Fred Hutch Cancer Center

Institutional Review Board

Policy/Procedure

Title:	Investigational New Drugs/Biologics (IND) and Investigational Device Exemptions (IDE)
Policy:	1.13
Version:	6.00
Effective Date:	March 28, 2023
Responsible Office:	Institutional Review Office (IRO)
Responsible Official / Approved By:	Meghan Scott, IRO Director

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POLICY STATEMENT

The Institutional Review Board (IRB) is responsible for reviewing and approving FDA regulated clinical investigations involving investigational biologics, devices or drugs in human research participants in accordance with the federal regulations which govern these test articles.

DEFINITIONS

See *HRP-001 - SOP - Glossary of Terms and Acronyms* for full definitions of the following:

FDA

Investigational Device Exemption (IDE)

Investigational New Drug Application (IND)

Investigator

Phase 1, 2, 3, 4 Drug Trials

PRINCIPLES/OVERVIEW

The IRB is responsible for reviewing and approving FDA regulated clinical investigations involving investigational biologics, devices or drugs in human research participants in accordance with the federal

regulations which govern these test articles. This policy outlines the IRB's process and reporting criteria for studies which may involve an IND or IDE and training requirements of sponsor-investigators.

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to Institutional Review Office (IRO) staff, IRB members, employees of Fred Hutch, and investigators from other institutions who submit research studies to the Fred Hutch IRB for review.

PROCEDURES

1. New research applications submitted for IRB review

Investigators create and complete a New Study SmartForm in Hutch IRB, attaching *HRP-259 - FORM - Drug Supplement and HRP-258 - FORM - Device Supplement*, as applicable*,* to describe the use of an investigational biologic, device or drug as required in *IRB Policy 2.1 New Application* (028). The Investigator will provide the IRB with the following information*:*

- Will a non-FDA approved drug or biologic be used in this study?
- Will a commercially available drug, biologic, or food supplement be used in a new way (e.g., off-label, new formulation, different route of administration or dosage level, or for a new indication or population)?
- Does this study involve the use of an investigational medical device or an FDA-approved medical device that is being used for a new indication?

If consultation is required for making the determination about the relevance of FDA regulations and oversight for the investigational product, the Clinical Research Support (CRS) Office of Regulatory Affairs will provide assistance to investigators and/or the IRB.

ICH Good Clinical Practice (GCP) training is required for investigators who hold either an IND or IDE at Fred Hutch, to ensure they are knowledgeable about their obligations and commitments outlined in the 1572, per 21 CFR 312.53 (1)(g). In addition, all investigators and staff involved in the conduct, oversight, or management of clinical trials must be trained in GCP. The CRS Office provides several courses on GCP training. Refer to *IRB Policy 2.20 Training* (038) for accepted courses.

2. Continuing review reports, modifications and adverse event reporting to IRB for approved clinical investigations

The investigator is responsible for ensuring that FDA regulated clinical investigations receive continuing IRB review and approval. The IRB requests a Continuing Review submission as defined in *IRB Policy 2.2 Continuing Review* (010).

Modifications or changes to research require prior IRB review and approval. The mechanism for submitting modifications is described in *IRB Policy 2.5 Modifications to Ongoing Activities* (025)*.*

Investigators will be responsible for submitting Reportable New Information (RNIs) to the IRB, which includes: a) adverse events or other unanticipated risks to research subjects or others, as described in *IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others* (0224)*;* and b) serious or continuing noncompliance with applicable laws and regulation, the Fred Hutch human research protection programs, or determination of the IRB as described in *IRB Policy 1.9 Noncompliance* (029).

