Clinical Research in Aesthetics Dermatology Practices

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Nuts and Bolts of Clinical Trial

All clinical investigators, sponsors, and contract research organizations (CROs) who conduct clinical studies on investigational drugs must comply with U.S. law and regulations covering good clinical practice (GCP).

GCP (Good Clinical Practice) training serves to:

- Help protect the rights, safety, and welfare of human research participants
- Ensure the integrity of clinical data on which product approvals are based

Standard Operating Procedures

a **Standard Operating Procedures (SOPs)** document is required by each research site to provide standardized written procedures that include detailed instructions to:

- Record routine operations and processes
- Help define the research site's practices
- Assure the execution of research tasks in accordance with institutional, state and federal guidance

This document should be reviewed and updated every 1-2 years

Principal Investigator (PI) the safety of all research participants is an integral responsibility

All adverse events, serious adverse events, and adverse events of special interest are to be reported to the Institutional Review Board (IRB)

IRB is an institutional entity that serves to provide ethical and regulatory oversight of research involving human participants, typically at the site level

Informed Consent Form (ICF)

The informed consent process **includes three main features:**

- **Disclosing** to potential research participants all information needed to make an informed decision
- **Facilitating the understanding** of what has been disclosed
- **Promoting the voluntariness** of the decision about whether or not to participate in the research

Phases of Clinical Trials

PHASES	PRIMARY GOALS	LENGTH	PATIENT MONITOR	TYPICAL # OF PARTICIPANTS	SUCCESS RATE	NOTES
Preclinical	Testing on non-human subjects to assess efficacy, toxicity, pharmacokinetics		Scientific Researcher	N/A		
Phase 0	Pharmacokinetic		Clinical Researcher	10		Often skipped
Phase 1	Safety & dosage	Months	Clinical Researcher	20-80 (or subjects w/ disease condition)	70%	Determines safety of drug
Phase 2	Efficacy & side effects ***End of phase 2: FDA & Sponsors determine how large-scale p3 will be	Months – 2 Years	Clinical Researcher	100s w/ disease condition	33%	Drug presumed to not have any therapeutic effect
Phase 3	Efficacy & monitoring of AE's (adverse effects)	1– 4 Years	Clinical Researcher & Personal Doctor	1000s w/ disease condition	25-30%	Drug presumed to have some effect
Phase 4	Safety & efficacy		Personal Doctor		N/A	Drug's long-term effect

Stages of Clinical Trial

Study startup – site submission of regulatory documents & CTA/budget negotiation

Participant screening/enrollment – inclusion & exclusion criteria, scheduling

Treatment administration (initial treatment, retreatment, etc.)

Maintenance - follow-up visits to be completed including data collection (i.e. questionnaires, diaries)

Study close-out – data cleaning, investigational product (IP) return/destruction, equipment returns, database lock

Drug Development Process

1. **Discovery & development** – begins in lab

2. **Preclinical research (3-6 years)** – drug undergoes lab and animal testing)

IND application
FDA has 30 days to review

3. **Clinical research (6-7 years)**

4. **FDA Review**

5. **FDA Post-market safety monitoring**

Pitfalls

- FDA / Company Audit Process
- Patient Retention

FDA Oversight

- **FDA** conducts clinical investigator inspections to determine if clinical studies are being conducted in compliance with applicable statutory and regulatory requirements
- All PIs are **required to permit FDA investigators to access, copy, and verify any records or reports made with regard to the disposition of the investigational product (IP) and participant case histories**
- This oversight function is **typically conducted by way of on-site inspections** designed to document how the study was actually conducted at the clinical investigator's site
- For **investigational drug studies, clinical investigators must retain study records for a period of two years** following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified
- The **FDA prioritizes participant safety, data integrity and transparency pertaining to financial disclosures of all research staff with regard to the sponsor company**

