not later than 15 calendar days after first knowledge by the investigator
Follow-up Report Timeline	Within 8 calendar days of the initial report	Within 8 calendar days of the initial report	Within 8 calendar days of the initial report	
***Local is defined as institution under the oversight of the NHG DSRB**				

DSRB Reporting Requirements for Local Deaths in Oncology Studies

Conditions for study:

- Most of such deaths occur when the subjects are in the treatment free follow-up phase (due to natural disease progression);
- The local death(s) is / are unrelated to the investigational product;
- The local deaths yield no clinically meaningful information that allows assessment of the risk-benefit relationship of the study;
- There are no significant implications on the rights and welfare of the subjects.

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Reporting Timelines for Local Deaths in Oncology Studies

Local Death Occurring Within 60 Days (or Less) After Last Dose of Treatment	Local Death Occurring More Than 60 Days After Last Dose of Treatment
Related (expected or unexpected) *Preliminary report by PI within 7 calendar days of first knowledge*	Related (expected or unexpected) *Preliminary report by PI within 7 calendar days of first knowledge*
Unrelated (expected or unexpected) *Preliminary report by PI within 7 calendar days of first knowledge*	Unrelated (expected or unexpected) *Routine reporting for Annual Continuing Review*

The PI is required to follow up with the detailed report within 8 calendar days after the preliminary report. Wherever possible, all unrelated and expected local death reports should be reviewed by a data and safety monitoring entity.

Expected SAE – For HBR Studies

Definition

A problem that is

1) related or possibly related to HBR
2) expected, and
3) serious

Reportable to DSRB

1) Any events meeting the above criteria

2) Applicable for both local Singapore sites and overseas sites. E.g. For multi-center HBR involving collaborations from local and overseas research sites for the same research protocol, any SAE which occurs in a participant during the research at the overseas site must also be reported to DSRB.

Reporting Timelines for Expected SAE – For HBR Studies

Initial Report
Within 7 days of PI's 1st knowledge of the event
Any additional information pertaining to the initial report
Within 8 days of making the initial report

Note: For studies approved by other IRB(s) via mutual recognition arrangement (e.g. NHG study approved by CIRB), expected SAE(s) reporting should follow the requirements set by the approving IRB.

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Non-Compliances

Definition

A **failure** by an investigator **to abide by the policies and procedures of DSRB** or **applicable regulations** governing the protection of human subject research. E.g.:

- ❑ Failure to obtain approval for research
- ❑ Failure to obtain informed consent when required
- ❑ Performance of an unapproved research procedure
- ❑ Failure to adhere to the approved protocol

What should PI do?

- PI is encouraged to report conduct of any non-compliance by him / herself, members of the research team or others.
- Information may be reported by:
  - Other members of the research team
  - Other staff of the institution
  - Monitoring reports
  - Audit reports
  - Complaints from research subjects
- Must be reported as soon as possible but not later than 14 days after first knowledge by the NHG investigator

Reminder:

All research conducted in institutions under the oversight of NHG DSRB, should be in compliance with the research proposal approved by the DSRB, with GCP, with DSRB requirements, institution requirements and applicable regulations.

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Questions?

Refer to www.research.nhg.com.sg

Or contact the NHG Research Education Unit @ researchcoord@nhg.com.sg

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