Concept of Operations

Integration of FDA Facility Evaluation and Inspection Program for Human Drugs

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FDLI Enforcement Litigation & Compliance Conference

December 7, 2017

ORA reorganization – May 15, 2017

- Creates distinct, product-based and vertically integrated regulatory programs. The new structure will enable staff to work more closely with FDA scientific and technical experts on complex regulatory challenges.
- ORA's inspection and compliance staff will specialize in an area:
  - Office of Biological Product Operations
  - Office of Bioresearch Monitoring Operations
  - Office of Human and Animal Food Operations
  - Office of Medical Device and Radiological Health Operations
  - Office of Pharmaceutical Quality Operations
  - Tobacco Operations Staff
- ORA import operation will be organized into five virtual divisions to allow the FDA to better target threats with specialized know-how.

Why Concept of Operations?

Needs

- Better oversight of increasingly complex and global manufacturing of drugs
- Improved efficiency in line with the ORA Program Alignment into vertically integrated, program aligned areas
- Enhanced IQA approach – alignment/integration between field professionals and review staff
- New commitments and improved coordination and efficiency of work performed under generic drug program as per GDUFA II

Concept of Operations Goals

Goals

- Create and implement a **formalized and streamlined facility evaluation and inspection program** that ensures:
  - Consistency, efficiency, and transparency in facility evaluations, inspections, and regulatory decision-making for marketing applications across the FDA;
  - Strategic alignment across CDER and ORA functional units by clarifying roles and responsibilities;
  - Improved FDA's operational capacity by enhancing collaboration between various CDER and ORA offices;
  - Enhanced quality and increased access to facility and regulatory decisional information across FDA;
  - Improved timelines for regulatory, advisory, and enforcement actions to protect public health and promote drug quality, safety, and effectiveness.

Concept of Operations Goals

Scope

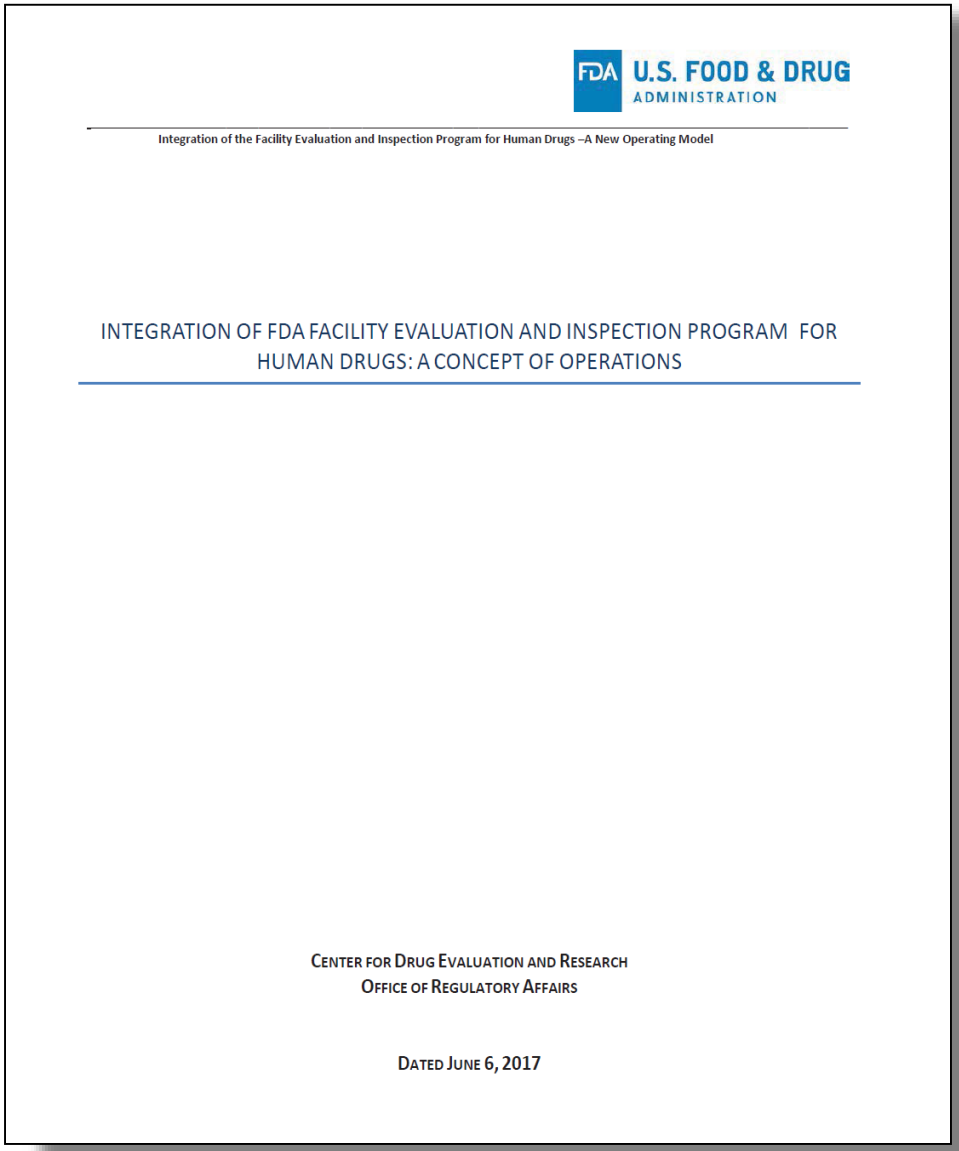
- **All quality inspections** - pre-approval, post-approval, surveillance, for-cause
- **All inspection locations -** domestic and international
- **Development, communication, implementation** of ConOps in
  - CDER
    - OPQ (OPPQ, OPF and OS)
    - OC OMQ
  - ORA
    - Office of Operations
    - Office of Pharmaceutical Quality Operations
    - Office of Medical Products and Tobacco Operations
    - Office of Policy and Risk Management

