

# Principal Investigator Role and Responsibilities



**Sponsor**

**Study  
Coordinator**

**PI**

**Research  
Ethics Board  
(REB)**

**Office of  
Research  
Services**

To Ensure Protection  
of the Study  
Participants



# Nuremberg Code

- 1946-1947 20 physicians of Nazi Germany were tried for murder, torture and other atrocities committed in the name of medical science
- Resulted in the 10 point Nuremberg Code which focuses on the ethical treatment of humans in non-therapeutic research, the elements described form the cornerstone for the guidelines and regulations we have today

# The Helsinki Declaration

- Adopted by the 18<sup>th</sup> World Medical Association General Assembly in Helsinki in June 1964 and amended periodically
- Last amended in 2004
- The WMA developed the Declaration as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects

- In medical research on human subjects considerations related to the well-being of the human subject should take precedence over the interests of science and society
- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic diagnostic and therapeutic methods as identified by the study

# The Belmont Report

- In 1979 the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research wrote: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
- Three Basic Principles:
  - Respect for persons
  - Beneficence
  - Justice

# International Conference on Harmonisation (ICH)

- Established in 1990 to maintain a forum between regulatory authorities and the pharmaceutical industry in the European Union, USA and Japan in order to ensure a more timely introduction of new medicinal products and their availability to patients

# ICH Guidelines

- The objective is to increase international harmonisation of technical requirements to ensure that safe, effective and high quality medicines are developed and registered in the most efficient and cost-effective manner
- To promote public health, prevent unnecessary duplication of clinical trials in humans and minimize animal testing without compromising safety and effectiveness

# Principal Investigator (PI)

- According to regulations (21 CFR 312.3)
  - An individual who actually conducts a clinical investigation
  - The person under whose immediate direction the investigational drug is administered or dispensed to a subject
  - The leader of the team of investigators
  - Usually a physician, although a Pharm D or PhD can be PI as long as a physician is a co-investigator

# Selection of the PI

## ➤ PI Eligibility

- Based on the assumption that the PI has sufficient training and experience for the responsible management of a sponsored project
- Requires a background that includes training, knowledge and familiarity of all the issues and areas of expertise related to the project or protocol

# Responsibility of the PI

- By signing the Qualified Investigator Undertaking (QIU) for Health Canada and/or the FDA 1572 the PI:
  - Agrees to comply with the regulations of CFR Title 21 which states the PI assumes the responsibility of the **entire** conduct of the study at his/her site
  - Is accountable for everything that happens during the course of the study

## QUALIFIED INVESTIGATOR UNDERTAKING

An undertaking must be completed by the qualified investigator responsible for the conduct of the clinical trial at the site specified below. The completed undertaking must be retained by the clinical trial sponsor for a period of 25 years.

Please note that the Qualified Investigator Undertaking should not be submitted to Health Canada unless requested.

<b>PART 1 - Clinical Trial Protocol Information</b>				
Please check one of the following: <b>Clinical Trial Application (CTA)</b> <input type="checkbox"/> <b>Clinical Trial Application Amendment (CTA-A)</b> <input type="checkbox"/>				
1. Clinical Trial Protocol Title			2. Clinical Trial Protocol Number (If Applicable)	
<b>PART 2 - Drug Product / Sponsor Information</b>				
<b>A) Drug Product Information</b>				
3. Brand Name				
4. Proper or Common Name				
<b>B) Sponsor of Clinical Trial</b>				
5. Company Name (Full Name - No Abbreviations)				
6. Street / Suite / PO Box	7. City / Town	8. Prov. / State	9. Country	10. Postal/ZIP Code
<b>C) Contact for THIS Clinical Trial</b>				
11. Contact Name			12. E-mail	
13. Company Name (Full Name - No Abbreviations)				
14. Street / Suite / PO Box	15. City / Town	16. Prov. / State	17. Country	
18. Telephone No.	19. Fax No.		20. Postal/ZIP Code	

PART 3 - Qualified Investigator Information			
<b>A) Clinical Trial Site</b>			
21. Name of Site (Full Name - Do Not Abbreviate)			
22. Street / Suite / PO Box	23. City / Town	24. Province	25. Postal Code
<b>B) Qualified Investigator</b>			
26. Name	27. Title	28. Language Preferred <input type="checkbox"/> English <input type="checkbox"/> French	
29. Street / Suite / PO Box	30. City / Town	31. Province	32. Postal Code
33. Email	34. Tel. No.	35. Fax No.	

In respect of the identified clinical trial, I certify, as the qualified investigator for this site that:

1. I am a physician or dentist and a member in good standing of a professional medical or dental association as defined in Part C Division 3 of the *Food and Drug Regulations*;
2. I will supervise the medical care and medical decisions respecting this clinical trial at this site;
3. I will conduct this clinical trial in accordance with Good Clinical Practices; and
4. I will immediately on discontinuance of the clinical trial by the sponsor, in its entirety or at a clinical trial site, inform both the clinical trial subjects and the Research Ethics Board for this site of the discontinuance, provide them with the reasons for the discontinuance, and advise them in writing of any potential risks to the health of clinical trial subjects or other persons.

