Welcome to the SWOG Fall Meeting 2026 Oishi Symposium

Chicago, Illinois



Remembering with honor and gratitude

Noboru Oishi MD

(1928 – 2020)

and

Jeri Oishi, RN

Founders of the Oishi Symposium

YOU are The ORP Committee!

"SWOG holds a fundamental conviction that the **O**ncology **R**esearch **P**rofessionals (ORP) play a crucial role in the successful development, implementation, and analysis of any SWOG clinical trial."

SWOG ORP Committee & Sub-Committees



Serving >10,000 ORPs

SWOG ORP Executive Committee

Chair: Connie Szczepanek

Vice-Chair: Dana Little



ORP Liaison

Co-Chairs:
Sandy Annis
Erin Cebula

Membership

Co-Chairs:
Anthony Hicks
Lisa Stoppenhagen

Education

Co-Chairs:
Kira Pavlik
Joyce Nancarrow Tull

Site Operations

Co-Chairs:
Connie Szczepanek
Caitlin Hutchinson
Nikki Stover
Christina Wiess

SWOG Cancer Research Network's Mission

To significantly improve lives through cancer clinical trials and translational research

ORP Committee's Mission

To support SWOG activities through promotion of integrity and excellence in clinical research through education, guidance, & collaborative contributions

ORP Executive Committee Members

Sandy Annis	Dana Little
Deb Bergevin	Jamie Myers
Annette Betley	Joyce Nancarrow-Tull
Erin Cebula	Kira Pavlik
Erin Fukaya	Lisa Stoppenhagen
Anthony Hicks	Connie Szczepanek
Caitlin Hutchinson	Nikki Stover

Join the ORP Committee

SWOG Website:
https://www.swog.org/member-resources/membership/committee-membership

Key Involvement Opportunities:

- Disease Specific Liaisons
- Liaisons at Large
- Education Team

*"SWOG holds a fundamental conviction that the **O**ncology **R**esearch **P**rofessionals (ORP) play a crucial role in the successful development, implementation, and analysis of any SWOG clinical trial."*

Welcome on Behalf of the ORP Committee!

- Chair, Connie Szczepanek, RN BSN
- Vice-Chair, Dana Little, MHA
- Committee Members:
  - Sandy Annis



Although there are no formal CE credits for this meeting,

PLEASE KEEP YOUR COPY

of the agenda to reflect your attendance

(For use with certification)

ORP Jeri & Noboru Oishi Symposium
Hyatt Regency, Chicago, Illinois
Friday, October 9, 2026 9:00 am – 11:30 am CDT

Topic	Time	Speaker(s)
Opening & Announcements	9:00 am – 9:10 am	Connie Szczepanek, RN, BSN Joyce Nancarrow Tull, RN, MSN
Medically Necessary. Standard of Care. Covered? Not Necessarily.	9:10 am – 9:55 am	Denise Quint, CPC, CHC, CHRC Denise Quint LLC *"What Research Teams Need to Know About Clinical Trial Billing"*
Quality Assurance Updates	9:55 am – 10:25 am	Laura Gonzales, RN, BSN; SWOG Cancer Research Network Quality Assurance Manager
FDA Focus & Updates	10:25 am – 11:20 am	Jennifer Adams, BS, MPH Commander, US Public Health Service Branch Chief, Bioresearch Monitoring Foreign Investigation Branch, U. S. Food & Drug Administration
Q & A	11:20 am – 11:30 am	Jennifer Adams, BS, MPH; Branch Chief Colleen E. Burke, RN, MSN; FDA Investigator Food and Drug Administration

PLEASE **KEEP** THIS AGENDA AND USE THE FILLABLE STATEMENT BELOW TO DOCUMENT YOUR EDUCATIONAL CREDITS.

I certify that I attended _____ hours of this meeting. The topics of the meeting contribute to my education and professional advancement in clinical research.

Signature _____ Date _____

Oishi Education Sub-Committee Co-Chairs:
Kira Pavlik, MPH, CCRP – kira.pavlik@yale.edu
Joyce Nancarrow Tull, MSN, RN – jntull@health.ucsd.edu

SWOG Training & Resource Announcements:

- **The SWOG ExpertusOne Learning Management System has moved to a new URL:**

  https://swog.expertusone.cloud/learner/swog/

  (login with ID.me credentials used to access NCI/CTSU secure IT systems)

- **SWOG posts the SWOG Oishi Symposium, Site Operations Meeting, NCORP Workshop and Take Action Symposium Meetings for enduring reference via ExpertusOne.**
  - Meeting materials are posted via ExpertusOne ~4 weeks after each Group Meeting.
  - After review, SWOG members can download a completion certificate to document their review.
  - You can locate online resources via keyword search within the ExpertusOne system, or
    - Refer to the: **Fall 2026 Oncology Research Professionals Resources (https://www.swog.org/fall-2026-oncology-research-professionals-resources)** for forthcoming Fall 2026 Site Operations and Oishi Symposium enduring course links.
    - Refer to the **Current List of Online Training Courses** webpage for forthcoming Fall 2026 NCORP Workshop enduring course links. Here, you can also find links to prior Group meeting materials.
- **Featured new online training course:**
  - **SWOG Specimen Labeling** : An overview of specimen labeling (for submissions to the SWOG Biospecimen Bank)

Training Resources | SWOG (https://www.swog.org/clinical-trials/training-resources)

Please join me in welcoming
our first Speaker,
Denise Quint, CPC, CHC, CHRC

Medically Necessary. Standard of Care. Covered? Not Necessarily.

What Research Teams Need to Know About Clinical Trial Billing

Denise Quint, CPC, CHC, CHRC

Jeri & Noboru Oishi Symposium | SWOG Fall Group Meeting
Friday, October 9, 2026 | 9:10 – 9:55 am CT | Regency BC, Hyatt Regency Chicago

Disclaimer

This presentation is informational only. It does not constitute legal advice.

Participants are encouraged to consult with their compliance department or legal counsel if concerns arise.

Meet your presenter



Denise A. Quint, CPC, CHC, CHRC
Principal Consultant, Denise Quint, LLC

- **40+ years in healthcare**, including three decades in research billing and hospital compliance
- **Clinical background** in cardiac catheterization and interventional radiology
- **Specialized expertise** in clinical trial billing, coverage analysis, and investigational device trials

These are the three things I hear most. None of them decides coverage.

"We always bill this and NEVER get denials."

"Other hospitals bill for this test for the same research study and NEVER have any problems! You are being so unreasonable."

"We billed and got paid, what's the problem?"

Start Here: NCD 310.1, Routine Costs in Clinical Trials

What it covers

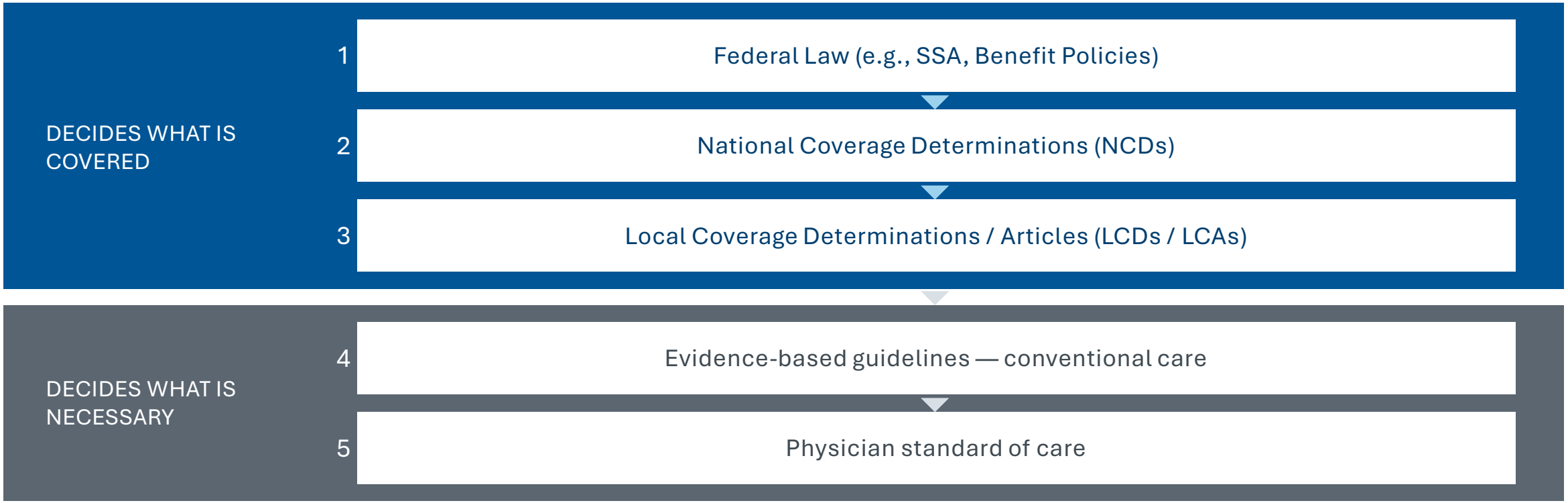
- Conventional care
- Items or services required solely for the provision of the investigational item or service;
- The clinically appropriate monitoring of the effects of the item or service;
- The clinically appropriate detection and prevention of complications; and
- Treatment of complications.

