Audit Like An Inspector

HEALTH AUTHORITY TOOLS FOR AUDITING & INSPECTION READINESS

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Outline

I. Introduction
II. FDA Tools Available to the Public
III. Questions?
IV. Contact Us

Introduction

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Scope: FDA-regulated Products

- Product Types Regulated by the US FDA: **Drugs**, **Food**, **Cosmetics**, **Medical Devices**, **Radiation-emitting products**, **Vaccines**, **Blood** and **Biologics**, **Animal and Veterinary**, and **Tobacco**,
- This presentation will focus on drugs, but the resources presented can be applied across other types of manufacturing.
- Principles can also be applied to ISO 9001 and other audits.

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Modern, Strategic Auditing: **Preparation is Key**

- Whether a government inspection or audit of a private company, time is always a constraint.
- Audits/inspections can range from a single day to weeks. Even the longest audit cannot give a complete picture of a company's compliance to applicable laws, regulations, and standards.
- How can you ensure the most efficient and effective audit? **Prepare like an inspector!**
  - The FDA provides inspectors with "dossiers"—a compilation of valuable information about a company (e.g., FARs, recalls, product listings) to assist in determining areas of highest risk during inspections.
  - The FDA website has many tools available to the public providing some of this same information (e.g., compliance dashboards) as well as other helpful resources (e.g., compliance programs).

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Modern, Strategic Auditing: **Use of Electronic Tools**

- Using modern tools to determine potential areas of concern and the ability to quickly access and analyze data are critical.
- **Electronic Tools Can Be Used To**:
  - **Determine specific areas of concern (pre-audit)**
    - **FDA**- compliance dashboards to access recalls, observation trends; databases (Search Databases | FDA)
    - **Industry**- Atlas-Compliance to access all 483s, WLs, EIRs, AI searches (Atlas (atlas-compliance.ai))
  - **Efficiently analyze data (during audit)**
    - **Excel**- during or before the audit, request data be presented in an electronic format to allow for sorting, filtering etc.
    - **SharePoint** – during an audit, companies can supply documentation through electronic systems, allowing for faster review and less printing.

Prepare Like An Inspector

FDA Inspector

Review the last Establishment Inspection Report (EIR) of the firm.

- What systems were cited in observations?
- What systems received verbal discussion?
- What systems were *not* covered during the inspection?

Review the firm's compliance history.

- FDA website: databases (e.g., recalls, previous FDA inspections)
- Inspection outcomes by other Health Authorities

Review information in the public domain.

- Firm website
- Regional issues that may impact product, e.g., recent catastrophic events, like flooding could impact water systems
- Internet searches – may illustrate wide-spread customer complaints on social media

Auditor

Review the last audit report(s) of the auditee.

Review the compliance history of the auditee.

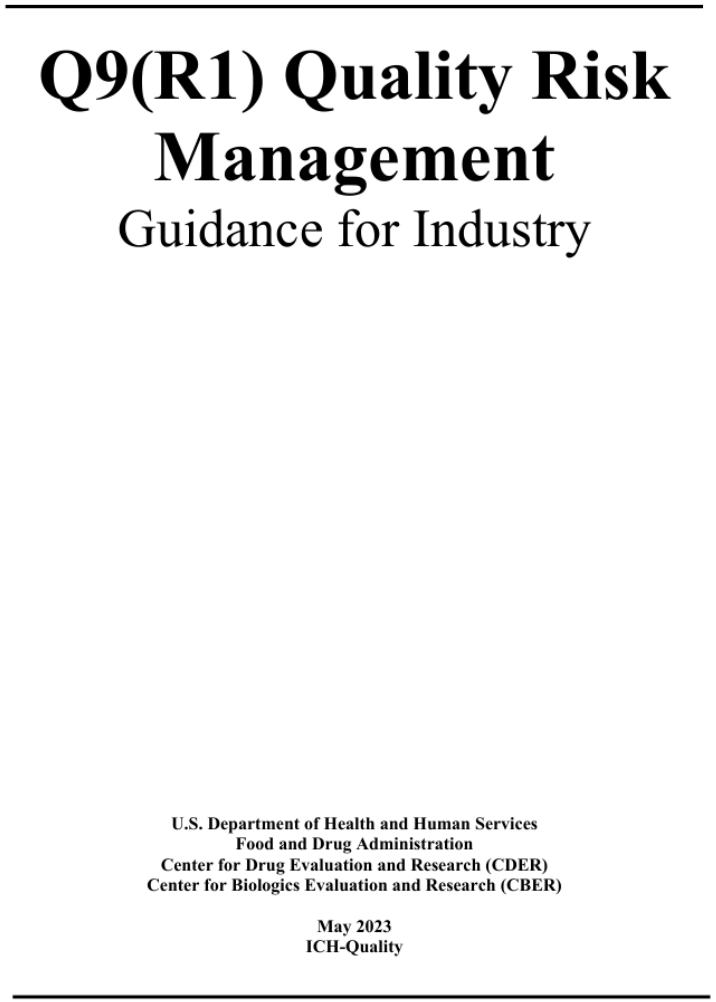
- If there was a recall(s) has the product quality issue been adequately addressed?
- Is there an adequate recall system in place, including SOP(s) and requirement for periodic mock recalls?
- Health Authority inspection results?

