Appendix

Chapter 2: Definitions

Sponsors: An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial [33].

Good clinical practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected [33].

Contract research organization (CRO): An organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor’s trial-related duties and functions [33].

Site management organization (SMO): An organization that provides clinical trial-related services to a CRO, a pharmaceutical company, a biotechnology company, a medical device company, or a clinical site. The site is usually a hospital or a similar health care institution that has adequate infrastructure and staff to meet the requirements of the clinical trial protocol.

Clinical research associate (CRA): A professional who monitors clinical trials and research studies. CRAs can be either employed by a Pharmaceutical or Biotech Company, CRO, Independent Consultant or may act as freelancers. CRAs practice FDA-approved methodology, monitor clinical trials, and ensure that clinical trials adhere to established guidelines, regulations, and standard operating procedures (SOPs) [40].

Internal review board (IRB): An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among
other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects [33].

Independent ethics committee (IEC): An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and nonmedical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving / providing favorable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects [33].

Covered entity: Defined in the HIPAA rules as (1) health plans, (2) health care clearinghouses, and (3) health care providers who electronically transmit any health information in connection with transactions for which HHS has adopted standards [28].
Feasibility Questionnaire

Please complete the form and return to Susie Q at susie@pharmacompany.com

Completion of the feasibility does not guarantee that your site will be selected to participate in any of the studies. Based on the feasibility criteria your site may be selected to participate in one study.

Completed forms are due within 5 business days

Estimated Study Timelines

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigator Meeting</td>
<td>January 2014</td>
</tr>
<tr>
<td>First Patient Entered</td>
<td>February 2014</td>
</tr>
<tr>
<td>Last Patient Entered:</td>
<td>August 2014</td>
</tr>
<tr>
<td>Last Patient Out:</td>
<td>December 2014</td>
</tr>
<tr>
<td>Expected Enrolment Per Site</td>
<td>10</td>
</tr>
</tbody>
</table>

Salutation:  □ Prof  □ Dr  □ Mr  □ Mrs  □ Ms  □ Other __________________________

First Name - Principal Investigator

Last Name - Principal Investigator

Institution/Practice Name

Type of Institution (e.g., hospital, university, private clinic)

Address

Country

Town / City

Zip Code/Postal Code

Business Phone Number

Business Fax Number

Email Address

Area of Specialty (check all that applies):  □ Dermatology  □ Other (Specify): __________________________

Principal Investigator Experience

1. Do you have previous experience conducting dermatology studies?  □ Yes  □ No

   If yes, please advise how many dermatology clinical trials you have conducted within the last 5 years: ______

2. Have you ever worked with DrugXYZ on a clinical trial?  □ Yes  □ No

3. Has your site worked on previous Pharmacompany clinical trials?  □ No  □ Yes,

   indicate Study Numbers/Indications: __________________________

4. Are you familiar or have you worked with the Global Skin Assessment Scale?  □ Yes  □ No
Please complete the table below to reflect your current and past experience in the conduct of clinical trials (over the past 5 years):

<table>
<thead>
<tr>
<th>Indication</th>
<th>Phase</th>
<th>Type of Study</th>
<th>Role on study (PI/sub-PI)</th>
<th>No. of Patients Enrolled at Site</th>
<th>Duration of Study</th>
<th>Enrolment Period (months)</th>
<th>Did the Study Recruit to Target/Timelines (if no, please comment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>Device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Drug - indicate class:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>Device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Drug - indicate class:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>Device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Drug - indicate class:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>Device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Drug - indicate class:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical Research Staffing & Experience

1. Please indicate the number of current studies that you are participating in as the Principal Investigator? _________

2. How many of these studies are currently enrolling patients? _________

3. How many total site staff members do you anticipate participating in the study? _________
   Will Sub-Investigators be assigned? □ Yes □ No
   If yes, how many? _________
   How many Study Coordinators are estimated to participate in the study? _________

4. Data entry of subject information is estimated to take 1 hour/subject/week. Do you have the appropriate data entry staff to complete the data entry task?
   □ Yes □ No

5. Do you anticipate being involved in any other related studies which may compete with this trial? □ Yes □ No

6. Are you and your staff/clinic available to conduct study visits on the weekends?
   □ Yes □ No

7. Please indicate your clinic holidays, your clinic/staff vacation schedules, or the dates you will have limited staff to complete study documentation and/or patient study visits

Patient Population/ Recruitment-related Issues

1. How many patients with skin condition x do you see at your site per month?
   _____ adult patients/month

2. How many patients with moderate skin condition x do you see per month?
   _____ adult patients/month

3. Based on the Inclusion/ Exclusion Criteria

   a) How many eligible patients would you anticipate screening per month for:
      _______ Pts/month

   b) How many eligible patients would you anticipate enrolling per month for:
      _______ Pts/month

   c) What screen failure rate (%) do you anticipate for:
      _______ %
What are the challenges that you may foresee in regards to recruitment (specific to your facility/ location, unique and/or seasonal in nature)?

Describe: ____________________________________________

How many months do you think it will take your site to enrol 10 patients? ___MONTHS__________

4. What techniques do you use/have used to pre-identify patients (check all that apply)?
   - Chart review
   - Staff meetings
   - Screening clinics
   - Advertising, please describe: ____________________________________________
   - Site database search
   - Other: ____________________________________________

5. Do you receive patient referrals from colleagues within your vicinity?
   - Yes  □ No
   
   If yes, please advise where these patients are referred from (check all that apply):
   - GP/Primary Care
   - Other Clinics
   - Walk-in Clinic
   - Other: ____________________________________________

6. Will your patients require informed consents and questionnaires in languages other than English?
   - Yes, specify: ____________________________________________
   - No

**Study Design & Procedures**

1. Do you have a dedicated room for subjects to stay while they are waiting for the next procedure or for at least 1 hour?
   - No □ Yes
   
   If yes, please describe: ____________________________________________

2. Do you have experience working with Photocentric, Inc. (photography)?
   - Yes □ No

3. Do you have experience using a central laboratory?
   - Yes □ No

4. Do you have a dedicated secure access/ lockable room to maintain study supplies for facial photography?
   - Yes □ No

5. Do you have a secure (locked) storage area (room temperature, no refrigeration required) to maintain the study medication?
   - Yes □ No If yes, describe area/location: ____________________________________________
☐ Yes  ☐ No
If yes, describe area/location: Study records/binders are stored in locked cabinets within a secured area of the clinic.

7. Do you have a dedicated Fax machine to receive laboratory reports and IVRS faxes?
☐ Yes  ☐ No

8. The expected courier for this study is FedEx. Are you able to use FedEx?
☐ Yes  ☐ No
If no, please provide availability of other services (company name, pick-up frequency):

9. Will your facility require the use of a satellite location in order to meet the enrollment goal? (For example, off site laboratory services, clinics where subjects will be seen other than the primary location)? NOTE: Any satellite location utilized for conduct of the study will require qualification and inspection.
☐ Yes  ☐ No
If yes, please describe and provide full address and distance from primary site:

10. Does your facility require the use of a pharmacy to dispense study medication?
☐ Yes  ☐ No
If yes, please list contact details as well as who would be responsible for receiving study drug supply shipments:

11. Do you have qualified personnel available to draw and process safety blood samples when needed
☐ Yes  ☐ No
If no, please comment:

12. Does your site have IATA certified personnel for specimen shipment when required?
☐ Yes  ☐ No
If no, are you willing to have them obtain IATA certification prior to study start?
☐ Yes  ☐ No

13. Has your site ever worked with ABC Central Laboratory, or any other central laboratory?
☐ ABC Central
☐ Other (Specify):

14. Who will be responsible for drug shipments (please list the contact details below)?

<table>
<thead>
<tr>
<th>Study Medication Shipments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact Name:</td>
</tr>
<tr>
<td>Address:</td>
</tr>
<tr>
<td>City / State:</td>
</tr>
<tr>
<td>Country:</td>
</tr>
<tr>
<td>Zip/Postal:</td>
</tr>
<tr>
<td>Phone:</td>
</tr>
<tr>
<td>Fax:</td>
</tr>
<tr>
<td>Email:</td>
</tr>
</tbody>
</table>
Equipment and Supplies

1. Do you have the following equipment/technology available at your site (check all that apply)?
   □ Scale to weigh study medication (within 0.01g measure) □ At site □ Other location
   □ Sphygmomanometer □ At site □ Other location
   □ Body weight and height scales □ At site □ Other location
   □ PC computer with Internet Explorer 6.0/7.0/8.0 or Mac computer with Safari 3.2.1
   □ High speed internet connection (for electronic data capture and IVRS/IWRS requirements)
   □ Centrifuge (for safety blood samples processing)
   □ -20°C or colder freezer which does not automatically defrost (for safety blood samples)

2. Does your site use a validated Electronic Medical Records system?
   □ Yes □ No □ Don’t know if it’s validated
   If Yes/Don’t know, would you be willing to print out hard copies and sign/date for the research files? ONLY FOR DOCUMENTATION OF MEDICAL HISTORY, NOT AS STUDY SOURCE.
   □ Yes □ No

3. Has your site used electronic data capture (EDC) in the past? If so, please specify:
   □ InForm □ ePRO
   □ IVRS □ Other, specify:__________________________

4. Does your site have wireless internet capabilities with high speed connection for electronic data capture and IVRS/IWRS requirements?
   □ Yes □ No

5. Does your site have an institutional firewall that would prevent from using an external device (such as a handheld electronic diary or tablet)?
   □ Yes □ No □ Don’t know
   If yes/don’t know, please provide the appropriate Information Systems contact:
**IRB Information**

Is there a requirement to use a specific IRB?  
- [ ] Yes  
- [x] No  

What type of IRB will you be using?  
- [ ] Central  
- [ ] Local  

If you selected CENTRAL IRB, which IRB has your site used (Check all that apply)?  
- [ ] Quorum  
- [ ] WIRB  
- [ ] Other, please specify: ____________________________  

For LOCAL IRB: Please list contact details below

IRB Name:  
Contact person’s name:  
Address 1:  
Address 2:  
City / State:  
Country:  
Zip/Postal:  
Phone:  
Fax:  
Website:  
Email:  
How often does your IRB meet?  
- [ ] Weekly  
- [x] 2x monthly  
- [ ] Monthly  
- [ ] Quarterly  
- [ ] As needed  

How much lead-time (in weeks) is required to submit a protocol/ ICF to be on the IRB agenda?  

Do you have IRB meeting dates?  
- [ ] Yes  
- [ ] No  

*If yes, please provide the dates of the next few meetings:*

<table>
<thead>
<tr>
<th>Submission Due Date</th>
<th>Meeting Date</th>
<th>Approx. Date of Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Additional comments on the IRB submission or requirements:*
1. Do you anticipate any aspect of the study design being unacceptable to your IRB committee?
   ☐ Yes ☐ No
   If yes, please comment: ____________________________________________________________

2. Will the patient population and/or your IRB at your site require translations of any written documents? (Examples: Informed consent form, patient authorization, patient questionnaires)
   ☐ Yes ☐ No
   If yes, please list languages: ________________

3. Does your IRB allow your site’s details to be displayed on advertising material?
   ☐ Yes ☐ No

4. Have the PI, SubI, and/or site ever been audited by FDA or any regulatory agency?
   ☐ Yes ☐ No,
   If yes, have you received a FDA 483 or other warning letter from another regulatory agency?
   ☐ Yes ☐ No
   If yes, please attach a copy of the letter with this document.

5. To your knowledge, is the PI or any site staff on any of the following lists:
   a. Ineligible/Restricted to Receive Investigational Products List (US Sites Only) ☐ Yes ☐ No
   b. Debarment List (US Sites Only) ☐ Yes ☐ No
   c. Routine Inspection for Cause List, with an Official Action Indicated (OAI) (US sites only) ☐ Yes ☐ No
   d. Office of the Inspector General (OIG) (US sites only) ☐ Yes ☐ No
   e. Other regional/country-specific lists (e.g., UK British Medical Association and General Medical Council (GMC) ☐ Yes ☐ No

6. Have the PI or Sub-I ever been investigated regarding his/her medical license or DEA permit?
   ☐ Yes ☐ No
   If yes, please attach a copy of related documentation.
Contracts and Financial Information

Do you agree to comply with the financial disclosure requirements FDA CFR Title 21 Part 54?

<table>
<thead>
<tr>
<th>Is there a contract office which oversees your research contracts?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes, approximately how long (in weeks) does the process take from submission to approval?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your site require more than one contract?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If yes, how many?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are there any contracts that are unique to your site/ institution you can share that may help to expedite the contracts approval process?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Who should payments/checks be made payable to?

Name:
Institution:
Address 1:
Address 2:
City/State:
Country:
Zip:
For the Attention of:
Tax ID Number:

For Clinical Trial Agreement purpose ("Notice" Section), please provide the name, title, address, telephone, fax number and email of the Institution’s representative that is designated to receive any notice in writing via hand-delivered, registered or certified mail, or facsimile transmission regarding the study.

Name:
Institution:
Address:
Address:
City/State:
Country:
Phone: Telephone
Fax: Fax:
Email: Email:

Name and title of the Institutional Signatory on the Clinical Trial Agreement (This representative must have the capacity to bind the institution.)

Name:
Title:

Person Completing Form: __________________________ Date: __________________________

Title / Role: ____________________________________________

Principal Investigator Signature: __________________________ Date: __________________________

Sample Financial Disclosure Form

The following information is requested by Pharmaceutical Company X, Inc. in accordance with 21 CFR Part 54—Financial Disclosure by Clinical Investigators, and is required to be completed by all individuals listed on the FDA Form 1572. Please complete all the information below and retain a copy for your records.
1. Protocol Number/Title: XYZ: A Multicenter, Randomized, Double-Blind, Vehicle-Controlled Study of the Safety and Efficacy of XYZ, in Adults With a Dermatologic Condition

2. Name: ☐ Principal Investigator ☐ Sub-Investigator

3. Institution Name (if applicable):

4. PI Name:

5. Address:

6. Telephone:

7. I am a full or part-time employee of Pharmaceutical Company X: ☐ Yes ☐ No

8. Information Collected at: ☐ Initial disclosure ☐ End of study ☐ One year post study completion

9. Please indicate below if any of these financial interests or arrangements of concern to FDA apply to you, your spouse, any of your dependent children or, with respect to the last item, the institution that supports your activities. If you answer YES to any of the items listed, please provide details.

