Centralised Institutional Review Board (CIRB) Researcher Handbook

Version 1.1 dated 14 Mar 2022

Contents

INTRODUCTION

What is an Institutional Review Board (IRB)?

It is an independent body constituted of medical, scientific, and non-scientific members that has been designated to review and approve research involving human subjects. An IRB has the authority to approve, require modifications (to secure approval) or disapprove research.

In SingHealth, the official name of the IRB is SingHealth Centralised Institutional Review Board (CIRB).

The purpose of IRB review is to ensure the protection of rights, safety and well-being of human subjects in research, both in advance (prior to initiation of such research) and by periodic reviews of such research. This includes ensuring that risks to participants are minimised, the selection of participants is equitable, and participants are informed fully of what their participation will entail and of the potential risks and benefits.

It is guided by ethical principles (*Respect for Persons*, *Beneficence*, *Justice*) outlined in the Belmont Report and legal mandates outlined in the International Conference for Harmonisation Guidelines for Good Clinical Practice (ICH GCP), the Human Biomedical Research Act (HBRA), the Health Products Act (HPA), the Medicines Act (MA) and its regulations.

PURPOSE OF THIS HANDBOOK

Is this Handbook for you?

This handbook is written specifically for the researchers (Principal Investigators, Co-Investigators, Study Team Members) and research administrators.

It is the researchers' responsibilities to obtain IRB approval before initiating a research and to conduct the research in compliance with institutional policies, the applicable guidelines and regulatory requirements.

Will this Handbook tell you everything you need to know?

No. This handbook serves as a guide for the research community planning for a research proposal. It provides a quick overview of the IRB submission process. It guides you through the process in determining if IRB review is required for your study all the way through the approval process.

Step 1	Step 2	Step 3	Step 4	Step 5
Do you need to submit for IRB review?	Before you submit for IRB review	How to submit for IRB review	After you submit for IRB review	After IRB approval

Reviewing each of the five steps will help you compile the information you need to prepare your research proposal, provide you with direction on how to submit a CIRB application on iSHaRe, as well as guidance after you have received an initial approval on how to submit request for amendment, renewal or closure.

What other materials should you read besides this Handbook?

You may find useful information and news on research regulations, compliance, and ethics via the followings:

- Ministry of Health (MOH) website on human biomedical research
- Health Sciences Authority (HSA) website on clinical trials
- SingHealth Docupedia on policies and procedures *(intranet only)*
- SingHealth Research Integrity, Compliance & Ethics (RICE) website
- Research e-Bulletin via SingHealth announcements

Step 1: Do you need to submit for IRB review?

Is it Research?

Research is defined as

"systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge"

Tips

The Ministry of Health (MOH) Singapore has a guidance table to help differentiate Research from Research-like activities. Click here.

Is it Human Subject Research?

Human subject research refers to study that:

(i) *Obtain information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyses the information or biospecimens; or*

(ii) *Obtain, uses, studies, analyses, or generates identifiable private information or identifiable biospecimens*

Important

Even if you are using coded information, data or specimens in the research, as long as you can determine a subject's identity or have access to identifiers, it is considered to be a Human Subject Research.

Examples of Human Subject Research

- Surveys, interviews, or observations (social sciences)
- Records review (e.g. medical records, health information databases)
- Research studies that involve the use of human biological materials (e.g. human tissue, blood samples, pathologic or diagnostic specimens)
- Outcomes research – Studies that seek to understand the end results of particular health care practices and interventions
- Clinical trials – Studies that utilise test subjects for new devices, drugs, or materials (biomedical)

What activities does not need CIRB review?

- Case report of one to two patients only
- Projects for internal management purposes
  - Quality assessment (QA)
  - Quality improvement (QI)
  - Service evaluation
  - Clinical audit
- Public health surveillance
- Outbreak investigations

What activities need CIRB review?

IRB review is required —before the project is initiated— If it involves:

- Activities that meet the definition of "Human Subject Research" AND conducted by SingHealth employees
- "Human Subject Research" that recruits SingHealth patients, SingHealth staff, and/or being conducted in premises of institutions under the oversight of CIRB
- Case series (i.e. case reports of three or more patients)
- Any QA/QI activity where participants are subjected to additional risks or burden beyond usual clinical practices
- Any QA/QI study which the PI has determined to have both the research intent and QA/QI objectives

  Click here (*intranet only*) for SingHealth PnP SHS-MI-201 Use of clinical, operational and research data for the purpose of Research and Quality Assurance/Service Improvement (QA/SI). Annex A: Checklist for Quality Assurance (QA)/ Service Improvement (SI) projects can be used to determine if a QA/SI project requires IRB review prior to its conduct.