Review information in the public domain.

Modern, Strategic Auditing: **Let Risk Be Your Guide**

- When selecting which areas, processes or products to audit, consider:
  - Those with the highest risk to the end user.
    - Vulnerable populations?
    - Product(s) with largest distribution?
    - High-risk processes, e.g., sterilization
  - Representative of multiple products
  - Encompass multiple Quality systems

- ICH Q9: Quality Risk Management
- ISO 31000: Risk Management



Q9(R1) Quality Risk Management

Guidance for Industry

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)

May 2023
ICH-Quality

Q9(R1) Quality Risk Management | FDA

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FDA Tools Available To the Public

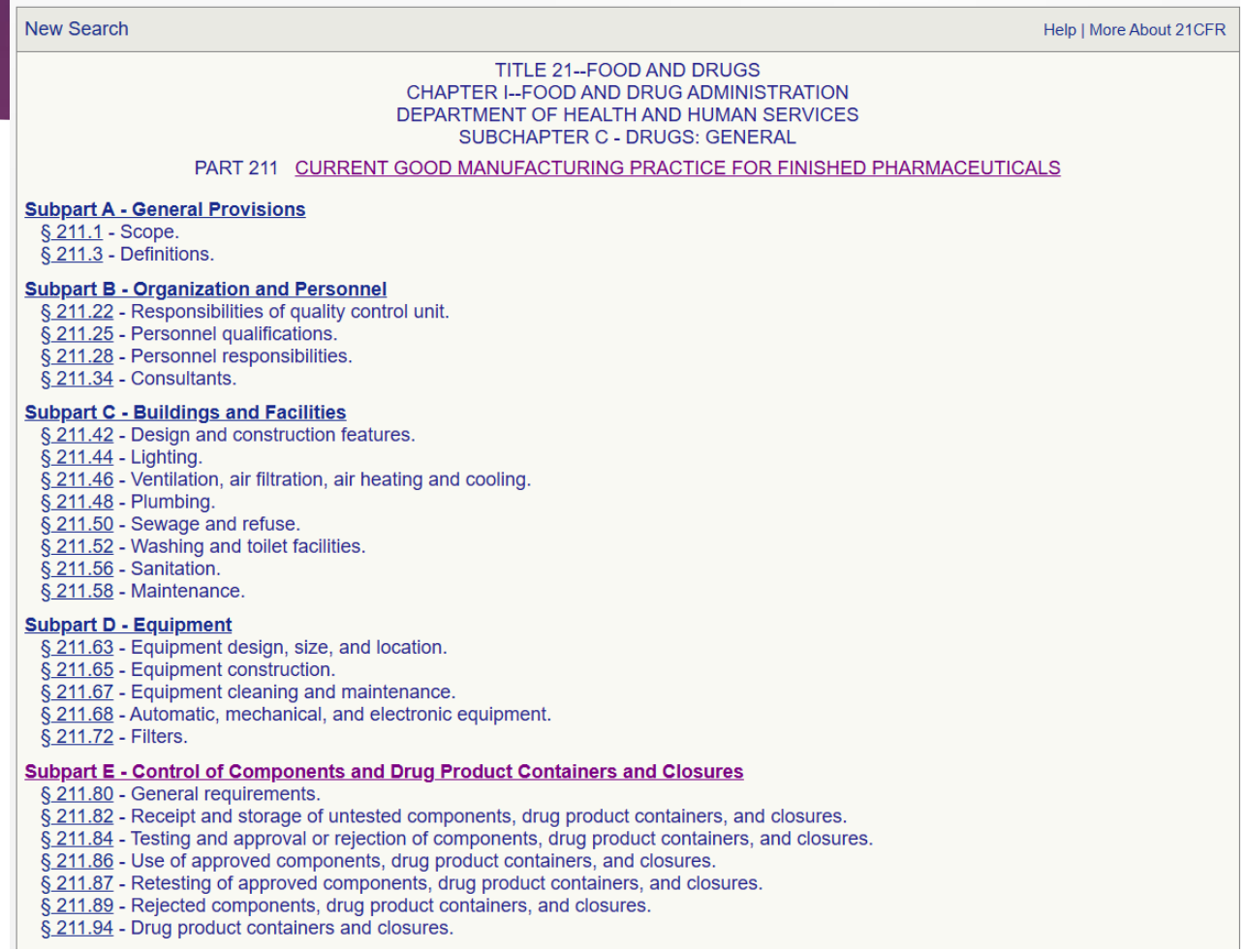
FDA Resources

Tool	Description	Access
Laws (e.g., FD&C Act)	Laws establish requirements or prohibitions and can form the basis for regulations, guidance, and policy.	US Federal government websites (end in .gov). For example, https://uscode.house.gov/
Regulations (e.g., 21 CFR 211)	Regulations are published by agencies (e.g., FDA) to clarify their interpretation of a law and how a law will be implemented.	FDA website or https://www.ecfr.gov
Guidance Documents	Guidance documents are published by agencies to further clarify how an they understand and implement existing laws and regulations.	FDA website, for example Search for FDA Guidance Documents | FDA
Compliance Programs	FDA's Compliance Programs provide instructions to FDA personnel for conducting activities to evaluate industry compliance with the Federal Food, Drug, and Cosmetic Act and other laws administered by FDA.	FDA website under *Compliance Program Manual* Compliance Program Manual | FDA