ConOps Agreement

- Covers Pre- and Post-Approval, Surveillance, and For-Cause Inspections at domestic and international drug facilities
- Does not cover compounding, and bioresearch monitoring, and Pre-Approval Inspections for biotech products
- For ORA and CDER staff involved in these inspections, outlines
  - workflow
  - roles and responsibilities (RACI charts;

R: Responsibility; A: Accountability;

C: Consulted; I: Informed)



FDA U.S. FOOD & DRUG ADMINISTRATION

Integration of the Facility Evaluation and Inspection Program for Human Drugs –A New Operating Model

INTEGRATION OF FDA FACILITY EVALUATION AND INSPECTION PROGRAM FOR HUMAN DRUGS: A CONCEPT OF OPERATIONS

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF REGULATORY AFFAIRS

DATED JUNE 6, 2017

Four Major Types of Drug-Related Inspections

- **Pre-approval:**
  - supports the review of marketing applications for drug products to ensure high-quality manufacturing
- **Post-approval:**
  - is initiated after drug application approval to verify that the commercial-scale manufacturing produces the drug as it was designed and approved
- **Surveillance:**
  - monitors the state of pharmaceutical manufacturing quality to satisfy our legal obligation to inspect production operations
- **For-cause**:
  - is initiated in response to a specific event or observation that brings into question the quality of a manufacturing facility, process, or drug product;
  - is meant to determine whether recalls or enforcement actions are necessary, particularly as a result of the initial cause for concern

ConOps Highlights

What is different?

- Improved communication with stakeholders
  - decisional letters
  - follow-up engagements
- Defined timelines
- Parity between domestic and international inspections
- Improved collaboration, communication, and information sharing between CDER and ORA
- Streamlined work flow
- Consistent work processes
- Clear roles and responsibilities
- Better use of quality knowledge to support facility evaluations (e.g., site dossiers)

The 90-Day Letter

- Goal
  - Increase engagement with industry by communicating the final inspection classification to the facility within 90 days of the end of the inspection
- Scope
  - Applies to any CDER led 56002 A-T inspection
- GDUFA II Commitment
  - "*By October 1, 2018, FDA agrees to communicate to the facility owner final inspection classifications that do not negatively impact approvability of any pending application within 90 days of the end of the inspection. FDA agrees to ongoing periodic engagement with industry stakeholders to provide updates on agency activities and seek stakeholder feedback*."

Some Q & A

Can all facility owners expect final inspection classification communications within 90 days of inspection closing?
CDER and ORA will start to issue the 90-day decisional letters by the end of 2017 with a goal of 90 percent in this timeframe in 2018.

Will domestic and international facilities be evaluated differently?
No, the ConOps will enhance FDA's commitments to provide, among other things, risk-based parity and consistent processes for domestic and international facility evaluation and inspection.

Will the ConOps help address problems at manufacturing facilities that have impacted approval of drug applications?
Companies retain the responsibility of ensuring that their products are manufactured in accordance with current good manufacturing practice (CGMP) regulations. The ConOps promotes transparency and communication between the agency and industry for facilities involved in manufacturing human drugs. The enhanced communication between FDA and facility owners may help them address problems more efficiently.

ConOps Current State & Next Steps

Future

- Operationalization of ConOps (began Fall 2017)
- 90-day decisional letters to communicate final inspection classifications within 90 days of the end of Surveillance, Post-Approval, or For-Cause inspections and within GDUFA or PDUFA application timeframes
- Program/staff-level SOPs related to inspection and surveillance activities
- Train CDER and ORA staff on ConOps workflows and associated roles and responsibilities, processes, and procedures
- Update documents such as MAPPs, CPGMs, IOM, RPM
  - 56002 updated 10/31/17
  - Others in process

ConOps Readings

- ConOps White Paper

https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/UCM574362.pdf

- Blog by FDA Commissioner, Scott Gottlieb, M.D., from Aug 31, 2017

https://blogs.fda.gov/fdavoice/index.php/2017/08/new-steps-to-strengthen-fdas-inspection-and-oversight-of-drug-manufacturing/#

- Q&A on ConOps

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm576309.htm