Sponsor-Investigator Research and Investigational New Drugs

Karen Corday
Senior Compliance Analyst
Research Compliance Office (RCO)
March 7, 2011

Definitions

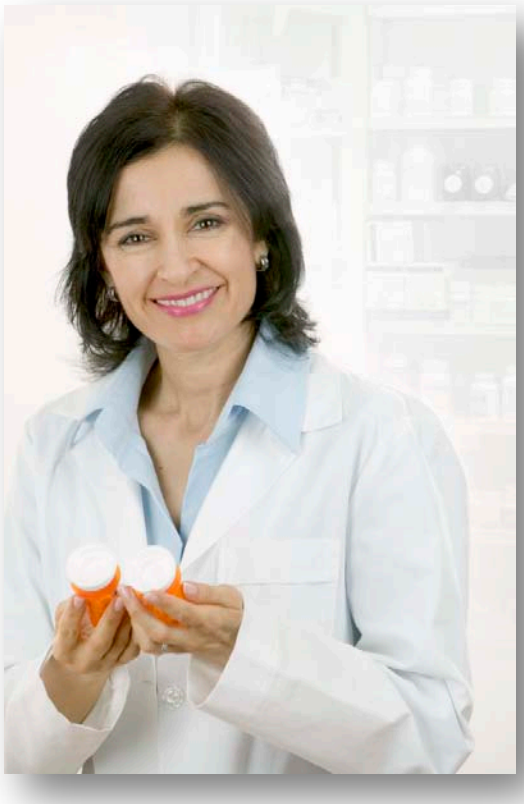
Sponsor-Investigator:

- ✓ Holds the IND (Investigational New Drug)
- ✓ Initiates and conducts an investigation
- ✓ Directs administration and dispensing of the drug