IRB Approval must be obtained before beginning any research activity involving human subjects

What's Next?

If submission to the IRB is not required, the Principal Investigator should seek his/her institution's advice with regards to compliance with institutional policies, the applicable guidelines and regulatory requirements. In case of publication, the project should not be described as research.

If submission to the IRB is required, continue to Step 2 for more details on the activities necessary before submission.

Step 2: Before you submit for IRB review

Complete the required training

All SingHealth researchers who are involved in the design, conduct, oversight or management of research must complete the following trainings.

<table>
<tr><th>Type of Research</th><th>Minimum Training</th><th>Additional Training</th></tr>
<tr><td>Clinical Trials regulated under Health Sciences Authority (H.S.A.)</td><td rowspan="2">PI/ Site-PI, Co-I, STM

CITI Program
“Biomedical Research Investigators and Key Personnel” course</td><td>PI/ Site-PI only

GCP</td></tr>
<tr><td>All other human subject research including
- Human Biomedical Research
- Tissue Banking Activities</td><td>PI/ Site-PI, Co-I, STM

SingHealth HBRA Essentials</td></tr>
</table>

Important

Researchers are required to submit in the CIRB application the CITI and GCP certificate. Submission of the SingHealth HBRA Essentials certificate is not required. Instead, researchers should file a copy to the study site file.

Note

Principal Investigator (PI) - An individual who is the lead researcher of a study. He/she will also be the primary contact person for the CIRB.

Site-Principal Investigator (Site-PI) - An individual who is the lead researcher of a study at a particular site.

Co-Investigator (Co-I) - An individual of the research/ clinical trial team who is designated and is under the direct supervision of the Principal Investigator/ Site-Principal Investigator at the study site to perform study-related procedure and/or make important research-related decisions.

Study Team Member (STM) - An individual who is directly involved in a research study which is under the direct supervision of Principal Investigator/ Site-Principal Investigator at the study site. For example: Performing intervention or having interaction with participants; obtaining and/or handling identifiable research data about the participants.

Collaborative Institutional Training Initiative (CITI) Training

***Approximate training duration: 2 hours**

If you are SingHealth staff, login to CITI Program (https://www.citiprogram.org/).

1. Add "Singapore Health Services Pte (SingHealth)" as your institution.

2. Select "Biomedical Research Investigators and Key Personnel" course.
   - If you are completing for the first time, select BASIC COURSE
   - If you are renewing CITI certification, select REFRESHER COURSE

Note

Your CITI course certificate should have these core modules:

- ☑ Belmont Report and CITI Course Introduction
- ☑ History and Ethics of Human Subjects Research
- ☑ Informed Consent
- ☑ Social and Behavioral Research (SBR) for Biomedical Researchers
- ☑ Records-Based Research
- ☑ Genetic Research in Human Populations
- ☑ Populations in Research Requiring Additional Considerations and/or Protections
- ☑ Vulnerable Subjects - Research Involving Prisoners
- ☑ Vulnerable Subjects - Research Involving Children
- ☑ Vulnerable Subjects - Research Involving Pregnant Women, Human Fetuses, and Neonates
- ☑ Conflicts of Interest in Research Involving Human Subjects

3. To access your CITI training completion certificate:
   - Click on "My Records".
   - Click on "View-Print-Share" under "Completion Report".

Important

SingHealth researchers should maintain a valid CITI certificate by completing the Basic course (initial) and then the Refresher course.

Researchers who are not from SingHealth institutions should complete the CITI course according to their institutions' requirements.

SingHealth Human Biomedical Research Act (HBRA) Essentials

***Approximate training duration: 2 hours**

Self-register the course here [*For SingHealth staff only.*]

Note

If you are logging into the system for the first time, the default login credentials will be:

- LoginID: Windows UserID (ADID)*
- Default Password: LMS2019 followed by your ADID in lower case (e.g. LMS2019xxxx where xxxx is your ADID)

*Do not include domain (e.g. singhealth/shhq/kkhad/sghad/shsc) in front of the UserID.

If you have forgotten your password or have problem logging in, please use the "Reset Password" function, or contact LMS Helpdesk for assistance.