☐ Financial arrangements with Pharmaceutical Company X whereby the value of the compensation for conducting the study could be influenced by the outcome of the study, such as compensation that could be higher for a favorable result, or compensation in the form of an equity interest in Pharmaceutical Company X or in the form of compensation tied to sales of the test product, e.g., a royalty interest. ☐ Yes ☐ No

☐ If Yes, please describe

☐ A significant equity interest in Pharmaceutical Company X such as ownership interest, stock options, or other financial interest whose value cannot be easily determined through reference to public prices; or any equity interest in Pharmaceutical Company X exceeding $50,000 during the time you conduct the study and for 1 year following completion of the study. ☐ Yes ☐ No

☐ If Yes, please describe

☐ A proprietary or financial interest in the test product such as a patent, trademark, copyright, or licensing agreement. ☐ Yes ☐ No

☐ If Yes, please describe

☐ Significant payments of other sorts from Pharmaceutical Company X (including payments to the institution that support your activities), exclusive of the costs of conducting the study or other clinical studies, that have a total monetary value of more than $25,000 (e.g., a grant to fund ongoing research, honoraria, compensation in the form of equipment, or retainers for ongoing consultation) during the time you conduct the study and for 1 year following completion of the study. ☐ Yes ☐ No

☐ If Yes, please describe

---

**Start-Up Checklist**

☐ Original signed and dated Form FDA 1572

☐ Original signed Protocol Signature Page

☐ Principal Investigator’s Curriculum Vitae (CV)—Current and signed within 2 years of study start-up

☐ Sub-Investigator’s CV—Current and signed within 2 years of study start-up

☐ Medical Licensure for PI
☐ Medical Licensure for Sub-Investigators (as applicable)  
☐ PI and all Sub-Investigator’s Financial Disclosures  
☐ IRB Approval Letter and Approved Consent Form(s)  
☐ Justification Form for Use of a Central IRB (as applicable for Quorum Review IRB)  
☐ Central IRB Questionnaire (as applicable for Quorum Review IRB)  
☐ Fully Executed Clinical Trial Agreement (CTA)  
☐ Finalized Study Budget  

**Other Essential Documents needed:**  
☐ W-9 form  
☐ IRB Statement of Compliance (Local Sites)  
☐ IRB Membership Roster (Local Sites)  

### Study BUDGET

<table>
<thead>
<tr>
<th></th>
<th>Screening</th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed consent</td>
<td>$100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics, history</td>
<td>$75</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical exam</td>
<td>$100</td>
<td>100</td>
<td>$100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin assessment</td>
<td>$75</td>
<td>$75</td>
<td>$75</td>
<td>$75</td>
<td></td>
</tr>
<tr>
<td>Data entry fees</td>
<td>$50</td>
<td>$50</td>
<td>$50</td>
<td>$50</td>
<td></td>
</tr>
<tr>
<td>Study coordinator fee</td>
<td>$100</td>
<td>$100</td>
<td>$100</td>
<td>$100</td>
<td></td>
</tr>
<tr>
<td>PI simple visit fee</td>
<td>$150</td>
<td></td>
<td>$150</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI complicated visit fee</td>
<td>$250</td>
<td></td>
<td>$250</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient incentive</td>
<td>$50</td>
<td>$50</td>
<td>$50</td>
<td>$50</td>
<td></td>
</tr>
<tr>
<td>Urine pregnancy test</td>
<td>$20</td>
<td>20</td>
<td>20</td>
<td>$20</td>
<td></td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>$120</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety labs</td>
<td>$75</td>
<td></td>
<td>$75</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$915</strong></td>
<td><strong>$645</strong></td>
<td><strong>$445</strong></td>
<td><strong>$750</strong></td>
<td><strong>$2,755</strong></td>
</tr>
</tbody>
</table>

| Screen failures up to 10 | 500 | 10 | **$5,000** |

**Invoiced fees**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB</td>
<td>$2,000</td>
</tr>
<tr>
<td>Pharmacy fees</td>
<td>$1,000</td>
</tr>
<tr>
<td>Start-up fee</td>
<td>$4,000</td>
</tr>
<tr>
<td>Advertisement</td>
<td>$5,000</td>
</tr>
<tr>
<td>Document Storage Fees</td>
<td>$1,000</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>$13,000</strong></td>
</tr>
</tbody>
</table>

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overhead</td>
<td>28.00 %</td>
</tr>
<tr>
<td>GRAND TOTAL</td>
<td>$58,304.00</td>
</tr>
</tbody>
</table>
Chapter 4: Glossary and Acronym Guide

Clinical trial: A planned, structured investigation of a device, treatment or drug on a group of volunteers.

Clinical study: See clinical trial.

Study site: A location where a clinical trial is conducted.

Human subject: A volunteer in a clinical trial or study.

Food and Drug Administration (FDA): The US Government agency that is responsible for overseeing the manufacture, use, testing, and conduct of clinical trials involving drugs and medical devices.

Protocol: The plan for conducting a clinical trial.

Cohort: A group of people treated or analyzed in a study.

Case–control study: A type of observational study in which two different groups are observed. One group has a particular condition or is treated a particular way and the other is not. This type of study is useful to discern differences between the groups.

Cross-sectional study: A type of observational study in which researchers record information about their subjects without altering the study environment.

Double-blind study: A type of interventional trial in which neither the investigator nor the subjects are aware of the treatment assignments in the study.

Vehicle-controlled study: A type of interventional trial in which the study intervention is compared to a placebo intervention designed to be identical in appearance for the purpose of blinding the subject and investigator to the treatment assignment.

Randomization: A method of assigning subjects at random to different intervention arms of a study.

Investigational new drug (IND) program: The means by which a pharmaceutical company obtains permission from the FDA to ship a drug across state lines for the purpose of human subject research prior to the approval of a marketing application.

Sponsor: The institution or firm providing the funding for a clinical trial.

Substantial equivalence: A term indicating that a device or drug has a similar efficacy and safety profile to an already marketed device or drug. Proving substantial equivalence is a key step to obtaining marketing approval.

510(k) clearances: A section of the Food, Drug and Cosmetic Act that requires device manufacturers to notify the FDA of their intent to market a medical device at least 90 days in advance. The FDA then will determine if the device is equivalent to a device already placed into one of three classification categories.
Food, Drug and Cosmetic Act (FD&C): A set of laws passed by congress giving authority to the FDA to oversee the safety of food, drugs and cosmetics.

Good clinical practices (GCP): A standard for designing and conducting clinical trials that provides assurance regarding the ethical treatment of trial participants, the integrity of clinical trial data, and the reporting of results.

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH): A joint, multi-country project bringing together regulatory authorities and pharmaceutical industry for the purpose of discussing scientific and technical aspects of pharmaceutical registration.

Declaration of Helsinki: A statement of ethical principles developed by the World Medical Association to provide guidance for those conducting or participating in biomedical research regarding the ethical treatment of human subjects.

Principal investigator (PI): A physician who is responsible for all aspects of a site’s performance of a clinical trial.

Subinvestigator (SubI): A person who helps design and conduct investigation at a study site.

Sponsor-investigator: An individual who both initiates and conducts a clinical trial without the involvement of a corporation or agency.

Source documentation: Location where information is first recorded including original documents, records, and data.

Source data: The information, observations, records, and results contained within the source documents that are required for evaluation of the study.

Clinical research coordinator (CRC) or study coordinator (SC): A specialized research professional working under the direction of a principal investigator.

Study monitor or clinical research associate (CRA): An individual responsible for ensuring proper data collection as well as documenting and reporting protocol deviations.

Protocol deviation: An unplanned excursion from the protocol that is not implemented or planned as a systematic change.

Medical research associate (MRA): An individual, usually employed by the sponsor, performs similar duties as the CRA.

Medical monitor (MM): An individual, usually a physician, who has responsibility to answer protocol and study related questions.

Contract research organization (CRO): An agency or firm providing trial management services.

Institutional review board (IRB): A committee established to review and approve research involving human subjects. The purpose of an IRB is to ensure that a study is safe and effective for human participation.
Site qualification survey (SQS): A process in which a sponsor or CRO determines a potential trial site’s suitability for a particular study.

Health Insurance Portability and Accountability Act (HIPAA): A stringent set of standards enacted in 1996 to protect the privacy and security of individually identifiable health information. The act also includes standards with respect to health insurance coverage and electronic health care transactions.

Investigator initiated study or trial (IIS or IIT): A trial concept conceived by an investigator that may be conducted with or without industry sponsorship.

Medical science liaison (MSL): An industry representative or employee that is particularly well versed and able to answer scientific questions regarding a drug or device offered by a sponsor.

Physician Payments Sunshine Act (Sunshine Act): A US federal law requiring manufacturers of drugs, medical devices and biologicals to report certain payments or items of value transferred to physicians and teaching hospitals. This information is intended for distribution on a publically searchable website.

Chapter 5

Active Unique Investigators Filing Form 1572s WorldWide. Source: FDA's Bioresearch Monitoring Information System File (BMIS)
## Adverse Event Tracking Log

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Start date of event</th>
<th>Date event resolved&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Description of event</th>
<th>Severity of event</th>
<th>Nature of event</th>
<th>Relationship of event</th>
<th>Action with study drug</th>
<th>Is this a UP involving risks to subjects or others?</th>
<th>Date report sent to HRPP&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. No action</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. Interrupted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3. Discontinued</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>All events should be resolved or noted as unresolved at the time of subjects discontinuation in the study (i.e., study complete or subject withdrawal)

<sup>b</sup>Report all adverse events in accordance with HRPP Guidelines
# Drug Shipment Receipt Log

<table>
<thead>
<tr>
<th>Date of receipt</th>
<th>Protocol number/name</th>
<th>Total number of boxes received</th>
<th>Ambient/refrigerated/frozen</th>
<th>Name of CRC notified of shipment</th>
<th>Initials of CRC confirming medication received/checked in/ and placed in drug room/refrigerator/freezer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## FDA AUDIT CHECKLIST

### INITIAL CONTACT

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff member who received initial contact.</td>
<td></td>
</tr>
<tr>
<td>Contact and notification date.</td>
<td></td>
</tr>
</tbody>
</table>

### FDA AUDIT VISIT INFORMATION

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit start date.</td>
<td></td>
</tr>
<tr>
<td>Estimated time of arrival.</td>
<td></td>
</tr>
<tr>
<td>Anticipated duration.</td>
<td></td>
</tr>
<tr>
<td>FDA Inspector contact information.</td>
<td></td>
</tr>
<tr>
<td>Additional FDA Inspectors' names.</td>
<td></td>
</tr>
</tbody>
</table>

### PURPOSE OF INSPECTION

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trial</td>
<td></td>
</tr>
<tr>
<td>Investigator</td>
<td></td>
</tr>
<tr>
<td>Routine</td>
<td></td>
</tr>
<tr>
<td>Directed (For Cause): If directed, consider notifying legal department</td>
<td></td>
</tr>
<tr>
<td>Follow-up (438, or warning letter)</td>
<td></td>
</tr>
<tr>
<td>If unannounced FDA inspector arrives notify legal department</td>
<td></td>
</tr>
</tbody>
</table>

### FDA REQUESTED DOCUMENTS

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific personnel requested (name, times available requested)</td>
<td></td>
</tr>
<tr>
<td>Specific documents requested.</td>
<td></td>
</tr>
<tr>
<td>Documents checked prior to inspection</td>
<td></td>
</tr>
<tr>
<td>Documents requested to be sent to FDA prior to inspection.</td>
<td></td>
</tr>
</tbody>
</table>

### NOTIFICATIONS OF INVOLVED PARTIES

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td></td>
</tr>
<tr>
<td>IRB</td>
<td></td>
</tr>
<tr>
<td>Investigator(s), Sub-Investigator(s)</td>
<td></td>
</tr>
<tr>
<td>Study Coordinator(s)</td>
<td></td>
</tr>
<tr>
<td>Staff</td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td></td>
</tr>
</tbody>
</table>
### Audit Preparation Team

<table>
<thead>
<tr>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designated inspection coordinator.</td>
</tr>
<tr>
<td>Designated FDA inspector escort to accompany inspector at all times.</td>
</tr>
<tr>
<td>Designated team member to make photocopies and take notes.</td>
</tr>
</tbody>
</table>

### Designated Inspection Workspace

<table>
<thead>
<tr>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large table or desktop cleared of all but requested documents.</td>
</tr>
<tr>
<td>Room #</td>
</tr>
<tr>
<td>Telephone number or extension</td>
</tr>
<tr>
<td>Copy machine available</td>
</tr>
</tbody>
</table>

### Clinic, Research and Staff Schedule

<table>
<thead>
<tr>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review staff, investigator, and clinic schedules</td>
</tr>
<tr>
<td>Avoid conflicts of key staff from vacations, appointments, etc.</td>
</tr>
<tr>
<td>Reschedule nonessential meetings.</td>
</tr>
<tr>
<td>Reschedule noncritical clinic visits.</td>
</tr>
<tr>
<td>Reschedule flexible clinical trial visits.</td>
</tr>
</tbody>
</table>