- ✓ ***Assumes sponsor responsibilities***

SIR:

- ➢ Sponsor-Investigator Research

I have an IND - What does the IRB Expect?



Complete eProtocol Application:

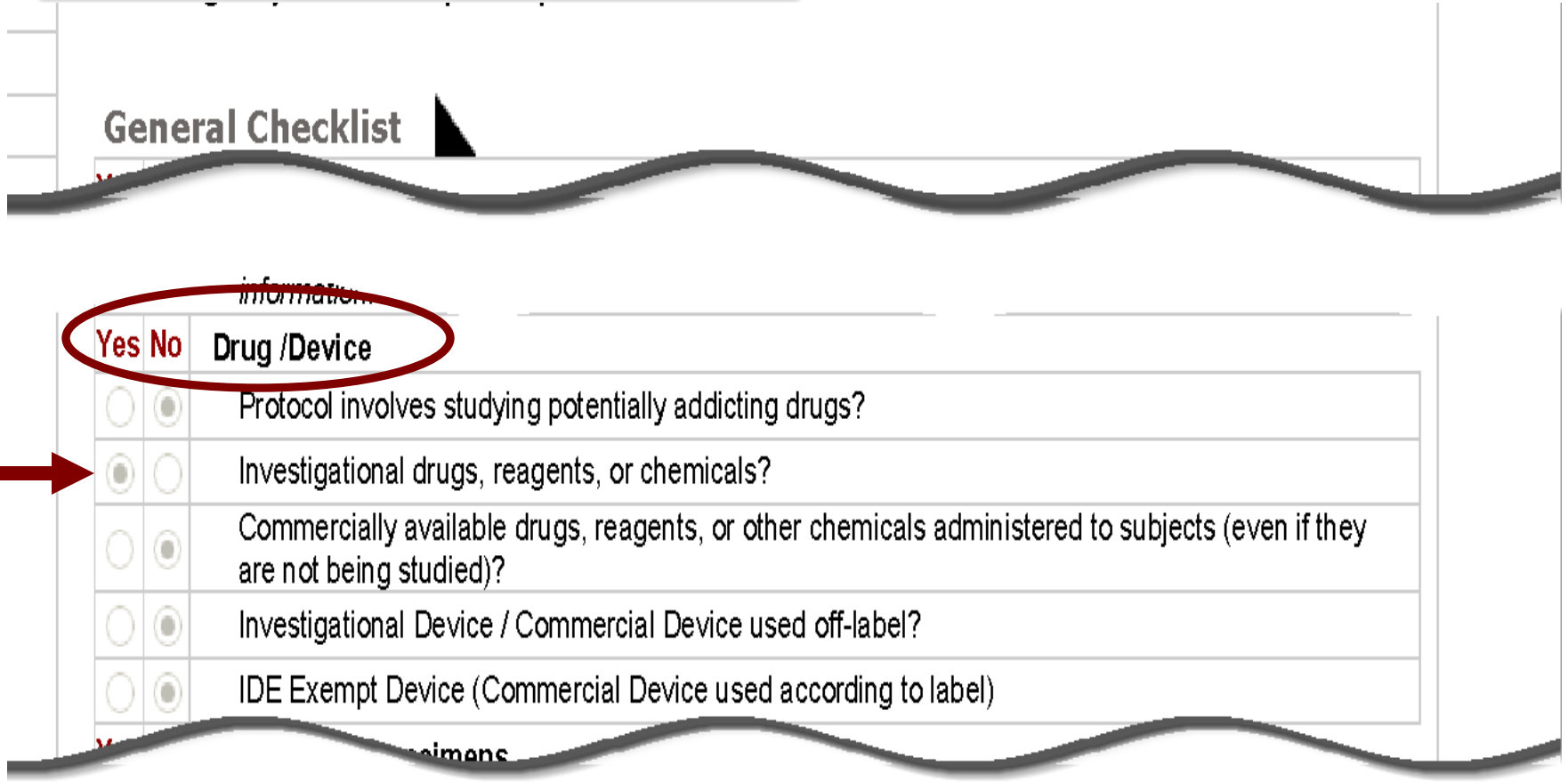
1. **General Checklist**
   - Investigational drugs, reagents, or chemicals?
2. **Protocol Information - Section 6**
   - Investigational Drugs
3. **Protocol Information - Section 16**
   - Attachments

