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

Research Compliance Office
# eProtocol General Checklist

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Drug / Device</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Protocol involves studying potentially addicting drugs?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Investigational drugs, reagents, or chemicals?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Investigational Device / Commercial Device used off-label?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IDE Exempt Device (Commercial Device used according to label)</td>
</tr>
</tbody>
</table>

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Investigational Drug Documentation

Research Compliance Office
## Investigational Drugs, Reagents, Chemicals

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

### 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.

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**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
Delay in sending Annual Report to the FDA

**Observations**
**IND Annual Report**

**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 Documentation:
- 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 Documentation:
- 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:**

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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.

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

- [ ] INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
- [ ] RESPONSE TO CLINICAL HOLD
- [ ] INITIAL WRITTEN REPORT
- [ ] FOLLOW-UP TO A WRITTEN REPORT

**PROTOCOL AMENDMENT(S):**
- [ ] NEW PROTOCOL
- [ ] CHANGE IN PROTOCOL
- [ ] NEW INVESTIGATOR

**INFORMATION AMENDMENT(S):**
- [ ] CHEMISTRY/MICROBIOLOGY
- [ ] PHARMACOLOGY/TOXICOLOGY
- [ ] CLINICAL

**IND SAFETY REPORT(S):**
- [ ] ANNUAL REPORT
- [ ] GENERAL CORRESPONDENCE

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**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