Good Clinical Practice (GCP)

***Approximate training duration: 2 days**

To complete the local GCP workshop offered by any of these institutions only: [*For PI and Site-PI conducting clinical trials only.*]

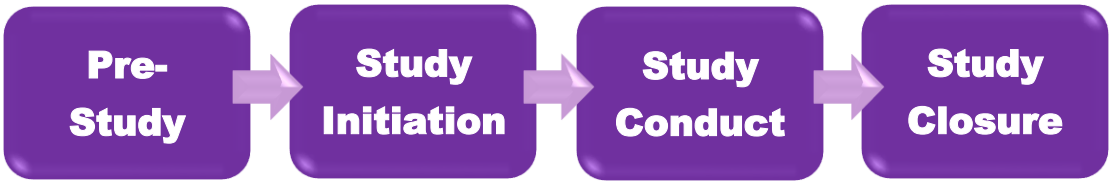
- SingHealth Academy
- National Healthcare Group (NHG)
- National University Health Systems (NUHS)

Important

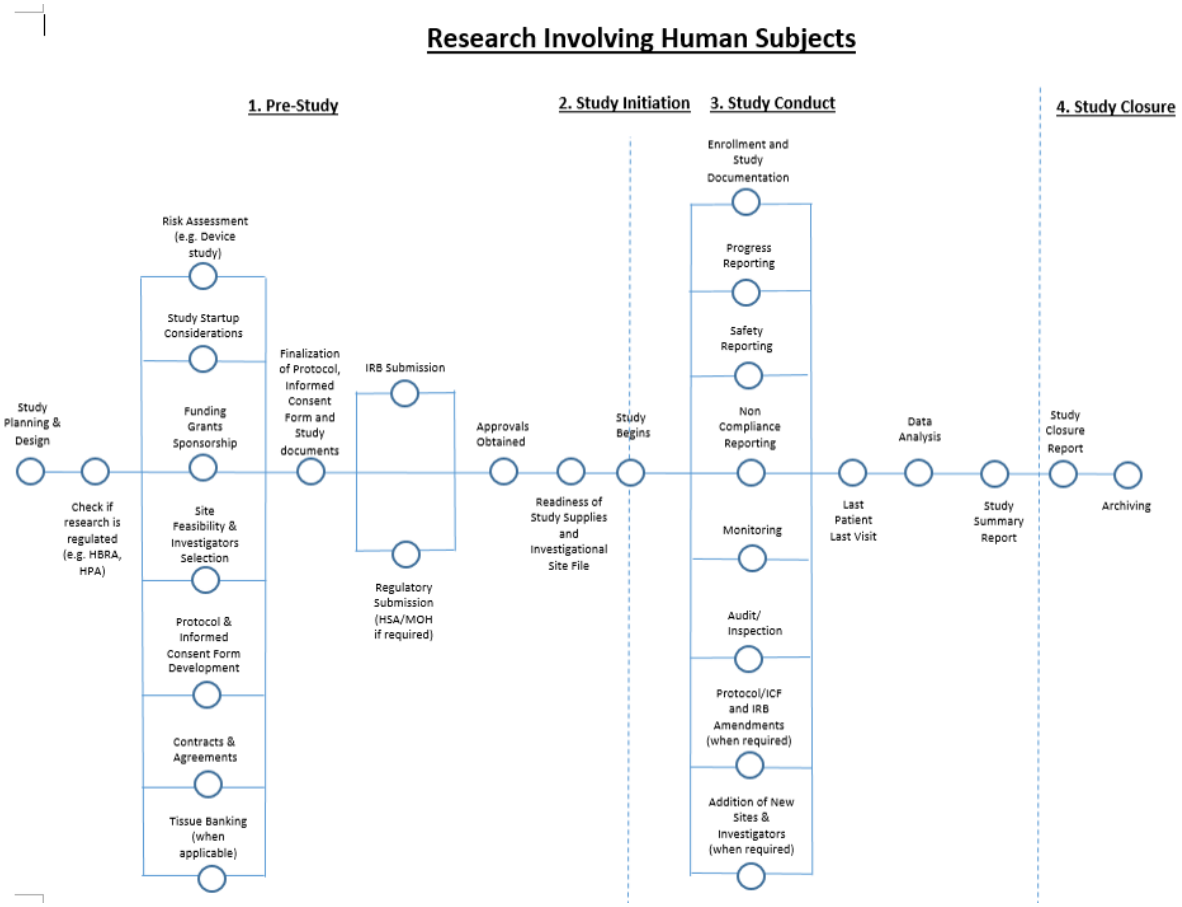
The CITI Program “Good Clinical Practice (GCP)” course is not acceptable.

Understand the research roadmap

To conduct a research study, it requires processes from various functions to start the study properly. This is to ensure that ethics, regulatory and institution expectations are met for the conduct of research.



This is an overview of the steps that you should follow when planning for and designing a research study.