What it does not cover

- The investigational item or service itself, unless otherwise covered outside of the clinical trial;
- Items and services provided solely to satisfy data collection, not used in the direct clinical management of the patient; and
- Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial.

All other Medicare rules apply. A routine cost is the beginning of the analysis, not the end.

The Coverage Hierarchy: Start with #1



"Physician practices should remember that 'necessary' does not always constitute 'covered'..."

HHS Office of Inspector General, Compliance Program Guidance — October 5, 2000

Coverage of Drugs in Oncology Trials

Coverage of drugs in oncology trials: Three questions

Question 1 · NCD 310.1 — is it a routine cost?

"Routine costs do not include … the investigational item or service, itself unless otherwise covered outside of the clinical trial."

Question 2 · Is the drug covered outside the trial?

Question 3 · § 50.4.5 — is the off-label use covered?

"Contractors shall recognize medically accepted indications as those that: are favorably listed in one or more of the compendia listed above, or, the contractor determines from a review of the peer-reviewed literature … that it is a medically accepted indication."

NCD 310.1, Routine Costs in Clinical Trials | SSA § 1861(t)(2) | CMS Medicare Benefit Policy Manual, Pub. 100-02, ch. 15, § 50.4.5

Coverage of drugs in oncology trials: Three questions

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NCD 310.1, Routine Costs in Clinical Trials | SSA § 1861(t)(2) | CMS Medicare Benefit Policy Manual, Pub. 100-02, ch. 15, § 50.4.5

What § 50.4.5 actually says:

B. Policy: CMS is recognizing the following as authoritative compendia and listing them in Pub. 100-02 of the Medicare Benefit Policy Manual, chapter 15, section 50.4.5 for use in the determination of a "medically-accepted indication" of drugs and biologicals used off-label in an anti-cancer chemotherapeutic regimen:

- American Hospital Formulary Service-Drug Information (AHFS-DI)
- NCCN Drugs and Biologics Compendium
- Thomson Micromedex DrugDex
- Clinical Pharmacology

Contractors shall recognize medically accepted indications as those that:

- are favorably listed in one or more of the compendia listed above, or,
- the contractor determines from a review of the peer-reviewed literature as described above that it is a medically accepted indication,

unless CMS has determined that the use is not medically accepted, or any of the listed compendia list the use as not medically accepted, or words to that effect.

What happens when nothing supports the use

Wellpoint Federal (formerly National Government Services) · LCD L33394

“Upon review, if the drug use is not on the FDA label, does not appear on the American Hospital Formulary Services (AHFS), Elsevier/Gold Standard Clinical Pharmacology, NCCN Drugs and Biologics Compendium, Truven Health Analytics Micromedex DrugDex® and/or Wolters Kluwer Lexi-Drugs® compendium or National Government Services has not published an LCD or article covering the off-label use as listed below, then the drug use is not approved and the use of the drug may be denied.”

LCD L33394, Drugs and Biologicals, Coverage of, for Label and Off-Label Uses | Wellpoint Federal Administrators

Coverage of Tests and Procedures in Oncology Trials

Good Medical Practice. Still Not Covered for Everyone.

What we see in the grid

- Baseline HIV and hepatitis testing, required by the protocol for every enrollee.

Why Medicare does not pay for it

- These enrollees are not symptomatic. NCDs 210.6, 210.7 and 210.13 each carry eligibility limits a trial population does not automatically meet.
- Testing without symptoms is screening per Medicare.

“NCCN supports this testing.”

- NCCN is Step 4 — a guideline. It says what good care looks like, not what Medicare covers.
- It warns the drug may cause hepatitis.
- It’s clinically appropriate to order**. It is not appropriate to bill.**

NCD 310.1, Routine Costs in Clinical Trials | NCDs 210.6 (HBV) · 210.13 (HCV) · 210.7 (HIV)

What about the 75-year-old in your trial?

NCD 210.7 — HIV screening, ages 15 to 65

- *“A maximum of one, annual, voluntary screening for all adolescents and adults between the age of 15 and 65, without regard to perceived risk.”*

Past 65, the rule changes

- *“…for adolescents younger than 15 and adults older than 65 who are at increased risk for HIV infection.”*
- Increased risk is defined in the NCD as specific behaviors and exposures. Age alone does not qualify anyone, and neither does a cancer diagnosis.

And the benefit is one per year

- A patient inside the covered age range who already had this year's screening has used the benefit. A protocol that requires one within the last six months does not create a second one.

NCD 210.7, Screening for the Human Immunodeficiency Virus (HIV) Infection | effective 4/13/2015

A real dispute: is the baseline ECHO/MUGA billable?

The disagreement

- Sponsor's coverage analysis: routine care, bill the patient.
- Institution's coverage analysis: bill to research.
- Principal investigator: billable — it is medically necessary.

His basis: published guidance advises pre-treatment cardiac assessment because of large IV fluid volumes and routine anthracycline use.

What the protocol says

- Baseline ECHO/MUGA required at baseline/screening
- No anthracyclines — no cardiotoxic agents in the treatment plan
- No follow-up cardiac imaging required
- No LVEF-based dose modification or stopping rules
- Rhythm risk monitored by serial 12-lead EKG
- Consent does not list cardiac toxicity as a material risk

How Medicare decides something is “screening”

THE STATUTE §1862(a)(1)(A)

- Medicare generally excludes examinations performed for a purpose other than the diagnosis or treatment of a specific illness, symptom, complaint, or injury, while listing exceptions for covered preventive services.

THE NCD None for echocardiography or MUGA

THE LCD

- *“Exposure to Cardiotoxic Agents (chemotherapeutic and external) … An initial complete TTE may be performed prior to first administration of the agent …”*
- *“Myocardial perfusion studies performed based on the presence of risk factors in the absence of cardiac symptoms … will be considered screening and denied as not covered by Medicare.”*

LCDs L33577 (TTE) · L33560 (Cardiovascular Nuclear Medicine) — Wellpoint Federal, MAC Jurisdictions J-6 and J-K

How it resolved

- No follow-up imaging. No LVEF-based dose modification or stopping rules.
- The question is never “is this clinically reasonable?” It is “how does this result change management for this patient?”
- And: what covered diagnosis supports it — for every patient enrolled?
- Not billable to the patient. The baseline imaging is an eligibility screen — charge it to the study.

The echo still happens. The only question was who pays.

Documentation Must Support Medical Necessity!

The coverage analysis is permission. It is not proof.

What it does

It tells you what MAY be billed under this protocol.

It is built before the patient is ever seen. It is a document about the study.

What it does not do

It does not create a medical record.

It cannot make a service necessary for this patient, on this day. That is decided in the chart.

Permission and proof are two different documents.

Example 1 — Documentation

What the coverage analysis says: Bill to Patient

Baseline exam, ECG and echo supported for a breast cancer trial on an anthracycline regimen. Cites NCD 310.1, LCD L33577 and NCCN.

What the record shows: the research nurse's note

Patient consented for Study XYZ. Pt seen by Dr. ___ for physical exam. ***Required screening procedures performed today****, blood samples and ECG. Pt is scheduled for Echo on Monday and we anticipate completing eligibility screening next week.*

What the record does not show: the physician's intent

No physician order or note for the ECG or echo. The echo order is coded Z01.818 — and the claim pays on it.