3. IRB review and response to investigators

The IRB will review the proposed research as outlined in *IRB Policy 2.1 New Application* (028) and will determine if the following have been met:

a. **INDs:** For studies which require an Investigational New Drug (IND) application, an IND number must be provided in the New Study SmartForm in Hutch IRB. The IND goes into effect 30 days after the FDA receives the IND application, unless the sponsor receives earlier notice from the FDA. Final IRB approval will not be granted until the IRB has reviewed documentation stating that the 30-day waiting period has elapsed. The IRO staff and IRB will confirm the IND number is valid.

b. **IND exemptions:** For studies that involve the use of an investigational drug/biologic which may be exempt from the IND requirements and the FDA has not already made an exempt determination, the IRB must determine if the following have been met:

   i. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

   ii. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

   iii. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

   iv. The investigation is conducted in compliance with the requirements for institutional review set forth in 21 CFR Part 56 and with the requirements for informed consent set forth in 21 CFR Part 50; **and**

   v. The investigation is conducted in compliance with the requirements of 312.7.

   Note: For scenario iii above, if the drug/biologic is used differently from product labeling, the investigator must submit a memo describing the difference in usage between the labeling and the proposed use, including an analysis of why there is not a significant increase in risk.

c. **IDEs:** For studies that will employ an investigational device, the IRB will determine if the device is:

   i. exempt from an IDE,

   ii. a “Significant Risk” device subject to an IDE, or

   iii. a “Non-Significant Risk” device subject to FDA abbreviated IDE requirements.

   The IRB will make such determination based on the information provided in the study SmartForm, *HRP-258 - FORM - Device Supplement,* and the device manual or manufacturer’s information.

   The investigator should consult the CRS Regulatory Affairs office to create a plan for the management, control and use of the investigational device.

   - Significant risk (SR) device under 21 CFR 812.3(m) means an investigational device that:
     - Is intended as an implant and presents a potential for serious risk to the health safety or welfare of a subject;
     - Is purported to be for use supporting or sustaining human life and presents a potential for serious risk to the health safety or welfare of a subject;
     - Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of the subject; **or**
     - Otherwise presents a potential for serious risk to the health, safety or welfare of a subject.
   - An IDE is required for significant risk devices. If the IRB determines the device is SR, the investigator is required to submit an application for an IDE to the FDA or request the FDA grant an NSR determination. The FDA’s determination is final.

     For research requiring an IDE, the IRO staff and IRB will confirm the IDE number is valid. The IDE goes into effect 30 days after the FDA receives the IDE application, unless the sponsor receives earlier notice from the FDA. Final IRB approval will not be granted until the IRB has reviewed documentation stating that the 30-day waiting period has elapsed.
   - Non-significant risk (NSR) devices are devices that do not meet the criteria for SR devices. Examples include devices such as crutches, elastic knee braces, medical chairs, and tongue depressors. NSR devices do not require an IDE application, and a study can begin with IRB approval and the determination by the IRB that the study is an NSR device study. The investigator is subject to the FDA’s abbreviated IDE requirements.

If the IRB is unable to determine whether a study is an NSR device study, the IRB may refer the investigator to the FDA for an NSR determination. The FDA's determination is final.

The outcome of the IRB's review will be communicated to the Investigator as outlined in *IRB Policy 1.6 Meeting and Meeting Records* (024).

SUPPORTING DOCUMENTS

IRB Policy 1.6 Meeting and Meeting Records (024)

IRB Policy 1.9 Noncompliance (029)

IRB Policy 2.1 New Application (028)

IRB Policy 2.2 Continuing Review (010)

IRB Policy 2.5 Modifications to Ongoing Activities (025)

IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others (0224)

IRB Policy 2.20 Training (038)

HRP-001 - SOP - Glossary of Terms and Acronyms

HRP-258 - FORM - Device Supplement

HRP-259 - FORM - Drug Supplement

REFERENCES

21 CFR 50

21 CFR 56

21 CFR 312

21 CFR 812

Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors (FDA): *Significant Risk and Non-significant Risk Medical Device Studies*

Information Sheets Guidance for IRBs and Clinical Investigators (FDA): "*Off-label" and Investigational Use of Marketed Drugs, Biologics and Medical Devices*