Source: SingHealth (RICE) homepage > Getting Started

Tips

SingHealth staff can self-register here (via e-Learning portal) for Human Subject Research Start-Up Training Course. It will equip learners with essential information and key elements to plan start-up and pre-study activities, and initiate Human Subject Research successfully.

Know the regulatory frameworks governing your research

All research studies reviewed and approved by CIRB must comply with CIRB's requirement, the institution's policy and the applicable regulatory requirements.

Regulations	Type of Research
Human Biomedical Research Act (HBRA) and its subsidiary legislation	• Human biomedical research • Tissue banking activities • Observational clinical trials • Class 1 cell, tissue & gene therapy products (CTGTP) clinical trials • Medical device clinical trials
Health Products Act (HPA) and its subsidiary legislation	• Therapeutic product clinical trials (e.g. chemical drugs, biologics) • Class 2 cell, tissue & gene therapy products (CTGTP) clinical trials
Medicines Act (MA) and its subsidiary legislation	• Medicinal product clinical trials (e.g. chinese Proprietary Medicines, health supplements)
Clinical Research Material (CRM) Regulations	• Any registered or unregistered therapeutic products, medicinal products, medical devices, applicable CTGTP, or placebo, that is manufactured, imported or supplied for the purpose of being used in clinical research
Personal Data Protection Act (PDPA) and its subsidiary legislation	• Any collection, use and disclosure of personal data (individually-identifiable data)

Familiarise with the resources available for you

The CIRB Policies & Procedures are accessible via SingHealth Docupedia (*intranet only*). Researchers should be aware of the following requirements while planning for research. The webpage also allows you to read up CIRB requirements on other research topics.

SHS-RSH-CIRB-233 Minimum Training and Requirements for Study Team Members

SHS-RSH-CIRB-231 Responsibilities of Principal Investigators

SHS-RSH-CIRB-234 Conflict of Interest - Study Team Members

RESEARCH TOOLKITS

The SingHealth Research Integrity, Compliance & Ethics (RICE) has prepared these Research Toolkits that consolidate the important guidances, reference documents, forms and templates as well as other resources essential for planning a research study, from the Pre-Study Activities, Study Initiation, Study Conduct till Study Closure.

RESEARCH HANDBOOK ***(intranet only)***

The SingHealth Office of Research (OoR) has put together this Research Handbook that comprises an overview and directory to research resources available in the Academic Medical Centre (AMC). It serves as a useful guide for researchers who are navigating research in SingHealth. *[On the webpage, click on "Resources", then "SingHealth Research Handbook".]*

NEWSLETTERS

The RICE newsletter and CIRB Illuminaté newsletter communicate updates on important laws, regulations, guidance, SingHealth policies and procedures, as well as topics specific to IRB and its processes.

The following webpages provides answers to some of the most commonly asked questions among the researchers.

Researchers FAQs

CIRB FAQs

Populations in research requiring additional considerations

For research involving individuals who are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, prisoners, or mentally disabled persons, additional safeguards should be included in the study to protect their rights and welfare.

To find out more about the additional protections and regulatory requirements for this type of research, read up the CIRB Policies & Procedures on SingHealth Docupedia (*intranet only*).

SHS-RSH-CIRB-224
Research Involving Pregnant Women, Foetuses and Neonates

SHS-RSH-CIRB-225
Research Involving Children

SHS-RSH-CIRB-226
Research Involving Cognitively Impaired Persons

SHS-RSH-CIRB-227
Research Involving Prisoners

Prepare your IRB application (gathering your study documents)

You should have the following items ready:

☑ Research protocol or a detailed description of the research:
- Aims
- Methodology (e.g. study design, eligibility criteria, recruitment details, informed consent process, etc.)
- Importance of proposed research to science or medicine
- Potential benefits and risks

> **Tips**
> For information on the details required to complete IRB submission, click here for the CIRB Application and Exemption Application Form Template.

☑ Study team members' qualifications (e.g. CV, training certificates)

☑ Consent forms and assent forms (if applicable)

☑ Recruitment materials (e.g. posters, brochures, advertisements, letter of invitation, scripts, etc.)

☑ Data collection forms (e.g. case report forms, questionnaires/ surveys)

☑ Other supporting documents (e.g. script for interviews, written/ video/ audio materials to be viewed by participants, etc.)

> **Tips**
> Click here to customise the sample Protocol, Consent Form, Assent Form (if applicable) for your research study. Guidance on the requirements for informed consent documents, as well as advertisements for recruitment of research participants are also available.