Discussion Papers	To facilitate and enhance mutual learning between the FDA and stakeholders (e.g., academia, manufacturers); the public can comment on these papers.	FDA website under *FDA Voices* FDA Releases Two Discussion Papers to Spur Conversation about Artificial Intelligence and Machine Learning in Drug Development and Manufacturing | FDA
Data Dashboard	Tool on FDA website that allows users to review inspection results, recalls, import refusals, compliance actions etc.	FDA Dashboards - Inspections
Other resources	Warning Letter database, Other manuals (e.g., IOM, RPM), and databases (e.g., eDRLS)	FDA website

Since the above is subject to change, always access from a government source to ensure the most current version.

Resources to Assist Auditors: **Regulations**

- Regulations are technically not law, but they have the force and effect of law, i.e., **they MUST be followed and penalties result if not followed**.
- Use of electronic CFR allows the user to CTRL + F and search for key terms in the regulations.



New Search | Help | More About 21CFR

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER C - DRUGS: GENERAL

PART 211 CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

Subpart A - General Provisions
§ 211.1 - Scope.
§ 211.3 - Definitions.

Subpart B - Organization and Personnel
§ 211.22 - Responsibilities of quality control unit.
§ 211.25 - Personnel qualifications.
§ 211.28 - Personnel responsibilities.
§ 211.34 - Consultants.

Subpart C - Buildings and Facilities
§ 211.42 - Design and construction features.
§ 211.44 - Lighting.
§ 211.46 - Ventilation, air filtration, air heating and cooling.
§ 211.48 - Plumbing.
§ 211.50 - Sewage and refuse.
§ 211.52 - Washing and toilet facilities.
§ 211.56 - Sanitation.
§ 211.58 - Maintenance.

