OPQ Policy Update

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Overview

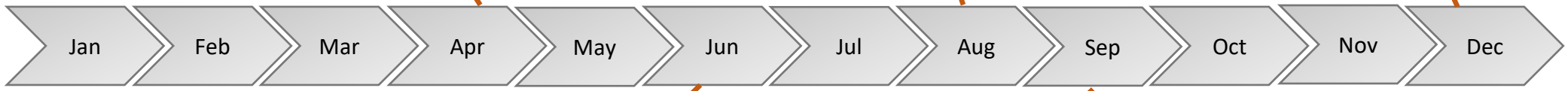
- COVID-related policy efforts
- Other recent quality guidance
- Quality policy priorities for 2021
  - Guidance/regs
  - Priority initiatives
- Challenge questions

COVID-related Quality Guidance - 2020

Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers

Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID-19 Public Health Emergency

Review Timelines for Applicant Responses to Complete Response Letters When a Facility Assessment Is Needed During the COVID-19 Public Health Emergency



Good Manufacturing Practice Considerations for Responding to COVID-19 Infection in Employees in Drug and Biological Products Manufacturing

Resuming Normal Drug and Biologics Manufacturing Operations During the COVID-19 Public Health Emergency

COVID-related Quality Guidance - 2021

Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers (Update)

COVID-19 Container Closure System and Component Changes: Glass Vials and Stoppers

Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting SARS-CoV-2 Infectivity

Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency

Other COVID-related Guidance 2020-2021

- Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)
- Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)
- Policy for the Temporary Use of Portable Cryogenic Containers Not in Compliance With 21 CFR 211.94(e)(1) For Oxygen and Nitrogen During the COVID-19 Public Health Emergency
- Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Outsourcing Facilities During the COVID-19 Public Health Emergency
- Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency
- Development of Monoclonal Antibody Products Targeting SARS-CoV-2, Including Addressing the Impact of Emerging Variants, During the COVID 19 Public Health Emergency

COVID-related Policy Implementation

- Internal working groups addressed numerous operational challenges associated with the impact of travel restrictions on pending applications
  - ✓ Alignment on approach across Centers (CBER, CDER, CVM, ORA)
  - ✓ Communications to applicants and DMF holders for different scenarios
  - ✓ Determining how inspections will be prioritized once travel restrictions are lifted
  - ✓ Documenting when records requests under section 704(a)(4) can be used in lieu of preapproval inspection
  - ✓ Guidance on review timelines for applicant responses to complete response letters
  - ✓ Communications to facilities regarding FDA assessment of records received pursuant to a 704(a)(4) request
  - ✓ Use of MRA 3rd country inspection reports

Other Recent Quality Guidance

- Draft - Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research (July 2020)
- Draft - Setting Endotoxin Limits During Development of Investigational Oncology Drugs and Biological Products (July 2020)
- Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products (July 2020)
- Immediate Final - Control of Nitrosamine Impurities in Human Drugs Guidance for Industry (September 2020)
- Draft - The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls (September 2020)

Quality Policy Priorities for 2021

- Guidance – draft/revised draft
  - ANDAs: Stability Testing of Drug Substances and Products Questions and Answers
  - Quality and Stability Testing of Drug Substances and Drug Products for NDAs, ANDAs, and BLAs and Associated Labeling Statements for Drug Products
  - Inspection of Injectable Products for Visible Particulates
  - Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations
  - Microbiological Quality Considerations in Non-Sterile Drug Product Manufacturing
  - CDER's Program for the Recognition of Voluntary Consensus Standards (final)

CARES Act Implementation

- New section 506C(j) to the FD&C Act – added requirement for risk management plans (RMPs)
- New subsection 510(j)(3) of the FD&C Act – added a requirement that persons who register drug establishments under section 510 report annually the amount of each listed drug manufactured for commercial distribution

Risk Management Plans

- CARES Act added Section 506C(j) to the FD&C Act:
  - Each manufacturer of:
    - a drug that is life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug used in emergency medical care or during surgery or any such drug that is critical to the public health during a public health emergency declared by the Secretary … that is not a radio pharmaceutical drug product or any other product as designated by the Secretary; or
    - any **active pharmaceutical ingredient** or any associated medical device used for preparation or administration included in the drug
  - shall **develop, maintain, and implement**, as appropriate, a **redundancy risk management plan** that identifies and evaluates risks to the supply of the drug, as applicable, for each establishment in which such drug or active pharmaceutical ingredient of such drug is manufactured
- FDA draft guidance *Risk Management Plans to Mitigate the Potential for Drug Shortages* in development

Reporting Amount of Listed Drugs

- CARES Act added Subsection 510(j)(3) to the FD&C Act:
  - "Each person who registers with the Secretary under this section with regard to a drug shall report annually to the Secretary on the amount of each drug listed under paragraph (1) that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution. Such information may be required to be submitted in an electronic format as determined by the Secretary."
  - "By order of the Secretary, certain biological products or categories of biological products regulated under section 262 of title 42 may be exempt from some or all of the reporting requirements…"
- FDA draft guidance on Reporting Amount of Distributed Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act in development

Other Quality Policy Priorities for 2021

- Proposed Rulemaking: Post Approval Changes to Approved Applications
- Internal: Implementation activities associated with “alternate tools” used when inspections cannot be accomplished due to travel restrictions
- Quality Management Maturity
- International Harmonization
  - ICH
  - PIC/S

International Harmonization

- Provides opportunities to reduce regulatory burden and incentivize continual improvement and innovation

Recently finalized:

- ICH Q12 *Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*
- ICH M9 *Biopharmaceutics Classification system-based Biowaivers*

Under development:

- ICH Q13 *Continuous Manufacturing*
- ICH Q2(R2)/Q14 *Analytical Procedure Development and Validation*
- ICH Q3E *Impurity: Assessment and Control of Extractables and Leachables for Pharmaceuticals and Biologics*

New work items:

- ICH Q9(R1) *Quality Risk Management*
- ICH M4Q(R1) *The CTD – Quality*

International Harmonization (cont.)

- Opportunities for further input to the ICH development process
  - Quality Discussion Group (QDG)
    - ICH Reflection Paper on Advancing Biopharmaceutical Quality Standards to Support Continual Improvement and Innovation in Manufacturing Technologies and Approaches (endorsed June 2018)
  - Informal Generics Discussion Group (IGDG)
    - ICH Reflection Paper on Further Opportunities for Harmonization of Standards for Generic Drugs (endorsed November 2018)
- PIC/S – Pharmaceutical Inspectorate Cooperation Scheme
  - Draft Recommendation “How to Evaluate/Demonstrate the Effectiveness of a Pharmaceutical Quality System in relation to Risk-based Change Management”

ICH Q12

Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

- Guideline finalized by ICH in November 2019 (https://ich.org/page/quality-guidelines)
- ICH IWG developing training materials for assessors and inspectors in cooperation with PIC/S, for use in all regions
- Final guidance (FDA version) awaiting publication
- Implementation of the full Q12 guideline in the U.S. begins with publication
  - Scope includes innovators, generics, biosimilars, CDER- and CBER-led combination products
  - Can be used for new products and already marketed products
- FDA guidance on details of implementation in the U.S. awaiting publication
- MAPP - *Implementation of Established Conditions as Described in ICH Q12* being developed

Challenge Question - #1

True or False?

The new requirement to develop, maintain, and implement, as appropriate risk management plans does not apply to any API manufacturers.

Challenge Question - #2

True or False?

ICH guidelines are relevant to generic drug products.

Thank You!