U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

Fiscal Year 2023 Report on the State of Pharmaceutical Quality

June 2024

Introduction

The Office of Pharmaceutical Quality (OPQ) in the U.S. Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER) assures that drugs legally marketed in the U.S. are safe and effective, and meet quality standards. This 6th Report on the State of Pharmaceutical Quality (FY2023[1]) was produced by OPQ's Office of Quality Surveillance as part of its mission to promote the availability of quality medicines for the American public. This report provides information about FDA-registered drug manufacturers[2] and the quality of the U.S. drugs supply, including biological products regulated by CDER.[3]

In addition to analyses and insights about drug manufacturers and their products, this report:

- Highlights two quality surveillance programs that are advancing CDER's quality oversight: the implementation of the CARES Act[4] Drug Amount Reporting Program and the development of a Quality Management Maturity (QMM) program. CARES amount reporting will provide FDA with deeper supply chain knowledge while QMM encourages manufacturers to foster a quality culture mindset.
- Describes new approaches, such as quantitative measures of natural hazard risk, to help FDA and its stakeholders better prevent or mitigate quality issues that may lead to supply chain vulnerability and drug shortages in a changing environment.
- Presents reasons for new drug shortages that occurred during calendar years (CY) 2022 and 2023.
- Provides data on recalls and global trends in quality and product failures.
- Shares findings from a recent assessment of the public health value of requests for records and other information under the Federal Food, Drug, and Cosmetic Act (FD&C Act) §704(a)(4).

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1 Fiscal Year 2023 (FY2023) was from October 1, 2022 to September 30, 2023.

2 A "manufacturer" is anyone engaged in manufacturing, preparing, propagating, compounding, processing, packaging, repackaging, or labeling of a drug.

3 This report covers CDER-regulated products and excludes products regulated by FDA's Center for Biologics Evaluation and Research (CBER), e.g., blood, vaccines, tissues, and certain other biological products.

4 The Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was enacted on March 27, 2020 to aid response and ease economic impacts of COVID-19.

Manufacturing Site Demographics

FY2023 Key Takeaways:

- CDER's Site Catalog has more than 4,800 manufacturing sites[5] globally, with almost 42% of sites located in the U.S.
- There were 776 drug quality assurance inspections, over 40% more than the 548 accomplished in FY2022.
- There were 187 Mutual Recognition Agreement (MRA) partner inspections classified under the MRAs, the highest number achieved to date.

Manufacturing Site Demographics

At the end of FY2023, the CDER Site Catalog[6] included 4,819 drug manufacturing sites (Table 1), which represents a 14% increase in the number of sites over the past five years. Of all FY2023 drug manufacturing sites, 40% are in the "No Application" sector, indicating that all products manufactured at those sites are marketed in the U.S. without approved FDA applications. The majority of this sector includes over-the-counter (OTC) monograph products, but also includes marketed unapproved prescription drug products and homeopathic products. The remaining 60% of sites manufacture at least one application product, including:

- Biological products licensed under Biologics License Applications (BLAs)[7]
- Innovator products approved under New Drug Applications (NDAs)
- Generic products approved under Abbreviated New Drug Applications (ANDAs)

5 Although they meet the definition of "manufacturer," medical gas manufacturers (based on existing CDER Site Catalog policy) and registered outsourcing sites (under section 503B of the FD&C Act) are excluded from the count and analyses presented in this report.

6 The CDER Site Catalog is the curated inventory of registered manufacturing sites, vetted by FDA as legally manufacturing human drugs for the U.S. market. Hence, not all registered human drug sites qualify as "manufacturers" for the CDER Site Catalog.

7 See FDA's webpage for further explanation of which therapeutic biological products are regulated by CDER per the original transfer and those subsequently deemed to be BLA products.

The five countries with the most sites in the FY2023 Site Catalog (U.S., India, China, Germany, and Italy) all had large net increases over the past five years, accounting for new registrations and removals.[8] Four countries, Germany, South Korea, Spain, and Mexico each experienced growth of least 15% increases in their number of sites. Curating an accurate Site Catalog is foundational to comprehensive quality surveillance.

Table 1. Inventory Shift Over FY2019-FY2023 for Countries with Greater Than 50 Sites

Country	Sites in FY2023 Catalog	5-Year Review of Sites in the Catalog			
		Sites Maintained	Sites Removed	Sites Added	% Net Change
United States	2,009	1,459	317	544	**11%**
India	585	438	54	146	**16%**
China	484	284	76	196	**25%**
Germany	195	153	12	42	**15%**
Italy	151	130	10	21	**7%**
France	142	113	11	29	**13%**
Canada	139	115	30	24	**-4%**
Japan	128	108	18	20	**2%**
United Kingdom	103	86	18	17	**-1%**
South Korea	93	42	27	50	**25%**
Spain	91	72	5	19	**15%**
Switzerland	79	60	9	19	**13%**
Mexico	74	47	8	27	**26%**
Ireland	59	49	4	10	**10%**
All Others	487	323	71	163	**19%**
Total	**4,819**	**3,479**	**670**	**1,327**	**14%**

The number of FDA-conducted drug quality assurance inspections, which includes surveillance and for-cause inspections, increased from 522 in FY2022 to 766 in FY2023; this is the highest number of inspections since the start of the COVID-19 Public Health Emergency (PHE)[9] (Figure 1).[10]

8 FDA removes sites from the CDER Site Catalog if they are not currently engaged in the manufacture of human drugs for the U.S. market and therefore are not subject to routine surveillance inspection. This commonly occurs when sites deregister or are no longer active in an approved application.

9 The duration of this PHE, as determined by the Secretary of Health and Human Services, was January 27, 2020 – May 11, 2023.

