Industry Trends and Training Expectations
FDA Partnership Opportunities

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CAPT Jane M. Kreis, R.Ph., MBA
Food and Drug Administration
Office of Regulatory Affairs
Office of Import Operations
Program Training Officer

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The information provided is only intended to be general summary information. It is not intended to take the place of either the written law or regulations.

Opinion Disclaimer:

The comments and opinions expressed are those solely of the presenter. They are not intended to take the place of either the written law or regulations

Getting Started

Pharmacist

Lessons Learned:

Communication

Critical Thinking

United States Public Health Service

Lessons Learned:

Clinical care

Scientific Research

Regulatory Service Tasks

Indian Health Service

Lessons Learned:

Clinical Care

Quality

Adult Learning

United States Food and Drug Association Office of Regulatory Affairs

Lessons Learned:

Regulatory

Protect the Public Health

Communication

Agenda

FDA Expectations

Trends in Training for the Industry

FDA Partnership Opportunities

Training

“Any type of modality in which individuals gain knowledge or skills to do their jobs … Note that the benefit to the organization derives not from what is learned but from what actually gets used… ”

Source

Kirkpatrick, J.D. and W.K. Kirkpatrick 2016 *Four Levels of Training Evaluation.* Alexandria VA :ATD Press

Question

Do all regulated firms need to have:

- procedures for training that includes how needs with be determined and
- records documenting that training occurred?

FDA Requirements

Training -- Ongoing and targeted training on issues ranging from allergen control, cleaning and sanitation procedures, incoming ingredient receipt protocol, and monitoring for employees, management, as well as suppliers

https://www.fda.gov/Food/GuidanceRegulation/CGMP/ucm110877.htm

Training Resource

- Module 1: GMP Regulation & Training
- Module 2: Food Safety: Microbes & Allergens
- Module 3: Personnel: Health & Hygiene
- Module 4: Plant Grounds & Pest Control
- Module 5: Plant Construction & Design
- Module 6: Sanitary Facilities: Water, Plumbing & Toilets
- Module 7: Sanitary Operations: Cleaning & Sanitizing
- Module 8: Equipment & Utensils
- Module 9: Plant Operations & Raw Materials
- Module 10: Manufacturing Operations: Process Controls
- Module 11: Warehousing, Food Disposition & Defects
- Module 12: Building Sanitation Procedures

https://instituteforfoodsafety.cornell.edu/trainings/good-manufacturing-practices-registration/

FDA Requirements

Food

- 21 CFR 123.10 Fish and Fishery Products

FDA Wrote in Warning Letter December 12, 2022

In addition to the above violations, we offer the following comment. To comply with 21 CFR § 123.10, you must have an individual who has successfully completed training in the application of HACCP principles to fish and fishery product processing that is at least equivalent to that received under a standardized curriculum recognized as adequate by the FDA or who may otherwise be qualified through job experience to perform the following functions: (1) the development of the HACCP plan, as required by 21 CFR § 123.6(b); (2) the reassessment and modification of the HACCP plan in accordance with the corrective action procedures specified in 21 CFR § 123.7(c)(5); (3) the reassessment and modification of the HACCP plan in accordance with the verification activities specified in 21 CFR § 123.8(a)(1);(4) the reassessment and modification of the hazard analysis in accordance with the verification activities specified in 21 CFR § 123.8(c); and (5) perform the record review required by 21 CFR § 123.8(a)(3). During the inspection you stated no one associated with your firm has completed seafood HACCP training. Further, based on the seafood HACCP violations described in this letter, it does not appear that any individual at your firm has sufficient seafood HACCP knowledge through job experience.

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/rdm-express-inc-643578-12122022

FDA Requirements

BioResearch Monitoring

- 21 CFR 312.60 Investigational Plan

FDA Wrote in Warning Letter March 14, 2023

Your failure to conduct the clinical study in accordance with the protocol resulted in the unnecessary administration of intrathecal methotrexate and the performance of invasive procedures, such as lumbar punctures and the sedation of a pediatric subject; and the initiation of study treatment cycles for a subject, despite that subject's not meeting the treatment eligibility criterion. This conduct raises significant concerns about your protection of the study subjects enrolled at your site, and also raises concerns about the validity and integrity of the data collected at your site.

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/robert-j-hayashi-mdwashington-university-school-medicine-department-pediatrics-654873-03142023

FDA Requirements

Devices

- 21 CFR 820.25 Quality System Regulation

FDA Wrote in Warning Letter June 17, 2021

Failure to have sufficient personnel with the necessary education, background, training, and experience to assure that all activities required by this part are correctly performed, as required by 21 CFR 820.25(a).