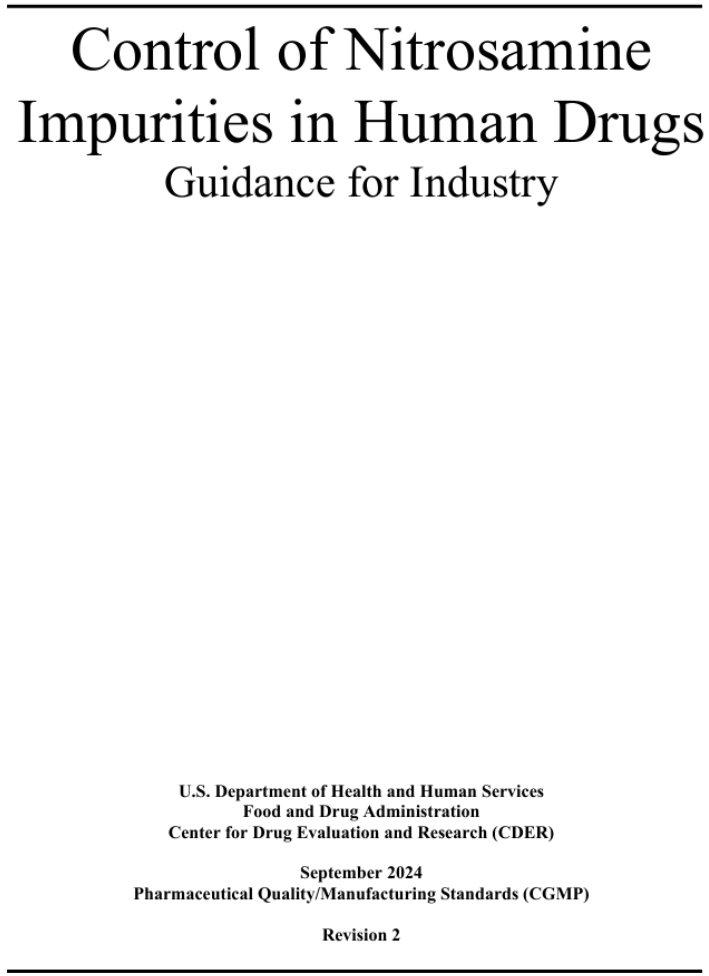
Subpart D - Equipment
§ 211.63 - Equipment design, size, and location.
§ 211.65 - Equipment construction.
§ 211.67 - Equipment cleaning and maintenance.
§ 211.68 - Automatic, mechanical, and electronic equipment.
§ 211.72 - Filters.

Subpart E - Control of Components and Drug Product Containers and Closures
§ 211.80 - General requirements.
§ 211.82 - Receipt and storage of untested components, drug product containers, and closures.
§ 211.84 - Testing and approval or rejection of components, drug product containers, and closures.
§ 211.86 - Use of approved components, drug product containers, and closures.
§ 211.87 - Retesting of approved components, drug product containers, and closures.
§ 211.89 - Rejected components, drug product containers, and closures.
§ 211.94 - Drug product containers and closures.

CFR - Code of Federal Regulations Title 21 (fda.gov)

Resources to Assist Auditors: **Guidance Documents**

- Guidance documents are NOT law or regulation. Therefore, they are not cited on an FDA 483, but they do provide the Agency's current thinking on a matter.
- As such, they are extremely helpful in adding the C ("current") to CGMP.
- **Note:** Ensure that you are referring to a "final" guidance not a "draft"; draft versions are subject to change.



Control of Nitrosamine Impurities in Human Drugs

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

September 2024
Pharmaceutical Quality/Manufacturing Standards (CGMP)

Revision 2

Search for FDA Guidance Documents | FDA

Resources to Assist Auditors: **Compliance Programs**

- Compliance Programs are documents that FDA inspectors use to ensure all requirements are covered during the inspection.
- **Similar to an audit checklist**.
- There are Compliance Programs for all types of inspections, e.g., PAI, sterile, API.