10 Counts were revised in August 2025 to remove the inadvertent inclusion of medical gas inspections.

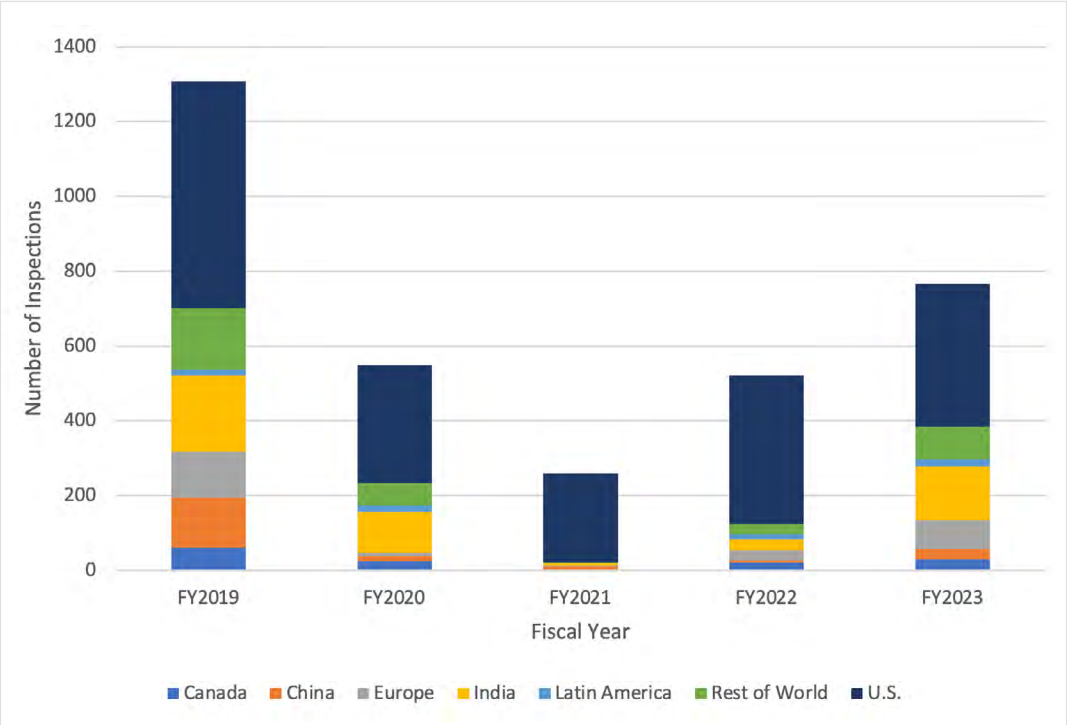

Figure 1. Drug Quality Assurance Inspections by Country and Region for FY2019-FY2023

Foreign inspections are accomplished by either conducting FDA drug quality assurance inspections or by assessing and classifying inspections from MRA partners. In the same timeframe, the number of inspections classified under the MRAs increased from 144 in FY2022 to 187 in FY2023, the highest number achieved to date. As travel restrictions eased with the end of the COVID-19 PHE, foreign inspections continued to increase, constituting approximately 59% of all FY2023 drug quality assurance inspections. This progress in foreign inspections was particularly evident in India, where 25% of Indian sites in the Site Catalog were inspected. By comparison, 6% of the Chinese sites and 20% of the U.S. sites in the Site Catalog were inspected in FY2023. For India, the higher inspectional coverage of sites in the Site Catalog was driven by for-cause inspections, while for China, travel restrictions continued for almost all of FY2023, delaying inspections. In comparison, Site Catalog coverage was 32% - 39% for those countries in FY2019.

Globally, 94% of all sites in the CDER Site Catalog received no action indicated (NAI) or voluntary action indicated (VAI) as their most recent inspection classification. The percent of sites that received NAI or VAI outcomes from their most recent inspection ranged from 89% for India to 98% for Europe (Table 2). It should be noted that inspection outcome is a measure of site current good manufacturing practice (CGMP) compliance and not a direct measure of drug product conformance to product specifications.

Table 2. Percent of Sites with Most Recent Inspection Outcomes of NAI or VAI by Country/Region as of FY2023

Country or Region	Count of Inspections	Count of NAI and VAI Outcomes	Percent of Sites
Canada	139	131	94%
China	308	293	95%
Europe	991	974	98%
India	500	444	89%
Latin America	82	75	91%
Rest of the World	315	298	95%
U.S.	2,135	2,000	94%
Global Average	**4,470**	**4,215**	**94%**

Drug Product Demographics

Key Takeaways:

1. At the end of FY2023, CDER's Product Catalog contained 17,519 application products (16,698 in FY2022) and 131,367 non-application product National Drug Codes (NDCs) (123,532 in FY2022).
2. Of the 168 CDER-regulated essential medicines, medical countermeasures, and critical inputs (EM), 80 drug products were solely reliant on foreign manufacturing sites for their active pharmaceutical ingredient (API).
3. Nearly all EM products (156 out of 168) had at least one domestic finished dosage form (FDF) manufacturer.
4. Risk management plans (RMPs) should be used to mitigate risks, including those caused by natural hazards.

The CDER Product Catalog is a regularly updated record of all application products (NDAs, ANDAs, and BLAs) and non-application products (OTC monograph products, marketed unapproved prescription drugs, homeopathic products, etc.). At the end of FY2023, the Product Catalog included 13,572 ANDAs, 3,593 NDAs, 354 BLAs, and 131,367 non-application product NDCs.[11] Some of these applications may include multiple NDCs, each with different strengths, concentrations, or package configurations. In FY2023, the number of applications in the catalog increased for all categories. The largest percent increase was observed for BLA products (9%) and the smallest increase was for NDA products (1.5%). Overall, the number of products listed increased 6% to 148,886 in FY2023.

11 The NDC is a 10- or 11-digit identifier for drugs listed with FDA that consists of three segments: "labeler code" (manufacturer or distributor), "product code" (drug product: formulation, dosage form, and specific strength), and "package code" (commercial package size and type).

Essential Medicines

In October 2020, FDA published its List of Essential Medicines, Medical Countermeasures and Critical Inputs as required by Executive Order 13944. To meet patient needs, CDER monitors the availability of 168 EM products that are manufactured at more than 1,600 facilities. The majority (63%) of these EM manufacturing facilities are foreign, and most EM products have foreign manufacturing sites for their API and finished dosage form (FDF) (Figure 2). In particular, only 18% of EM API manufacturing facilities and 42% of EM FDF manufacturing facilities are located in the U.S. However, more than half of the EM products have at least one domestic source of API, and nearly all EM have at least one domestic FDF manufacturer.

When considering dosage form, most (67%) EM products are injectables, 44% of which are solely reliant on foreign manufacturing facilities for API. EMs that fall into other dosage form categories (including solid oral dosage forms and inhalation products) have even greater reliance on foreign API manufacturing. These data demonstrate the importance of efforts to strengthen U.S. domestic supply chains for the most medically necessary drug products.