> **Important**
> All study documents must be given an appropriate document title (to reflect content of the document), version number and version date and pagination (Good Documentation Practice).
>
> The CIRB decision letter will list the study documents approved. If you require the document to be titled a specific way, make sure you state the title (e.g. Questionnaire - Phase 1) within the document.

Access to iSHaRe e-CIRB

The Integrated System in Healthcare for Research (iSHaRe) is a web-based platform accessible by both internal and external users. It has two research ethics modules which allows for Principal Investigator (PI), Co-Investigator (Co-I), Study Team Member (STM), Protocol Administrator (PA) and Institutions to track, monitor and manage their research portfolios and ethics applications more efficiently in one centralised location.

IRB submission for research involving human subjects is made through the iSHaRe e-CIRB module.

To login to iSHaRe, go to https://ishare.singhealth.com.sg/.

Important

New users must register for an iSHaRe account before they can access the system. Click here for the account registration guide.

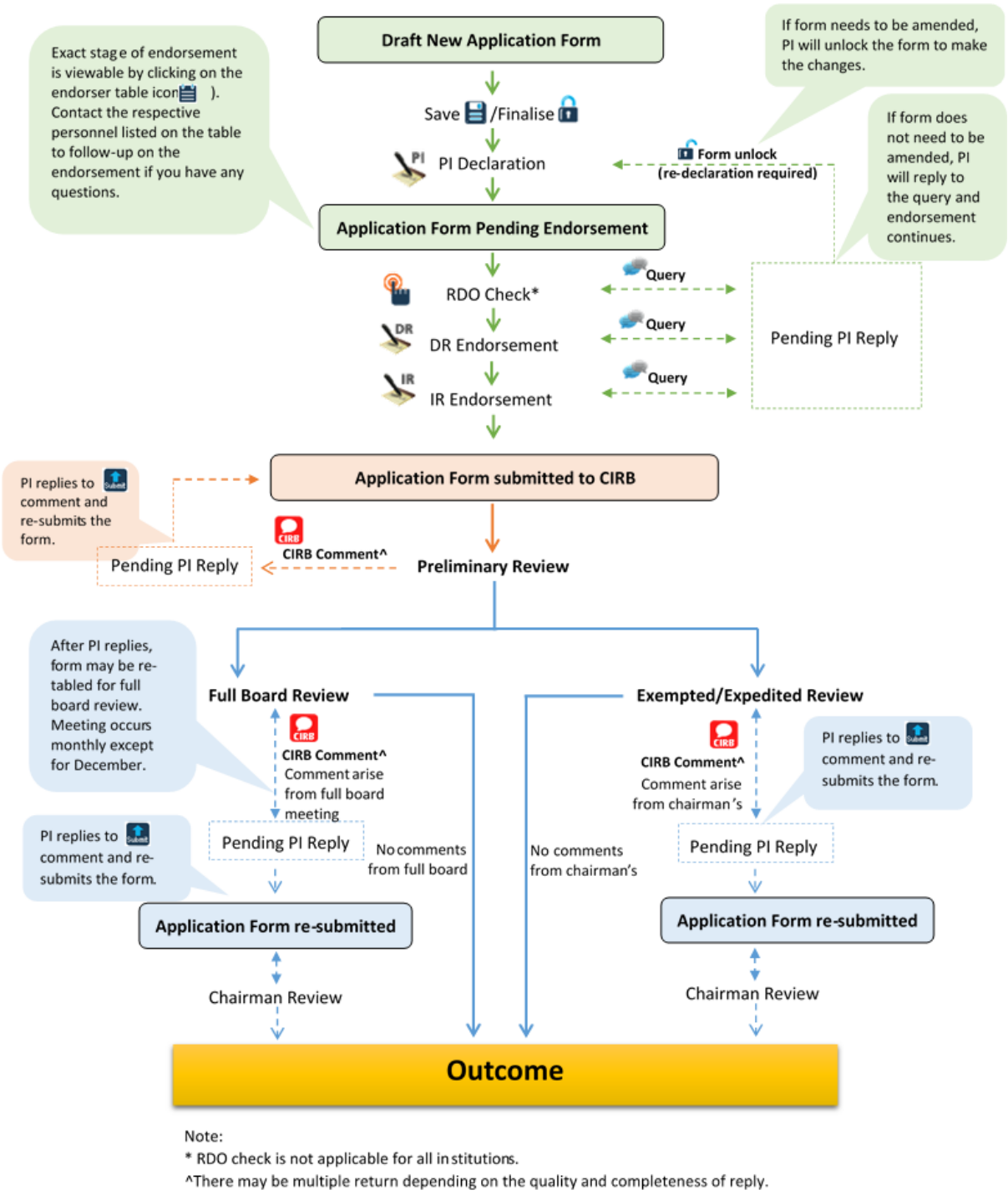
What's Next?