### Retrieve Records

<table>
<thead>
<tr>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrieve records from storage, or print from cloud.</td>
</tr>
<tr>
<td>Retrieve electronic stored records or CDs, DVDs.</td>
</tr>
<tr>
<td>For hospitalized SAEs, make sure inpatient records are accessible.</td>
</tr>
<tr>
<td>Have all drug accountability records available on site.</td>
</tr>
<tr>
<td>Follow-up (438, or warning letter)</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Regulatory Documents</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Current list of PI's active research protocols.</td>
</tr>
<tr>
<td>Copies of all signed agreements between PI, Sponsor, CRO.</td>
</tr>
<tr>
<td>All versions of the protocol available and dated and signed by PI.</td>
</tr>
<tr>
<td>All protocol amendments and clarifications available.</td>
</tr>
<tr>
<td>All versions of the Investigator's Brochure.</td>
</tr>
<tr>
<td>All package inserts.</td>
</tr>
<tr>
<td>All Instructions for handling IP and trial-related materials.</td>
</tr>
<tr>
<td>All IND Safety reports</td>
</tr>
<tr>
<td>DSMB summary reports, submission documents to IRB if applicable.</td>
</tr>
<tr>
<td>All versions of IRB approved Consent Forms.</td>
</tr>
<tr>
<td>Original IRB Approval Letter.</td>
</tr>
<tr>
<td>All documentation related to additional IRBs involved in study.</td>
</tr>
<tr>
<td>IRB protocol amendment(s) and approval letter(s).</td>
</tr>
<tr>
<td>IRB continuing review approval letters.</td>
</tr>
<tr>
<td>IRB approval letters for revised Informed Consent Forms.</td>
</tr>
<tr>
<td>IRB approval letters for translated Informed Consent Forms.</td>
</tr>
<tr>
<td>IRB approval of subject compensation.</td>
</tr>
<tr>
<td>Documentation of all payments to subjects.</td>
</tr>
<tr>
<td>IRB approval letters for subject recruitment (handouts, ads, videos).</td>
</tr>
<tr>
<td>IRB approval letters for Case Report Forms.</td>
</tr>
<tr>
<td>Correspondence from the Investigator to the IRB</td>
</tr>
<tr>
<td>Correspondence from the Sponsor to the Investigator &amp; vice-versa.</td>
</tr>
<tr>
<td>Original IRB letters acknowledging receipt of SAE submissions.</td>
</tr>
<tr>
<td>Original IRB letters acknowledging receipt of protocol deviations.</td>
</tr>
<tr>
<td>Original IRB letters acknowledging receipt of protocol violations.</td>
</tr>
<tr>
<td>Original letters acknowledging receipt of safety reports, SAEs, AEs.</td>
</tr>
<tr>
<td>Completed subject screening/enrollment log.</td>
</tr>
<tr>
<td>Completed site personnel log with signed authorization of duties.</td>
</tr>
<tr>
<td>Documentation of a trial initiation monitoring visit.</td>
</tr>
<tr>
<td>Signed and dated monitoring visit log.</td>
</tr>
<tr>
<td>All versions of FDA Form 1572 signed and dated.</td>
</tr>
<tr>
<td>Financial disclosures for the PI and all sub-investigators.</td>
</tr>
<tr>
<td>Signed and dated current CVs for the PI and all sub-investigators.</td>
</tr>
<tr>
<td>Current licenses of the PI, Sub-I, and all other key study staff.</td>
</tr>
<tr>
<td>GCP/HSP training documentation for everyone on FDA 1572.</td>
</tr>
<tr>
<td>GCP/HSP documentation for anyone with more than minimal involvement in the study.</td>
</tr>
<tr>
<td>Signed and dated current CVs for the study coordinator(s).</td>
</tr>
<tr>
<td>Documentation of staff protocol training.</td>
</tr>
<tr>
<td>Documentation of additional staff training.</td>
</tr>
<tr>
<td>Documentation of protocol submission, approval, activation.</td>
</tr>
<tr>
<td>Appendix</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Documentation of protocol deregistration if applicable.</td>
</tr>
<tr>
<td>Any other correspondence related to the study.</td>
</tr>
<tr>
<td>IRB committee membership roster.</td>
</tr>
<tr>
<td>Documentation of any unblinding procedures and events.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appendix</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV of pharmacist, current, signed, dated</td>
</tr>
<tr>
<td>CV of key pharmacy personnel.</td>
</tr>
<tr>
<td>Licenses of pharmacy personnel</td>
</tr>
<tr>
<td>Sample labels attached to IP containers</td>
</tr>
<tr>
<td>Signature list.</td>
</tr>
<tr>
<td>Delegation log.</td>
</tr>
<tr>
<td>IP accountability logs.</td>
</tr>
<tr>
<td>Records of study product dispensed to appropriate staff member.</td>
</tr>
<tr>
<td>Shipping receipts and records for IP and related study materials.</td>
</tr>
<tr>
<td>Documentation of study drug transfer, return, disposal.</td>
</tr>
<tr>
<td>Temperature logs.</td>
</tr>
<tr>
<td>Calibration and maintenance records for all equipment.</td>
</tr>
<tr>
<td>Certificate of analysis of IP shipped.</td>
</tr>
<tr>
<td>Certificates of analysis of new batches of IP.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appendix</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV of laboratory director (Central Lab, Local Lab)</td>
</tr>
<tr>
<td>CVs of key laboratory personnel</td>
</tr>
<tr>
<td>Licenses of laboratory personnel</td>
</tr>
<tr>
<td>Lab certifications (CAP, CLIA, State Lab) and expirations.</td>
</tr>
<tr>
<td>Other lab certifications.</td>
</tr>
<tr>
<td>Laboratory normal values used throughout the study.</td>
</tr>
<tr>
<td>Updates to normal values included in the protocol.</td>
</tr>
<tr>
<td>Updates of laboratory procedures or tests.</td>
</tr>
<tr>
<td>Specimen logs.</td>
</tr>
<tr>
<td>Chain of custody SOP.</td>
</tr>
<tr>
<td>Clinical equipment temperature logs are complete and up to date.</td>
</tr>
<tr>
<td>Clinical equipment maintenance logs are complete and up to date.</td>
</tr>
<tr>
<td>Complete</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td><strong>SOP</strong></td>
</tr>
<tr>
<td>Source Documents and medical records for each subject. Must be attributable, legible, contemporaneous, original, and accurate.</td>
</tr>
<tr>
<td>Signed, dated, complete CRFs for each subject.</td>
</tr>
<tr>
<td>CRF corrections properly documented (single line crosses out error, new value entered, initialed, and dated by team member).</td>
</tr>
<tr>
<td>Inclusion and exclusion criteria for each participation have been met and are documented.</td>
</tr>
<tr>
<td>Original signed and dated Consent Forms are on file for each subject.</td>
</tr>
<tr>
<td>All visits are conducted within protocol windows.</td>
</tr>
<tr>
<td>Correct laboratory blood volume in correct tube is drawn at each required visit.</td>
</tr>
<tr>
<td>Protocol required tests and evaluations have been documented clearly, and appropriately.</td>
</tr>
<tr>
<td>All labs are correctly labeled and match their corresponding subjects.</td>
</tr>
<tr>
<td>All laboratory tests have been reviewed by the PI or other protocol indicated medical professional.</td>
</tr>
<tr>
<td>Laboratory tests have been signed by the reviewing PI or medical professional.</td>
</tr>
<tr>
<td>Laboratory values outside the normal range evaluated as &quot;Clinically Significant&quot; or &quot;Not Clinically Significant.&quot;</td>
</tr>
<tr>
<td>Concomitant medications documented.</td>
</tr>
<tr>
<td>AEs documented.</td>
</tr>
<tr>
<td>SAEs reported to the IRB.</td>
</tr>
<tr>
<td>All AEs and SAEs reported to sponsor.</td>
</tr>
<tr>
<td>Study endpoints corrected identified and reported.</td>
</tr>
<tr>
<td>Protocol violations and deviations reported along with corrective action plans.</td>
</tr>
<tr>
<td>Early study termination of subjects documented.</td>
</tr>
<tr>
<td>Study product use by all subjects documented.</td>
</tr>
<tr>
<td>Subjects lost to follow-up documented.</td>
</tr>
<tr>
<td>Study subject recruitment and retention plan documented.</td>
</tr>
</tbody>
</table>
During audit,
Do not volunteer additional information.
Do not argue with the inspectors.
Do not sign affidavits without legal counsel.

Red flags for auditors
Lack of any errors or corrections on CRFs.
Subjects who follow protocols perfectly.
All screened subjects enroll in the study to completion.
Study staff lack knowledge about the study.
Equipment or resources at the site don’t match documentation.

Common deficiencies
Failure to follow the protocol.
Protocol deviations which are not properly documented.
Failure to obtain informed consent,
Lack of accurate, complete, and current records.
Lack of accountability for investigational product.
Failure to obtain IRB approval.

Regulations do not require responding to a 483, but it is expected. A good response shows that you understand the concerns of the inspector, that you are committed to compliance and improvement, that you are serious about establishing your credibility as an investigator, and may help you avoid a warning letter.

You can respond to a 483 in person during the exit interview, or in writing. A written response tends to be more reflective, more comprehensive, and a more neutral and professional tone. Send a response within 14 days.

A good response should contain the following elements:
1. A willingness from the senior investigative team members to address the agency’s concerns.
2. A point-by-point response to each deficiency noted by the inspector.
3. Corrective actions you intend to take.
4. A time course for corrective actions.
5. A plan for monitoring the effectiveness of the correction.

You may consider sending a follow-up letter to the agency which documents the results of any corrective actions you have taken. If you have any disagreement with the findings, stick to facts, and back up your facts with incontrovertible and verifiable evidence or data.

The FDA may respond after an audit with a letter. If no deviations or compliance issues are found, no letter may be sent or a general letter may be sent stating the investigator is in compliance with applicable regulations.

An Informational or Untitled Letter outlines deviations from regulations and statutes that do not meet the threshold for Warning Letters. These letters typically merit a response from the investigator.

A Warning Letter identified significant violations of regulation, and requires prompt action, which must be detailed in a written response.

A Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) is sent when an investigator repeatedly or intentionally fails to comply with the protocol or its regulations or intentionally submits false information to the FDA, the IRB, or the sponsor. In these cases, the FDA will try to disqualify the investigator from participating in clinical studies and may refer the investigator to appropriate agencies for further sanctions.

## Note-to-File Template

A note to file should:

- Be composed as needed based on individual cases.
- Contain clearly verifiable references to the volunteer and the protocol.
- Have a contemporary and dated signature.
- Preferably be typed or printed in neat, clear handwriting.
• Contain a succinct, precise, and accurate explanation for any errors, discrepancies, or departures from the protocol, and future corrective steps.
• Have a follow-up plan.
• Be placed in the correct section of the study binder to which it applies.

Example Note to File:

<table>
<thead>
<tr>
<th>PROTOCOL #:</th>
<th>AMG-2015-CTAB4044-A</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE:</td>
<td>Comparison of CTAB to 4404-A on transepidermal water loss in neonates with harlequin ichthyosis</td>
</tr>
<tr>
<td>From:</td>
<td>Wake Research Associates</td>
</tr>
<tr>
<td></td>
<td>[Kim Papadopolis, Sub Investigator]</td>
</tr>
<tr>
<td>To:</td>
<td>Study Volunteer File</td>
</tr>
<tr>
<td>Re:</td>
<td>Subject# 05-JDP</td>
</tr>
<tr>
<td>Date:</td>
<td>July 31, 2015</td>
</tr>
</tbody>
</table>

Dr. Jones consented the subject on July 15, 2014. Dr. Jones, in error dated the delegation of authority log July 15, 2019. The incorrect date does not reflect the date of delegation but is the result of illegible handwriting and mistranscription. Dr. Jones was reminded to print dates clearly and his staff were encouraged to question Dr. Jones if they are in doubt about the clarity of her handwriting in the future.

Signature:

Site Temperature Log

Facility Name: __________________________
Thermometer Name&No.: __________________________ Other information: __________________________
Sponsor: _____________ Protocol: _______________ Site #: __________ Pl: _______________
Test material name/number: ____________________
Required temperature range _____________ Other information as per sponsor: ____________________

<table>
<thead>
<tr>
<th>Date ddmmyyyy</th>
<th>Time</th>
<th>Actual temperature</th>
<th>Minimum temperature</th>
<th>Maximum temperature</th>
<th>Initials/signature for first time on current log sheet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Standard Operating Procedures Manual

Table of Contents

PART A: OUTPATIENT STUDIES

SECTION 1: PREPARATION, ISSUE, AND REVISION
SECTION 2: ORGANIZATION CHART
SECTION 3: MASTER STUDY FILES AND RECORD RETENTION
SECTION 4: QUALITY ASSURANCE
SECTION 5: PATIENT/SUBJECT RECRUITMENT
SECTION 6: SCREENING PROCESS
SECTION 7: PHONE SCREENS
SECTION 8: INFORMED CONSENT
SECTION 9: MONITORING SCHEDULING
SECTION 10: STUDY VISITS
SECTION 11: STUDY INITIATION VISITS
SECTION 12: STUDY DATA COLLECTION AND REVIEW
SECTION 13: DRUG INVENTORY AND ACCOUNTABILITY
SECTION 14: REPORTING OF PROTOCOL DEVIATIONS AND ADVERSE EVENTS TO THE IRB
SECTION 15: FDA AUDIT PREPARATION
SECTION 16: CLOSE-OUT VISITS
SECTION 17: HIPPA COMPLIANCE POLICY
SECTION 18: PROCEDURES FOR ON-CALL PERSONNEL
SECTION 19: STUDY MEDICATIONS/DEVICE TRANSPORTATION
SECTION 20: USE OF MEDICATION/DEVICE TRANSPORTATION
SECTION 21: TRANSPORTING LAB SPECIMENS

(continued)
SECTION 22: TRANSPORTING SOURCE DOCUMENTS
SECTION 23: DATA ENTRY

PART B: INPATIENT STUDIES

SECTION 1: CRASH CART INVENTORY AND RESTOCKING
SECTION 2: ADMISSION AND DISCHARGE PROCEDURES
SECTION 3: PK COLLECTION, PROCESSING, HANDLING AND SHIPPING
SECTION 4: SHIFT CHANGE REPORT
SECTION 5: UNBLINDING PROCESS
SECTION 6: MEDICAL EMERGENCY PROCEDURES