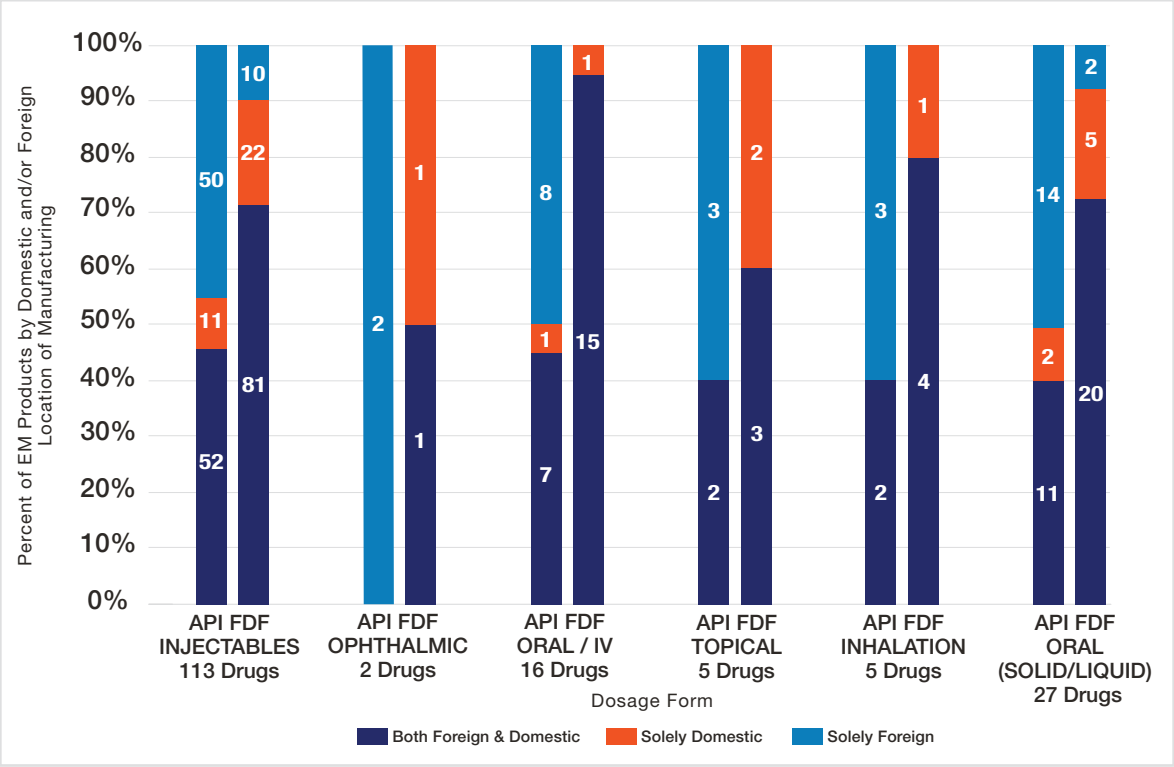

Figure 2. Domestic vs. Foreign Manufacturing for the 168 CDER-Regulated EM Products by Dosage Form

Geographic Information System (GIS) Analysis of Domestic CDER-Regulated EM Sites

The severity and prevalence of natural hazards may be exacerbated by climate change. Natural hazards may adversely affect drug quality and availability by compromising storage conditions (e.g., heat stress), deteriorating infrastructure, and reducing water quality. Natural hazard risks are one type of risk that can be mitigated by the development of RMPs.[12] Implementing RMPs enables the proactive identification and implementation of preventive measures and contingency plans that support business continuity and product availability. As a first step to understanding potential impacts to the global drug supply chain, FDA mapped the Federal Emergency Management Agency (FEMA) National Risk Index (NRI)[13] for the 575 sites in the contiguous U.S.[14] that manufacture CDER-regulated EM.[15] This GIS map[16] (Figure 3) illustrates how risk from multiple natural hazards could increase supply chain vulnerability. While this map is merely a snapshot for the U.S., it highlights the need for all parties in the drug supply chain to be informed and prepared for potential climate-related impacts.

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12 Under section 3112(b) of the CARES Act, Congress added section 506C(j) to the FD&C Act, which requires certain manufacturers to 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."

13 The NRI provides county-level natural hazard risk for the U.S. It is a holistic index that integrates the likelihood and consequence of 18 natural hazards (avalanche, coastal flooding, cold wave, drought, earthquake, hail, heat wave, hurricane, ice storm, landslide, lightning, riverine flooding, strong wind, tornado, tsunami, volcanic activity, wildfire, and winter weather) with community risk factors (a function of social vulnerability and community resilience) to provide a baseline risk measure.

14 This does not include the 20 EM sites in Puerto Rico. There are no EM sites in Alaska and Hawaii. There are 1,176 EM sites globally.

15 Pursuant to Executive Order 13944, FDA monitors supply chains for the drug and biological products on its October 2020 List of Essential Medicines, Medical Countermeasures, and Critical Inputs (EM). Of the 227 EM products, 168 are CDER regulated drug products. The other 59 are CBER-regulated products including vaccines and plasma products.

16 This GIS map was created using ESRI ArcGIS Pro 3.1.0.

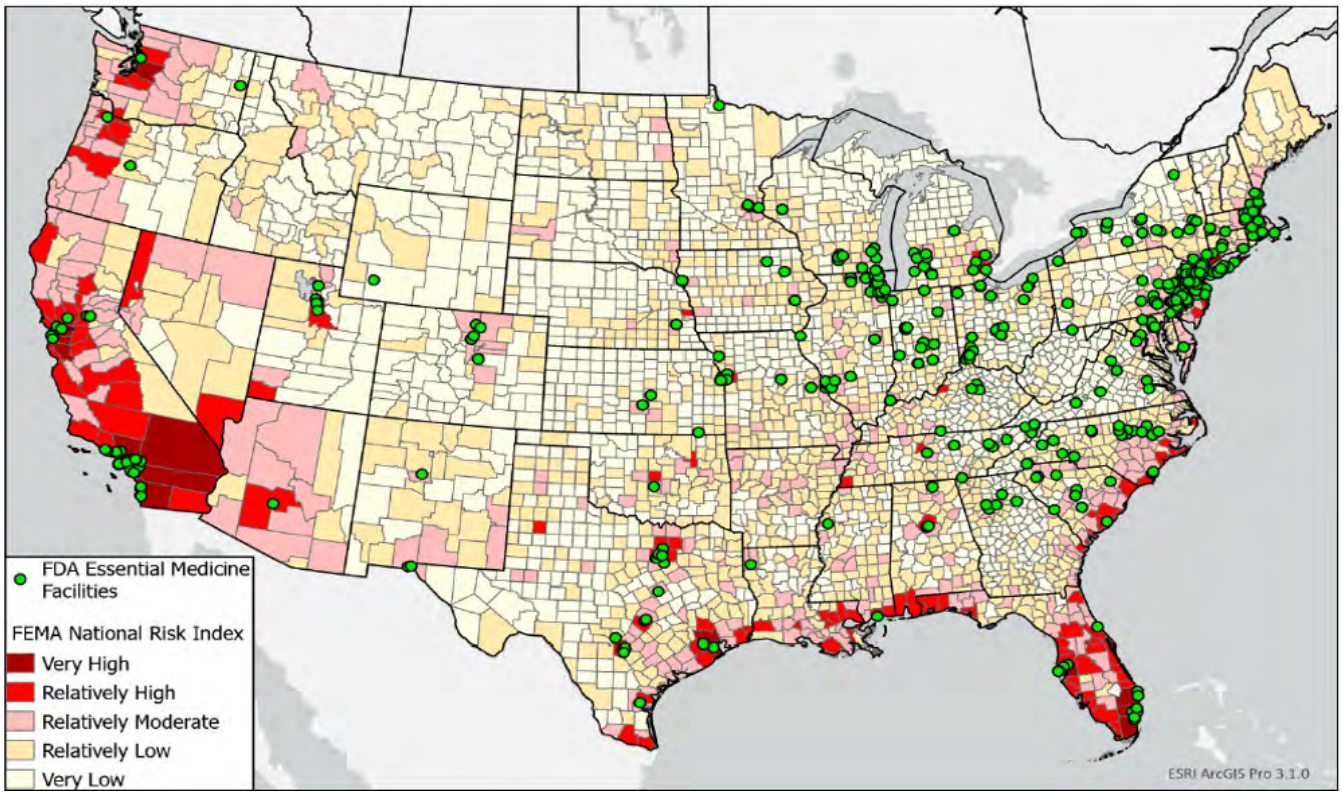

Figure 3. FEMA National Risk Index map with sites that manufacture CDER-regulated Essential Medicines

Based on the FEMA NRI, most domestic EM manufacturing sites are in U.S. counties with no more than "relatively moderate risk"; however, 34% are in counties with relatively high or very high risks (Table 3). These high-risk U.S. counties are located primarily on coastal areas of the Pacific Ocean, Gulf of Mexico, and southern Atlantic Ocean. Their higher risks are due to the confluence of hazards that include coastal flooding, riverine flooding, and wildfires. In addition, drought, earthquakes, heat waves, landslides, and tsunamis contribute to the higher risks on the west coast, while hurricanes and lightning contribute to the higher risk on the Gulf coast and southern Atlantic regions. Many of the higher risk counties in California and Florida are home to multiple EM manufacturers. This analysis is subject to evolving information; but for now, it prompts consideration of natural hazards and potential climate-related effects while encouraging informed decision-making for all stakeholders.