For example, your firm has not demonstrated it had any prior knowledge of U.S. FDA regulations and requirements including 21 CFR Part 820 - Quality System regulation.

- https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/tianjin-bolang-science-technology-development-co-ltd-614851-06172021

FDA Requirements

Drugs

- 21 CFR 211.25 Finished Pharmaceuticals

FDA Wrote in Warning Letter March 14, 2022

Your firm failed to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and experience, or any combination thereof, to enable that person to perform his or her assigned functions (21 CFR 211.25(a)).

You failed to ensure that all personnel are qualified for the CGMP operations they perform. For example, your co-owner stated that he is the sole proprietor of the Magic Heal formulation, had full knowledge of the process, and performed all manufacturing operations. However, you lack evidence that your co-owner has the adequate experience to perform these functions nor has received the appropriate CGMP training.

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/premier-trends-llc-621313-03142022

Question

How many people believe that FDA requires that drug manufacturers provide annual training on current good manufacturing practices?

Drugs 21 CFR 211

211.25(a)

- "Each person…shall have education, training, and experience (or any combination)…to enable that person to perform the assigned functions."

- "Training shall be in the particular operations that the employee performs and in current good manufacturing practice…as they relate to the employee's functions."

Drugs 21 CFR 211

211.25(a)

- "Training in current good manufacturing practice shall be conducted by ***qualified individuals*** ***on a continuing basis and with sufficient frequency*** to assure that employees remain familiar with CGMP requirements applicable to them."

Drugs 21 CFR 211

- 211.25(b)
  - "Each person ***responsible for supervising*** the manufacture, processing, packing, or holding of a drug product shall have the ***education, training, and experience***, or any combination thereof,…
    - **21CFR 210.3(b)(12):** ***Manufacturing, processing, packing or holding of a drug product*** _ includes packaging and labeling operations, testing and quality control of drug products.

Drugs 21 CFR 211

211.25(b)

- …***to perform assigned functions in such a manner as to provide assurance*** that the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to possess."

211.25(c)

- "There shall be an ***adequate number of qualified personnel*** to ***perform*** and ***supervise*** the manufacture, processing, packing, or holding of each drug product."

Comment 107 from the Preamble

Many comments questioned the frequency of the "continuing training" required in 211.25(a), asked for a definition of the word "continuing," and questioned who should receive what type of training. **The requirement that training be on a continuing basis is intended to mean, for example, that a single training course at the time an employee is hired, with no subsequent training activities, is not sufficient. Subsequent training should be sufficiently frequent to assure that employees remain familiar with CGMP requirements.**

Comment 107 from the Preamble

The Commissioner does not believe it would be prudent to specify time intervals for training in view of the broad nature of the drug industry and the wide range of employee functions covered by these regulations. The Commissioner believes this section is sufficiently clear in identifying "who should receive what training" in stating that each person engaged in the manufacture, processing, packing or holding of a drug product must have training in current good manufacturing practice that relates to that person's functions in the firm.

References

References:

21 CFR 211.25

Preamble:
https://www.fda.gov/downloads/drugs/developmentapprovalprocess/manufacturing/ucm206779.pdf

FDA Wrote in Warning Letter March 20, 2019

Compounding Pharmacy

Your firm failed to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and experience, or any combination thereof, to enable that person to perform his or her assigned functions (21 CFR 211.25(a)).

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/apollo-care-574756-03202019

FDA Wrote in Warning Letter May 13, 2020

International Inspection Korea

Your firm failed to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and experience, or any combination thereof, to enable that person to perform his or her assigned functions (21 CFR 211.25(a)).

> Your firm failed to ensure that all personnel are trained as appropriate. Training deficiencies were noted for personnel operating in management, production, quality assurance, and quality control positions. For example, employees engaged in the manual visual inspection of **(b)(4)** drug products were not trained at the intervals specified in your SOP; analysts who perform foreign matter (visible particulate) testing were not certified as required by your SOP; and some personnel lacked training records.
>
> We also observed laboratory data deficiencies during the inspection, which you attributed to inadequate SOPs, software, and training.

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/samchundang-pharm-co-ltd-599255-05132020

5 Key Questions about Personnel

DOJ investigations also focus on people to determine responsibility.