An Example of Regulatory Binder Table of Contents Is Below

<table>
<thead>
<tr>
<th>Sec.</th>
<th>Essential Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>STUDY TEAM</td>
</tr>
<tr>
<td></td>
<td>Study Team Contact List</td>
</tr>
<tr>
<td></td>
<td>Study Team Signature and Delegation Log</td>
</tr>
<tr>
<td></td>
<td>CVs, Licenses, Financial Disclosures, Applicable Certifications of Key Study Personnel</td>
</tr>
<tr>
<td>2</td>
<td>PROTOCOL</td>
</tr>
<tr>
<td></td>
<td>Study protocol + amendments</td>
</tr>
<tr>
<td></td>
<td>IRB Stamped Consent Document and Translations</td>
</tr>
<tr>
<td></td>
<td>IRB Stamped Advertisements</td>
</tr>
<tr>
<td></td>
<td>Investigator Brochure (IB)</td>
</tr>
<tr>
<td></td>
<td>Safety update letters for inclusion in IB</td>
</tr>
<tr>
<td></td>
<td>Sample of Questionnaires/survey forms</td>
</tr>
<tr>
<td></td>
<td>Sample of Diary cards</td>
</tr>
<tr>
<td></td>
<td>Sample of memory aids for study procedures</td>
</tr>
<tr>
<td></td>
<td>Any other written information given to the patient</td>
</tr>
<tr>
<td></td>
<td>Sample of CRF</td>
</tr>
<tr>
<td>3</td>
<td>REGULATORY</td>
</tr>
<tr>
<td></td>
<td>Committee for Protection of Human Subjects (IRB)</td>
</tr>
<tr>
<td></td>
<td>IRB Submission Forms (initial, amendments, renewals, etc.)</td>
</tr>
<tr>
<td></td>
<td>IRB Outcome Letters (Approvals, Acknowledgments, etc.)</td>
</tr>
<tr>
<td></td>
<td>IRB Correspondence (or location)</td>
</tr>
<tr>
<td></td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td></td>
<td>Form FDA 1572 for all Key Study Personnel</td>
</tr>
<tr>
<td></td>
<td>Copy of IND/IDE submission</td>
</tr>
<tr>
<td></td>
<td>FDA Correspondence</td>
</tr>
<tr>
<td></td>
<td>Annual Reports</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Sec.</th>
<th>Essential Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4</strong></td>
<td><strong>PATIENT LOGS</strong></td>
</tr>
<tr>
<td></td>
<td>Screening log</td>
</tr>
<tr>
<td></td>
<td>Enrollment log</td>
</tr>
<tr>
<td></td>
<td>Subject Visit Schedule Log</td>
</tr>
<tr>
<td></td>
<td>Signed Informed Consent Forms (or location)</td>
</tr>
<tr>
<td><strong>5</strong></td>
<td><strong>UNANTICIPATED PROBLEMS</strong></td>
</tr>
<tr>
<td></td>
<td>Copies of AE reports if not included in CRF</td>
</tr>
<tr>
<td></td>
<td>AE log for events in non-site subjects</td>
</tr>
<tr>
<td></td>
<td>AE log for events in site subjects</td>
</tr>
<tr>
<td></td>
<td>Adverse Event reports</td>
</tr>
<tr>
<td></td>
<td>Protocol Deviation Logs</td>
</tr>
<tr>
<td><strong>6</strong></td>
<td><strong>DRUG/DEVICE ACCOUNTABILITY</strong></td>
</tr>
<tr>
<td></td>
<td>Package Insert/Prescribing Information</td>
</tr>
<tr>
<td></td>
<td>Drug/Device Receipt (Shipping Records)</td>
</tr>
<tr>
<td></td>
<td>Drug/Device Accountability Log</td>
</tr>
<tr>
<td></td>
<td>Drug Disposal Records</td>
</tr>
<tr>
<td></td>
<td>Sealed unblinding envelopes (or location)</td>
</tr>
<tr>
<td></td>
<td>Individual treatment codes (or location)</td>
</tr>
<tr>
<td></td>
<td>Temperature Logs</td>
</tr>
<tr>
<td><strong>7</strong></td>
<td><strong>LABORATORY</strong></td>
</tr>
<tr>
<td></td>
<td>Laboratory Name and Contact Address</td>
</tr>
<tr>
<td></td>
<td>Logistic Arrangements with lab (if local lab is used)</td>
</tr>
<tr>
<td></td>
<td>Lab certifications and normal ranges</td>
</tr>
<tr>
<td></td>
<td>Biological specimen sampling, labeling, storing and shipping procedure</td>
</tr>
<tr>
<td></td>
<td>Biological specimen log</td>
</tr>
<tr>
<td></td>
<td>Shipping records (if central lab is used)</td>
</tr>
<tr>
<td></td>
<td>Temperature Logs</td>
</tr>
<tr>
<td><strong>8</strong></td>
<td><strong>MONITORING</strong></td>
</tr>
<tr>
<td></td>
<td>Monitoring log</td>
</tr>
<tr>
<td></td>
<td>Monitoring reports</td>
</tr>
<tr>
<td></td>
<td>Initiation meeting information (sign in sheet, agenda, minutes, etc.)</td>
</tr>
<tr>
<td></td>
<td>Correspondence</td>
</tr>
<tr>
<td><strong>9</strong></td>
<td><strong>FINANCIAL DOCUMENTS (may be stored in separate location)</strong></td>
</tr>
<tr>
<td></td>
<td>Clinical Trial Agreement</td>
</tr>
<tr>
<td></td>
<td>Budget</td>
</tr>
<tr>
<td></td>
<td>Financial expenditure records</td>
</tr>
<tr>
<td></td>
<td>Billing statements</td>
</tr>
<tr>
<td><strong>10</strong></td>
<td><strong>Other Documents</strong></td>
</tr>
<tr>
<td></td>
<td>Completed CRFs (location)</td>
</tr>
<tr>
<td></td>
<td>Study Closure Documentation</td>
</tr>
<tr>
<td></td>
<td>Publications, presentations, manuscripts, etc.</td>
</tr>
</tbody>
</table>
Example of Forms, Logs, and Checklist

Study Drug Dispensing Verification Form

Protocol Number: ___________________________ PI: ___________________________

Date of Visit: ___________________________

Subject Number: ___________________________ Initials: ___________________________

Assigned IP to Be Dispensed *: ___________________________ Amount: ___________________________

*If Assigned via IXRS, confirmation print out must be present for verification

Dosing Instructions:
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Coordinator Dispensing Drug: ___________________________ Date: ___________________________

Coordinator Verifying *: ___________________________ Date: ___________________________

*MUST be coordinator listed on the delegation of authority log as authorized by the Principal Investigator to prepare/dispense investigational product
Appendix A: Informed Consent Checklist (Please Refer to DHS HHS OHRP 45 CFR 46 §46.116 for Details)

<table>
<thead>
<tr>
<th>Basic elements</th>
<th>Indicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the study involves research</td>
<td>□  □</td>
</tr>
<tr>
<td>An explanation of the purposes of the research</td>
<td>□  □</td>
</tr>
<tr>
<td>The expected duration of the individual’s participation</td>
<td>□  □</td>
</tr>
<tr>
<td>A description of the procedures to be followed</td>
<td>□  □</td>
</tr>
<tr>
<td>Identification of any procedures which are experimental</td>
<td>□  □</td>
</tr>
<tr>
<td>A description of any reasonably foreseeable risks or discomforts to the participant</td>
<td>□  □</td>
</tr>
<tr>
<td>A description of any benefits to the participant or to others which may reasonably be expected from the research</td>
<td>□  □</td>
</tr>
<tr>
<td>A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant</td>
<td>□  □</td>
</tr>
<tr>
<td>A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained</td>
<td>□  □</td>
</tr>
<tr>
<td>For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained</td>
<td>□  □</td>
</tr>
<tr>
<td>An explanation of whom to contact for answers to pertinent questions about the research and participant’s rights, and whom to contact in the event of a research-related injury to the participant</td>
<td>□  □</td>
</tr>
<tr>
<td>A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the individual is otherwise entitled, and the individual may discontinue participation at any time without penalty or loss of benefits, to which he/she is otherwise entitled</td>
<td>□  □</td>
</tr>
<tr>
<td>A statement that must contain the following language: “A description of the clinical trial will be available on <a href="http://www.ClinicalTrials.gov">http://www.ClinicalTrials.gov</a>, as required by the US Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search the Website at any time/”</td>
<td>□  □</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional elements, as appropriate</th>
<th>Indicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the intervention may involve risks to the individual (or to the embryo or fetus, if the individual is or may become pregnant), which are currently unforeseeable</td>
<td>□  □</td>
</tr>
<tr>
<td>Anticipated circumstances under which the individual’s participation may be terminated by the investigator without regard to the subject’s consent</td>
<td>□  □</td>
</tr>
<tr>
<td>Any additional costs to the individual that may result from participation in the research</td>
<td>□  □</td>
</tr>
<tr>
<td>The consequences of an individual’s decision to withdraw from the research and procedures for orderly termination of participation by the individual</td>
<td>□  □</td>
</tr>
<tr>
<td>A statement that significant new findings developed during the course of the research, which may relate to the individual’s willingness to continue participation, will be provided to the individual</td>
<td>□  □</td>
</tr>
<tr>
<td>The approximate number of study participants</td>
<td>□  □</td>
</tr>
</tbody>
</table>
Appendix B

First Payment: $33,534.02

Variable Events not included in the PSF and incurred to:

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Frequency</th>
<th># of Subjects</th>
<th>NullException Rate</th>
<th>Total Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintegrated left (LME)</td>
<td>1</td>
<td>20</td>
<td>2,940.00</td>
<td>23,200.00</td>
</tr>
<tr>
<td>Unintegrated left (MFE)</td>
<td>1</td>
<td>960.00</td>
<td>65,559.00</td>
<td>65,559.00</td>
</tr>
<tr>
<td>Blood loss, (emergency bypass)</td>
<td>1</td>
<td>150.00</td>
<td>1,360.00</td>
<td>1,360.00</td>
</tr>
<tr>
<td>Delayed Cardiac Visit</td>
<td>1</td>
<td>8</td>
<td>2,161.00</td>
<td>16,359.00</td>
</tr>
<tr>
<td>Abnormal left ejection fraction</td>
<td>1</td>
<td>5</td>
<td>1,521.00</td>
<td>5,142.00</td>
</tr>
<tr>
<td>Early withdrawal</td>
<td>1</td>
<td>1</td>
<td>3,046.75</td>
<td>29,737.50</td>
</tr>
<tr>
<td>Surgery QRS</td>
<td>1</td>
<td>1</td>
<td>3,046.75</td>
<td>4,063.00</td>
</tr>
<tr>
<td>Issues related to 3</td>
<td>1</td>
<td>3</td>
<td>1,884.10</td>
<td>5,568.31</td>
</tr>
<tr>
<td>Total Products/Related Events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Appendix
Appendix

Joe Smith, MD, PhD
Big Pharma
9899/6XMA
11/1/11
A Randomized, Double-Blind, Double-Dummy, Parallel-Group Study To Evaluate The Efficacy And Safety Of Study Drug In Comparison To Standard of Care Drug in Patients With Serious Disease

Salary Breakdown

<table>
<thead>
<tr>
<th>Role</th>
<th>Months</th>
<th>Effort</th>
<th>Base</th>
<th>Salary</th>
<th>Benefits</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joe Smith, MD, PhD</td>
<td>Investigator</td>
<td>Fringe: 26.00%</td>
<td>5.000%</td>
<td>170,000</td>
<td>2,125.00</td>
<td>552.50</td>
</tr>
<tr>
<td></td>
<td>co-inv</td>
<td>Fringe: 26.00%</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>co-inv</td>
<td>Fringe: 26.00%</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>co-inv</td>
<td>Fringe: 26.00%</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Amy Smith</td>
<td>Nurse</td>
<td>Fringe: 34.00%</td>
<td>1.000%</td>
<td>136,560</td>
<td>364.40</td>
<td>117.78</td>
</tr>
<tr>
<td>Judy Smith</td>
<td>CRC</td>
<td>Fringe: 34.00%</td>
<td>14.92%</td>
<td>44,450</td>
<td>829.82</td>
<td>552.78</td>
</tr>
<tr>
<td>Gene Smith</td>
<td>staff</td>
<td>Fringe: 34.00%</td>
<td>2.000%</td>
<td>95,738</td>
<td>478.68</td>
<td>162.75</td>
</tr>
<tr>
<td></td>
<td>staff</td>
<td>Fringe: 34.00%</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>staff</td>
<td>Fringe: 34.00%</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Supplies
8.87

Computing/Data Processing
59.26

Other Expenses
- General, Automobiles & Employee Liability insurance@$0.58 per $100 of wages
- Desktop Support, ITS
- CHIL initial review fee
- Pharmacy Set-up fee, uncomplicated
- Pharmacy close-out fee
- G290 CNS start-up fee is $1,500 if needed, add
- Off-campus rent for 3 months ($750/month)

Patient Payment Cards

Study Team Direct Cost Total: $13,698.00

<table>
<thead>
<tr>
<th>Role</th>
<th>Months</th>
<th>Effort</th>
<th>Base</th>
<th>Salary</th>
<th>Benefits</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budget Analyst</td>
<td>Analyst</td>
<td>Fringe: 34.00%</td>
<td>6.600%</td>
<td>92,700</td>
<td>1,289.55</td>
<td>520.05</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fringe: 34.00%</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Supplies
119.10

Computing/Data Processing
15.50

Other Expenses
- General, Automobiles & Employee Liability insurance@$0.58 per $100 of wages
- Desktop Support, ITS

NCRA Preaward Direct Cost Total: $2,206.00

NCRA 10%: $1,598.80
Dept. Total Direct Costs Start-up: $17,467.80
Indirect Cost Total: $5,545.85

Grand Total Due from Sponsor: $22,034.62

Standard Budget Calculations
- Computing/Data Processing support calculated as: 3 months*$53.54*sum(all effort)
- ITS desktop exchange calculated as: 3 months*$35*sum(all effort)

Budget Notes
- study team: $6,308.60
Please provide the following information to produce a first draft of a clinical research project budget.

### Project Title
A Randomized, Double-Blind, Double-Dummy, Parallel-Group Study To Evaluate The Efficacy And Safety Of Study Drug In Comparison To Standard Of Care Drug In Patients With Serious Disease

<table>
<thead>
<tr>
<th>Primary sponsor</th>
<th>Big Pharma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor protocol number</td>
<td>999976XMA</td>
</tr>
<tr>
<td>Budget negotiation contact</td>
<td>Jane Smith</td>
</tr>
<tr>
<td>phone &amp; email</td>
<td><a href="mailto:Jane_Smith@bigpharma.com">Jane_Smith@bigpharma.com</a></td>
</tr>
<tr>
<td>Contract negotiation contact (if different)</td>
<td>Jane Smith</td>
</tr>
<tr>
<td>phone &amp; email</td>
<td><a href="mailto:Jane_Smith@bigpharma.com">Jane_Smith@bigpharma.com</a></td>
</tr>
<tr>
<td>Anticipated or actual CHR approval date</td>
<td>11/1/11</td>
</tr>
<tr>
<td>Type of disease</td>
<td>serious disease</td>
</tr>
<tr>
<td>Phase and/or intent of study</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Anticipated complications</td>
<td></td>
</tr>
</tbody>
</table>

### Protocol Complexity Rating (subjective)
Low, Medium, or High | High

### Name personnel paid from the award

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>% Effort and/or Project Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joe Smith, MD, PhD</td>
<td>Principal Investigator</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>co-inv</td>
<td></td>
</tr>
<tr>
<td></td>
<td>co-inv</td>
<td></td>
</tr>
<tr>
<td></td>
<td>postdoc fellow</td>
<td></td>
</tr>
<tr>
<td>Amy Smith</td>
<td>Nurse</td>
<td>0.2</td>
</tr>
<tr>
<td>Judy Smith</td>
<td>CRC</td>
<td>0.5175</td>
</tr>
<tr>
<td>Gene Smith</td>
<td>staff</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>staff</td>
<td></td>
</tr>
<tr>
<td></td>
<td>staff</td>
<td></td>
</tr>
</tbody>
</table>

### Comments:

### Project Periods

- Estimated start date for deliverables will be submitted to the CHR: 10/31/14
- Estimated number of UCSF subjects: 10
- Estimated subject accrual rate: 2 per month
- Length of time a subject is expected to participate: 146 weeks