Table 3. Summary of FEMA NRI ratings for CDER-regulated EM manufacturing sites in the contiguous U.S.

FEMA Risk Rating	Number of EM sites	Percent of EM sites
Very Low	26	5%
Relatively Low	92	16%
Relatively Moderate	258	45%
Relatively High	134	23%
Very High	65	11%

Postmarket Quality Defects (PQDs)

CDER receives PQD reports from all over the world. Pursuant to FDA's postmarket regulations in 21 CFR 314.81(b) and 21 CFR 600.14, application holders are required to notify the FDA of any significant quality defect in marketed products within three working days for Field Alert Reports (FAR) and within 45 days for Biological Product Deviation Reports (BPDR), respectively. The MedWatch (MW) reports and consumer complaints (CC) are voluntary reports that consumers, patients, and healthcare professionals submit when product quality fails to meet expectations. During FY2023, CDER received 12,549 quality-related MW reports[17] (1.6 % increase from FY2022), 3,792 FAR (8.3% increase from FY2022), 347 BPDR (77% increase from FY2022), and 398 quality-related CC (53.7% increase from FY2022).

Overall, the total volume of PQD reports increased by 5% to 17,086 in FY2023. Like prior years, MW reports constitute 73% of all postmarket reports and 43% of MW reports come from CDER biologics (BLAs), even though they represent less than 1% of the Product Catalog. The high proportion of MW reports for BLAs can be attributed to many BLAs being drug-device combination products that have multiple components, are self-administered, and require training for usage. The moderate increase in FAR reports was caused primarily by complaints of leaky bags for saline products. The significant increase in the number of BPDRs is due to numerous reports regarding a single biologic, which represented 56% of all BPDRs in FY2023 and 26% of BPDRs in FY2022. The substantial increase in CCs during FY2023 can be associated with recalls of OTC eye drops and gel products due to microbial contamination. In addition, FY2023 saw an increase in complaints about the therapeutic effect of drugs that treat attention-deficit/hyperactivity disorder.

17 Quality-related MW reports are voluntary post-market reports from health professionals, patients, and consumers concerning product quality issues (not adverse events) such as defective components, contamination, poor packaging, and suspected counterfeit products.

Import Alerts, Recalls, and Warning Letters

Key Takeaways:

1. There were more drug quality-related import alert additions in FY2023 (93) than during FY2021 and FY2022 combined (77).
2. 17% of recalled products were associated with ophthalmic drug products.
3. The number of recalls was 26% less than in FY2022 but similar to the five-year average.

Import Alerts

Import Alerts help stop products from entering the U.S. During FY2023, FDA added 93 companies to import alerts[18] for reasons related to drug quality (Figure 4).[19] Most of the sites placed on quality-related import alert (90%) are manufacturers of OTC monograph drug products. The number of quality-related import alert additions was significantly higher than in FY2021 and FY2022 (which had 49 and 28, respectively) due to:

- 48 import alert additions for sites that refused to respond to FD&C Act §704(a)(4) record requests and 24 for sites whose CGMP deficiencies were identified through FD&C Act §704(a)(4) record review to meet the threshold for regulatory action.
- An increase in import alert additions related to site inspections (19 in FY2023 compared with 6 and 7, respectively, in FY2022 and FY2021).

The import alert additions due to §704(a)(4) records requests were driven primarily by FDA's efforts to help stop the importation of hand sanitizer products that did not meet quality standards, with over a third of import alert additions related to §704(a)(4) record requests for hand sanitizer sites (31 of 93, 33%). Similarly, FDA has continued to ensure products entering the U.S. do not contain diethylene glycol (DEG) or ethylene glycol (EG), highly hazardous materials that have caused

18 This count includes import alert additions that were initiated by CDER and ORA.

19 The subset of import alert reported here are for 66-40 (GMP-based) 704(a)(4), 66-40 (GMP-based) Inspection, 66-78 (Testing-based), 66-79 (Refusal-based) Inspection, 55-03 (GMP-based) Heparin, 55-05 (Testing-based), and 66-79 (Refusal-based) 704(a)(4).

poisonings resulting in fatalities. The §704(a)(4) deficiencies related to these sites (e.g., failure to respond, not conducting appropriate DEG/EG testing) supported 28% (26 of 93) of import alert additions. Most of the 93 import alert additions were associated with sites in China (33%), South Korea (18%), and India (16%). This is a disproportionate number of import alert additions for sites in China and South Korea given that they represent only 17% and 3%, respectively, of foreign sites in the catalog.