36. Signature of Qualified Investigator	37. Date		
	Year	Mo	Day

# Qualified Investigator Undertaking

## ➤ PI certifies that:

- Physician or dentist and a member in good standing of a professional medical or dental association as defined in Part C Division 4 of the Food and Drug Regulations
- Will supervise the medical care and medical decisions respecting this clinical trial at this site

- Will immediately on discontinuation of the clinical trial by the sponsor, in it's entirety or at a clinical trial site, inform both the clinical trial subjects and the Research Ethics Board for this site of the discontinuation, provide them with the reasons for the discontinuation and advise them in writing of any potential risks to the health of clinical trial subjects or other person

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0014.  
Expiration Date: May 31, 2009.  
See OMB Statement on Reverse.

**STATEMENT OF INVESTIGATOR**  
**(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)**  
(See instructions on reverse side.)

**NOTE:** No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR
2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED. <input type="checkbox"/> CURRICULUM VITAE <input type="checkbox"/> OTHER STATEMENT OF QUALIFICATIONS
3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED.
4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY.
5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES).
6. NAMES OF THE SUBINVESTIGATORS (e.g., research fellows, residents, associates) WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S).
7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

- FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION, INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED.
- FOR PHASE 2 OR 3 INVESTIGATIONS, AN OUTLINE OF THE STUDY PROTOCOL, INCLUDING AN APPROXIMATION OF THE NUMBER OF SUBJECTS TO BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY, THE CLINICAL USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION, THE KIND OF CLINICAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF THE STUDY, AND COMPLETE DESCRIPTION OF CASE REPORT FORMS TO BE USED.

9. COMMITMENTS

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 312.50 and Institutional Review Board (IRB) review and approval in 21 CFR Part 312.59 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64.

I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in making the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.61.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 312 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

**INSTRUCTIONS FOR COMPLETING FORM FDA 1572  
STATEMENT OF INVESTIGATOR:**

1. Complete all sections. Attach a separate page if additional space is needed.
2. Attach curriculum vitae or other statement of qualifications as described in Section 2.
3. Attach protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND).

10. SIGNATURE OF INVESTIGATOR \_\_\_\_\_

11. DATE \_\_\_\_\_

**(WARNING: A willfully false statement is a criminal offense: U.S.C. Title 18, Sec. 1001.)**

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Control Products Division  
5901-B Annapolis Road  
Beltsville, MD 20725-1288

Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research (CBER)  
1401 Rockville Pike  
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

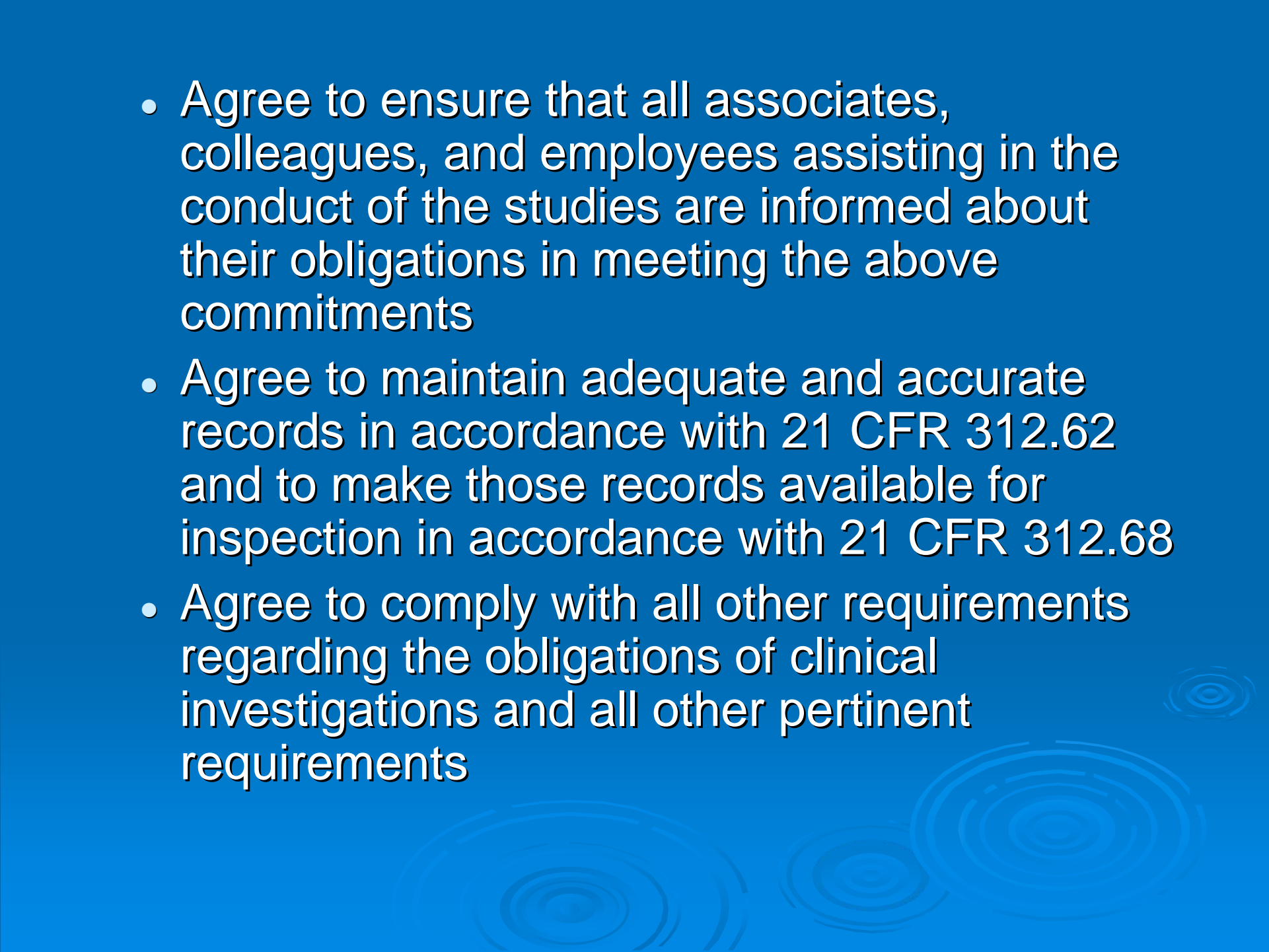
Please DO NOT RETURN this application to this address.