Continue to Step 3 on how to submit a CIRB application.

Step 3: How to submit for IRB review

Understand the initial application submission workflow

This is an overview of the initial application submission and review process.



Source: SingHealth (RICE) homepage > IRB Submissions & Review Fees

Submit an initial review

CIRB Application – This is the first (initial) submission that you make when you create your study in the iSHaRe e-CIRB system. It describes the research you intend to do and the methodology you intend to use.

To create and submit a CIRB application, click here for "New Application Submission", which provides a step-by-step guide.

When drafting the CIRB application, bear in minds the followings:

- Clarity in language
- State research aim clearly – be precise about what you are going to do
- Cross check information in CIRB application and study documents – ensure the information matches up
- If you cut-n-paste, ensure to modify the language in terms of context

Tips

Click here for "Initial Application Checklist" that serves to facilitate the researchers in preparing the CIRB application for submission on iSHaRe.

Click here for "Useful Tips for CIRB Application".

Important

The initial submission must be approved before any research can begin.

What's Next?

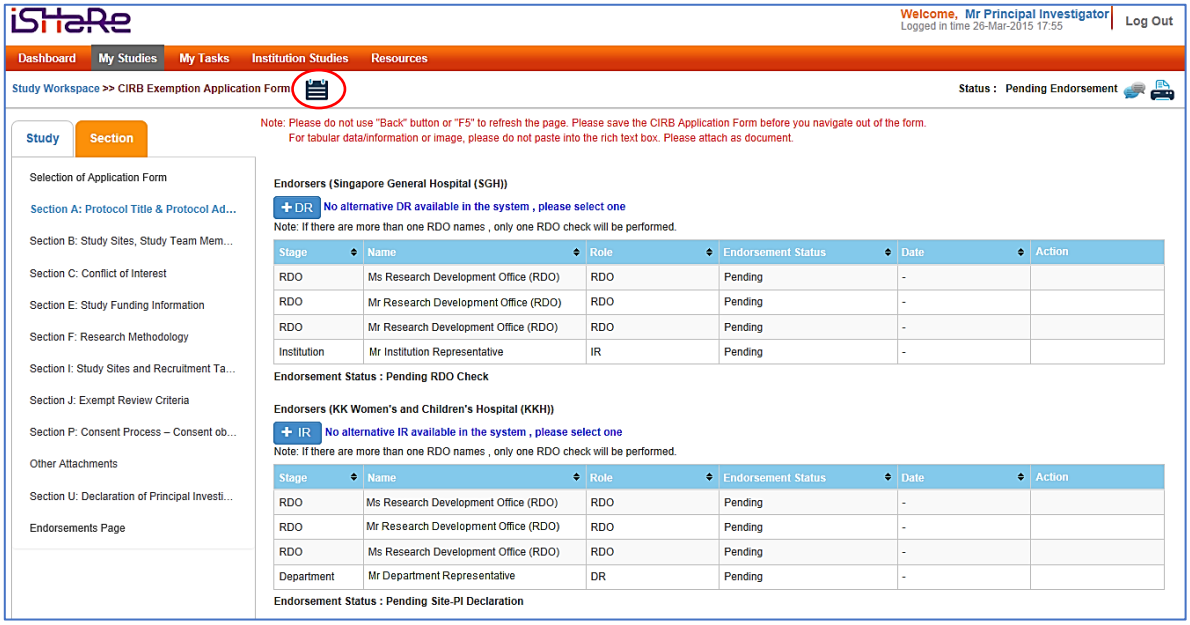
Learn about what happens in the review process in Step 4.

Step 4: After you submit for IRB review

Institution's endorsement

Once the Principal Investigator has submitted the initial application, it will be automatically routed to the institution's Research Development Office (RDO) if applicable, Department Representative (DR) and subsequently, the Institution Representative (IR) for endorsement.

To check on endorsement progress or to view the endorser list, click on the "endorser" ( ) icon as shown below.



Your institution's RDO, DR or IR may raise queries to your application during the endorsement process. If you need clarifications to the queries raised, please contact the institution's research office directly.

Tips

Click here for the step-by-step guide on how to view and reply to the queries raised by the institution's RDO, DR or IR.

Important

The application reaches CIRB for review only after institution's endorsement has completed.

Ready for CIRB review

Once the application reaches CIRB, a preliminary review will be conducted on completeness of the submission. If the submission is incomplete or lack clarity, the CIRB Secretariat may request for clarifications or modifications. After which, the study is assigned a review type.