NCD 310.1, Routine Costs in Clinical Trials | LCD L33577, Transthoracic Echocardiography | SSA § 1862(a)(1)(A)

Example #1 — Continued

What the physician note should have said for the ECG and echo to be billable:

Physician note — as it should read

Stage II breast cancer, Study XYZ regimen includes anthracyclines. Will order ECG and echo to establish baseline cardiac function before anthracycline therapy.

Diagnosis codes — supported by that note

Z01.818, Z00.6, C50.919

Reason for the test · qualifying clinical trial · breast cancer

NCD 310.1, Routine Costs in Clinical Trials | LCD L33577, Transthoracic Echocardiography | SSA § 1862(a)(1)(A)

Example #2

The justification doesn't stand on its own

Coverage analysis

TSH: Nivolumab linked to both hyper and hypothyroidism. Baseline not billable, but subsequent TSH is covered under NCD 190.22.

Use **ICD-10 Z79.899** for monitoring for chemo toxicity/complications.

Use **ICD-10 Z08** for post-treatment follow-up.

Medical record

Order says "Reason for test" is "C22.0 Hepatocellular carcinoma."

Claims scrubbed — all deleted for medical necessity. Not Covered

NCD 190.22, Thyroid Testing | ICD-10-CM Z79.899 · Z08

Example #2 — Continued

TSH during chemotherapy

Physician note: Thyroid cascade ordered to monitor for Nivolumab toxicity/complications.

Order diagnosis codes: **Z79.899, C22.0, Z00.6**

TSH post-treatment

Physician note: “Thyroid cascade ordered to ensure no toxicity/complications post Nivolumab treatment.”

Order diagnosis codes: **Z08, C22.0, Z00.6**

Same test, same patient — the covered diagnosis depends on why it was ordered that day.

Documentation

Documented "reason for exam" on CT chest/abdomen with and w/o contrast.

Good

Newly diagnosed primary CNS lymphoma. He has a dominant mass in the right thalamus/hypothalamus with 2 punctate satellite lesions. Need chest/abdomen CT to determine whether there is a metastatic source.

Insufficient

"Brain tumor"

SSA § 1862(a)(1)(A), reasonable and necessary | Documentation must support the service billed

Medical Necessity

Research Nurse note says:

Called Mrs. Smith and told her that, per study protocol, her hemoglobin needs to be above 9.2 and hers is 8.7. Dr. X says she will need a transfusion to get into the study. Patient agrees. Scheduled for a transfusion tomorrow.

NCD 310.1, Routine Costs in Clinical Trials | SSA § 1862(a)(1)(A), reasonable and necessary

Three things to take back

“It’s medically necessary.”

- Necessary is decided by the clinician. Covered is decided somewhere else, by someone else, under rules that do not care how good the medicine is.
- Ask what the service was FOR in this study — treatment, eligibility screening, or data. That decides which rule you are under.

“We have journal articles.”

- Compendial listing is what you can rest on; the literature route belongs to the contractor.
- When the rule does not reach your facts, ask the MAC. Send the journal articles from different centers — not manufacturer publications, not abstracts.

“The coverage analysis said it was billable.”

- That is permission, not proof. The record still has to say why this patient needed this service on this day.
- “Per protocol” is not an indication and an order is not a note. You control the order — flag the gap before the claim goes out.

Necessary is not covered. Standard of care is not covered.

Questions & discussion

Denise Quint, CPC, CHC, CHRC

denise@dq-compliance.com | 802-881-8721

dq-compliance.com

Thank you Denise!

Please join me in welcoming our next speaker Laura Gonzales, RN, SWOG QA Manager who comes in the spirit of ‘love and education’.

Welcome Laura!

Oishi Symposium
Quality Assurance Updates

Speaker

Laura Gonzales, BSN, MA, RN, OCN

SWOG Quality Assurance Manager

SWOG QA Audits: By the Numbers (1/1/26-9/30/26)

- 20 treatment audits (triennial audits)
- 47 LungMAP audits
- 1 S1806 audit
- 39 S2302 audits

- No audits have had an unacceptable component

SWOG QA Audits: Audit Findings

Common Major Deficiencies:

Patient Case:
Eligibility:
Tests/scans conducted out of window

Adverse Events:
Late reporting of SAEs

SWOG QA Audits: Audit Findings

Common Major Deficiencies:

Correlative Studies, Tests, and Procedures:

- Specimens not collected/submitted
- QOLs/PROs not administered per protocol

Data Quality:

- Delinquent data submission

SWOG QA Audits: Recommendations

Eligibility – Tests/Scans Conducted out of Window

- Refer to Section 5 of the protocol for eligibility criteria
- Use an Eligibility Checklist and have two people review prior to patient registration

SWOG QA Audits: Recommendations

Adverse Events - Late Reporting of SAEs

- Document date of discovery for all SAEs in RAVE
- Any questions about reporting SAEs, contact ADR@swog.org

SWOG QA Audits: Recommendations

Correlative Studies, Tests and Procedures - Specimens Not Collected/Submitted

- Refer to Section 15 of protocol
- Confirm patient consented to specimen submission
- Refer to Specimen Requirements Summary in Specimen Tracking System on CRA Workbench
- If unable to collect specimen, document in the research record and in Specimen Tracking System

SWOG QA Audits: Recommendations

Correlative Studies, Tests and Procedures – QOLs/PROs Not Collected/Submitted

- Refer to Section 15 of the protocol
- Confirm patient consented to QOL participation (if applicable)
- Generally, QOLs/PROs can be administered via phone/telehealth/mail or at next study visit
- Site staff should review SWOG: Patient Reported Outcomes Questionnaires course available in CLASS

SWOG QA Audits: Recommendations

Data Quality – Delinquent Data Submission

- Refer to Section 14 of protocol for data submission requirements
- Any questions regarding data submission in RAVE, contact the data coordinators at the SWOG Statistics and Data Management Center (SDMC) via the email listed on the Protocol Contact Information page of the protocol

Questions?

QAmail@swog.org

FDA BIMO Inspections

CDR Jennifer Adams, Branch Chief
Colleen Burke, Investigator
FDA/OII/OBMI

Agenda

- Regulatory Requirements
- The Inspection Process
- Best Practices
- Case Study

REGULATORY REQUIREMENTS

Food, Drug, and Cosmetic Act (FD&C Act)

Title 21

Code of Federal Regulations

Guidance Documents

Sponsor Responsibilities – 21 CFR 312



SELECT QUALIFIED INVESTIGATORS



MONITORING TRIAL PROGRESS



INVESTIGATION CONDUCTED IN ACCORDANCE WITH PLAN



NOTIFY OF NEW RISKS

Investigator Responsibilities – 21 CFR 312



FOLLOW INVESTIGATIONAL PLAN



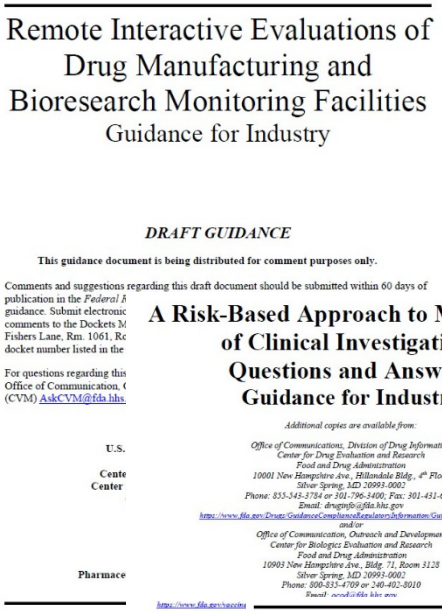
OBTAIN INFORMED CONSENT



PROTECT RIGHTS, SAFETY, AND WELFARE OF PARTICIPANTS



CONTROL INVESTIGATIONAL PRODUCTS


Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal R* guidance. Submit electronic comments to the Dockets M Fishers Lane, Rm. 1061, Rc docket number listed in the

For questions regarding this Office of Communication, ((CVM) AskCVM@fda.hhs.

U.S.