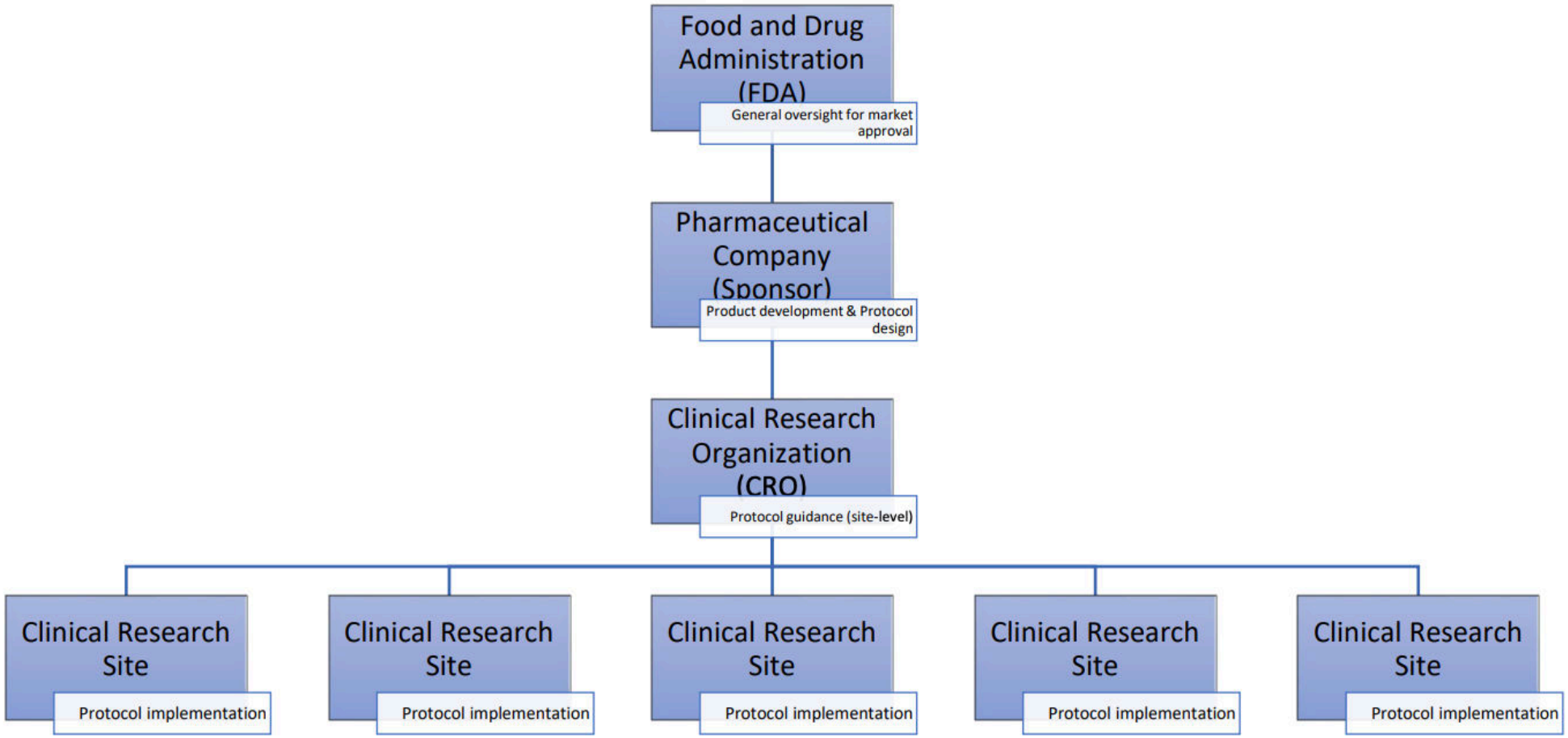
FDA Oversight

- **To best prepare for an FDA audit,** immediately notify the study sponsor
- A sponsor contact will provide invaluable guidance as well as supplementary documents, if requested
- At the end of an audit, the FDA investigator conducts an exit interview with the PI whereby a review and discussion of findings is provided
- If deficiencies were found, the PI will be issued a written Form FDA 483 which describes any inspectional observations that, in the opinion of the FDA investigator, represent deviations from applicable statutes and regulations

FDA Oversight

- If no deficiencies were found, the FDA investigator who conducted the inspection will prepare a written Establishment Inspection Report (EIR)
- This EIR will describe how there is no action indicated (NAI), which means no objectionable conditions or practices were found during the inspection
- Upon receipt of the EIR, the site is to notify the sponsor and provide update on the FDA audit findings

Clinical Trial Chain Of Command



Participant recruitment & retention

- Manage participant expectations
- Awareness of trial duration & commitment required
- Diversity of participant pool (FST & males/females)
- Participants meet all criteria per study protocol
- IRB-approved materials can be used as tools for recruitment (ads, newsletters, etc.)

On-site Monitoring

- Prior to site selection, the Clinical Research Organization (CRO) affiliated with the study will assign your site a Clinical Research Associate (CRA)
- This CRA will be your site's primary contact for guidance from start-up throughout the entirety of the trial (if selected)
- After site selection, a Site Initiation Visit (SIV) and subsequent Interim Monitoring Visits (IMVs) will be conducted on-site roughly every 6-10 weeks
- IMVs serve to provide the CRA time to review source documents and study related materials and to ensure protocol and regulatory compliance at your site
- The final study visit during the close-out stage is called the Close Out Visit (COV) whereby the CRA will ensure all final steps to end the trial have been completed

Site Feasibility

- To qualify as a clinical research site, the CRA will conduct a Pre-selection Visit (PSV) which is typically conducted on-site.
- The PSV serves to clarify the capabilities of a site for running the trial, and includes a tour of the facilities.
- If all goes well and all start-up documentation is in order, the PSV will yield a site selection letter shortly thereafter

Site Feasibility criteria includes:

- Robust and well-trained research team available to take on the following roles: a PI, a sub investigator (Sub-I), Clinical Research Coordinators (CRCs). If a blinded study, a Blinded Live Evaluator (BLE/BE), and/or an Independent Drug Reconstitutor (IDR) may also be necessary.
- Sufficient office space to conduct participant vitals, EKG, lab draws
- Sufficient and lockable space to store photography, source/regulatory binders, and other trial related equipment

Site Feasibility criteria cont'd:

- Sufficient, lockable and **completely separate** facilities to keep IP at required temperature. It is imperative to keep all study IP and IP supplies isolated from your office's product stock. This space must be monitored by a calibrated thermometer throughout the duration of the trial.
- Access to a willing and diverse patient population (all FST, male & female)
- Proximity to emergency services and/or crash cart in case of need
- All instruments must be annually calibrated

CTA/Budget

- Prior knowledge of protocol deliverables is key to negotiating a fair budget and Clinical Trial Agreement (CTA)

- Prepare a list of non-negotiable costs (i.e. storage, supply reimbursement, etc.)

- Be prepared to provide budget justification documents (if requested by sponsor)

Regulatory docs

- Trial start-up will require many regulatory documents to be reviewed and signed by PI.
- The CRO will be in close communication with you and your team to ensure all IRB documents are submitted and complete.

Virtual Tour

What are the wins from doing clinical research?


Whew!
After all that you still want to do research…???
OH YEAH!

Research Benefits

- Engaging with other top physicians and key opinion leaders in your specialty
- Behind the scenes fund of knowledge regarding new products and indications
- The opportunity to be at the forefront of your specialty
- Participants able to access cutting-edge new products/treatments