Introduction

This section provides information on the Office of Pharmaceutical Quality's report on the state of pharmaceutical quality, including drug manufacturers, quality surveillance programs, supply chain vulnerability, drug shortages, recalls, and global trends in quality and product failures.

* The Office of Pharmaceutical Quality ensures the safety and effectiveness of drugs in the US market.
* The report highlights the implementation of the CARES Act Drug Amount Reporting Program and the Quality Management Maturity program.
* New approaches, such as quantitative measures of natural hazard risk, are discussed to prevent quality issues and supply chain vulnerability.
* The report provides data on drug shortages, recalls, and global trends in quality and product failures.

Manufacturing Site Demographics:

The FY2023 report highlights key findings on drug manufacturing sites, inspections, and outcomes, including an increase in inspections and the highest number of inspections classified under MRAs.

* The CDER Site Catalog includes over 4,800 drug manufacturing sites globally, with 42% located in the U.S.
* There were 776 drug quality assurance inspections in FY2023, a 40% increase from the previous year.
* The number of inspections classified under MRAs reached 187, the highest to date.
* The majority of drug manufacturing sites in the U.S. are in the "No Application" sector, indicating products are marketed without FDA approval.
* Biological products, innovator products, and generic products are manufactured at the remaining 60% of sites.
* The U.S., India, China, Germany, and Italy had the most sites in the FY2023 Site Catalog, with significant net increases over the past five years.
* Foreign inspections accounted for approximately 59% of all drug quality assurance inspections in FY2023.
* The majority of sites in the CDER Site Catalog received NAI or VAI outcomes from their most recent inspections, ranging from 89% for India to 98% for Europe.

Drug Product Demographics

This section discusses CDER's Product Catalog, which contains application and non-application products, as well as the reliance on foreign manufacturing sites for essential medicines. It also highlights the importance of risk management plans in mitigating risks, including those caused by natural hazards.

* The CDER Product Catalog at the end of FY2023 contained 17,519 application products and 131,367 non-application product National Drug Codes (NDCs).
* 80 out of 168 CDER-regulated essential medicines were solely reliant on foreign manufacturing sites for their active pharmaceutical ingredient (API).
* Nearly all essential medicines had at least one domestic finished dosage form (FDF) manufacturer.
* Risk management plans (RMPs) should be used to mitigate risks, including those caused by natural hazards.
* The number of products listed in the CDER Product Catalog increased by 6% in FY2023.
* Most essential medicines are injectables, with 44% solely reliant on foreign manufacturing facilities for API.
* The FEMA National Risk Index (NRI) was used to assess natural hazard risks for EM manufacturing sites, with 34% located in high-risk counties.
* CDER received 12,549 quality-related MedWatch reports, 3,792 Field Alert Reports, 347 Biological Product Deviation Reports, and 398 consumer complaints in FY2023.

Import Alerts, Recalls, and Warning Letters:

The section discusses the increase in drug quality-related import alerts and recalls in FY2023, with a focus on the reasons behind the increase, the countries involved, and the types of defects leading to recalls.

* In FY2023, there were 93 drug quality-related import alert additions, more than the combined total of FY2021 and FY2022.
* Ophthalmic drug products accounted for 17% of the recalled products.
* The number of recalls in FY2023 decreased by 26% compared to FY2022 but was similar to the five-year average.
* The majority of import alert additions were for manufacturers of OTC monograph drug products.
* The increase in import alert additions was driven by sites that refused to respond to record requests and CGMP deficiencies identified through record review.
* A significant number of import alert additions were related to hand sanitizer sites that did not meet quality standards.
* China, South Korea, and India had a disproportionate number of import alert additions compared to their representation in the foreign sites catalog.
* The most common defect group for recalls was CGMP deficiencies, and the highest number of recalls came from the U.S. and India.
* FY2023 saw an increase in recalls due to contamination, including sterility assurance issues and foreign material/particulate contamination.
* The USPTC of antibacterials had the highest percentage of recalls, followed by therapeutic nutrients/minerals/electrolytes and anxiolytics.
* Six recalls were attributed to unapproved drug products marketed in the U.S. without conforming to an OTC monograph or receiving FDA approval.
* FDA issued 94 warning letters to drug manufacturing sites, with the majority of sites manufacturing OTC monograph products.
* Over a quarter of the warning letters resulted from refusal to respond to records requests or CGMP issues identified during records review.

Analyses on the State of Pharmaceutical Quality

This section discusses the impact of record requests on FDA actions and enforcement, as well as the reasons for drug shortages and potential solutions.

* Record requests under §704(a)(4) have been effective in identifying quality problems and have led to warning letters and import alert additions.
* Quality problems and increases in demand are the main causes of drug shortages, each accounting for 40% of shortages in the past two years.
* Inspections and §704(a)(4) records requests have resulted in an increasing number of actions and enforcement by the FDA.
* The number of inspections decreased in FY2021 due to travel restrictions during the COVID-19 pandemic.
* §704(a)(4) records requests peaked in FY2021 and have since leveled off.
* The FDA classifies drug shortages based on seven reasons, including quality issues, manufacturing delays, and product discontinuation.
* Previously, 62% of shortages were caused by quality issues, but in the past two years, quality problems and increases in demand have each caused 40% of new drug shortages.

Sampling and Testing:

FDA's testing of hand sanitizer products from domestic manufacturers during the COVID-19 pandemic revealed a high incidence of violative samples. Out of 310 products tested, 71.6% of the manufacturers had violative products. The FDA continues to educate consumers about safe use of hand sanitizers.

Commitment to Quality:

This section discusses the compliance for CARES Act annual amount reporting and the improvements to the CDER NextGen portal. It also highlights the stakeholder engagement in the development of the Quality Management Maturity (QMM) program.

* Compliance for CARES Act annual amount reporting is expected to increase with improvements to the CDER NextGen portal.
* The final guidance on Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the Federal Food, Drug, and Cosmetic Act was published in February 2024.
* Less than half of the active products listed in FDA's eDRLS have submitted drug amount reports.
* The publication of the final guidance and enhancements to the NextGen portal are expected to improve reporting levels.
* CDER has engaged with more than ten stakeholder groups and received 23 responses about the voluntary QMM program.
* CDER has developed a prototype assessment protocol for the QMM program and initiated the voluntary Quality Management Maturity Prototype Assessment Protocol Evaluation Program.

Assurance of Quality:

This report by the U.S. Food and Drug Administration (FDA) aims to improve drug manufacturing and increase awareness about quality and availability risks. FDA's monitoring efforts include assessing adverse events, evaluating inspection outcomes, and conducting product testing to enhance the availability of quality medicines.