FOOD AND DRUG ADMINISTRATION
COMPLIANCE PROGRAM PROGRAM 7356.002

CHAPTER 56—DRUG QUALITY ASSURANCE

SUBJECT:	IMPLEMENTATION DATE:
Drug Manufacturing Inspections REVISION: Revised to add elements of International Council for Harmonisation (ICH) guidances for industry *Q9 Quality Risk Management, Q10 Pharmaceutical Quality System,* and *Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management;*[1] control of nitrosamine impurities; and alternative tools for evaluating facilities.	10/17/2022

DATA REPORTING

PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
All Human Drugs Industry codes: 50, 54-56, 59, 60-66	Domestic/Foreign current good manufacturing practice (CGMP) inspections covered under this compliance program, 7356.002, include inspection of any establishment that does not have a specific program:

PAC	Type	Subject
56002	Full	Drug Process Inspections (DPI)
56002H	Abbreviated	Drug Process Inspections (DPI)

Report CGMP coverage of the programs specified below under PACs as follows (using the appropriate compliance program):

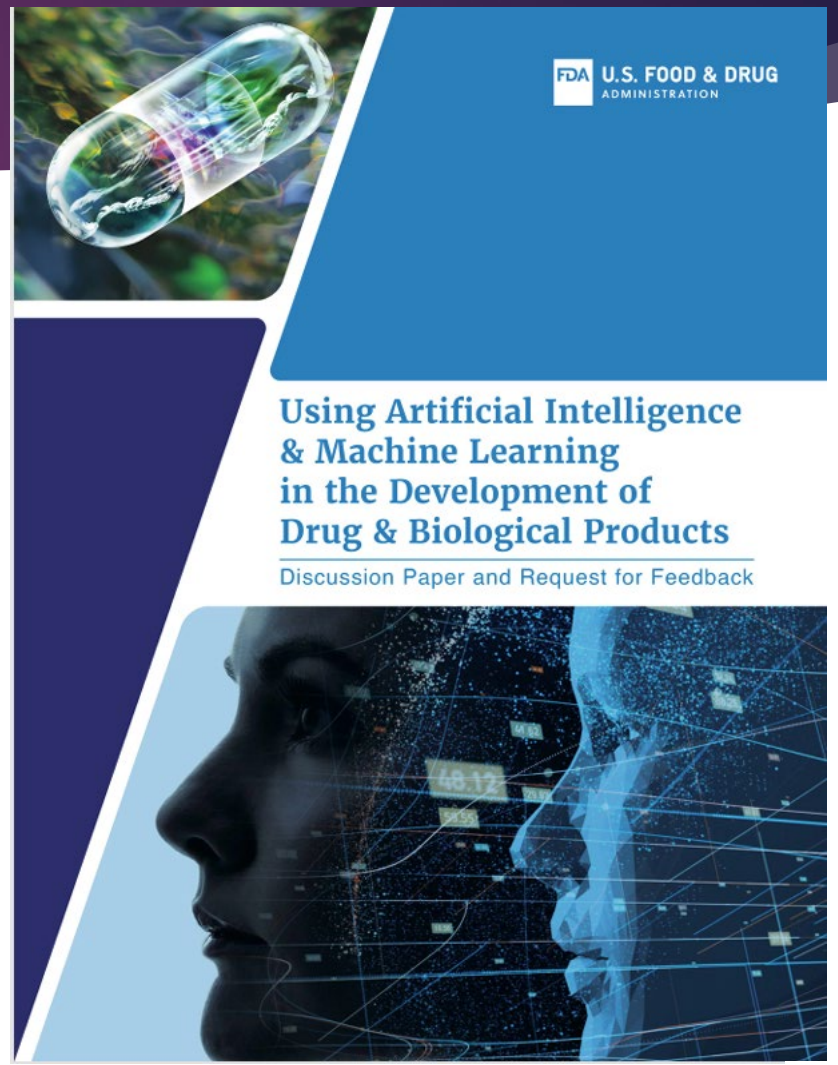
PAC	Type	Subject
56002A	Full	DPI/Small Volume Parenterals (compliance program 7356.002A—*Sterile Drug Process Inspections*)
56002I	Abbreviated	DPI/Small Volume Parenterals (compliance program 7356.002A)
56002B	Full	DPI/Drug Repackers and Relabelers
56002J	Abbreviated	DPI/Drug Repackers and Relabelers
56002C	Full	DPI/Radioactive Drugs
56002K	Abbreviated	DPI/Radioactive Drugs
56002F	Full	Active Pharmaceutical Ingredient Process Inspections
56002L	Abbreviated	Active Pharmaceutical Ingredient Process Inspections