Studies generally fall into one of the three categories: Exempt, Expedited, or Full Board review. The determination of the review type is to be made by CIRB and based on the level of risk in which research participants are exposed to.

	Exempt Review	Expedited Review	Full Board Review
Criteria	Research meets one of the exempt categories (1-6)	Research meets the criteria for expedited review	Research that do not qualify for exempt/ expedited review
Risk[1]	Minimal/ less than minimal risk	Minimal/ less than minimal risk	More than minimal risk
Reviewer	Board Chairperson or designee	Board Chairperson or designee	Convened meeting of the board at which a quorum[3] is present
Submission Deadline	Submit anytime	Submit anytime	First working day of the month (except December)
Review Timeline[2]	Within 30 calendar days from date of receipt	Within 30 calendar days from date of receipt	Within 60 calendar days from date of receipt

[1]***Note**: Minimal risk is defined as "the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life, or during the performance of routine physical or physiological examinations or tests."*

[2]***Note:** This could vary depending on several factors such as the completeness, and quality of the application, complexity of the study and response time to CIRB's queries.*

*[3]**Note:** The Board will conduct Full Board review at a convened meeting monthly (with the exception of the month of December) wherein a quorum is present. A quorum is defined as five members including the Chairperson (a medical practitioner), at least one external Scientific Member and one external Lay Member. Click here for the Full Board Meeting Dates.*

Clarifications requests (CIRB comment)

The CIRB may request for clarifications or modifications during the review of the initial submission. Such requests will be made through the "CIRB comment" function within the form submission.

The “CIRB comment” function is the official communication with the CIRB. While email exchanges and/or phone calls with a CIRB secretariat may be helpful to understand the clarifications, the study team must respond to the requests for clarification within iSHaRe.

When you revise any study documents in response to CIRB’s requests for clarifications or modifications, make sure the changes you have made are easily identifiable. Reviewers must be able to clearly determine what changes have been made.

After you have made the necessary changes to the CIRB application and replied to the CIRB’s comment, you will need to re-submit the form so CIRB is able to receive your responses and proceed with the review and coming to a review outcome.

Click here for the Quick Guide on how to use the “CIRB comment” function.

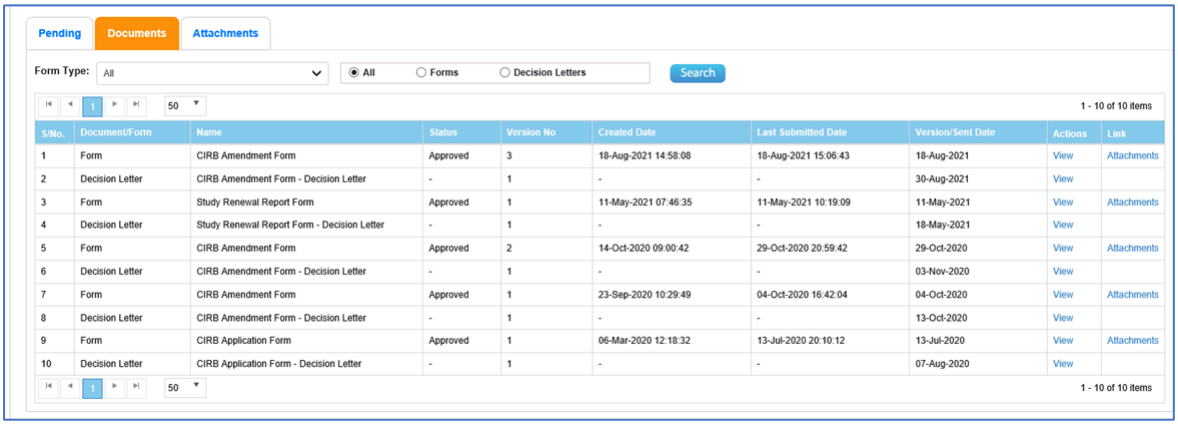
CIRB review outcome

Upon reviewing the application, modifications made and responses to the CIRB’s comment, a CIRB review outcome will be issued.

The PI, Site-PI (if applicable), Protocol Administrator (PA) and study team (Co-Investigator and Study Team Member) would be notified via system and email notification.