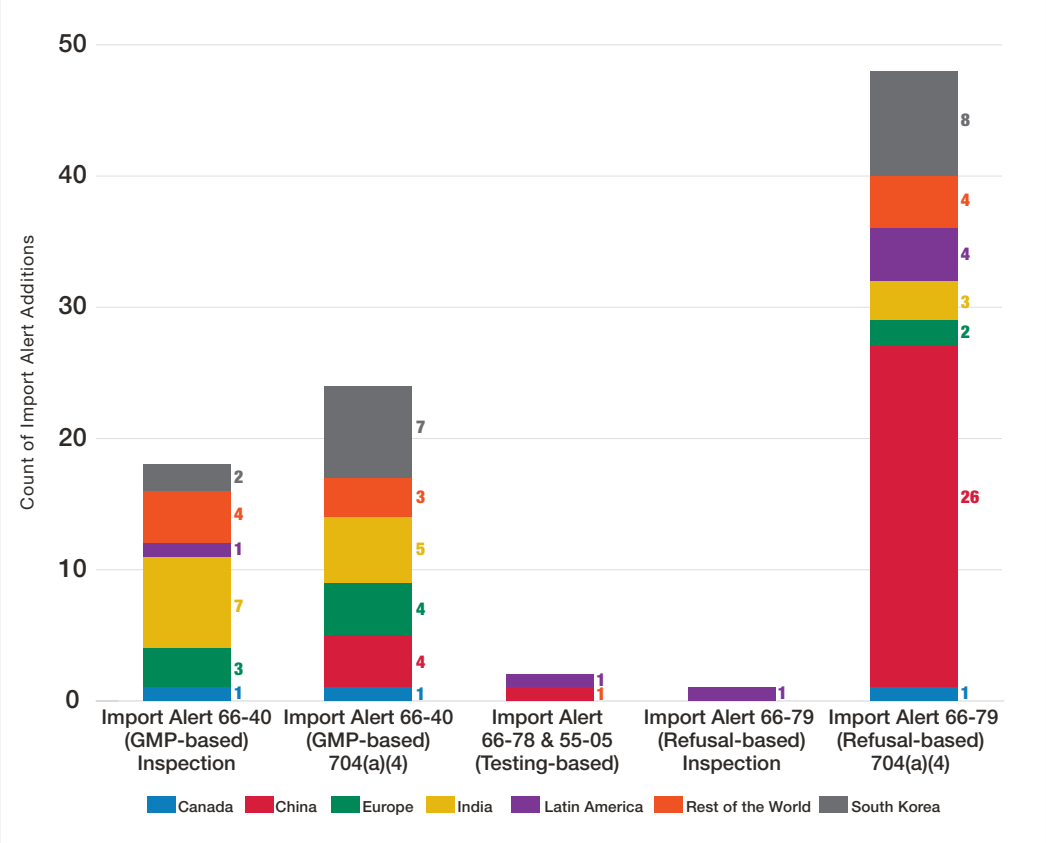

Figure 4. FY2023 Drug-Quality-Related Import Alerts Additions by Type and Region

Recalls

In FY2023, there were 674 drug products recalled,[20] down 26% from the high of 912 in FY2022. The FY2023 recalls were from 158 sites that generated 225 recall events (Figure 5). As in prior years, the most common defect group for recalls was CGMP deficiencies (52%). The countries whose sites had the highest number of FY2023 recalls were the U.S. (58%) and India (33%), followed by Jordan (3%), Switzerland (2%), and China (1%). In FY2023 there were no recalls related to temperature abuse (i.e., inappropriate storage conditions), which represents a change from FY2022 when 15% of recalls were related to temperature abuse. FY2023 saw an increase in recalls attributable to contamination, up by 58% from FY2022. Contamination-related recalls included sterility assurance issues (38%), foreign material/particulate contamination (31%), microbial contamination (17%), product mix-up/cross contamination (8%), and chemical contamination (6%). During FY2023, 35% of recalled products were associated with five specific events:

- 86 product recalls attributed to a single manufacturer that went out of business and was, therefore, unable to maintain CGMP requirements for distributed drugs, such as stability testing.
- 67 product recalls attributed to a single drug manufacturing site for data integrity issues identified during an inspection.
- 52 product recalls attributed to a single drug manufacturing site for lack of assurance of sterility.
- 17 product recalls attributed to a single manufacturing site for data integrity issues identified during an inspection.
- 17 product recalls attributed to a single manufacturing site for lack of assurance of sterility.

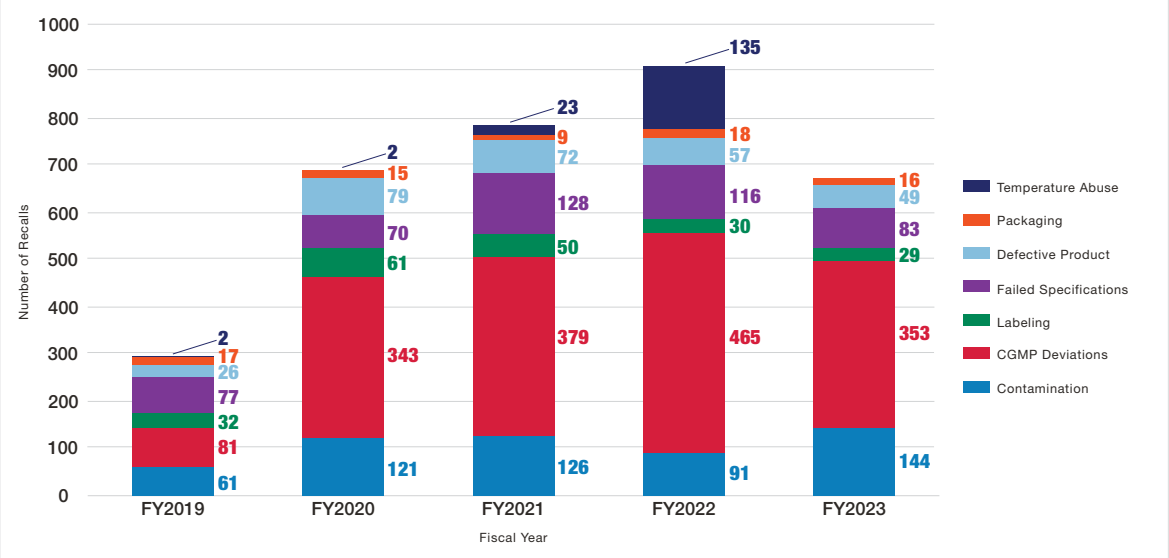

Figure 5. Recalls by Defect Group for FY2019-FY2023

20 Recalls can be analyzed by product NDC numbers recalled (recall number) or by recalling event. Multipleproduct NDC numbers and lot numbers may be listed within a single recall event. All recall classes (I, II, III) initiated in FY2023 are included in this analysis. Recalls of drug products not in the CDER Product Catalog (e.g., compounded drugs and those marketed without an approved application) are not included in this analysis.

In FY2023, the United States Pharmacopeia Therapeutic Category (USPTC) of antibacterials had the highest percentage of recalls (Figure 6). In February 2023, FDA notified consumers to stop using eye drops made in India by Global Pharmaceutical Healthcare because of microbial contamination. Ophthalmic agents moved up from eighth in FY2022 to third, accounting for 17% of FY2023 recalls. Multiple incidents of contaminated eye drops that could cause blindness were identified and a warning letter was issued in October 2023. In December 2023, FDA issued a draft guidance, Quality Considerations for Topical Ophthalmic Drug Products, that revised the earlier October 2023 draft. It added microbiological considerations related to product sterility for all ophthalmic drug products and prevention of contamination for ophthalmic drug products in multidose containers.