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Compliance Program Manual | FDA

Resources to Assist Auditors: **Discussion Papers**

- FDA is becoming more collaborative with industry as technology is incorporated into manufacturing.

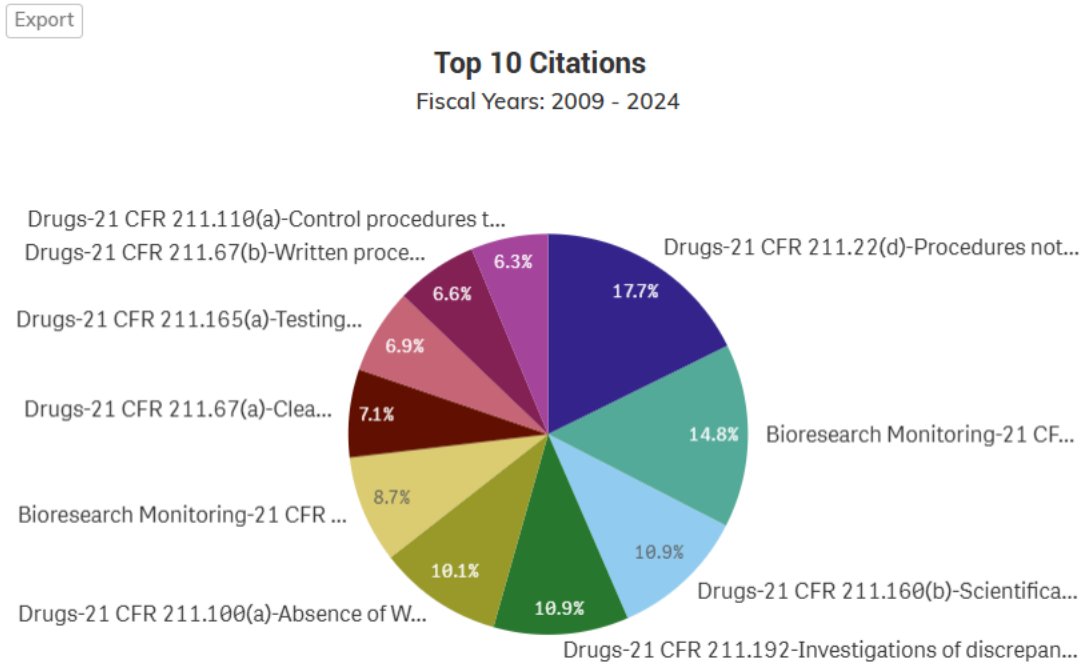


Using Artificial Intelligence & Machine Learning in the Development of Drug and Biological Products (fda.gov)

Resources to Assist Auditors: **Data Dashboards**

- Provides compliance information and observation trending.
- Allows user to review recalls.
- Allows user to filter inspections by:
  - Product Type – foods/cosmetics, drugs, devices etc.
  - Region/Country
  - Inspection Classification – OAI, NAI, VAI
- Users can access *some* 483s but not all.

