GMP Inspection Overview
U.S. Food and Drug Administration

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CDER Manufacturing Inventory by the Numbers

Sites:

- Approximately 7,000 human drug manufacturing sites of obligation (as defined by regulations and policy)
  - 2,000 Medical Gas manufacturers (nearly all in U.S.)
  - 5,000 Non-Medical Gas manufacturers
    - ~ 40% domestic
    - ~ 60% foreign

Products (all approximates):

- 97,000 unique NDCs for Final Dosage Forms
- 14,000 unique NDCs for Active Pharmaceutical Ingredients
- 1,100 unique NDCs for Medical Gas

Note: *Based on current listings in eDRLS. One product could be listed under multiple NDC's by private label distributors, manufacturers and/or repackers.*

Site Selection Model (SSM)

- Routine surveillance inspections are prioritized using a site selection model (SSM)
- Manual of Policies & Procedures (MAPP) 5014.1: *Understanding CDER's Risk-based Site Selection Model*
  - Published 9/5/18 (Effective 9/26/18)
  - https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM619302.pdf

CDER-ORA Site Selection Model (SSM)

PURPOSE

- ***Risk management tool developed to support*** the prioritization of both domestic and foreign manufacturing surveillance inspections.
- ***Implement a consistent, science-based approach*** to identify and allocate resources to sites that can potentially impact public health.

OBJECTIVE

- ***Rank*** drug manufacturing sites for CGMP surveillance inspections ***based on risks to drug quality***.

SSM Compliance with the FD&C Act

Risk-based inspection frequency considers:

(A) The **compliance history** of the establishment.

(B) The record, history, and nature of **recalls** linked to the establishment.

(C) The **inherent risk of the drug** manufactured, prepared, propagated, compounded, or processed at the establishment.

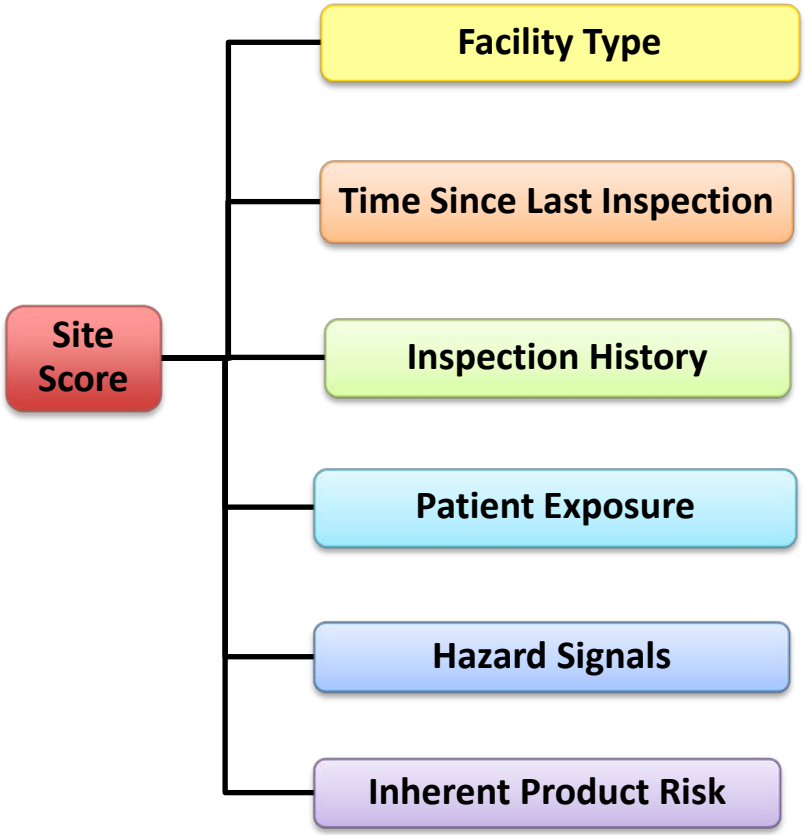
(D) The **inspection frequency and history** of the establishment, including whether the establishment has been inspected pursuant to section 704 within the last 4 years.

(E) Whether the establishment has been **inspected by a foreign government** or an agency of a foreign government recognized under section 809 (EU Mutual Recognition Agreement).

(F) **Any other criteria deemed necessary** and appropriate by the Secretary for purposes of allocating inspection resources.

Started November 1, 2017!

Current SSM Factors



Sub-factors of Inherent Product Risk

- Dosage form
- Route of administration
- Products intended to be sterile
- API load (concentration of API in dosage form or unit dose)
- Biologic drug substance or drug product
- Therapeutic class
- Narrow Therapeutic Index (NTI) drugs
- Emergency use drugs

Understanding Time Since Last Inspection

- 510(h) of the FD&C Act was amended in 2012
  - Biennial inspection frequency for domestic establishments (i.e., sites) replaced with requirement that FDA inspect domestic ***and*** foreign drug establishments "in accordance with a risk-based schedule" that considers establishments' "known safety risks."
- Promotes parity in inspectional coverage
- Assures FDA resources address the most significant public health risks.

Understanding Time Since Last Inspection

- Foreign regulators should ***not*** expect a fixed inspection interval for FDA inspections.
  - The model "hard stop" establishes a maximum interval
- Our export certificates (Certificate of Pharmaceutical Product) no longer have the date of the last inspection on them
  - Our online inspection classification database can be found at https://www.fda.gov/iceci/inspections/ucm222557.htm
- Our current approach ensures riskier sites are inspected more frequently, while less risky sites could be inspected less often

Updates to FDA's Public Inspection Classification Database

The database includes...

- an update **every 30 days** that covers all drug surveillance inspection **final classifications** (i.e., compliance status). The final classification is generally completed within 90 days of the end of a surveillance inspection, which means the entry for the site will be within 120 days of the close of an inspection.
- inspections of sites involved in the conduct or analysis of **human drug bioanalytical or clinical bioequivalence/bioavailability** studies
- **MRA partner** inspection assessment classifications
- a link from the introductory page to **definitions of final inspection classifications**—NAI, VAI, OAI—and to a new FAQs page

New Inspection Protocols Project (NIPP)

- Modernize inspections through collecting structured data that can be analyzed over time:
  - Quantitate the state of pharmaceutical quality
  - Accelerate the pace of making informed, data-driven decisions
    - Pre-approval: application decisions
    - Surveillance: resource allocation
  - Lead to more efficient inspections in the future
    - Proactively identify issues to investigate
  - Identify policy and outreach opportunities across the industry
  - Provide evidence for addition or modification of regulations

NIPP

- Identify attributes of an effective quality system and introduce these elements into the protocol
  - Integration of quality culture elements
  - Establish relationship with data collected in protocol
- National Roll-out for Sterile Pre-Approval and Surveillance Inspections 10/29/18

Acknowledgements

- Jennifer Maguire, Ph.D., FDA CDER
- Carla Lundi, FDA CDER
- Rosa Motta, FDA CDER

THANK YOU!