Cente Center

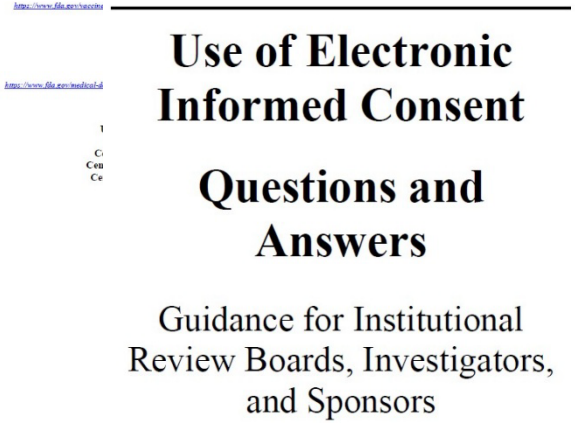
Pharmace

A Risk-Based Approach to Monitoring of Clinical Investigations
Questions and Answers
Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
and/or
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov

https://www.fda.gov/vaccine

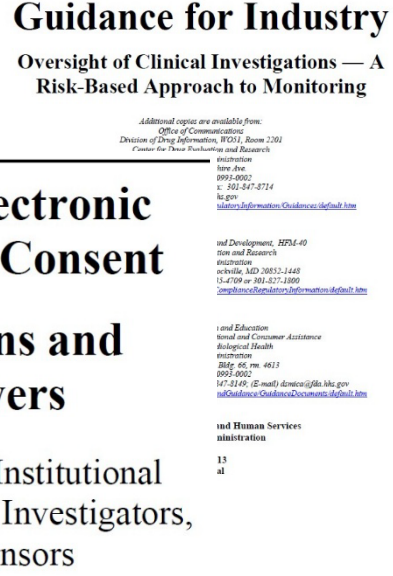

Use of Electronic Informed Consent

Questions and Answers

Guidance for Institutional Review Boards, Investigators, and Sponsors

Processes and Practices Applicable to Bioresearch Monitoring Inspections
Guidance for Industry

Additional copies are available from:
Office of Field Regulatory Operations, Office of Inspections and Investigations,
Food and Drug Administration
12420 Parklawn Drive,
Rockville, MD 20857


Guidance for Industry

Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

Additional copies are available from:
Office of Communications
Division of Drug Information, WO51, Room 2201
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Silver Spring, MD 20993-0002
Phone: 301-796-3400; Fax: 301-847-8714
Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

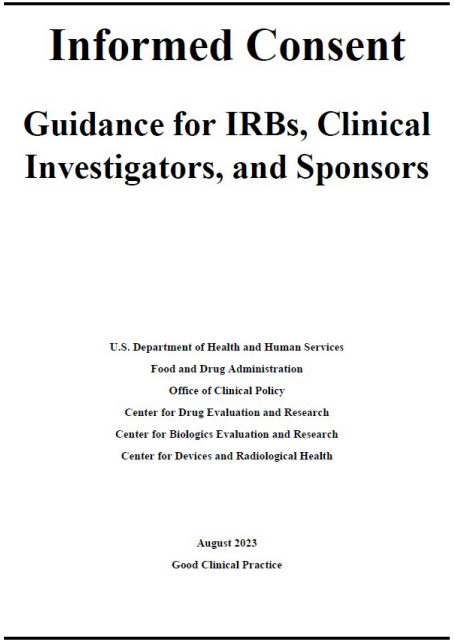
https://www.fda.gov/medical-d

Use of Data Monitoring Committees in Clinical Trials

Guidance for Industry

Additional copies are available

Office of Communications, Division of Dr
Center for Drug Evaluation and R
Food and Drug Administrati
10001 New Hampshire Ave., Hillandale


Informed Consent

Guidance for IRBs, Clinical Investigators, and Sponsors

U.S. Department of Health and Human Services

Food and Drug Administration

Office of Clinical Policy

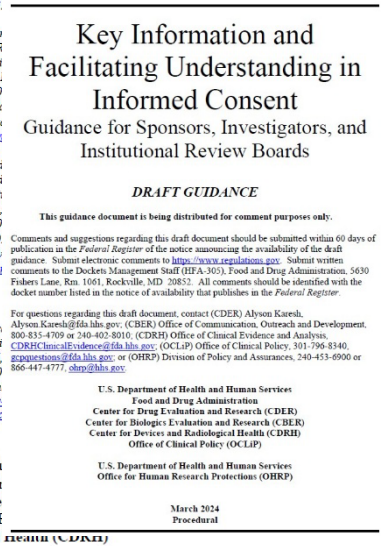
Center for Drug Evaluation and Research

Center for Biologics Evaluation and Research

Center for Devices and Radiological Health

August 2023

Good Clinical Practice


Key Information and Facilitating Understanding in Informed Consent
Guidance for Sponsors, Investigators, and Institutional Review Boards

DRAFT GUIDANCE

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Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Alyson Karesh, Alyson.Karesh@fda.hhs.gov; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; (CDRH) Office of Clinical Evidence and Analysis, CDRHClinicalEvidence@fda.hhs.gov; (OCLIP) Office of Clinical Policy, 301-796-8340, gcpquestions@fda.hhs.gov; or (OHRP) Division of Policy and Assurances, 240-453-6900 or 866-447-4777, ohrp@hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Clinical Policy (OCLIP)

U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)

March 2024
Procedural

[Guidance]

THE INSPECTION PROCESS



President Ronald Reagan (4/12/86)

"The nine most terrifying words in the English language are:

'I'm from the government and I'm here to help.'"

Office of Bioresearch Monitoring Inspectorate



Chrissy J. Cochran, PhD

Director, OBMI

David Glasgow

Deputy Director

Mishelle Harriger

DD Div 1 (acting)

Christine Smith

DD Div 2

Audrey Vigil

DD Div 3 (acting)

Audrey Vigil

DD Div 4 (acting)