### Comments:

### Financial Information

- Is this an Investigator initiated project: No
- List all addresses where research is conducted: 350 Parnassus and then Mission Bay in Spring 2012
- Will this contract require subcontracts to other sites: No
- Will this contract require inpatient hospital services: GRCG infusions
- Will any part of this project be billed to insurance: No
- per subject dollar figure or total budget targets, if any: 54,554

### Comments:

All the blinding requires additional labor on the budget and increases the complexity.
<table>
<thead>
<tr>
<th>Process expectations:</th>
<th></th>
</tr>
</thead>
</table>
| NCRA Preaward Analyst | *completes information submitted by the PI (or designee) into a standard, budget template*  
*returns a first draft budget to the PI for review within 5 business days*  
*negotiates a budget and payment terms with the Sponsor, if requested*  |
| Principal Investigator | *submits a budget requisition with another meaningful document representing the scope of work (AKA the protocol)*  
*provides required proposal documents to the NCRA as they become available*  
*may negotiate a budget and payment terms with a Sponsor and, when doing so, is acting as an agent of the University and must follow University contracting policies*  |

<table>
<thead>
<tr>
<th>Checklist for submitting required, electronic documents to the assigned, preaward analyst</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed Consent (ICF)*</td>
<td>submit the most current version</td>
</tr>
<tr>
<td>Protocol*</td>
<td>submit the most current version</td>
</tr>
<tr>
<td>CHR application**</td>
<td>submit when the final is available</td>
</tr>
<tr>
<td>Sponsor’s contract</td>
<td>submit when a draft is available</td>
</tr>
<tr>
<td>Sponsor’s budget and payment terms</td>
<td>submit when a draft is available</td>
</tr>
<tr>
<td>CTSI CRS services quote</td>
<td>(if utilized)</td>
</tr>
<tr>
<td>Pharmacy services quote</td>
<td>(if utilized)</td>
</tr>
<tr>
<td>List other documents that impact the budget</td>
<td>(and submit these documents as they become available)</td>
</tr>
</tbody>
</table>

*If the protocol and/or ICF is not written yet, note this and identify big expense items, such as scans, lumbar punctures, etc. in financial comments on the budget requisition spreadsheet.*  
**If a contract amendment is triggered from changes to a protocol, submit the summary of changes from the CHR application to the preaward analyst.*

Send a message to the budgeting team in the box below regarding time sensitivity, unusual circumstances or items, etc.
Off-site Storage Fees Assessment for Clinical Trials Budgeting

Source Reference:
http://www.campuslifeservices.ucsf.edu/distribution/storage/storage_rates/

Cost Development Assumptions
10 boxes
15 years

<table>
<thead>
<tr>
<th>Storage fees for Start-up Costs</th>
<th>Rate</th>
<th>Units</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Std. file box per month</td>
<td>$0.54</td>
<td>1800</td>
<td>$972.00</td>
</tr>
<tr>
<td>Warehouse service hourly rate</td>
<td>$54.46</td>
<td>8</td>
<td>$435.68</td>
</tr>
<tr>
<td>Records destruction per box</td>
<td>$3.23</td>
<td>10</td>
<td>$32.30</td>
</tr>
<tr>
<td>Driver delivery charge</td>
<td>$70.00</td>
<td>2</td>
<td>$140.00</td>
</tr>
</tbody>
</table>

$1,579.98

Direct Cost Std. Charge $1,579.98 $158.00 per box

Notes
- electronic files can be about 5 boxes
- paper files can be about 10 boxes
- big trials can be 20 boxes

REVISED 9/9/11 via phone call. Rates are no longer listed on web page.

STUDY CALENDAR

<table>
<thead>
<tr>
<th>Protocol Activity</th>
<th>Screening</th>
<th>Baseline</th>
<th>DHC1</th>
<th>DHC1</th>
<th>Day 1, add'l cycles</th>
<th>Scans</th>
<th>ECT</th>
<th>Off Treatment Follow-up Visit</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Appendix C: Participant Screening/Enrollment/Withdrawal Log

<table>
<thead>
<tr>
<th>Date of screening</th>
<th>ICD(^a) on file?</th>
<th>Was participant given a copy of the ICD?(^b)</th>
<th>Was participant enrolled?</th>
<th>Y/N. If yes, note date</th>
<th>Participant ID #</th>
<th>Early withdrawal from research participation? Y/N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td></td>
<td></td>
<td>If yes:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Note reason</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. Did participant undergo study termination visit?</td>
</tr>
</tbody>
</table>

\(^a\)Informed consent document (ICD)  
\(^b\)If “no” note reason

### Appendix D: Site Personnel Signature Log

Study IRB #:______________________________  
Study Title:______________________________________________________________  
Principal Investigator:_____________________________________________________

<table>
<thead>
<tr>
<th>Name</th>
<th>Title/role (PI, coordinator, etc.)</th>
<th>Signature</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Page ____ of ____
Appendix E: The SMOG Readability Formula

Step 1: Take the entire text to be assessed.

Step 2: Count 10 sentences in a row near the beginning, 10 in the middle, and 10 in the end for a total of 30 sentences.

Step 3: Count every word with three or more syllables in each group of sentences, even if the same word appears more than once.

Step 4: Calculate the square root of the number arrived at in Step 3 and round it off to nearest 10.

Step 5: Add 3 to the figure arrived at in Step 4 to know the SMOG Grade, i.e., the reading grade that a person must have reached if he is to understand fully the text assessed.

SMOG grade = 3 + Square Root of Polysyllable Count

The SMOG formula is considered appropriate for secondary age (fourth grade to college level) readers.

The premises of McLaughlin’s SMOG formula are:

1. A sentence is defined as a string of words punctuated with a period, an exclamation mark, or a question mark.
2. Consider long sentences with a semi-colon as two sentences.
3. Words with hyphen are considered as a single word.
4. Proper nouns, if polysyllabic should be counted.
5. Numbers that are written should be counted. If written in numeric form, they should be pronounced to determine if they are polysyllabic.
6. Abbreviations should be read as though unabbreviated to determine if they are polysyllabic. However, abbreviations should be avoided unless commonly known.
7. If the text being graded is shorter than 30 sentences, follow the steps below:
   i. Count all the polysyllabic words in the text.
   ii. Count the number of sentences in the text.
   iii. Divide the figures obtained in (i) by the figure obtained in (ii) to arrive at average polysyllabic words per sentence.
   iv. Multiply the figure obtained in (iii) with the average number of sentences short of 30.
   v. Add the figure obtained in (iv) to the total number of polysyllabic words.
   vi. Compare the number of polysyllabic words in the SMOG conversion table.
SMOG conversion table

<table>
<thead>
<tr>
<th>Total polysyllabic word count</th>
<th>Approximate grade level (+1.5 grades)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–6</td>
<td>5</td>
</tr>
<tr>
<td>7–12</td>
<td>6</td>
</tr>
<tr>
<td>13–20</td>
<td>7</td>
</tr>
<tr>
<td>21–30</td>
<td>8</td>
</tr>
<tr>
<td>31–42</td>
<td>9</td>
</tr>
<tr>
<td>43–56</td>
<td>10</td>
</tr>
<tr>
<td>57–72</td>
<td>11</td>
</tr>
<tr>
<td>73–90</td>
<td>12</td>
</tr>
<tr>
<td>91–110</td>
<td>13</td>
</tr>
<tr>
<td>111–132</td>
<td>14</td>
</tr>
<tr>
<td>133–156</td>
<td>15</td>
</tr>
<tr>
<td>157–182</td>
<td>16</td>
</tr>
<tr>
<td>183–210</td>
<td>17</td>
</tr>
<tr>
<td>211–240</td>
<td>18</td>
</tr>
</tbody>
</table>

SMOG Readability Calculator
http://www.readabilityformulas.com/free-readability-formula-tests.php

Appendix F: Subject Visit Tracking Log

Study IRB #:________________
Study Title:____________________________________________________________
Principal Investigator:____________________________________________________

<table>
<thead>
<tr>
<th>Subject Study ID #</th>
<th>Visit # Date</th>
<th>Visit # Date</th>
<th>Visit # Date</th>
<th>Visit # Date</th>
<th>Date</th>
<th>Final study visit</th>
<th>Date and reason if early termination (please initial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example #001</td>
<td>Projected:</td>
<td>2/01/12</td>
<td>3/02/12</td>
<td>4/05/12</td>
<td>5/05/12</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td>1/10/12</td>
<td>2/01/12</td>
<td>3/06/12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Projected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Actual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Page _____ of_______
# Appendix G: Training Log

This log is designed to be study specific. You may customize this log to be the training record for an individual in the study team.

<table>
<thead>
<tr>
<th>Name of individual</th>
<th>Training (manual of operating procedures, standard operating procedures, study initiation visit, etc.)</th>
<th>Date of training</th>
<th>Initials of supervisor/PI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Glossary

**Adverse reaction (AE)** This is a side effect for an adverse reaction or an unanticipated or undesired effect of the experimental therapy. Adverse reactions may be further classified as routine adverse reactions and serious adverse reactions. Serious adverse reactions or serious adverse events may have specific reporting requirement time frames.

**Amendment** This is a change in the protocol that requires IRB approval prior to implementation. Studies may have several amendments, and these all require IRB approval, and they should be placed in the investigators brochure.

**Bias** This is a subjective impartiality which may affect the validity of the scientific results of the study. Bias may be controlled by factors such as randomization, blinding, and avoidance of conflict of interest.

**Blinded** Blinding occurs when one or more parties involved in a clinical trial are unaware of whether they are receiving treatment, placebo, or a control medication or intervention. Parties involved in blinding may comprise subjects, those dispensing medication, and those evaluating subjects, including investigators.

**Case-control study** This is a type of scientific trial that compares two cohorts. One cohort may have a disease (such as skin cancer) and be compared to a similar that does not have the disease. The study may for example examine the levels of exposure to carcinogens such as arsenic in each group up prior to the appearance of the disease to determine potential causality.

**Case report form (CRF)** This form is used to enter data related to protocol study procedures. CRFs may be paper or electronic (eCRFs). The latter have become more popular for a number of reasons, including real-time gathering and assessment of data. Case report forms are unique to each subject and the principal investigators responsible for maintaining the accuracy of the data in case report forms. In the case of a review by a sponsors monitor or an audit by regulatory agency, the accuracy of the data will be verified comparing CRF information with source documentation.

**Collaborative IRB training initiative (CITI)** This is a portal for certifying all levels of clinical research training including GCP (good clinical practices) training.
**Code of federal regulations (CFR)** These are the permanent rules and regulations published in the Federal Register by government agencies. Also known as administrative law, they contain sections and parts which govern human subjects’ research.

**Clinical research associate (CRA) or CCRA (certified clinical research associate)** This individual is often referred to as the monitor. The clinical research associate is typically employed by the sponsor to monitor clinical trial. The CRA makes sure that all trials were conducted according to the protocol and within guidelines mandated by GCP or the ICH.

**Clinical research coordinator (CRC)** This individual is also known as the study coordinator. The study coordinator typically administers the clinical trial at the investigative site. The study coordinator may be responsible for the collection of all documents related to the study and distribution of supplies at the investigative site.

**Clinical trial** Human subjects’ clinical trials are also known as clinical studies. These trials are designed to test a drug, medical device, or a biologic in a small population to determine whether its use can be considered safe and effective for a wider general population.

**Community-based clinical trial (CBCT)** This is a clinical trial typically conducted in a private practice setting as opposed to a large academic medical center.

**Contract research organization (CRO)** This is an agency contracted by a sponsor such as a pharmaceutical company to oversee clinical research at investigative sites.

**Control group** This is a group of human subjects to which the investigative intervention is compared. The control group may receive a placebo or may receive an established standard therapy for their disease.

**Controlled trials** This is a type of trial in which two groups are compared. The control group is either given standard therapy for disease or placebo and another group is given the experimental therapy.

**Crossover trial** This is a type of study in which all human subjects participating in the study receive both interventions: placebo and investigational product. At a point in time defined by the protocol, the control group receives the intervention and the intervention group receives placebo.

**Data safety monitoring board (DSMB)** This is an independent committee comprised of the board of experts that review clinical trial while it is in progress. The purpose of the data safety monitoring board is to ensure that subjects are not exposed to untoward risk. A data safety monitoring board may suspend a study early if there are concerns about human subjects’ safety or if the goals of the trial have been successfully demonstrated.

**Data safety monitoring plan (DSMP)** This is a plan designed to make certain that clinical trials have appropriate oversight and monitoring of their conduct. The purpose of a data safety monitoring plan is to ensure the safety of human subjects and to ensure the integrity and validity of trial data.

**Declaration of Helsinki** This is a manifesto published in the 18th world medical assembly in Helsinki, Finland in 1964. The Declaration of Helsinki covers...
ethics of biomedical research involving human subjects. Key principles of the declaration of Helsinki to ensure human subjects safety include documentation of valid informed consent and review by an ethics committee.

Demographic data These key features are characteristics of study groups which are pertinent to clinical trial study findings and include items such as gender, ethnic origin, age, medical history, family history, and social history such as occupation or smoking history of participants.

Deviation This is an isolated departure from an IRB protocol and tends to be unintentional. It is often identified retrospectively, after an event has occurred.

Device Devices are used to diagnose or treat or prevent disease and do not achieve their action through chemical means or by altering metabolic function in the human body. Devices maybe tools, apparatus, machines, contrivances, implants, or reagents.

Diagnostic trial These are clinical trials designed to discover more effective or efficient diagnostic tests for a particular disease.

Double-blind study In these studies, their participants nor investigators, Borst and his staff know which human subjects are receiving investigational therapy or which are receiving placebo or standard therapy.

Efficacy This is the ability of therapy or intervention to produce a beneficial result for a human subject. The degree of benefit is defined by the protocol, and the validity of efficacy is defined by statistical criteria.

Eligibility criteria These are criteria defined in the protocol, such as inclusion criteria and exclusion criteria, to allow investigators to determine which screened volunteers may participate in the study.

Endpoint This is the final outcome mentioned in the protocol which the study is attempting to evaluate.

Exclusion/inclusion criteria These are demographic and clinical criteria which determine whether the subject maybe eligible to participate in the clinical trial or maybe excluded from such participation. Typical inclusion and exclusion criteria may include subject age, gender, pregnancy status, presence or degree of disease, prior treatments, concurrent medical therapies, and confounding medical conditions.

Food and Drug Administration (FDA) This is a branch of the Department of Health and Human Services in the United States and is primarily responsible for protecting the public by ensuring the safety and efficacy of all Biologics drugs vaccines medical devices and in safeguarding nation's blood supply.

FDA form 1571 This form tabulates the commitments required by the study sponsor for drug or biologic therapy.