1. *Do you have the right people?*
2. *Do your people have the right incentives to see problems, to report problems, and to fix problems?*
3. *Are your people satisfied and engaged?*
4. *Are your people and policies working in harmony? or, do your policies acknowledge how real people work and what they are capable of?*
5. *Do you personally have visibility into what your people are actually doing?*

•*At CBI's 10th Annual Pharmaceutical Compliance Congress, Maame Ewusi-Mensah Frimpong, deputy assistant attorney general, consumer protection branch, civil division, at the US Department of Justice*

http://www.pharmexec.com/five-compliance-questions-ask-yourself-doj

Tips for Training

Use real-life examples- people tend to relate more and remember them.

Discuss compliance cases, FDA-483s and WLs- you may find similar situations in your company. Be proactive!

Ensure employees understand purpose of cGMPs and regulations. Legislation and regulations many times come after tragedies.

Tips for Training

Identify subject matter experts to assist with training. Establish Train the Trainer program; ensure they can teach.

Have small group discussions about SOPs, deviations, investigations, etc.

Key Points

Employees are your biggest variable to quality.

Managers should develop personnel qualifications for each position and should assign appropriate responsibilities according to the nature and risk of operations.

Key Points

Ensure employees' training is up to date and they understand the significance of their actions.

- Defect awareness and consequences

Train to prevent errors, deviations and non-compliance.

Key Points

Training done by qualified individuals on a continuing basis and with sufficient frequency.

Managers should verify that skills gained from training are implemented.

- Skills assessment
- Supervisory oversight is critical

Key Points

Training periodically assessed

- Quality system data should capture, trend, investigate and follow-up (CAPA) human errors.
- Use quality system data, such as complaints, failure investigations (lab and manufacturing), audit results, batch record reviews, etc., to assess training needs and effectiveness

Document, document, document.

Training for Top Management

The regulation does not exempt top management from training.

211.25(a)

- "Each person…shall have education, training, and experience (or any combination)…to enable that person to perform the assigned functions."
- "Training shall be in the particular operations that the employee performs and in current good manufacturing practice…as they relate to the employee's functions."

Top management must understand their authority and responsibility to manage a regulated business.

Training for Top Management

They must understand the regulations and their intent. They can be held accountable for the company's violative practices even if they were not aware of them (Park Doctrine).

Top Managers can be held as the responsible corporate officers with the authority and responsibility to prevent and correct F,D, & C Act violations.

Training for Top Management

Must understand the importance of sufficient resources and trained personnel.

They must understand the company's quality policy or other quality procedures or policies, i.e. complaints, recalls, etc.

If VPs or Senior Directors, they must be trained on those procedures applicable to their job function.

Some Recommendations for Training of Contractors

The firm is ultimately responsible for training of all employees including contractors.

Evaluate the risk of the work or service provided by the contractor or vendor.

Some Recommendations for Training of Contractors

Identify education, training and experience of contractors and determine training needs.

Determine what training can be done by “parent” company and how it will be evaluated and documented.

Some recommendations for Training for Contractors

Specify training responsibilities in quality agreements.

Develop audit program for contractors and vendors to verify training plan implementation.

Some recommendations for Training for Contractors

Periodically assess training effectiveness.

Ensure training records are accessible if requested during inspections.

Qualification & Training

21CFR 211.25: Each person engaged in the ***manufacturing, processing, packaging or holding*** of a drug product shall have the education, training, and experience (or any combination) to enable that person to perform their assigned functions.

– Qualifications, e.g. C.V., can be requested during inspections to verify a person's education and experience.

Effectiveness Tests

Currently, there is no specific requirement in the drug regulations for effectiveness checks or specific documentation to be kept.

Under the Quality System Guidance, Managers are expected to establish training programs that include the following:

- Evaluation of effectiveness of training
- Documentation of training and/or re-training

Risk Assessment

Design training based on risk of impact to the quality, safety and effectiveness of the drug.

- What can happen if the employee is not adequately trained?

Classify risk (i.e. high, medium, low, none) and document it.

For example,

- Low risk (minor SOP revision)- Read, Understand and Document training
- High Risk (process change)- Read, Discuss, Demonstrate & Evaluate

Questions

Training effectiveness: Whole program and Smaller session what is the measurement the industry should be looking at?

This varies considerably across systems.

Firms should evaluate their quality management systems at appropriate intervals to assess training effectiveness both (1) as a whole program and then (2) as a sub-element within the systems by looking at root cause failures for each issue detected/investigated.

Training effectiveness is successful when the training “sticks” (the employee truly understands the concepts) and detected failures are not tied to training deficiencies.

Questions

Does Quality need to be involved or review creation, revision or inactivation of curricula?