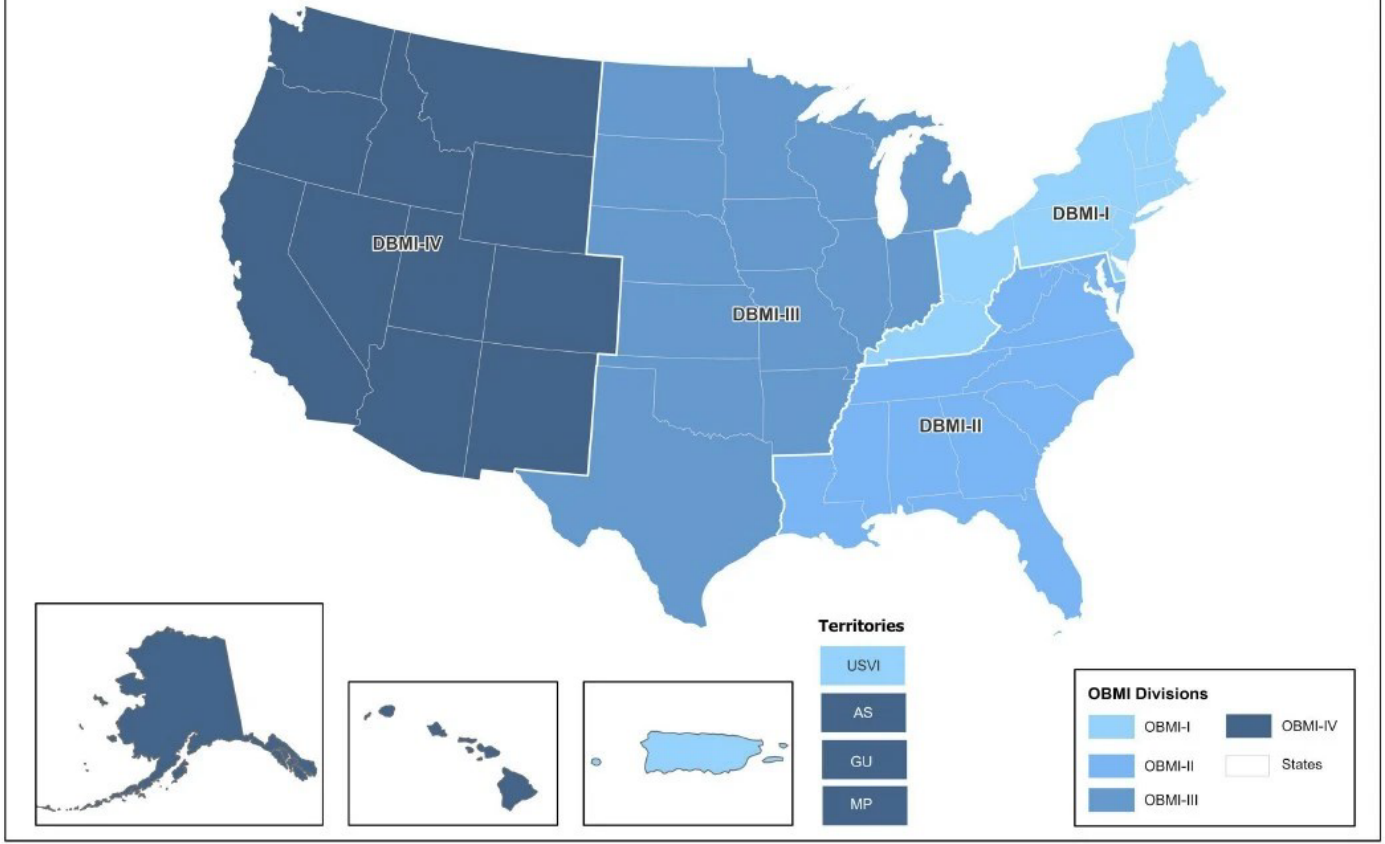
CDR Jenna Adams

Foreign Cadre Branch Chief

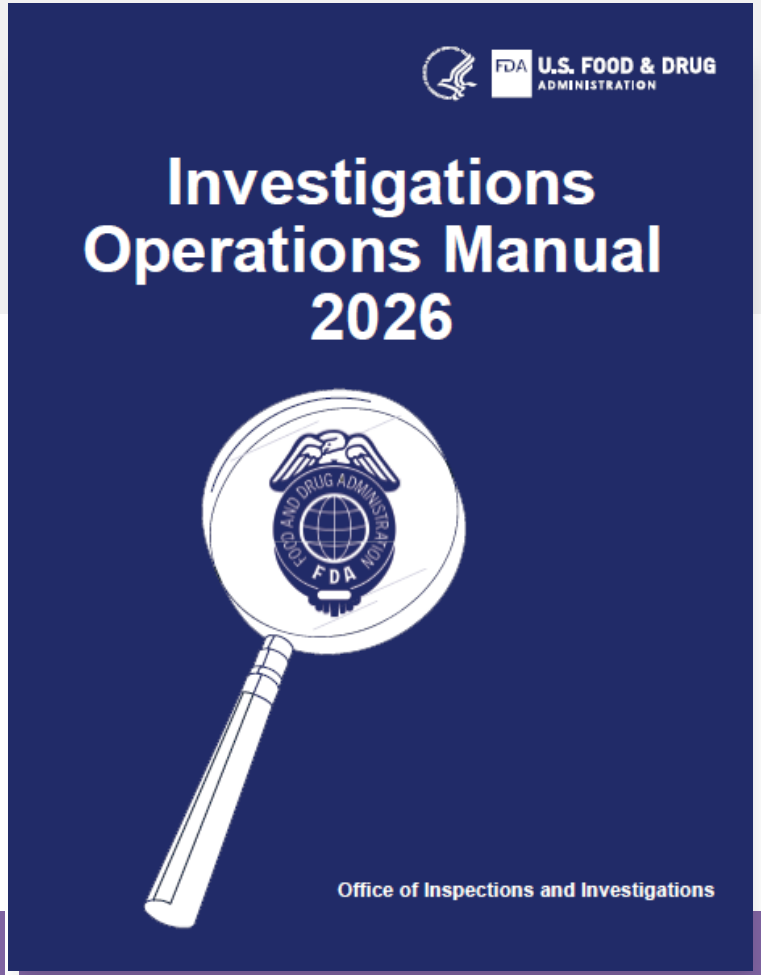
CDR Nicole Bell

Staff Director

Office of Bioresearch Monitoring Inspectorate (OBMI)



Prepared by ORA GIS Program, DAES, 2024



Know what we know…

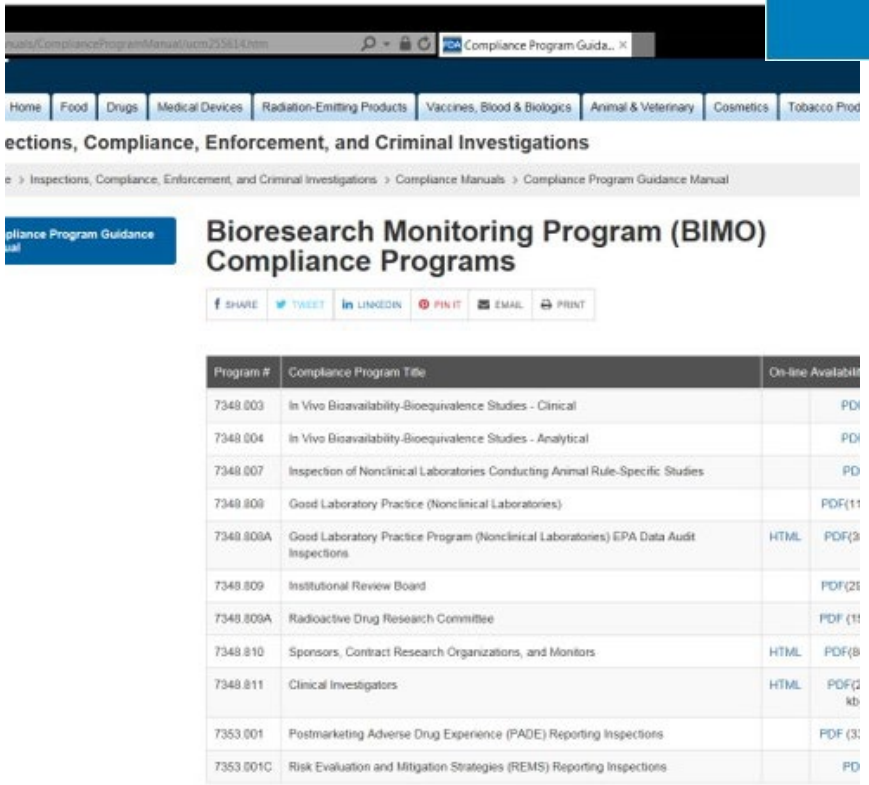
Investigations Operations Manual (IOM)

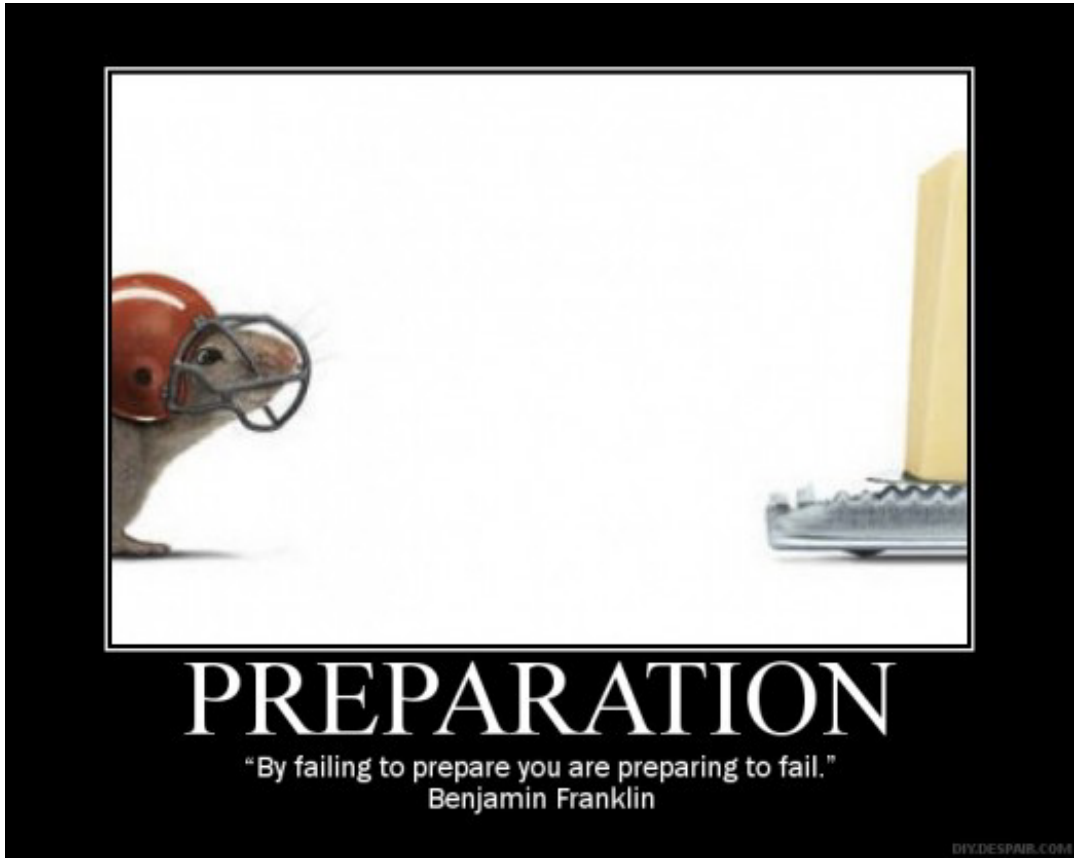
- https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/investigations-operations-manual
- Chapter 5: Establishment Inspections