FDA form 1572 This form numerates the commitments and conduct required by the principal investigator performing a drug or biologic study.

Good clinical practices (GCP) These are internationally recognized standards for the ethical conduct of research involving human subjects. The chief aims of GCP standards are twofold: to protect human safety, and to ensure data integrity.

Good laboratory practices (GLP) These are internationally recognized rules for ensuring the quality, integrity, and reliability of data from non-clinical safety studies.
**Good manufacturing practices (GMP)** These are internationally recognized rules for the manufacture of pharmaceuticals or food products that meet high quality standards and do not pose a hazard to consumers or the public.

**The Health Insurance Portability and Accountability Act of 1996 (HIPAA)** This legislation is establishing standards in the United States for electronic healthcare transactions and it gives national identifiers for healthcare providers, health plans, and employers. The purpose of the act is to regulate and ensure the security and privacy of health data.

**Human subject** Also known as a participant or a volunteer or a patient, the human subject is an individual participating and a clinical research trial.

**Hypothesis** Theory is being tested in a clinical investigation.

**Informed consent** This is a verification of a human subject’s willingness to participate in a clinical trial. Informed consent involves more than a document, rather, it is a process of ensuring that the investigator subject is fully informed of all potential risks and benefits of participating more/not participating in the clinical trial. Participation in clinical trials is strictly voluntary and maybe withdrawn at any time and this should be explicitly discussed during the informed consent process. Informed consent is not static. It may change as new information develops during the course of the trial.

**Informed consent document (ICF)** Also known as the informed consent form (ICF), this is a document. By the sponsor as part of the protocol is provided to investigators and subjects for discussion and verification of the informed consent process. He informed that the consent document must describe the types of human subjects participating in the trial, have specific information about the study such as its purpose blank and interventions required during the study. It should contain contacts of key individuals involved in the study as well as the risks and potential benefits of participating in the trial. If subjects agree to the contents of the informed consent and the discussion they will be asked to sign the document. Subjects must know that participation in the trial is voluntary and subjects may withdraw at any time without any penalty or loss of benefit rights to which they are entitled.

**Institutional Review Board (IRB)** This is an oversight committee which reviews clinical trials to make sure that they are conducted in an ethical manner which protects the rights of participating human subjects. The Board consists of a committee of community members, researchers, statisticians, and physicians. In addition to being responsible for determining whether a trial may be approved, institutional review boards also have a responsibility to periodically review research, for example on an annual basis, to ensure that the rights of human subjects during the course of the study are protected.

**Intent to treat** This is a trial data analysis which includes results from study participants even if they did not receive treatment.

**International Conference on Harmonization (ICH)** A consortium which has developed global standards on the conduct of clinical research involving human subjects. The purpose of the ICH is to meet or exceed standards in all member nations to allow subject safety, data integrity, and data validity to be streamlined and to prevent inefficiencies and duplications across study sites.
Investigational device exemption (IDE)  This permits an approved investigational device to be used in a clinical trial to collect safety and efficacy data. An approved IDE allows a device to be legally shipped to sites conducting investigations without violating other laws under the Food, Drug, and Cosmetic Act (FD&C Act) which prohibits commercial distribution of unapproved devices.

Investigational new drug (IND)  This is an application submitted to the FDA requesting permission for human subject testing of a new biologic, antibiotic, drug, or application of a biologic product used for in vitro diagnostic purposes.

Investigator's brochure  This is a compilation of all pertinent clinical and non-clinical data compiled in a trial of a drug biological or device at the study site by the principal investigator.

In vivo  This is testing in living organisms such as animals, or human subjects.

In vitro  This is testing outside of living organisms such as a test tube, petri dish, tissue culture, or organ culture.

Joint Commission on Accreditation of Healthcare Organizations (JCAHO)  This is a non-profit US-based organization that accredits and certifies healthcare organizations. It is governed by a 28-member board which includes physicians, nurses, healthcare consumers, medical directors, labor representatives, ethicists, educators, and employers.

Meta-analysis  This is a statistical analysis derived from pooled data of similar studies to measure an effect which might be difficult to measure from the results of a single study. The purpose of meta-analysis is often to generate new hypotheses for further studies.

Multicenter trial  This is a clinical trial with a single protocol which is conducted at multiple sites with multiple independent investigators. Multicenter trials may occur in one country or maybe worldwide.

National Institutes of Health (NIH)  This is one of 11 agencies of the Department of Health and Human Services which is responsible for finding basic science clinical research and conducting studies including the funding of multicenter national clinical studies.

National Cancer Institute (NCI)  This is one of 11 agencies of the Department of Health and Human Services charged with cancer research and training.

New drug application (NDA)  This is a petition submitted by a sponsor to the FDA for market approval of a new drug designed for human use in interstate commerce in the United States.

Observational study  This is a trial which does not involve any intervention or therapy. In studies, disease processes are allowed to be involved actually, and statistical analyses are used to determine whether characteristics separating one group from another are related in any way to health outcomes. Examples of observational studies include case-control studies and cohort studies. One study for example compared the diet history of hospitalized patients with melanoma to hospitalized cancer patients without.

Off label use  This is the practice of using a drug device for a condition other than that which is approved by the FDA.
Office for human research protections (OHRP) Under the umbrella of the Department of Health and Human Services, the OHRP is involved in protecting the rights, welfare, and wellbeing of human subjects involved in research supported by DHHS. It is also involved in compliance oversight, and regulatory oversight human clinical studies.

Open label trial This is a clinical trial in which investigators and subjects are aware of the treatment or intervention at the time it is being given.

Orphan drugs These are therapies designed to treat rare diseases. When the sponsor or manufacturer is given an orphan drug status for investigational product, he receives special incentives to bring its therapy to market.

Outcomes study This is a type of trial that assesses the effects of a medication or intervention on study subjects. Interventions may include drugs or treatments with devices, and outcomes may include changes and extent of disease, patient morbidity, or mortality.

P value This is a statistical value which represents the probability of the null hypothesis being true. Standard value of $P$-value $<0.05$ means that the probability of the null hypothesis being true is less than 5%.

Parallel study A parallel study evaluates the results of an intervention on two distinct populations of patients.

Pharmacology This is the discipline studying the effects of drugs on living tissues and organisms. Pharmacology studies how drugs interact with biological processes to lead to a change in function.

Pharmacodynamics (PD) This is a study of the relationship between the concentration of a drug at its site of action, and its effects.

Pharmacokinetics (PK) This is a study of the time course of drug or vaccine absorption, distribution, metabolism, and excretion and a cell, tissue, or living organism.

Pharmacovigilance This is an evidence-based process of assessing the effects of a medication, biological product, alternative medicine product, and traditional medicine product after market approval. Information on adverse effects is collected from healthcare providers and patients in the community. Collated data are then scrutinized for hazards and the information is disseminated to prevent further harm to patients. Sometimes pharmacovigilance results in withdrawal of an approved medication if it is determined that continued use presents a serious hazard to the public.

Phase 0 clinical trial This is a study where there is human exposure to minute doses of study drug, with no expected therapeutic goal. Examples of phase 0 trials include microdosing trials and screening trials.

Phase 1 clinical trial This trial often involves a small number of patients around 20–80 and is also called a dosing study. In phase 1 trials, volunteers may be healthy or may have a disease that is being targeted by the therapy. A phase 1 clinical trial typically evaluates different routes of administration of an intervention, timing of doses, as well as safety.
Phase 2 clinical trial  This phase of clinical research assesses safety and efficacy. In phase 2 trials, a significant proportion of the study population contains a disease of interest for which the therapy is being used. Phase 2 clinical trials are slightly larger than phase 1 clinical studies and may involve 100–300 subjects.

Phase 3 clinical trial These are larger clinical trials encompassing 1,000–3,000 subjects or more and may be carried out at multiple institutions or clinics in one country or globally. Phase three clinical trials typically compare a new intervention to the standard of care and assess safety efficacy and adverse events.

Phase 4 clinical trial These are trials conducted after market approval and are used to refine understanding of therapy including its risks, benefits, and ideal use.

Pivotal study This is typically a phase 3 clinical study which contains the data used by regulatory agencies such as the FDA when making a decision for marketing approval. Pivotal studies tend to have excellent controls, randomization, and tend to be double blinded.

Placebo This is an inert or inactive treatment which has no pharmacologic therapeutic value. It is given as a sham intervention in order to compare its effects to the experimental therapy.

Placebo-controlled study In this type of study, there are two groups of subjects: one group is administered a sham intervention (placebo), the other group is given an active drug or therapy. The two groups are compared to see if the active drug is more effective than the placebo.

Placebo effect This is a favorable physical or psychological outcome of a sham intervention that occurs outside of any special property of the inert substance or interactive therapy given. The placebo effect may occur because of expectations of improvement by the subject, or by the investigative team.

Preclinical studies These are studies performed in the laboratory either in vitro or in animals before a drug or device is tested in human subjects.

Prevention trials These are trials conducted to prevent the appearance of the disease and subjects who are healthy to prevent the recurrence of the disease and subjects who are in remission. Interventions in prevention trials may consist of pharmacologic therapies, alternative medicine, vaccines, or lifestyle changes. An example would be a prospective trial looking at the effects of sunscreen use on the prevention of skin cancer.

Principal investigator (PI) This is the individual and investigative site responsible for the conduct of a clinical trial according to the protocol and according to good clinical practices. If there are number of clinicians (sub-investigators or sub-Is) at a particular site, the investigator who is the leader of the team would be called the principal investigator.

Prospective study This is a trial in which study subjects receiving treatment or intervention is assessed over time to evaluate their outcomes according to criteria or endpoints delineated in the protocol.

Protected health information (PHI) This is an individually identifiable health information, including demographic information, relating to a subject’s physical or mental health. PHI needs to be de-identified if it is to be disclosed electronically without violating HIPAA. Identifiers such as names, geographic location, dates, and social security numbers.
**Protocol** This is the template upon which a clinical trial is based. The protocol establishes a rationale for a particular study and is designed with the primary focus being the protection of the health and safety and ethical rights of human subjects. Protocol is designed to answer a specific research question and does so with a clear description of the type of study being conducted, all study procedures, all medications and devices, all doses, inclusion and exclusion criteria for all subjects, details regarding informed consent, study end points, and the duration of the study.

**Quality assurance (QA)** This is the practice of ensuring optimal quality of product in pharmaceutical development through SOPs and practices which address every stage of the process from resource acquisition, to product manufacture and delivery.

**Quality control (QC)** This is the practice of testing sample batches of product in pharmaceutical development and comparing them to the desired or optimal specification.

**Randomization** This is a statistical method of assigning study subjects into different treatment groups in order to eliminate selection bias.

**Randomized trial** This is a trial in which study subjects are assigned by random chance to one or more treatment arms of a clinical trial. This allows investigators to test different treatments in similar subject populations.

**Report of prior investigations (ROPI)** This is included in all IDE submissions and contains relevant literature surveying all prior clinical, animal, and laboratory testing of the device.

**Retrospective study** In these trials, subjects have already been treated and their data are selected from experiences and outcomes that they have had in the past. Retrospective studies are often plagued with bias because investigators can select patient populations with known outcomes.

**Screening trial** These are clinical trials designed to test methodologies for the diagnosis of a disease.

**Side effects** These are harmful undesired effects and investigational drug or device. Drugs and devices must be evaluated for immediate, short-term, and long-term side effects.

**Serious adverse event (SAE)** This is any study related event which can result in death, a life-threatening situation, hospitalization, or prolonged hospitalization disability incapacity or congenital defect in study subjects or their offspring.

**Single blind study** In this type of trial, participants are unaware of the intervention or drugs they are receiving, while the investigator or the investigative team is aware.

**Source documentation** This is the first place where data are recorded. Source documents can be original data, certified copies of data or observations, or any other information necessary. Henry constructing and evaluating the events occurring during the conduct of the study.

**Sponsor** This is an individual, group, or organization that funds and manages a clinical trial. To avoid conflict of interest, the sponsor may not directly conduct the investigation.
**Standard operating procedures (SOP)** These are specific written instructions for the management conduct of a clinical trial and are designed to ensure consistency and efficiency.

**Statistical significance** This is the probability that observed difference occurred by chance alone. And in clinical trials, statistical significance is dependent on the size of the population studied, as well as the size of the differences being measured.

**Statistician** An expert in statistics. And in most trials, statisticians play a key role in the early stages of design of trial. On going statistical methodology can make the difference between a successful and an unsuccessful trial. Furthermore, one of the principles of ethics of conducting a clinical trial is to minimize harm to subjects in society and to maximize benefit. Statisticians play a central role in determining optimal participant size in a clinical trial.

**Study endpoint** This is a clinical outcome point designed to assess the safety or efficacy of an intervention.

**Surrogate endpoint** This is a biomarker or some other substitute for a clinical endpoint. A surrogate endpoint should have demonstrated validity in predicting a clinical endpoint.

**Suspended** This is when a study has stopped recruiting participants early, but may start doing so again in the future.

**Terminated** This is when a clinical trial has ended early and is not starting again. Subjects are not offered further study-related examinations or therapies.

**Toxicity** This is an adverse effect caused by a therapy which is harmful to the participant's health. Toxicity may be related to the active investigational product as well as the health of the participant. Depending on the severity of the disease being studied, a certain level of toxicity may be acceptable.