IRB Pre-Approval Requirement:

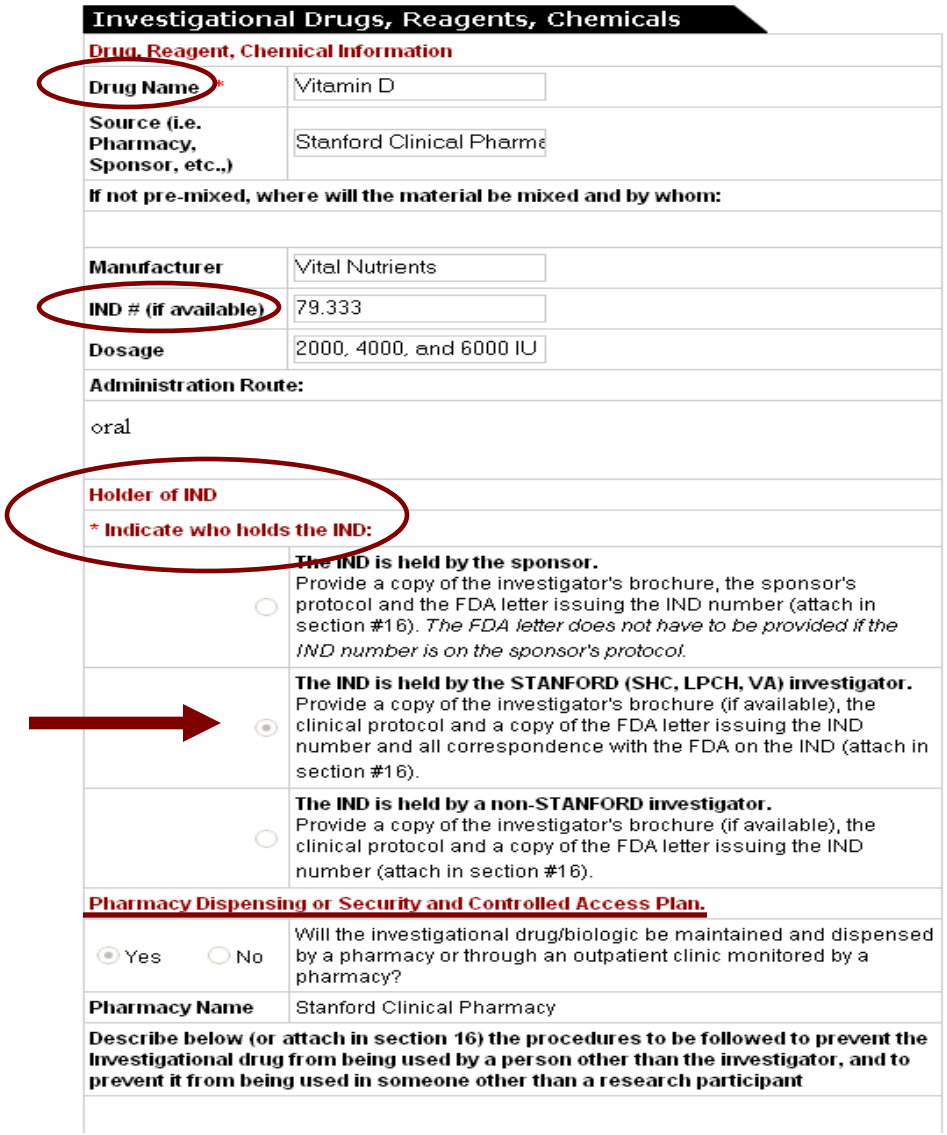
- **Complete SIR Training**

Investigational Drug Documentation

ePROTOCOL General Checklist



Investigational Drug Documentation



Investigational Drugs, Reagents, Chemicals

Drug, Reagent, Chemical Information

Drug Name *	Vitamin D
Source (i.e. Pharmacy, Sponsor, etc.,)	Stanford Clinical Pharma
If not pre-mixed, where will the material be mixed and by whom:	
Manufacturer	Vital Nutrients
IND # (if available)	79.333
Dosage	2000, 4000, and 6000 IU
Administration Route:	
oral	

Holder of IND

*** Indicate who holds the IND:**

○	**The IND is held by the sponsor.** Provide a copy of the investigator's brochure, the sponsor's protocol and the FDA letter issuing the IND number (attach in section #16). *The FDA letter does not have to be provided if the IND number is on the sponsor's protocol.*
◉	**The IND is held by the STANFORD (SHC, LPCH, VA) investigator.** Provide a copy of the investigator's brochure (if available), the clinical protocol and a copy of the FDA letter issuing the IND number and all correspondence with the FDA on the IND (attach in section #16).
○	**The IND is held by a non-STANFORD investigator.** Provide a copy of the investigator's brochure (if available), the clinical protocol and a copy of the FDA letter issuing the IND number (attach in section #16).

Pharmacy Dispensing or Security and Controlled Access Plan.

◉ Yes ○ No	Will the investigational drug/biologic be maintained and dispensed by a pharmacy or through an outpatient clinic monitored by a pharmacy?
Pharmacy Name	Stanford Clinical Pharmacy

Describe below (or attach in section 16) the procedures to be followed to prevent the investigational drug from being used by a person other than the investigator, and to prevent it from being used in someone other than a research participant

ePROTOCOL Section 6

- ✓ Drug Name
- ✓ Manufacturer
- ✓ IND number
- ✓ Dosage
- ✓ Administration route
- ✓ Holder of the IND
- ✓ Pharmacy Dispensing or Security and Controlled Access Plan

Investigational Drug Documentation

ePROTOCOL Section 16 - Required Attachments

- FDA IND acknowledgement letter or *letter of no objection*
- Clinical Protocol
- Investigator's Brochure (IB) or *Product Information*
- ALL correspondence with FDA on IND
  - e.g., clinical holds and annual reports
- Other IRB Approvals, if coordinating a multi-site study

I have an IND - What are IRB Expectations at Continuing Review?

