OPQ Policy Update

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Outline

- GDUFA II commitments focused on pharmaceutical quality
- Quality policy initiatives & collaborations
- Best practices that can help reduce quality issues during ANDA reviews

GDUFA II commitments focused on pharmaceutical quality

Pre-submission Facility Correspondence

- Impacts review performance goals for:
  - Priority original ANDAs
  - Priority major ANDA amendments and priority PASs where preapproval inspections are required
- Pre-Submission Facility Correspondence Information
  - Must be submitted 2 months in advance
  - Must be complete, accurate, and remain unchanged

Pre-submission Facility Correspondence

- Facility Name
- Facility Contact Name
- FEI
- Facility Address
- DUNS
- Operations Performed
- Confirm that facilities are ready for inspection
- Description of Mfg. Process
- DMF Completeness Certification

Communication Regarding Inspections

- May 31, 2018
  - For facilities named in an ANDA, PAS, or Type II DMF, if outstanding issues that could prevent approval are identified, applicants will be notified through an Information Request (IR), Discipline Review Letter (DRL) or Complete Response Letter (CRL)
- October 1, 2018
  - FDA will notify facility owners of final inspection classifications that do not negatively impact approvability within 90 days of the end of the inspection.

Site-selection model

- Guidance outlining:
  - Risk factors in the model
  - How the model is used to identify establishments for surveillance inspection in a given year

Post approval changes to Type II DMFs

- October 1, 2018 deadline to issue guidance
  - Includes submission mechanisms for ANDA applicants who reference Type II DMFs

IID Improvements

- Enhancements to the database by October 1, 2020 to allow users to electronically query:
  - Maximum daily intake
  - Maximum daily exposure
- Updates on an on-going basis and quarterly notices of updates made
- IIDUpdate@fda.hhs.gov

Quality Policy Initiatives & Collaborations

Mutual Recognition Agreement

- Agreement between FDA and EU
- Member state assessments conducted by FDA prior to relying upon inspection results
- Avoids duplication of inspections
  - Less burden on facilities in capable EU member states
- Prioritization of resources in areas of greater risk

Mutual Recognition Agreement

- A capable inspectorate:
  - has the legal and regulatory authority to conduct inspections against a standard for GMP;
  - manages conflicts of interest in an ethical manner; evaluates risks and mitigates them;
  - maintains appropriate oversight of manufacturing facilities within its territory;
  - receives adequate resources and uses them;
  - employs trained and qualified inspectors with the skills and knowledge to identify manufacturing practices that may lead to patient harm; and
  - possesses the tools necessary to take action to protect the public from harm due to poor quality drugs or medicinal products.
- Not required to have identical procedures

OPQ International Activities

- ICH guideline development
  - Q12 Pharmaceutical Product Lifecycle Management
  - M9 Biopharmaceutics Classification System-Based Biowaivers
  - M10 Bioanalytical Method Validation
- PIC/S – participation on expert circles to develop aide memoires and delivering training
- Engagement with international consensus standards development organizations (e.g., ISO)
- Outreach and training delivered in collaboration with FDA foreign offices

CDER 2017 Guidance Agenda

- Pre Submission Facility Correspondence for Priority ANDAs in GDUFA II
- CMC Postapproval Manufacturing Changes for Specified Biological Products to be Documented in Annual Reports
- Container Closure Systems for Packaging Human Drugs and Biologics; Revised Draft
- Drug Master Files; Revised Draft
- Drug Products, Including Biological Products, That Contain Nanomaterials
- GDUFA II Priority ANDA Pre-Submission Communications
- Harmonizing Compendial Standards with Drug Application CMC Approval Requirements Using the USP Pending Monograph Process
- In-vitro Methods for Evaluation of Abuse Deterrent Properties of Opioid Products

CDER 2017 Guidance Agenda (cont.)

- Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products - Chemistry, Manufacturing, and Controls Documentation; Revised Draft
- Child Resistant Packaging Statements in Drug Product Labeling
- Gluten in Drug Products and Associated Labeling Recommendations
- Type V Drug Master File (DMF) for Combination Products with CDER Jurisdiction Utilizing a Device Part with Electronics or Software
- Use of the FDA Inactive Ingredient Software (IID)
- Visual Inspection of Injectable Drug Products
- Current Good Manufacturing Practice for Medical Gases; Revised Draft
- Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products; Revised Draft
- Field Alert Report Submission
- Repackaging of Certain Drug Products by Pharmacies and Outsourcing Facilities

Best Practices That Can Help Reduce Quality Issues During ANDA reviews

Understand the supply chain

- Lack of communication with suppliers has led to delays in ANDA approvals
- Relationship with suppliers requires ongoing effort throughout the product lifecycle
- Identify and take steps to mitigate weak points in the supply chain
  - Careful audits of potential suppliers
  - Monitor and trend relevant metrics
  - Sole source suppliers
- Work with suppliers and contract manufacturers or labs before there is a problematic inspection. Your success is tied to their success!

Communicate regularly with suppliers and contractors

- DMF holders
  - Last minute (unsolicited) DMF amendments can delay ANDA approvals
- Contract manufacturers / laboratories
  - Lack of transparency regarding adverse inspection outcomes can lead to delays in ANDA approval
  - It can be difficult for the applicant to know whether the issues can be easily addressed or whether an alternative manufacturer/lab should be pursued

Monitor the USP and the PF

- For products covered by a monograph
  - Nomenclature must be the same as the monograph title
  - Product must meet monograph standards if tested
- New monographs may be introduced at any time
  - If USP is proposing a monograph that your product would not meet, respond to the PF (Pharmacopeial Forum)

USP Pending Monographs Guideline

- Encourages timely use of the USP pending monograph process for situations where ANDA approvals expected to differ from official USP monographs
  - To have an official USP-NF monograph consistent with FDA approval criteria as soon as possible after FDA approval of an application
  - Allows progress of USP internal processes and publication of 'Notice of Intent to Revise' before FDA approval has been granted to an applicant
  - http://www.usp.org/sites/default/files/usp_pdf/EN/USPNF/pendingStandards/2015-06-01-pending-monograph-guideline.pdf
  - FDA to provide further guidance on the topic

FDA U.S. FOOD & DRUG ADMINISTRATION

Thank You!

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