**Withdrawn** This is a type of recruitment status, indicating that a clinical trial has ended before enrolling any participant.
Index

A
Abrams, M., 168
Actinic keratosis (AK), 70, 81
Active Unique Investigators Filing
Form 1, 294
Adams, D.R., 188
Adams, V., 260
Adult and pediatric clinical research
ethical and federal standards, 161–162
RCTs, 161
Adverse event
description, 102
IND safety reports, 103–104
“life-threatening”, 103
reaction, 104
tracking log, 295
Agarwal, S., 24
Agner, T., 248
AK. See Actinic keratosis (AK)
Alam, M., 74, 262
Alexiades-Armenakas, M., 69
Anderson, B.E., 188
Anderson, K., 262
Anderson, L.L., 31
Apremilast, atopic dermatitis, 233
Arlette, J.P., 18
Armstrong, A.W., 153
Arndt, K., 69
Assent process, pediatric
child/adolescent, 162
informed consent, 170
IRB requirements, 216
Assessment and Accreditation of Laboratory
Animal Care International
(AAALAC) guidelines, 146
Astrup, A., 16
Audits
FDA guidelines, 218
good note taker, 217
‘high enrollers’, 216
inspectors, 219–220
investigator, 218
Notice of Inspection on FDA Form 482,
218–219
preparation, 217
protocols review, 219
study-related, 218
Autoimmune bullous dermatoses, 266–267
Autonomy
monetary incentives, 147
patients’ personal and best interests, 147
pediatrics
informed consent process, 168
participation, 169
placebo control groups, AAP, 169
prisoners, research subjects, 148
prison systems, 148

B
Bachmann, M.F., 8
Bailly, J.S., 23
Balkrishnan, R., 191
Barankin, B., 143–157
Barcat, D., 188
Bauer, J., 170
Baum, B., 162
Baumgaertner, P., 8
Beauchamp, T., 146
Bebo, B.F. Jr., 261

© Springer International Publishing Switzerland 2015
A. Nasir (ed.), Clinical Dermatology Trials 101: A Primer for Dermatologists,
DOI 10.1007/978-3-319-09027-6
patient care, 268–269
percentage of world population, 266, 267
pet theories/methods, 274
resources allocation, health care, 247–248, 252–253
speaking engagements, 268
Clinical research associate (CRA)
description, 279
and MRA, 29–30
protocol deviations, 65
site selection process, 33, 34
Sponsor Team, The, 29–30
Clinical research coordinator (CRC)
and CRA, 29
description, 64
monitoring, 102
protocol-specific training, 270
salaries, 116
support staff, 90
Clinical trial budget
activities, 115
checklist, 118–119
CRO, structure, 119
data collection and management, 116
description, 309–315
equipment and storage, 120–121
factor, 120
laboratory cost, 116
PICAS, 120
recruitment phase costs, 93
research coordinator salaries, 116
sponsors, 118
study start-up costs, 117–118
techniques, 120
Clinical trials
ACRP, 75
actinic keratosis, 81
advantages, training, 42–43
adverse event, 102–104
advertising, 99–101
ancient origins, 1–2
antibiotics, 5–6
anti-kickback statutes and stark law, 41
Avicenna, 4
biased knowledge, 177
bias trial results, 185
billing, 91
blood and circulation, 4
budget (see Clinical trial budget)
characteristics, 190
contract, 121–131
CRC, 74–75
CROs and SMOs, 41–42, 82
dermatology (see Dermatology)
device (see Device clinical trials)
drug development, 14–18, 24–26
drug storage and accountability, 108
equipment, 75
ethical feasibility, 114
factors, site selection, 31–32
feasibility, 32–41, 80
financial disclosure form, 289–290
financial perspective, 131–132
Food and Drug Act, 7
Galen, 3
global investigative site landscape, 74
Hippocrates, 3
Imhotep, 2
improvement, 191–192
indemnification, 14
informed consent, 97–99
initiation visit, 93
investigator, 113
investigator-initiated trials, 76
investigator responsibilities, 85–88
IRB, 88–90
medical device trials, 12–13
middle ages, 4
monitoring, 102
observational plan, 21, 184
patient database, 76
patient perspective, 155–156
pharmaceutical research, 6–7
PI qualifications, 28
pre-study visit/site qualification visit, 91–92
project management tips, 110
protocol design, 7–12
psoriasis, 16
quality assessment, 184
RCT, 22–23
record keeping, 104
registered physicians, 74
regulatory binder
authority log, 105
contents, 105
ICH GCP guidelines, 104–105
IRB approval, 106
lab certificates/reference ranges, 107
protocol deviations and violations, 106–107
screening, 105
reproducibility, 185–187
research study designs, 21–22
scientific feasibility, 113
scurvy, 4
Shen Nong, 2–3
site adequacy, 28–31
Clinical trials (cont.)
- site management organizations, 76
- site monitoring visits, 114
- smallpox vaccination, 5
- SMOs and TMOs, 73–74
- SOPs (see Standard operating procedures (SOPs))
  - space, 75
  - sponsors, 73, 76, 82, 279
  - start-up checklist, 290–291
- study feasibility checklist
  - administrative support, 83
  - compliance, 83
  - coordinates monitor activities, 84
  - manages logistics, 84
  - protective equipment, 83–84
- study flow and tracking, 90–91
- study subject recruitment, 93–97
- study subject retention, 108–109
- Sushruta, 3
- training and certification, 77
- US drug law, 26–27
- web advertising, 102
- worksheets, 91

Clinical trials contract
- agreement termination, 126–127
- anti-Kickback legislation, 121–122
- confidentiality, 125–126
- CRO, 127–129
- eCRFs, 124
- facilities letters, 123
- hospital laboratory services, 124
- indemnification clause, 122
- medicare and billing, 121
- medicare/medicaid, 124
- patent and inventions clauses, 122
- payment schedules, 121
- pharmaceutical company, 123
- publications clause, 122
- SMO, 129–130

Code of ethics
- ethical dilemmas, resolving, 144
- medical associations, 144
- Nuremberg Code, 144–146
- Cognetta, A.B., 69

Collaborative Institutional Training Initiative (CITI) program
- GCP training, 321
- standard web-based training courses, 271

Collyer, J., 262

Community research, 263

Comparative effectiveness research (CER)
- ARRA demonstration, 260–261
- diabetic foot ulcers, 262
- noninferiority thresholds, 263
- PhIRD-SD, 243–244
- psoriatic arthritis, 262
- systematic collaborations and reviews, 262
- therapies evaluation, 261

Conducting research studies, 14, 61, 139, 268
Connelly, E.A., 162

Consent. See also Informed consent
- assent process, 170
- by proxy, 169–170

Consent regulation
- Belmont Report, 136
- components, 137, 138

Contract research organizations (CROs)
- cost, patient per phase, 128
- and CRA, 29
- feasibility, 32
- institutional and community practice sites, 42
- medical monitor, 30
- and MRA, 29–30
- pharmaceutical companies, 127–128
- pharmaceutical company/sponsor, 128
- site management responsibilities, 129
- and SMO, 33
- and sponsors, 30
- worldwide employee size, 129

Cook, B., 248
Cowpox scabs, 163
CRA. See Clinical research associate (CRA)
Craig, S., 260
CRO. See Contract research organizations (CROs)
Cutaneous leishmaniasis (CL), 178

D

DAILY. See Disability-adjusted life year (DALY)
Datta, S.K., 248
Day, R.M., 234
DeGroot, J., 23
de Korwin-Krokovski, J.D., 188
Dellavalle, R.P., 178
Dermatological photographs
- GP, 209, 210
- mobile devices, 209

Dermatology. See also Randomized controlled trials (RCTs)
- academic vs. nonacademic, 56
- biostatistical consultation, 48
- budget and contract development, 51
- clinical trial conduct, 51–52
- code of ethics, 143–146
crossover design, 48
data analysis, 55
description, 143
enrollment visit, 53
IND, 50
IRB, 49–50
NDA, 55
placebo-controlled trial, 48
“practice” and “research”, 47
protocol, 49
recruitment, appropriate subjects, 52
regulatory issues, 51
resources, clinical trials training, 56
review publication, 55
safety and data monitoring, 54
screening, 52–53
skin, 47–48
study visits timing, 54
Dermoscopy, 197–198
Device clinical trials
AK, 70
cases and controls, 60
CIRB model, 65–66
class I and II, 63
CRA, 65
CRC, 64
and drug, 63
GCP, 64
IIS, 70
IND and FDA, 61–62
interventional study, 60
IRB, 65
MSL, 67–68
observational study, 59–60
office-based, 66
pharmaceuticals, 61
PMN, 63
prospective clinical investigators, 64
protocol items, 71
registry, 66–67
reporting requirements, 66
retrospective studies, 60
sponsor, 61
SQS, 66
steps, beginning study, 68
types, 61
Di Chiaccio, N., 208
Diepgen, T.L., 248
Digital cameras
DSLR, 196–198
PAS, 196, 197
Digital epiluminescence microscopy, 197–198
Digital single-lens reflex (DSLR) cameras
blurring, foreground scene, 196, 198
camera settings, 203–204
description, 196, 197
lenses with varying ability, optical
zoom, 200
macro lens attachment, 196, 202
Diot, E., 188
Disability-adjusted life year (DALY), 253
Doussau, A., 188
Dover, J., 69
Doyle, R., 24
Drug development
big data, 17
efalizumab, 18
FDA, 14, 24
FDA Amendments Act, 25–26
GLP, 24–25
ICAM-1, 15
medication research, 14
melanoma and Parkinson’s disease, 8–10, 18
nanotechnology, 15
PDUFA, 14
post-marketing surveillance, 25
regulatory agencies, 17–18
safety and efficacy, 25
Drug Shipment Receipt Log, 296
Drug storage and accountability, 108
DSLR. See Digital single-lens reflex (DSLR) cameras
Duarte, A.M., 162
Duffin, K.C., 261
Dummer, R., 8
Du Pasquier, R.A., 18
Durant, C., 188
E
EASI scores per Cohort over time, 235
Eczema education, 248
EDC. See Electronic data capture (EDC)
Edison, K.E., 248
efalizumab, 7, 15, 18
Eichenfield, L.F., 161–174
Eichenfield, L.F., 248
Efalizumab, 7, 15, 18
EIR. See Establishment Inspection Report (EIR)
Electronic case report forms (eCRFs), 124
Electronic data capture (EDC)
lifesaving trials, 240
physical requirements, 65
pros and cons, 240
Eliason, M.J., 34
Emanuele, E., 177–193
Engasser, H., 248
Enokihara, M.Y., 208
Establishment Inspection Report (EIR), 220
### Ethical issues
- Confidentiality and adverse events, 137
- Principles, 137
- Safety and voluntary participation, 137

### Ethical principles, dermatology
- Autonomy and beneficence, 146
- Non-maleficence and justice, 146

### Ethnicity
- Caregivers, 258
- Disease variability, 256–257

### Ethical issues
- Confidentiality and adverse events, 137
- Principles, 137
- Safety and voluntary participation, 137

### Ethical principles, dermatology
- Autonomy and beneficence, 146
- Non-maleficence and justice, 146

### Ethnicity
- Caregivers, 258
- Disease variability, 256–257

### F
- Fabbrocini, G., 208
- Fatal, P.M.L., 18
- FDA. See Food and Drug Administration (FDA)

### Feasibility
- Billing and claims, 40–41
- Budgeting, 40
- Contract and payment terms, 40
- Description, 39–40
- IRB, 38–39
- Patient population, 32
- Questionnaire, 32, 281–289
- Regulatory documents, 38
- Site equipment, 38
- Site selection process, 33, 34

### Federal regulations
- 41, 65, 139, 167
- Feldman, S.R., 191
- Fernandez, H.H., 18
- Ferris, L., 69
- Fiorentino, D., 234
- Fisher, R.A., 182
- Fitzar–Attas, C., 18
- Fogelberg, A.C., 188
- Food and Drug Act, 7

### Food and Drug Administration (FDA)
- Antibiotics, 6
- Audit checklist, 297–302
- Centers, 14
- Enforcement tools, 15
- Federal Register parts, 213
- IRB/IEC, 145
- Marketing approval, 13
- Pharmaceutical industry, 145
- Regulatory process, 213
- Resource allocation, 214
- Safety and welfare, human subjects, 213
- Statistical requirements, 5

### Gender imbalance
- Antidepressants and antiarrhythmics, women, 249
- Clinical research, 249
- Male bias and male norm, 249
- Quinacrine, uterus sterilization, 250
- Retention improvement, women, 250
- Tissue culture cells, origin, 249

### G
- Gao, X.H., 167
- Gap trials, 226–227
- Garbe, C., 170
- GCP. See Good clinical practices (GCP)
- Geiker, N.R., 16
- Geldhof, C., 8
- Gelfand, J.M., 261

### Good clinical practices (GCP)
- Clinical research trials, 28
- FDA rules, 214
- ICH, 70, 104
- Storage temperature logs, 107

### Good laboratory practices (GLP)
- 24–25

### Googe, P., 69
- Gordon, J., 62
- Goreshi, R., 235
- Gottlieb, A.B., 234
- Grach, E., 73–110, 113–132
- Grandoulier, A.S., 188
- Grattan, C., 24
- Grichnik, J.M., 69
- Gross, K., 69
- Gutkowicz-Krusin, D., 69

### H
- Hachulla, E., 188
- Hammann-Haenni, A., 8
- Hamzavi, I.H., 67
- Hanami, E., 21–43
- Hansen, C.D., 34
- Hansen, P.R., 16
- Hassan, M.N., 18
**Index**

Health and Human Services (HHS)
- covered entity, 280
- and IRB, 136
- OHRP, 138–139

Health Insurance Portability and Accountability Act (HIPAA), The
- clinical ethics, 208
- covered entity, 280
- description, 207
- and HITECH compliance, 210
- privacy rule, 66, 207–208
- security rule, 208
- subject recruitment services, 118

Health literacy, 251–252
HHS. See Health and Human Services (HHS)

Hickerson, R.P., 34

HIPAA. See Health Insurance Portability and Accountability Act (HIPAA), The

Hirata, S.H., 208
Hoesly, F.J., 62
Holbrook, J.S., 62
Hong, Y., 168
Hornblum, A., 147
Hsiej, H.J., 24
Huang, J.T., 168
Hu, C.C., 234
Hudson, M.L., 260

Human medical research
- ethical issues (see Ethical issues)
- federal agencies, 138–139
- laws, protection of, 136
- Tuskegee syphilis experiment, 135–136

Human subjects
- clinical trials, 268
- HIPAA training, 105

Huo, W., 167
Hutcherson, S.L., 34

I
- Ibler, K.S., 248
- IBM’s Watson, 17, 152, 221, 230
- Ibrahim, O., 62
- ICAM-1. See Intercellular adhesion molecule-1 (ICAM-1)

ICH. See International conference on harmonization (ICH), The

Imaging
- digital cameras (see Digital cameras)
- digital epiluminescence microscopy, 197–198

IND. See Investigational new drug (IND)

Independent ethics committee (IEC), 145, 280

Industry
- agencies, 237
- approval process, 238
- clinical drug development, phase III, 235, 236
- globalization, 244
- information technology and genomics, 244
- investors, 236
- PASI, NASI scores and DQLI, 236
- pharmaceutical companies, 238
- pharmaceutical research fund, proportion, 233, 235
- PhIRD-SD, 243–244
- Public Citizen attributes, 232
- regulatory agencies, 237
- regulatory process, 232
- risk aversion, 237
- safety culture adoption, 244
- Valley of Death phase, 231, 232

Inflammatory signals, phosphodiesterase inhibitors, 233

Informative technology, 230

Informed consent
- checklist, 308
- clinical investigations, 216
- components, 137, 138
- elements, 98–99, 215, 216
- IRB, 98, 216
- participants, clinical trial, 181
- required elements, 97
- written consent, 98