Know what we know…

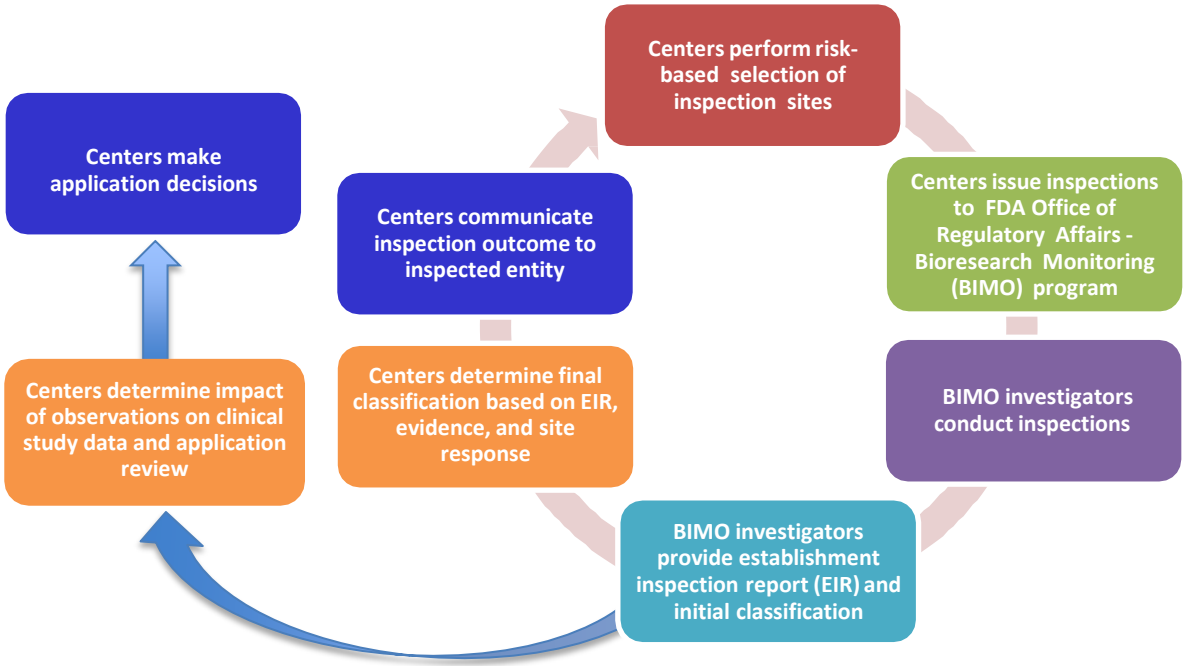
Compliance Program Guidance Manual (CPGM)

- Compilation of Compliance Programs (CPs) that supplement the IOM and provide specific procedures and guidance to staff
- https://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/ucm255614.htm




PREPARATION
"By failing to prepare you are preparing to fail."
Benjamin Franklin
DIY.DESPAIR.COM

Inspection Process



Why Me?


Application filed
Prior inspection history
Inspection
Data outliers
Complaints

Trust but Verify

Data integrity

- Can the data be relied upon?
- Support safety and effectiveness profiles?
- Fraud, recordkeeping issues?
- Failure to follow investigational plan?

Human subject protection

- Were participants informed?
- Were participants protected?

What to do when FDA calls…

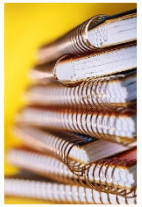
- Identify any commitments which cannot be changed (annual conferences, surgery, etc.)
- Mark your calendar
- Gather your records
- Allocate time and workspace