- Report enrollment at other sites, if multi-site study
- Attach in eProtocol Section 16
  - ✓Completed FDA Annual Report

If applicable:

  - ✓ Safety Reports
  - ✓ DSMC Reports
  - ✓ Updated IB
  - ✓ FDA Correspondence
- Send consent forms, if requested

FDA Documentation Expectations

- Correspondence/Communication *(including phone conversations)* between Sponsor (IND holder) and:
  - FDA
  - IRB
  - Study team
  - Manufacturer
  - Monitors
  - Contract Research Organization (CRO)
- All Documents should be:
  - A – attributable (e.g., signed, initialed)
  - L – legible
  - C – contemporaneous
  - O – organized
  - A – accurate

Continuous Quality Improvement (CQI) IND Compliance Activities

- Arrange for SIR Training *for each study*
- Review (annually) non-cancer SIR studies
  - Regulatory Binders
  - Subject Binders
  - Informed Consents
- Provide regulatory feedback/advice
- Collaborate with CCTO and Spectrum

Observations
IND Annual Report

- **Delay in sending Annual Report to the FDA**

Regulation: 21 CFR 312.33

"A sponsor shall, within 60 days of the anniversary date that the IND went into effect, submit a brief report of the progress of the investigation that includes…"

Observations, cont.

- **Annual Report –**
  Should include, for example:
  - ✓ **IND number**
  - ✓ **Individual study information**
    - title, purpose, population, status
  - ✓ **Summary information, such as:**
    - narrative/tabular summary of SAE's *by body system*
    - all safety reports
    - deaths/causes
    - subjects who dropped out/why
  - ✓ **Investigational Plan *for the coming year***

Observations

- **IND Regulatory Binder <u>Documentation:</u>**
  - Forms and documents sent to the FDA
  - Protocol modifications – *with dates or version numbers*
  - Protocol training for study staff – *throughout the study*
  - Delegation of Authority log
  - Study Monitoring – *follow plan, establish timelines*
  - Reports from other investigators (multi-site studies)
- **Subject Binder <u>Documentation:</u>**
  - Inclusion/Exclusion Criteria for each subject *(e.g., checklist)*
  - Source documents and Case Report Forms (CRFs)

What is a 1571?

All Purpose IND Cover Form:

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*

- ☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
- ☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):

- ☐ NEW PROTOCOL
- ☐ CHANGE IN PROTOCOL
- ☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):

- ☐ CHEMISTRY/MICROBIOLOGY
- ☐ PHARMACOLOGY/TOXICOLOGY
- ☐ CLINICAL

IND SAFETY REPORT(S):

- ☐ INITIAL WRITTEN REPORT
- ☐ FOLLOW-UP TO A WRITTEN REPORT

- ☐ RESPONSE TO FDA REQUEST FOR INFORMATION
- ☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
- ☐ ANNUAL REPORT
- ☐ GENERAL CORRESPONDENCE
- ☐ OTHER _____ *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

- ☐ **TREATMENT IND 21 CFR 312.35(b)**
- ☐ **TREATMENT PROTOCOL 21 CFR 312.35(a)**
- ☐ **CHARGE REQUEST/NOTIFICATION 21 CFR312.7(d)**

Guidance and HRPP Policies

Located under Topic Drugs:

- Special Considerations for the Oversight of Research Protocols in FDA-regulated Drug or Device Studies (GUI-26m)
- Guidelines for Studies Involving Human Volunteers Receiving Potentially Addicting Drugs (RPH 7.6)
- Orphan Drugs
- Sponsor-Investigator Research Requirements (When a STANFORD investigator holds the IND) (GUI-3m)

Located under Topic Compassionate Use:

- "Compassionate" and "Humanitarian" Use [FDA] (GUI-36m)
  - ✓ Treatment IND
  - ✓ Single-Patient Treatment IND

Researcher Resources

(available by request)

- Sponsor-Investigator IND Checklist
- IND Annual Report Template and Checklist
- Multi-site IND Checklist
- Note to file template
- Sample Template Logs:
  - ✓ Enrollment
  - ✓ Delegation of Authority
  - ✓ Drug Accountability

- Research Compliance Office/CQI - KCorday@stanford.edu
  650-723-6900
- CCTO
- Spectrum