Ingraffea, A.A., 209

Innovative trials, 227–228

Institutional Review Board (IRB)
- advertisement, 89
- clinical trial setup, academic setting, 49
- criteria for approval, 140, 141
- description, 38–39
- FDA Form, 89
- individuals, 140
- informed consent form, 50
- investigator qualifications, 88
- “local” and “independent”, 88
- medical, scientific and non-scientific members, 279
- and PI, 90
- risks, 140–141
- study protocol, 89

Intercellular adhesion molecule-1 (ICAM-1), 15

International conference on harmonization (ICH), The, 39, 41, 226
Investigational new drug (IND)

drug vs. device trials, 50
and FDA, 50

Investigator initiated study (IIS), 70

IRB. See Institutional Review Board (IRB)

Isaacson, S.H., 18

J

James, R., 163
Jemec, G.B., 248
Jenner, E., 162, 163
Jensen, P., 16
Jiang, Y., 168
Jilek, S., 18

Justice, dermatology
description, 153
ODA, 154
PASI and DQLI, 154–155

K

Kabelev, N., 69
Kalb, R.E., 261
Kaplan, A., 24
Kapur, K., 248
Kaspar, R.L., 34
Khamabalia, A., 23
Kieseier, B.C., 18
Kimball, A.B., 153
Kimberly, M.B., 171
Kim, N., 234
Kim, N.A., 262
King, R., 69
Kipnis, C., 234
Kirsner, R.S., 63
Kornbrust, D.J., 34
Kostrzewa, E., 188
Krafchik, B., 23
Krejci-Manwaring, J., 191
Krueger, G.G., 261
Krueger, J.G., 234
Kumar, N., 234
Kündig, T.M., 8
Kurian, A., 143–157
Kvedar, J.C., 18
Kwasny, M., 62

L

Langley, R.G., 234
Lattouf, C., 162
Lavoisier, A., 23
Leachman, S.A., 34

Leadership
career investigative dermatologists, 269
FDA, CDER/CBHR, 269
principal investigator, 269
quality assurance, 270
Lebwohl, M., 31
Lee, T.D., 63
Lenane, P., 23
Lepreux, S., 188
Lew, M.F., 18
Lind, J., 4, 12
Lindschou Hansen, J., 248

Line extensions
adaptive clinical trials, 243
clinical trials migration, 242
FDA, 243
pharmaceutical companies, 242
Lin, J.P., 168
Li, X.D., 168
Li, Y.H., 168
Lolis, M.S., 135–141
Lowe, N.J., 227
Lowe, P.L., 227
Lugo-Somolinos, A., 21–43
Luther, H., 170

Macarthur, C., 23

Macrophotography
camera mode dial, 201
macro lens, DSLR cameras, 201
PAS, 200

Mahmoud, B.H., 67
Mahon, F.X., 188
Maintenance of Certification (MOC), 273
Makredes, M., 153
Marston, W.A., 63
Martini, M., 69
Marty, L., 248
Mather, C., 163
Matheson, R.T., 234
Maurer, M., 24
Mchepange, U.O., 168
McLean, I., 34
McLeod, M., 162

Medical ethics. See Dermatology

Medical Research Associate (MRA), 29–30, 65
Medical science liaison (MSL), 67
Mehregan, D.A., 67
Melanoma diagnosis, 208
Melgaard, A., 31
Menikoff, J., 227
Mentor

- career development, 272
- investigator turnover, 254
- MTPCI program, 271
- pediatric clinical trials, 172
- Peer review process, 272
- shortage, skilled workforce, 223

Michalany, N.S., 208
Michielin, O., 8
Mihic-Probst, D., 8
Mihm, M., 69
Mikhailov, A., 195–210
Miller, S., 260
Milstone, L.M., 34

Minimal risk standard
- categories, 167
- children risk, 167
- federal regulation codes, pediatric research, 166
- personal investigator (PI), 168
- vulnerable population, 165

MOC. See Maintenance of Certification (MOC)

Mohan, S.V., 47–56
Molho, E., 18
Molluscum contagiosum, 95
Monheit, G., 69
Monoranu, C.M., 18
Moritz, T.E., 248
Motyka, D., 248
MRA. See Medical Research Associate (MRA)

MSL. See Medical science liaison (MSL)

N

NAI. See No action indicated (NAI)

Nail Psoriasis Severity Index (NAPSI), 236, 274

Nanotechnology, 15–17, 139–140

Nardone, B., 62

National Childhood Vaccine Injury Act (NCVIA), 163

National Institutes of Health (NIH)
- free GCP training, 64
- loan repayment programs, 273
- minority investigators, 251
- and NTD, 229
- scientific record keeping, 272

National Pediatric Research Network Act, 174

Neglected tropical diseases (NTDs), 229–230, 253, 254

Nelson, D., 225

New Drug Application (NDA), 25, 55, 218

No action indicated (NAI), 220

Non-maleficence
- and beneficence, 152
- description, 151
- ethical principles, 146
- ethics committee, 153
- risks, 152

Note-to-file template, 302–303

NTDs. See Neglected tropical diseases (NTDs)

Nuremberg Code
- certification, 77
- comparison, 145, 146
- concentration camps, 144
- guidelines, 145
- informed consent, 7

O

OAI. See Official action indicated (OAI)

ODA. See Orphan Drug Act (ODA)

Office based clinical research, 71, 78

Office for Human Research Protections (OHRP)
- description, 138
- and HHS, 139

Official action indicated (OAI), 220

Off-site storage fees assessment, 315

Omalizumab treatment, 24

Ondo, W.G., 18

Orphan Drug Act (ODA), The, 154

Overseas trials
- challenges, 223
- cultural concern barriers, clinical research, 225
- drawbacks, 222
- drivers, 221–222
- health care, 226
- migration of, 221
- quality of studies monitoring, 220
- quinolone (Trovan), meningitis, 225–226
- technology, 226
- vulnerable population, 223–224

Overton, M., 21–43

Ozog, D.M., 67

P

Pace, N., 62

Paller, A.S., 168

Papp, K.A., 234

Paraneoplastic autoimmune bullous dermatoses, 267

Parental permission and child assent, 167
Participant screening/enrollment/withdrawal log, 316
PAS. See Point-and-shoot (PAS) cameras
PASI. See Psoriasis Area and Severity Index (PASI)

Pediatric clinical trials
  collaboration, 172–173
ethics and relationships, 173
mentoring, 172

Pediatric dermatological research vs. adult clinical research, 161–162
antihistamines, 195
anti-inflammatory therapy, 195
autonomy, 198–199
consent, 199–200
history of, 162, 164–165
incentivizing participation, 171
minimal risk standard (see Minimal risk standard)
tetracycline class of antibiotics, 165

Photography
  clinical (see Clinical photographs)
daguerreotype process, 195–196
dermatologic (see Dermatological photographs)
dermatological imaging (see Imaging)
patient privacy, 207–208
storing (see Storing photographs)
submission to journals, 205–207
visual context, 195

Plantar warts treatment, 167–168
Point-and-shoot (PAS) cameras
  advanced, 196, 197
  and DSLR, 196–198

Regression to the mean, 185–186, 191

Randomized controlled trials (RCTs)
  advantages, 23
  annual citations, PubMed, 179
classification scheme for bias, 178, 179
clinical trials designing, 23
dermatological conditions, 189–190
description, 22
design, blinding and implementation,
dermatology, 180
drug effectiveness, 187
eezema trial results, 178
flow chart, 180, 181
HRQoL, 187
methodological interventions, 189
negative results, 188
omalizumab, 24
systematic reviews (SRs), 179

Ranishoff, R.M., 18
Rare Diseases Group (RDG)
  Biomarker Qualification Process, 229
  FDA, 229
  product evaluation, 228
  and TRND, 228

Reda, D.J., 248

Research assessments, 28, 30
site selection process, 33, 34

Prior, J.O., 8

Protocol design
  blinding, 12
  components, 11
crossover study, 12
parallel study, 12
sponsors, 7

Psoriasis, 16
Psoriasis Area and Severity Index (PASI)
dermatologists, 154
description, 273
for psoriasis, 48
termination criteria, 11

Pullen, S., 248

Q
Qi, R.Q., 167
Quemeneur, T., 188

R
Rabinovitz, H., 69
Rademaker, A., 168, 262
Raju, S., 248

Renton, B., 69

Reda, D.J., 248

Regression to the mean, 185–186, 191

Regulatory binder table of contents, 305–306
Renton, B., 69
Research. See also Clinical trials
  academic medicine, 64
  antibiotic, 5
  CRA, 65
  marketing phase, 33
  medication, 2
  participation, 54
  pharmaceutical, 144
  SMOs, 74
  TMO, 76
Research Study Feasibility Process, 84
Research training, 90, 105, 165, 321
Resource allocation
  DALYs, 253, 254
  disease-resistant bacteria, 253
  diseases under consideration, 254
  NTDs, 253, 254
  public private partnerships, 254
  Sanofi-Aventis, 254
Roberts, J.C., 227
Robinson, S.N., 21
Robyn, P., 34
Roekervisch, E., 261
Rohane, P., 234
Rosenberg, D., 69
Rosén, K., 24
Rosoph, L., 234
Russell, K., 260

S
  Sackett, D.L., 22
  Saini, S., 24
  Samrao, A., 235
  Schaad, B.K., 16
  Schachner, L.A., 162
  Schaeverbeke, T., 188
  Schleicher, S.M., 261
  Schlesinger, T.E., 59–71
  Schmitt, J., 261
  Schneider-Hohendorf, T., 18
  Schram, M.E., 261
  Schulz, K.F., 22
  Schwab, N., 18
  Schwartz, M.E., 34
  Schwarz, K., 8
  Scervy study, 4
  Seneschal, J., 188
  Shin, D.B., 261
  Simpson, E.L., 235
  Sindowski, T., 248
  Singer, C., 18
  Site management organization (SMO)
    administrative, 11
Center Watch website, 74
cite management organizations, 130
vs. CRO, 41–42, 131
network size, 130
and TMOs, 73
Site personnel signature log, 316
Site qualification survey (SQS), 66, 69
Site temperature log, 303–304
Skills development, dermatologists, 276
Skov, L., 16
Slade, H.B., 63
Smallpox vaccination, 5
Smith, S., 262
SMO. See Site management organization (SMO)
SMOG readability formula, The, 317–318
Snyder, R.J., 63
Sofen, H., 234
Solanilla, A., 188
Solliman, T., 182
Sparsa, A., 188
Speiser, D.E., 8
Sperber, B.R., 261
Sponsor
  characteristics, 28–30
  CRAs, 29–30
  CROs, 41, 76
  IND, 61–62
  IRBs, 100
  motivation and resources, 69
  MRA, 29–30
  pharmaceutical/device, 65
  PICAS, 120
  protocol design, 7–11
  regulatory agencies, 17
  Site/Investigator feedback, 81
  SMOs, 41
Spuls, P.I., 261
SQS. See Site qualification survey (SQS)
Srivatsa, G.S., 34
Standard operating procedures (SOPs)
  emergency action plan, 79
  research staff, 78
  source document, 79
Standard operating procedures manual, 304–305
Statistics
  ethical considerations, 181
  importance, power, 182–183
  industry-funded trials, 183
  informed consent, 181
  methods, 182
  participants selection, 183
  RCTs (see Randomized controlled trials (RCTs))
  trial outcomes, 184
Staugaitis, S.M., 18  
Steinemann, J.M., 261  
Stender, S., 16  
Stevens, R.M., 234  
Stierstorfer, M.B., 261  
STOP GAP trial, 189–190  
Storing photographs  
  cataloging images, 205  
  image file types, 204–205  
Strand, V., 234  
Strober, B., 234  
Study drug dispensing verification form, 119, 307  
Study subject recruitment  
  healthcare community, 96–97  
  molluscum contagiosum, 93  
  phase costs, 93  
  post-herpetic neuralgia study, 95  
  site enrollment performance, 94  
Study subject retention, 108–109  
Subject visit tracking log, 317  
Sun, X.P., 167  
Sutton, J.P., 18  
Swanson, N., 31  
Systemic eczema therapy, 261  
Systemic psoriasis therapy, 261  

T  
Taeib, A., 188  
Teledermatology, 248  
Therapeutics for Rare and Neglected Diseases (TRND) program, 27, 228  
Thomsen, S.F., 248  
Thottapurathu, L., 248  
Tlougan, B., 168  
Toledano, A., 69  
Tosti, A., 208  
Totri, C.R., 161–174  
Toyka, K.V., 18  
Training log, 319  
Trial migration factors  
  abuses, 259  
  CER, 260–263  
  cost savings, 258  
  cultural sensitivity, 259–260  
  disease variability, 256–257  
  FDA response to overseas trials, 260  
  investigator turnover, 254–255  
  overseas growth  
    breakdown of, 257  
    drawbacks, 257–258  
    potential subjects, 256  
  protocol bloat, 255  
  recruitment, 255  
  reduced regulatory burden, 256, 257  
  technology, 256  
Trials. See Clinical trials  
TRND. See Therapeutics for Rare and Neglected Diseases (TRND) program  
Troxel, A.B., 261  
Tse, T., 227  

U  
Ulzheimer, J.C., 18  
US Drug Law  
  FDA, 27  
    timeline, evolution, 26  

V  
Vaccine Adverse Event Reporting System (VAERS), 163  
Vaccines  
  and antibiotics, 163  
  CBER, 14  
  NCVIA, 163  
Valley of Death phase, 231, 232  
von Voorhees, A.S., 261  
Varner, M., 260  
“Virus-Toxin Law”, 164  
Voluntary action indicated (VAI), 220  
Volunteer bias, 183  

W  
Wan, J., 261  
Warshaw, E.M., 248  
Warycha, M., 62  
Watson, A.J., 153  
Web advertising, 102  
Weisman, J.D., 261  
Welch, W., 18  
Wendler, D., 167  
West, D., 62  
West, D.P., 262  
Whited, J.D., 248  
White, L.E., 262  
Wiecker, T.S., 170  
Wiendl, H., 18  
Willers, J., 8  
Williams, H.C., 178  
Winkel, P., 247  
Wojton, M., 69
Index

Wolf, J.E. Jr., 18
Woodcock, J., 243
Wright, D.R., 67

X
Xiao, B.H., 168
Xiao, T., 168
Xu, L.Y., 67
Xu, Z., 31

Y
Yang, K., 143–157
Yankura, J.A., 188

Z
Zachariae, C., 16
Zarin, D.A., 227
Zeldis, J.B., 234
Zhang, L., 168
Zip Code Analysis
  Project, 263
Zithromax (antibiotic), 238
Zoom, digital cameras, 200