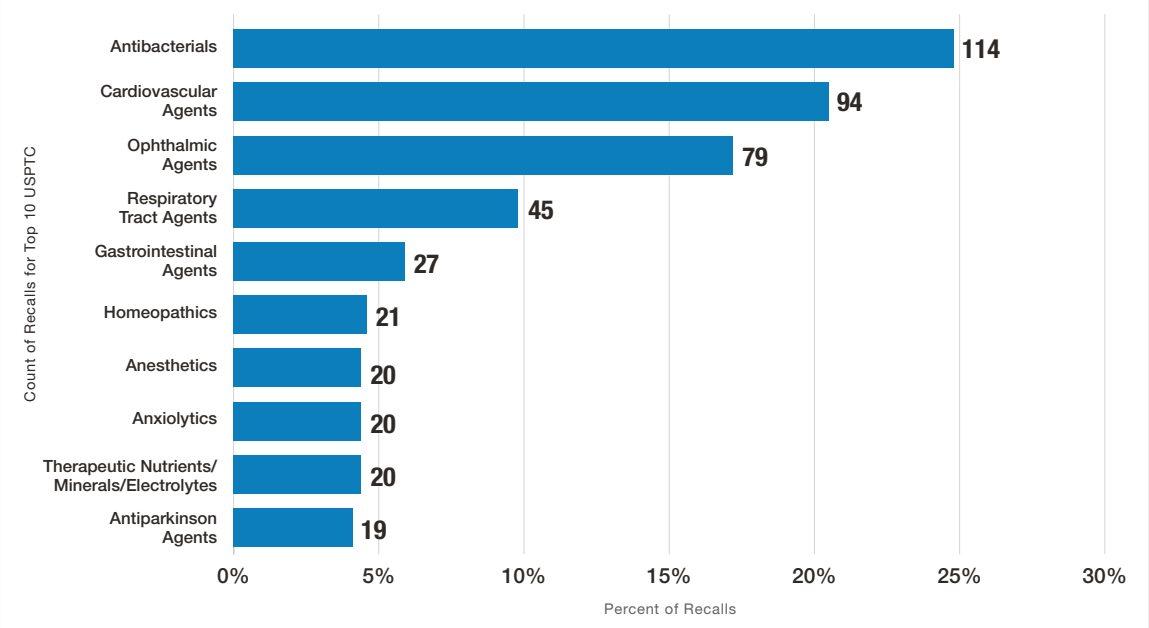

Figure 6. Top Ten Recalls in FY2023 by USP Therapeutic Category

In addition to the data presented, six recalls were attributed to unapproved drug products marketed in the U.S. without conforming to an OTC monograph or receiving FDA approval, a decrease from 28 in FY2022. Unapproved drugs are not included in the CDER Product Catalog.

The non-proprietary names of the five most recalled drug products are levothyroxine sodium (oral solutions and tablets), simvastatin (tablets), fexofenadine hydrochloride (tablets), glimepiride (tablets), and multiple types of ophthalmic products (solutions, suspensions, and ointments). Most of these products were recalled due to contamination or CGMP deficiencies.

Warning Letters

In FY2023, FDA issued 94 warning letters to drug manufacturing sites for reasons related to drug quality. Figure 7 shows warning letter trends by country and region for the past five years. Of the sites that received warning letters, 80% manufacture OTC monograph products, even though such sites accounted for less than 20% of FY2023 inspections. Of those sites, over half manufactured hand sanitizer or products that could be contaminated with DEG or EG.

During FY2023, FDA continued to effectively leverage records requests under FD&C Act §704(a)(4) to identify sites with quality issues. Over a quarter of the FY2023 warning letters resulted from refusal to respond to a §704(a)(4) records review or a CGMP issue identified during a §704(a)(4) records review. Details about FDA's warning letters are available through a searchable database.

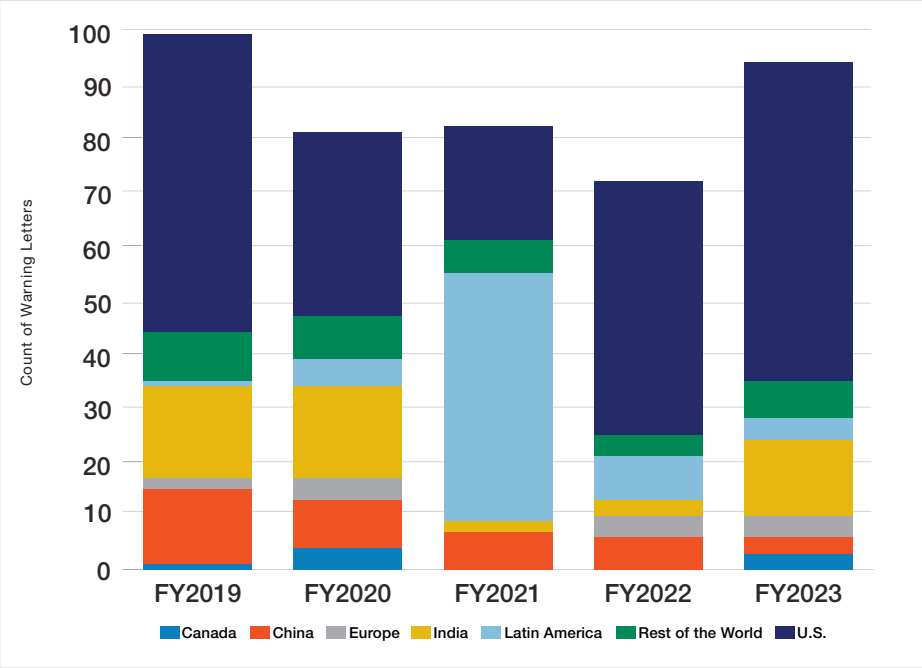

Figure 7. Warning Letters by Country and Region for FY2019-FY2023

Analyses on the State of Pharmaceutical Quality

Key Takeaways:

1. Record requests under §704(a)(4) have shown utility as the basis for import alert additions and warning letters.
2. Quality problems remain one of the most common reasons for drug shortages; however, during the past two years, increases in demand caused the same percentage of shortages (40%).

Value of Record Requests under FD&C Act §704(a)4

FD&C Act §704(a)(4) provides an effective quality surveillance tool for assessing establishment records and verifying the accuracy of the CDER Site Catalog. In addition, these record requests have resulted in the issuance of warning letters and import alert additions. An analysis of inspections and §704(a)(4) records requests during FY2018 – FY2023[21] compared how often each was the basis for FDA actions and enforcement (warning letters and import alert additions). For this analysis, inspections were divided into two groups: (1) the initial drug quality assurance inspection for a site and (2) subsequent drug quality assurance inspections. Starting in FY2020, the number of inspections decreased (with a low in FY2021) due to travel restrictions during the COVID-19 PHE. In contrast, the number of §704(a)(4) records requests peaked in FY2021 and has since leveled off. These record requests have led to an increasing number of actions and enforcement, and since FY2020, record requests have been the basis for dozens of actions and enforcement each year (Figure 8). This demonstrates the utility of §704(a)(4) records requests.

21 The relevant fiscal years for warning letter and import alert additions were defined by the inspection end date or the request date for the §704(a)(4) records request.