To view and/or download CIRB decision letter,

- Access to “Study Workspace”
- Click on “Document” tab
- Click on “View” under “Action” for the decision letter



S/No.	Document/Form	Name	Status	Version No	Created Date	Last Submitted Date	Version/Sent Date	Actions	Link
1	Form	CIRB Amendment Form	Approved	3	18-Aug-2021 14:58:08	18-Aug-2021 15:06:43	18-Aug-2021	View	Attachments
2	Decision Letter	CIRB Amendment Form - Decision Letter	-	1	-	-	30-Aug-2021	View	
3	Form	Study Renewal Report Form	Approved	1	11-May-2021 07:46:35	11-May-2021 10:19:09	11-May-2021	View	Attachments
4	Decision Letter	Study Renewal Report Form - Decision Letter	-	1	-	-	18-May-2021	View	
5	Form	CIRB Amendment Form	Approved	2	14-Oct-2020 09:00:42	29-Oct-2020 20:59:42	29-Oct-2020	View	Attachments
6	Decision Letter	CIRB Amendment Form - Decision Letter	-	1	-	-	03-Nov-2020	View	
7	Form	CIRB Amendment Form	Approved	1	23-Sep-2020 10:29:49	04-Oct-2020 16:42:04	04-Oct-2020	View	Attachments
8	Decision Letter	CIRB Amendment Form - Decision Letter	-	1	-	-	13-Oct-2020	View	
9	Form	CIRB Application Form	Approved	1	06-Mar-2020 12:18:32	13-Jul-2020 20:10:12	13-Jul-2020	View	Attachments
10	Decision Letter	CIRB Application Form - Decision Letter	-	1	-	-	07-Aug-2020	View	

What’s Next?

Continue to Step 5 to learn about managing submissions after CIRB approval and closing a study.

Step 5: After approval

Submit amendment, renewal, closure or reporting to CIRB

After you have received an initial approval for your study, you will be able to make the following types of submissions, if required. All the submissions are to be submitted via iSHaRe.

Amendment – If you wish to change any of the details of the study after it has been approved, you must submit an amendment, which must be approved before you can proceed to implement the changes. Amendment will be linked with the initial application and you will make revisions to the initial application based on the amendment you are proposing.

Renewal – When a study is nearing its expiration date, you must submit the renewal request and provide update on study progress in order to continue with the research. Click here for quick guide on study renewal submission.

Protocol Deviation/ Non-Compliance – You must submit a report to inform CIRB of any protocol deviation or non-compliance.

Local Serious Adverse Event – You must submit a report to inform CIRB of any serious untoward medical occurrence in participants recruited by the study sites. Click here for the reporting requirement and timeline.

Closure – A closure submission indicates that the research is complete and will not be continued.

- The study is permanently closed to enrollment; and
- Study interventions with participants have ceased; and
- No identifiable information is being collected; and
- The analysis of the identifiable information has concluded.

Other Reportable Events – All other events/ notifications to CIRB.

Tips

Click here for more information on submission requirement and process for each form types.

Monitoring and audit post IRB approval

Monitoring and audit is an integral part of the research roadmap. It is to ensure that the IRB-approved research is conducted in accordance with the IRB-approved protocol, the institutional policies and applicable regulations.

Monitoring is an integral part of ICH-GCP and ensures a research is conducted in compliance with international standards and guidelines.

Notes

For Industry-Sponsored Research/ Trial, the Sponsor is responsible to ensure the research/trial is adequately monitored.

For Investigator-Initiated Research/ Trial, the monitoring functions are usually assumed by the Institution or Investigator. Within SingHealth, RICE has developed a risk-based research monitoring framework to address the different types of research and to harmonize the monitoring approaches.

Click here to find out more.

Research Internal Audit completes the research governance framework in SingHealth through an audit programme which fulfils the Quality Assurance and Quality Improvement functions required under the various regulations and guidelines.

Notes

SingHealth RICE's audit programme is targeted to help researchers ensure and implement responsible conduct of human biomedical research. The programme covers all human biomedical research and activities conducted in SingHealth institutions, including investigator-initiated research monitored by external parties and research sponsored by other agencies.

Click here to find out more.

Whom do I contact with enquiries and questions?

IRB related matters

For enquiries or questions regarding IRB related matters, please contact CIRB at irb@singhealth.com.sg.

If your queries are study-specific and the application has not reached CIRB (pending RDO check/ endorsement), please contact your research office.

If your queries are study-specific, please contact the relevant board secretariat.

Research compliance

For enquiries or questions regarding research compliance, monitoring, audit and integrity, please contact ORIC at oric@singhealth.com.sg.

Tissue bank compliance

For enquiries or questions regarding tissue bank registration and compliance, please contact ORIC at singhealthtissuebank@singhealth.com.sg.

Revision History

Version Number and Date	Description
Version 1 dated 28 Oct 2021	Initial release
Version 1.1 dated 14 Mar 2022	Updated affected hyperlinks due to the migration exercise of SingHealth Docupedia