FDA Dashboards - Inspections



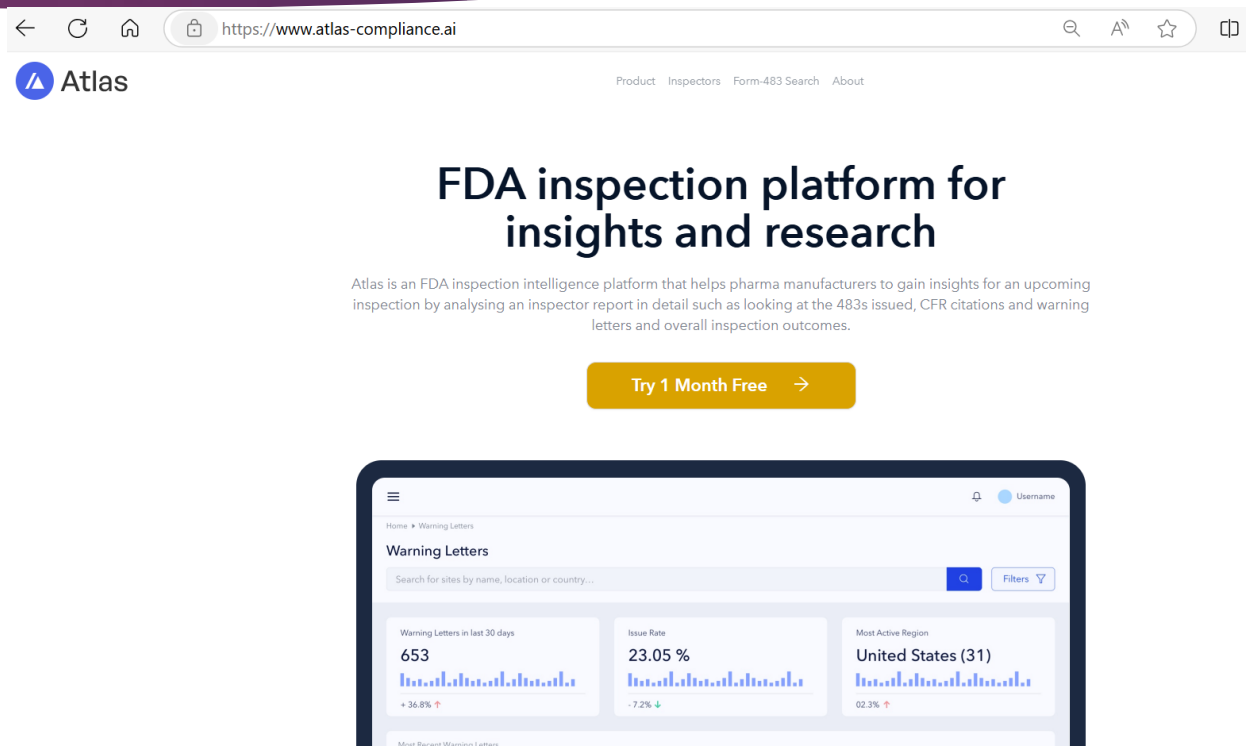
Accessed 9/15/24 @ 10:05pm EST

In Summary

- **How to audit like an inspector?**
  - **Prepare like an inspector**
    - Gather as much data about the auditee, product, process as possible using previous audit reports, FDA resources (e.g., compliance database) and information in the public domain (e.g., company website, internet searches) to determine potential areas of concern.
  - **Audit using modern tools**
    - Efficiently utilize resources during the audit (e.g., SOPs and data shared electronically instead of printed versions) and fast data analyses (e.g., sort/filter complaints, deviations using Excel or similar software).
    - Utilize FDA resources like compliance programs as auditing checklists and guidance documents to ensure you are auditing according to "current" GMPs.
  - **Use risk-based principles**
    - Select products/processes using risk analyses.

Inspection Readiness

- The resources previously discussed are also helpful in inspection readiness.
  - Regulations
  - Guidance Documents
  - Compliance Programs
  - Discussion Papers
  - Data Dashboards
- Private Companies like, Atlas-Compliance, provide FDA 483s, Warning Letters, EIRs, inspector intelligence reports, artificial intelligence (AI) searches etc.



[Atlas (atlas-compliance.ai)]

Questions?

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Want More Information?

Polymath Regulatory Consultants LLC are quality and compliance professionals having decades of experience with FDA-regulated and ISO-certified products. We perform audits, conduct trainings, provide QMS and inspection-related services, and assist with complex quality and compliance issues.

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