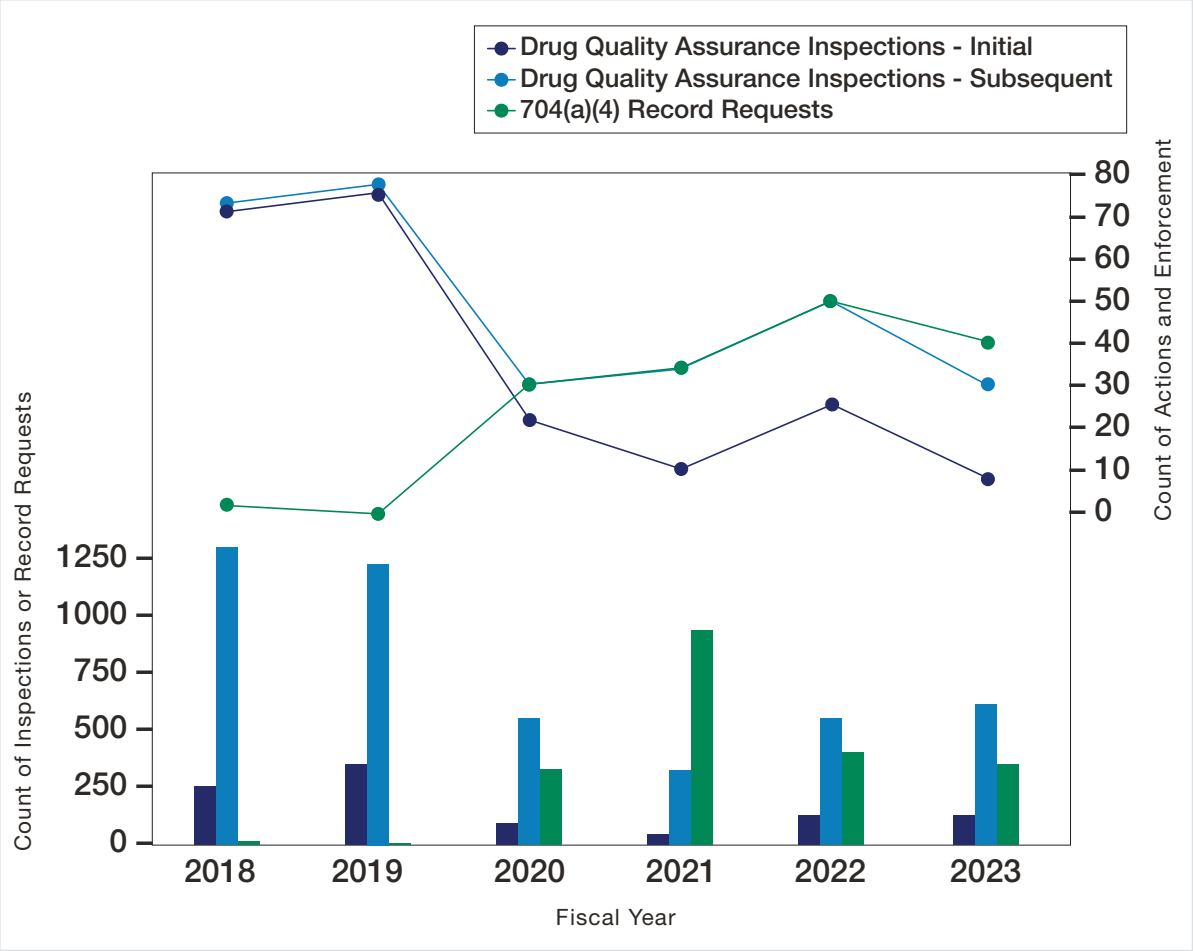

Figure 8. Counts of Inspections and §704(a)(4) Record Requests: Impacts on Actions and Enforcement (FY2018-FY2023)

Drug Shortages

The CDER Drug Shortage Staff classifies drug shortages by reason. Pursuant to FD&C Act §506E, FDA maintains a drug shortage list. When drugs are added to the list, the shortage is attributed to one of seven reasons listed in §506E(b)(3) or to "other." To enable targeted mitigation, FDA usually requests additional information from the impacted manufacturer that more specifically describes the shortage's cause(s). This includes product-specific quality issues (e.g., particulates and sterility issues), facility quality issues (e.g., manufacturing line or plant issues), raw material issues (e.g., quality issues or delays), increased overall demand, loss of manufacturing sites, and permanent discontinuations. The Drug Shortage Staff then captures different sets of reasons for shortages: 1) Quality Issues/Manufacturing Delays, 2) Increase in Demand, 3) Availability of API, 4) Product Discontinuation, or 5) Natural Disaster / PHE. The reasons for the 81 new shortages in CY2022-CY2023 (Figure 9) and can be compared with 2013-2017 data in the 2019 report Drug Shortages: Root Causes and Potential Solutions. Previously, 62% of shortages were caused by quality issues, but during the past two years, quality problems and increases in demand have each caused 40% of new drug shortages.

Quality problems have previously been the most common reason for shortages. These quality problems can be either related to specific quality defects in individual drugs or quality problems at the manufacturer; examples include production lines breaking down, delays in the ability of the Quality Assurance department to approve or reject batches, or facility-related breakdowns that lead to a lack of sterility assurance. Since the COVID-19 PHE began, there has been a rise in drug shortages due to increases in demand. These demand-driven shortages provide new challenges for FDA because this type of shortage has no clear notification requirements. The consolidation of API manufacturers, which can mean that multiple FDF manufactures rely on one or two API sources, may also be contributing to potential shortages. Product discontinuations continue to rise as manufacturers leave the marketplace or consolidate and trim portfolios.

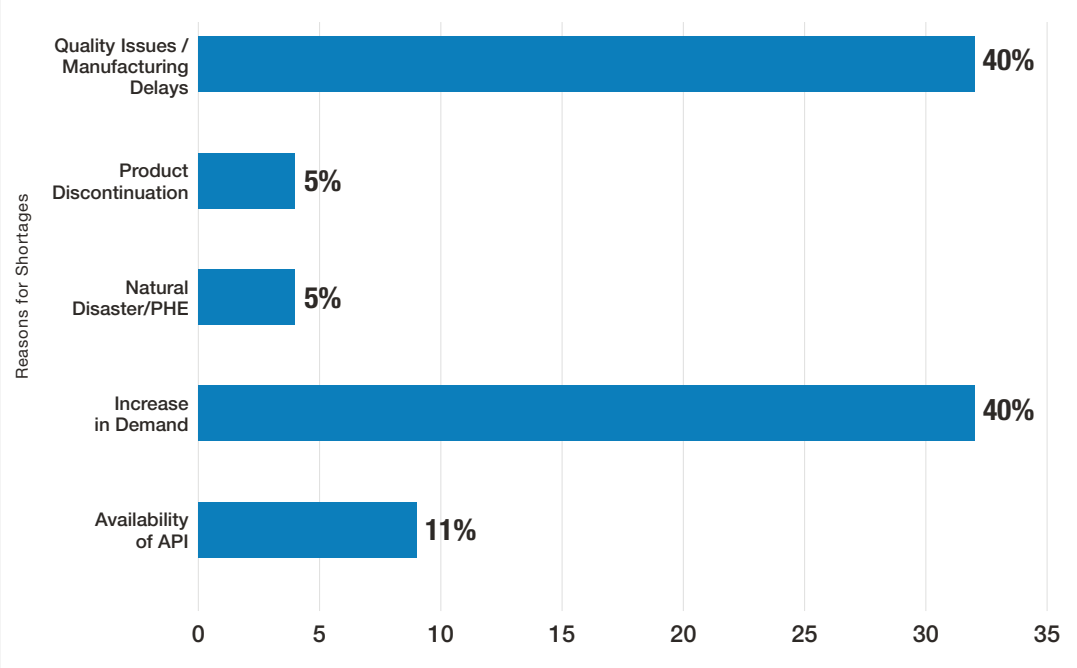

Figure 9. Reasons for New Shortages in CY2022 and CY2023

Sampling and Testing

Key Takeaway:

1. Testing of hand sanitizer products from domestic manufacturers that began manufacturing during the COVID-19 PHE revealed a high incidence of violative samples.

