Inspections and ANDA Review: CDER/OC/OMQ’s Role

Francis Godwin, Acting Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

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Outline

• OMQ’s Mission
• Enforcing CGMP
  — What OMQ Evaluates
  — Generics
  — Pending ANDAs
• How Cases Come to OMQ
• Recent OMQ Actions
OC/OMQ Mission

• CDER Office of Compliance (OC) Mission Statement:

  Promote and protect the public health through strategies and actions that minimize consumer exposure to unsafe, ineffective, and poor quality drugs.

• OMQ supports the OC mission by focusing on drug manufacturing
What OMQ Does

• Evaluate compliance with CGMP and other quality issues, primarily for marketed drugs
• Evaluate inspection reports and evidence gathered by FDA investigators in ORA, collaborating with other offices.
• Review information from other FDA offices including OPF and OS
What OMQ Evaluates
Manufacturing Facility Types

• Finished dosage form (FDF) manufacturers
• Active pharmaceutical ingredient (API) manufactures
• Repacking and relabeling operations
  – Finished dosage forms
  – Active pharmaceutical ingredients
• Laboratories
  – Internal
  – Contract labs
• Contract manufacturers
• Others
Drug Profile Types

- Sterile injectables
- Ophthalmics
- PET drugs
- Topical (sterile and non sterile)
- Transdermal patches
- Tablets & capsules
- Solutions and suspensions

- API by chemical synthesis
- API by fermentation
- Crude API
- Medical gas
- Intermediates
- Excipient
- Components
- Others
Regulatory Pathways: CGMP for All

- Prescription
- Over-the-Counter (OTC)
- Biologics (BLA)
- Innovators (NDA)
- Generics (ANDA)

- Unapproved drugs
- Monograph
- Homeopathic
- Pharmacy compounded
  - CGMP & insanitary conditions
How Generics Fit In

• Generics – just one subset of drug manufacturers OMQ evaluates.
• We apply the same CGMP requirements to generics as to other drugs.
• OMQ’s focus: surveillance CGMP inspections & violations/deviations for distributed drugs.
• Sometimes OMQ reviews pre-approval inspections if indicative of marketed product issues.
Facility Requirements for ANDAs

FDA cannot approve an application if:

...the methods used in, and the facilities and controls used for, the manufacture, processing, and packaging of such drug are inadequate to preserve its identity, strength, quality, and purity. FD&C Act § 505(j)(4)

What does this mean for OMQ cases?
Pending ANDAs & OMQ Cases

• OMQ does not review pending ANDAs.
• But, if a facility named in an application is not compliant with CGMP, FDA cannot approve the application.
• OAI classification may trigger a variety of different enforcement outcomes in addition to affecting application approval.
• OMQ cases focus on enforcement for OAI matters; we do not make review decisions.
How Cases Come to OMQ
How Cases Come to OMQ

- OMQ cases evaluate questions about deficient CGMP or other manufacturing standards.
- Case referrals can come from
  - OPQ (including OPF and OS)
  - ORA
  - Other Compliance sub offices
  - Other Centers (usually other compliance office)
- Some are initiated in OMQ:
  - Informants
  - Incidents, complaints, signals
Recent OMQ Actions
OMQ Actions
January-September 2016

- Import Alerts 66-40, 19
- Import Alerts 99-32, 21
- Regulatory Discretions, 22
- Warning Letters Issued & Cleared, 37
- Injunctions, 2
- Pharmacy Compounding Letters, 42
- Regulatory Meetings, 20
- Untitled Letters, 3
Recent Warning Letter Trends: CGMP Violations and Deviations

- Data manipulation, deletion, and falsification
  - Manufacturing process and analytical and micro labs
  - Electronic and paper
- Falsified supply chain/pedigree information
- Controls over incoming components/raw materials
- Sterility assurance
- Basic CGMP
  - No release testing
  - Dirt, mold, rodents, insects, & pests in manufacturing areas
- Delay, denial, refusal, and/or limitation of inspections
Questions?