# FDA 1572

## ➤ Commitments:

- Agree to conduct the studies in accordance with the relevant, current protocol and will only make changes in a protocol after notifying the sponsor except when necessary to protect the safety, rights or welfare of subjects
- Agree to personally conduct or supervise the described investigations

- Agree to inform any patients or any persons used as controls, that the drugs are being used for investigational purposes and will ensure that the requirement relating to obtaining informed consent in 21 CFR Part 50 and REB review and approval in 21 CFR Part 56 are met
- Agree to report to the sponsor adverse experiences that occur in the course of the investigation in accordance with 21 CFR 312.64
- Have read and understand the information in the Investigator's Brochure, including the potential risks and side effects of the drug

- Agree to ensure that all associates, colleagues, and employees assisting in the conduct of the studies are informed about their obligations in meeting the above commitments
  - Agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68
  - Agree to comply with all other requirements regarding the obligations of clinical investigations and all other pertinent requirements
- 

- To ensure that the REB complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. Also agree to promptly report to the REB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Will not make changes in the research without REB approval except where necessary to eliminate apparent immediate hazards to human subjects

# Further Responsibilities of PI

## ➤ Pre-award

- To review the protocol and ensure the study budget includes all study related activities including patient expenses allowed by REB
- Coordinate contract, REB submission, training of staff
- Attend Investigator Meetings and Initiation Meetings
- Ensure patient population exists for study inclusion/exclusion criterion
- Develop enrolment strategies with Co-investigators and study staff
- Fill out financial disclosures accurately

# Clinical Trial Recruitment

- Efficient, effective, inclusive and consistent enrollment in clinical trials has been a long-standing challenge
- Twenty years ago, only 3-5% of eligible adult cancer patients participated in clinical trials (the percentage is the same today)
- 94% of Americans said that their physician has never talked about clinical trials

- About 20% of eligible patients are offered a clinical trial
- 75% of those offered a clinical trial – enroll
- 92% of those enrolled are satisfied with their experience

# Barriers to Enrolment

- Lack of awareness about the clinical trials that may benefit patients
- Protocol or eligibility criteria that are too rigid
- Lack of time/person power to explain the clinical trial to patients

# Successful Strategies to Enrolment

- Physicians are considered a “trusted source” of information and patients are more likely to participate in a clinical trial if their physician suggests it to them
- Advertisement
- Dedicated health care professional to identify potential candidates (dedicated recruiter)
- Clinical trial to be considered a treatment option
- Positive discussion between doctor and patient is key in eliminating preconceptions regarding clinical trial participation

# Good Clinical Practice

- PI is responsible for conducting the study in accordance with the standards of Good Clinical Practice (GCP)
- GCP is a standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials
- GCP establishes the conduct of the study according to the protocol and protecting human subjects at all times

# More Responsibilities of PI

- PI is responsible for assigning personnel to perform various study related activities (from Co-investigators to study coordinators) as specified by the sponsor
- PI is responsible to ensure that all designated personnel are trained to perform study related activities
- PI is responsible to ensure that GCP/ICH guidelines are followed and documented

# Ultimate Responsibility of PI

- The PI will protect the safety and well-being of all participants in the clinical study at all times

# Disqualification of PI

- Does not comply with the regulations governing clinical research
- Falsify data in the investigation or reports to the sponsor and/or Health Canada/FDA
- Fines/Imprisonment
- Black List at [www.fda.gov](http://www.fda.gov)
  - List of restricted and disqualified investigators
  - Once on the list – always on the list