Scope



Facilities & Equipment



Participant Files



Communications

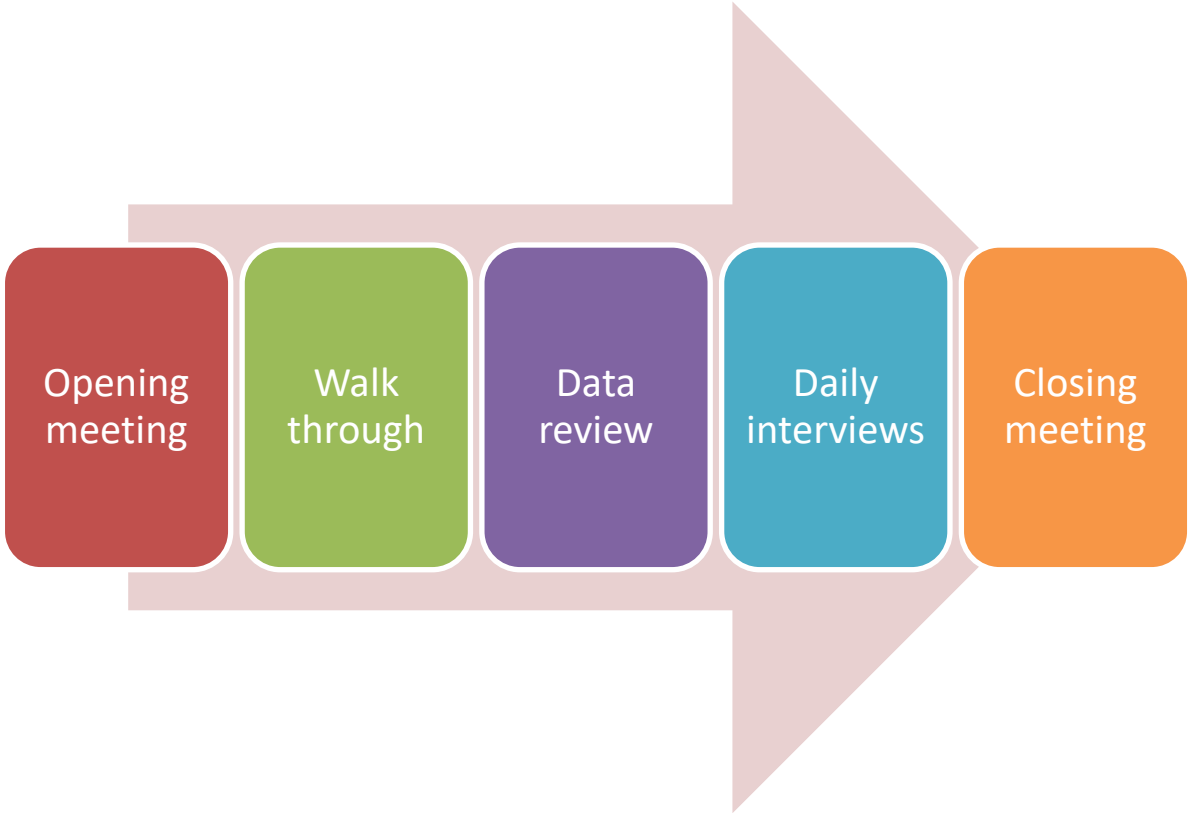


Test Article Accountability

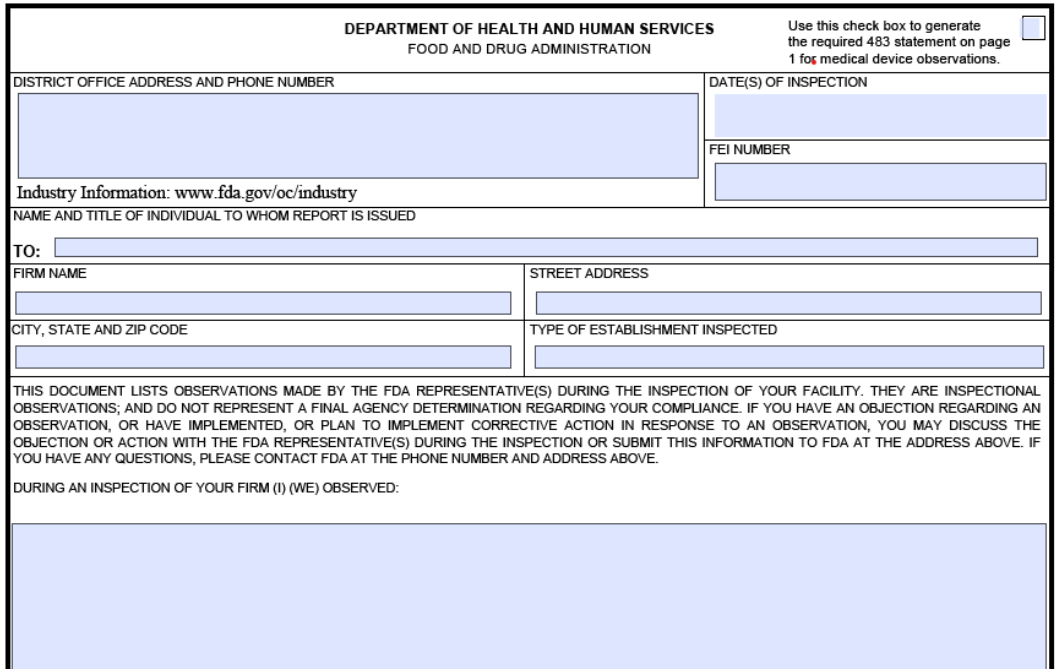


Delegation of Authority

Inspection Flow



FDA 483 Inspectional Observations



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Use this check box to generate the required 483 statement on page 1 for medical device observations.

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

DATE(S) OF INSPECTION

FEI NUMBER

Industry Information: www.fda.gov/oc/industry

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO:

FIRM NAME

STREET ADDRESS

CITY, STATE AND ZIP CODE

TYPE OF ESTABLISHMENT INSPECTED

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

- Issued at the inspection close
- Significant objectionable conditions
- Not a final Agency determination

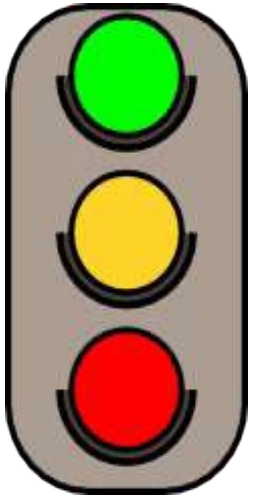
Contact Information

- Form FDA 483 response/correspondence
  - OIIBIMODivision1Correspondence@fda.hhs.gov
    - ME, VT, NH, MA, RI, CT, NY, NJ, DE, PA, OH, KY, PR
  - OIIBIMODivision2Correspondence@fda.hhs.gov
    - MD, WV, VA, TN, NC, SC, GA, MS, AL, LA, FL, DC
  - OIIBIMODivision3Correspondence@fda.hhs.gov
    - ND, SD, NE, KS, OK, TX, AR, MO, IA, MN, WI, IL, IN, MI
  - OIIBIMODivision4Correspondence@fda.hhs.gov
    - WA, OR, CA, NV, ID, MT, WY, UT, CO, AR, NM, AK, HI
- Inspection issues
  - Div 1: Mishelle.Harriger@fda.hhs.gov
  - Div 2: Christine.Smith@fda.hhs.gov
  - Div 3&4: Audrey.Vigil@fda.hhs.gov
  - Foreign Inspections: Jennifer.Adams@fda.hhs.gov



Inspection/Compliance Classifications

- No Action Indicated (NAI)
  - No objectionable conditions or practices
- Voluntary Action Indicated (VAI)
  - Objectionable conditions or practices
  - Not at threshold to take or recommend administrative or regulatory action
- Official Action Indicated (OAI)
  - Serious objectionable conditions found
  - Regulatory action recommended



BEST PRACTICES

Acceptable Subject Records are **ALCOA-C**

Attributable to the person creating the data

Legible and permanent

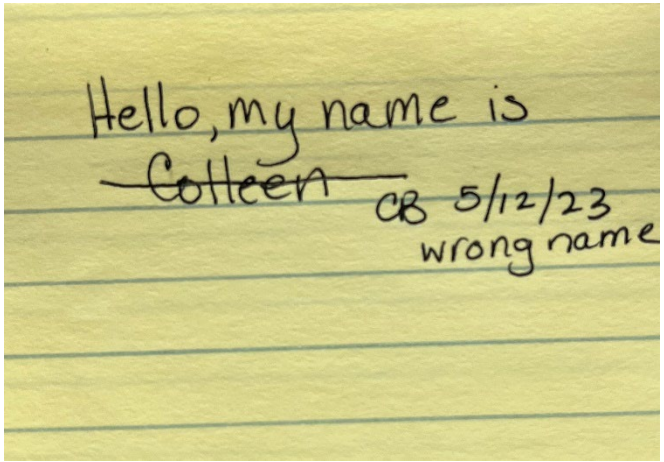
Contemporaneously recorded

Original or a true copy

Accurate

Complete

+Plus



What Is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?

- For each study site, there must be a distinct individual identified as the investigator who has supervisory responsibility for the site
- Any subinvestigator at a site should report directly to the investigator
- The subinvestigator should not be delegated the primary supervisory responsibility for the site

What Is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?

- The investigator should have sufficient time to properly conduct and supervise the clinical trial
- The level of supervision should be appropriate to the staff, the nature of the trial, and the subject population



Factors that may affect the ability of the CI to provide adequate oversight

- Inexperienced staff
- Inadequate number of staff
- Protocol complexity (eligibility, assessments, critical timing, length of study, numerous amendments)
- Large number of subjects enrolled at a site
- Seriously ill subject population (large numbers of adverse events and concomitant medications)

Factors that may affect the ability of the CI to provide adequate oversight (cont.):

- Conducting multiple studies concurrently
- Conducting a study at multiple sites



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Records on the Ready

Regulatory Binders

- Protocol with amendments
- Investigator's Brochure
- IRB, sponsor, site correspondence
- FDA-1572 / Statement of Investigator
- Financial Disclosure Forms
- CVs/resumes
- Recruiting materials (TV/newspaper/radio advertisements/social media posts)