FDA seeks to minimize the exposure of U.S. patients and consumers to non-compliant drug products. As part of comprehensive drug quality surveillance Drug Quality Sampling and Testing (DQST) uses knowledge from the product lifecycle to identify or confirm potential product quality issues. Then FDA samples and tests prescription drugs, OTC products, and API.

Alcohol-Based Hand Sanitizer Products

Since July 2020, FDA has been sampling and testing alcohol-based hand sanitizer products to ensure the availability of safe and effective products. This includes the development and validation of a test method for the product quality of such hand sanitizers. The full findings of this product quality study were recently published in *The AAPS Journal*. In brief, of 310 products from 196 newly registered[22] domestic manufacturers tested, 71.6% of the manufacturers in the study had violative products. This research paper provides a statistical analysis and a deeper understanding of how FDA manages risks in the face of uncertainty through testing and assessing OTC products. FDA continues to educate consumers about the safe use of hand sanitizers and maintains a webpage listing hand sanitizer products that should not be used.

22 These sites began manufacturing drugs during the COVID-19 PHE.

Commitment to Quality

Key Takeaways:

1. Compliance for CARES Act annual amount reporting is expected to increase with improvements to the CDER NextGen portal and publication of the final guidance.
2. CDER continued active stakeholder engagement with development of the Quality Management Maturity (QMM) Program, including a prototype assessment protocol that will be evaluated with volunteer establishments.

Drug Amount Reporting

The 2020 Coronavirus Aid, Relief, and Economic Security (CARES) Act provided authorities to enhance FDA's ability to identify, prevent, and mitigate possible drug shortages. It requires registrants to report annually the amount of each listed drug they manufactured for commercial distribution[23]. Registrants can submit reports with templates that match the type of drug being reported. The NextGen Portal for receiving drug amount data uses improved tools for parsing and validating submitted data elements and can inform registrants how to make corrections.

For active products listed in FDA's Electronic Drug Registration and Listing System (eDRLS), less than half of NDCs[24] have drug amount reports submitted (Figure 10). All three reporting years[25] had low rates of drug amount data submission. FDA expects that the publication of the final guidance and enhancements to the NextGen portal will improve reporting levels. In addition to education, outreach, and delinquency notifications, FDA will take action as appropriate to ensure compliance with CARES Act Drug Amount Reporting.

23 In February 2024 FDA published its final guidance on Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the Federal Food, Drug, and Cosmetic Act. In contrast to the 2021 draft, this final guidance describes enhancements to the drug amount submission process including the introduction of reporting by drug types and packaging (e.g., Drug Products in Finished Package Form, Drug Products Not in Finished Package Form, Drugs that consist of API alone, or Drugs that consist of API with other ingredient(s) but that are not in finished dosage form).

24 CARES amount data current as of November 2023.

25 CARES amount reporting is based on the calendar year (CY). CY2023 amount reporting is not due until July 31, 2024.

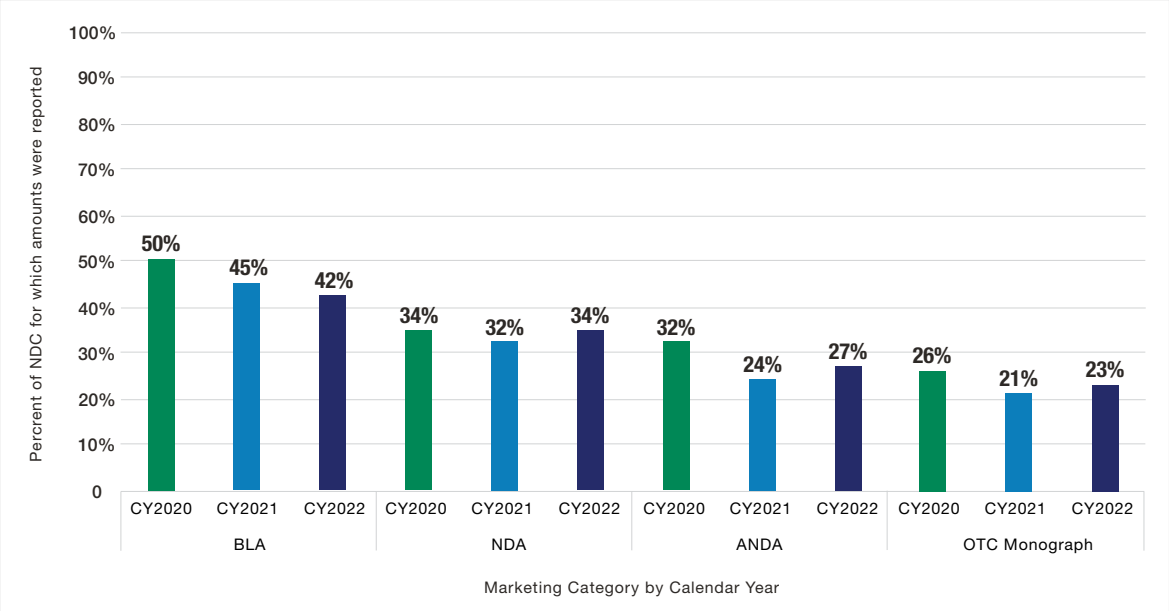

Figure 10. Percent of NDC in eDRLS for Which Amount Reports were Submitted by Marketing Category

Quality Management Maturity (QMM)

During the November 2-3, 2022 meeting of FDA's Pharmaceutical Science and Clinical Pharmacology Advisory Committee, CDER committed to seek input from stakeholders who could be impacted by a future QMM program. Throughout 2023, CDER engaged with more than ten stakeholder groups through facilitated discussions and established a public docket (September 15-December 14, 2023) that received 23 responses about the voluntary QMM program. Leveraging the lessons learned from two FY2021-2022 QMM pilots, CDER developed a prototype assessment protocol, which was described in an August 2023 white paper. In January 2024, CDER announced the voluntary Quality Management Maturity Prototype Assessment Protocol Evaluation Program for a limited group of manufacturers to gain experience with the prototype assessment protocol and for FDA to evaluate use of the protocol.

Assurance of Quality

This report seeks to advance OPQ's mission to assure that quality medicines are available for the American public. By communicating the state of pharmaceutical quality through data, findings, and insights, OPQ seeks to provide stakeholders with valuable information that can be used to improve drug manufacturing and increase awareness about quality and availability risks. FDA continues to monitor sites and products by assessing adverse events, evaluating inspection outcomes, and conducting product testing. FDA anticipates that improved tools and processes for quality surveillance will assist proactive identification of quality problems, improve inspections, and add value to quality programs, which will enhance supply chain resilience and the availability of quality medicines.

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