Depends on which department owns the training program and if the curriculums are treated as controlled records.

In general, training curricula should be approved and owned by the area manager and QA wouldn't need to sign off on changes to every employee curriculum change --- unless there has been some issue which demonstrated the need for QA to provide oversight on each change.

However, Quality is responsible for the oversight and effectiveness of the entire training system for the firm.

Questions

Is formal ownership of curricula prevalent or rare in the industry?

It’s common for curricula to be owned by an area management representative who is responsible for ensuring employees are current on required training.

Questions

Is assignment of curricula or lack thereof an issue in inspections?

Only if it’s fueling a systemic problem or failure.

Questions

Do you think complete removal of Read and Understand of SOPs in a curriculum, is a compliance problem or risk if it is replaced by Competency Based Learning?

Decide what works best for your firm as long as the training is controlled (via established procedures), consistent, and monitored for effectiveness (the training “sticks”).

Investigator Resources

IOM
https://www.fda.gov/iceci/inspections/iom/default.htm

Compliance Programs

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-manuals/compliance-program-manual

Top Citations 2018 to present

Biologics

21 CFR 606.100(b)

Establish, maintain and follow manufacturing SOPs

Top Citations 2018 to present

Bioresearch Monitoring

21 CFR 312.60

FD-1572, protocol compliance

21 CFR 312.62(b)

Case history records- inadequate or inadequate

Top Citations 2018 to present

Devices

21 CFR 820.100(a)

Lack of or inadequate procedures

21 CFR 820.198(a)

Lack of or inadequate complaint procedures

21 CFR 820.75(a)

Lack of or inadequate process validation

21 CFR 820.50

Purchasing controls, Lack of or inadequate procedures

21 CFR 803.17

Lack of Written MDR Procedures

21 CFR 820.90(a)

Nonconforming product, Lack of or inadequate procedures

Top Citations 2018 to present

Drugs

21 CFR 211.22(d)

Procedures not in writing, fully followed

21 CFR 211.160(b)

Scientifically sound laboratory controls

21 CFR 211.100(a)

Absence of Written Procedures

21 CFR 211.192

Investigations of discrepancies, failures

Top Citations 2018 to present

Foods

21 CFR 117.80(c)

Manufacturing, Processing, Packing, Holding – Controls

21 CFR 117.10

Personnel

21 CFR 1.502(a)

Develop FSVP

21 CFR 123.11(b)

Sanitation monitoring

21 CFR 117.35(a)

Sanitary Operations - Plant Maintenance

Site Visit Training Program for Office of Pharmaceutical Quality Staff

Federal Register Notice: 84 FR 55970, October 18, 2019

Federal Register :: Site Visit Training Program for Office of Pharmaceutical Quality Staff; Information Available to Industry

Site Visit Training Program for Office of Pharmaceutical Quality (OPQ) Staff

This site visit program is designed to offer experiential and firsthand learning opportunities that will provide OPQ staff with a better understanding of the pharmaceutical industry and its operations, as well as the challenges that impact a drug's developmental program and commercial life cycle. The goal of these visits is to enhance OPQ staff exposure to the drug development and manufacturing processes in industry; therefore, a tour of pharmaceutical company facilities including manufacturing and laboratory operations, is an integral part of the experience.

- Drug products
  - Solutions, suspensions, emulsions, and semisolids
  - Modified- and immediate-release formulations
  - Drug-device combination products (*e.g.,* inhalation products, transdermal systems, implants intended for drug delivery, and pre-filled syringes)

- Active pharmaceutical ingredients
  - Made entirely by chemical synthesis
  - Derived from a biological source (*e.g.,* fermentation, mammalian cell culture)

- Design, development, manufacturing, and controls
  - Engineering controls for aseptic processes
  - Novel delivery technologies
  - Hot melt extrusion
  - Soft-gel encapsulation
  - Lyophilization
  - Blow-Fill-Seal and isolators
  - Spray-drying
  - Process analytical technology, measurement systems, and real-time release testing

- Emerging technologies
  - Continuous manufacturing
  - 3-dimensional printing
  - Nanotechnology

Selection of potential facilities will be based on the priorities developed for OPQ staff training, the facility's current compliance status with FDA, and in consultation with the appropriate FDA district office.

All travel expenses associated with this program will be the responsibility of OPQ; therefore, selection will be based on the availability of funds and resources for the fiscal year.

OPQ will not provide financial compensation to the pharmaceutical site as part of this program.