Patient Binders

- Informed Consent Forms
- Case Report Forms
- Medical records

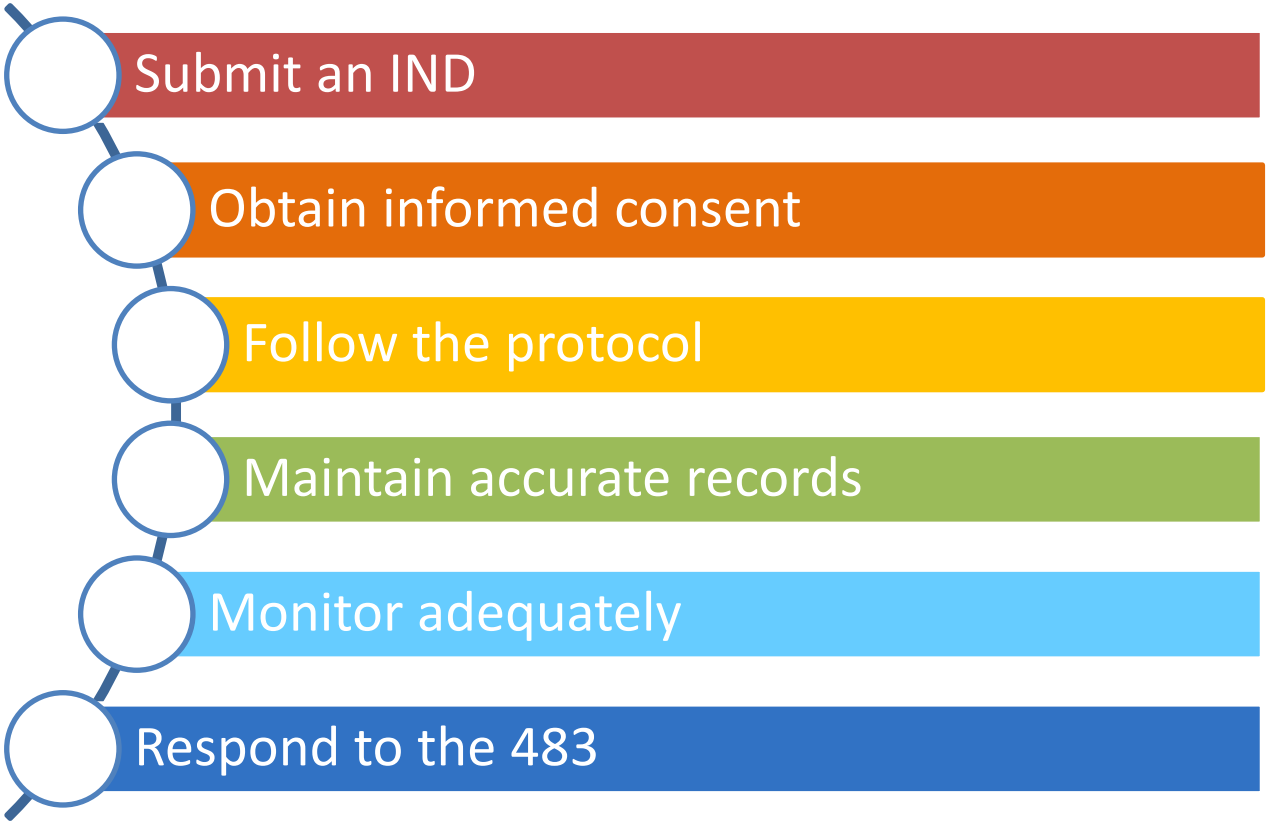
IP Records

- Test article accountability

Other Records

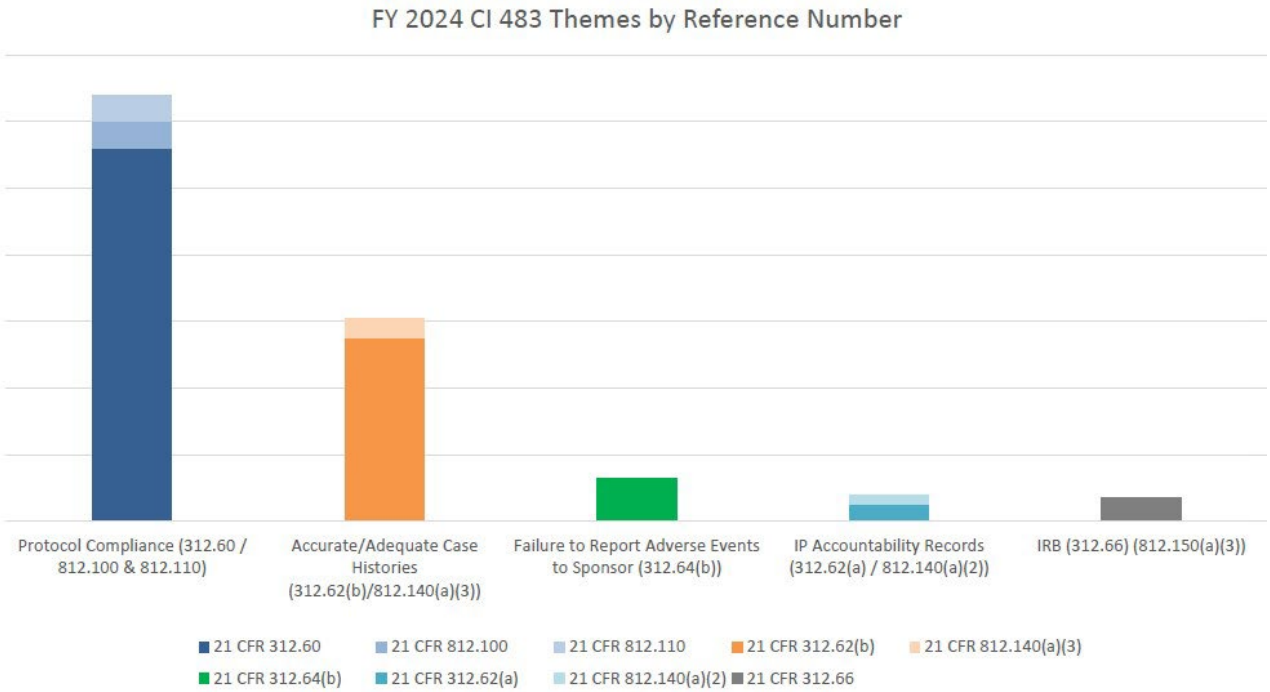
- CI's List of studies

Basic Tips

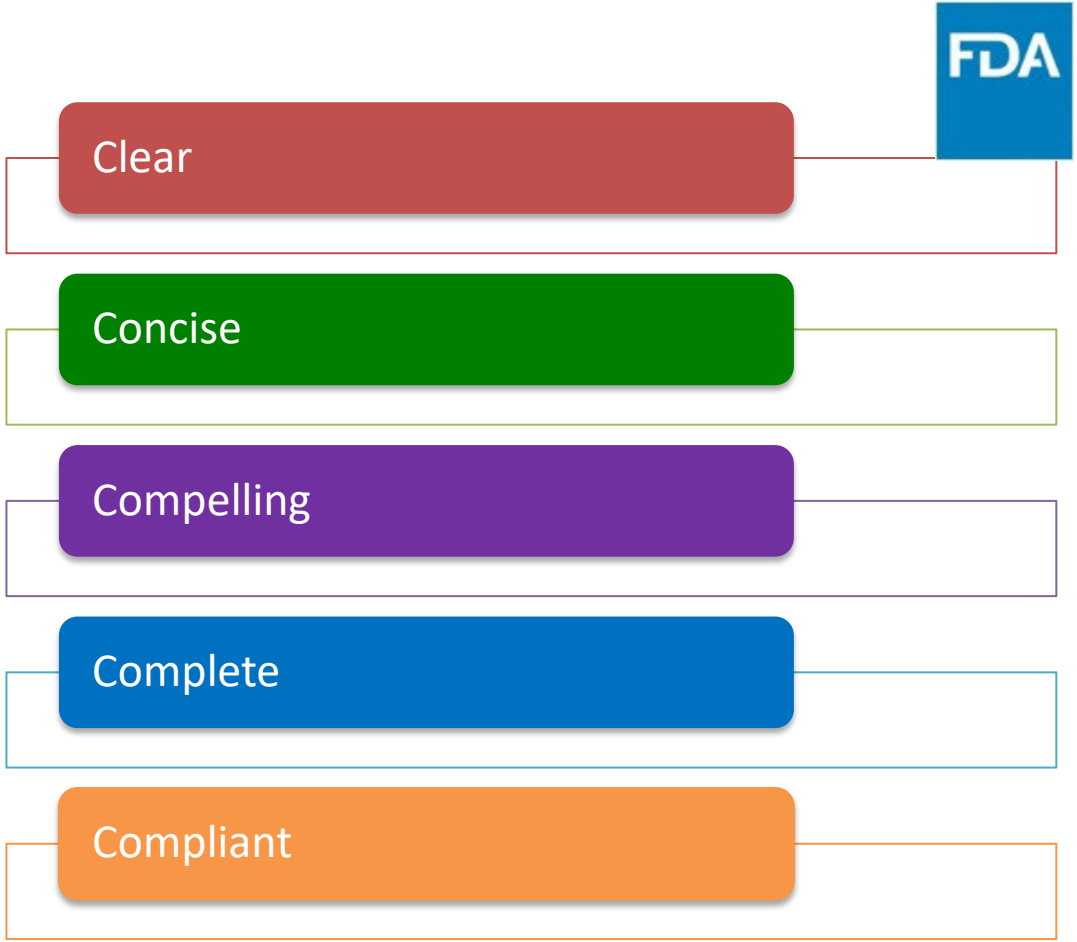

Submit an IND
Obtain informed consent
Follow the protocol
Maintain accurate records
Monitor adequately
Respond to the 483

FDA 483 Analyses

Analysis of all FDA 483s issued within a FY for inspection type



Form FDA 483 Responses



Case Study

- Clinical Investigator Inspection
- New biologic for Relapsed/Refractory Lung Cancer
- Phase II Study
- High enroller

Case Study

- Focus on:
  - Informed Consent
  - Eligibility
  - Efficacy Endpoints
  - Safety Endpoints

Case Study

- Observations
  - Eligibility
  - Adverse Event Reporting
- Classification: VAI

Contact Information

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FDA
U.S. FOOD & DRUG
ADMINISTRATION