Center for Devices and Radiological Health: Experiential Learning Program

The 2023 Fall Experiential Learning Program (ELP) Proposal Submission Period is **CLOSED**. Please check back in July 2023 for the Fall 2024 collection period.

- https://www.fda.gov/science-research/fda-stem-outreach-education-and-engagement/cdrhs-experiential-learning-program

Center for Devices and Radiological Health: Experiential Learning Program

This training is intended to provide CDRH and other FDA staff with an opportunity to understand laboratory practices, quality system management, patient perspective/input, and challenges that impact the medical device development life cycle.

The purpose of the FR document is to invite medical device industry, academia, and health care facilities, and others to participate in this formal training program for CDRH and other FDA staff, or to contact CDRH for more information regarding the ELP.

Areas of Interest

The Training Areas of Interest reflect topics identified by CDRH managers and are listed on the website twice a year during the two Fiscal Year ELP Training Solicitation Periods.

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Active Pharmaceutical Biotechnology

Tour of

- Manufacturing
- Production
- Facilities
- Warehouse
- Laboratory

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Personalized Immunotherapy

Tour of

- Manufacturing
- Production
- Facilities
- Warehouse
- Laboratory

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Active Pharmaceutical Ingredient Powder

Tour of

- Manufacturing
- Production
- Warehousing
- Laboratory
- Facilities

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Drug Substance Biotechnology

Tour of

- Manufacturing
- Production
- Warehousing
- Laboratory
- Facilities

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Sterile Biotechnology

Tour of

- Manufacturing
- Production
- Warehousing
- Laboratory
- Facilities

Past Site Visit Training Program for Office of Regulatory Affairs (ORA)

Non-Sterile Dosage Forms

Tour of

- Manufacturing
- Production
- Warehousing
- Laboratory
- Facilities

FDA Partnership Training Visit

Lessons Learned From:

- New equipment/technology design and capabilities presented
- Observation of firm's high quality culture
- Review of various visual management tools throughout the facility
- Q&A opportunities
  - FDA Subject Matter Experts
  - Firm's management

Advantages Industry

Investigators process knowledge can lead to shorter inspection time for voluntary participating companies

Qualified training site-name recognition

Better understanding of compliance expectations

Protect Public Health

Advantages FDA

Provide technical training to investigators, analysts, supervisors and compliance officers

Update on new and novel technologies in food, feed, medical products, cosmetics, and tobacco for investigators, analysts, supervisors and compliance officers

Protect Public Health

Disadvantages Industry

Concern about regulatory actions

Budget

Resource allocation

Production interruption

Disadvantages FDA

Budget

Workplan

Question

True or False

FDA is receptive to partnering with industry and foreign governments to provide training for FDA employees.

Answer: **True**

Reference:

Federal Register Notice: 84 FR 55970, October 18, 2019

Federal Register :: Site Visit Training Program for Office of Pharmaceutical Quality Staff; Information Available to Industry

Answer: **True**

Reference:

To fulfill its mission to monitor and ensure the safety of the supply chain for food, feed, medical products, cosmetics, and tobacco products that enter the United States from other parts of the world, the FDA engages in partnerships with foreign governments, regulatory coalitions, development organizations, academic institutions, among others.

https://www.fda.gov/internationalprograms/partnerships/default.htm

Question

True or False

FDA has an extensive array of online courses to train industry personnel about how FDA regulates pharmaceuticals and medical devices. Some of these classes are complimentary and for other industry need to pay a fee.

Answer: **False**

Free Resources:

CDER World

https://www.accessdata.fda.gov/scripts/cderworld/

CDERLearn

https://www.fda.gov/Training/ForHealthProfessionals/default.htm

CDRHLearn

https://www.fda.gov/Training/CDRHLearn/default.htm

OTP Learn--Biologics

OTP Learn | FDA

Tobacco Training

FDA Tobacco Compliance Webinars | FDA

Healthcare

Training and Continuing Education | FDA

Information for Industry

For Industry | FDA

Quote of the Day

“We must never forget that wisdom is impossible without learning, but learning does not -- not by the longest measure -- bring wisdom."

Remarks at Georgetown University's Bicentennial Convocation, October 1, 1988 Ronald Reagan

Discussion- Q & A

Thank You!

Jane M. Kreis, R.Ph., MBA

Pharma and BIMO Program Training Officer

jane.kreis@fda.hhs.gov

Rozelle Smith, MSQSM, CQA

Pharma Investigator

rozelle.smith@fda.hhs.gov


FDA
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ADMINISTRATION