Report on the State of Pharmaceutical Quality (RSPQ)

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Learning Objectives

- Understand the purpose of the RSPQ.
- Describe one impact of the COVID-19 PHE on drug quality surveillance.
- Know the approximate distribution of sites in the CDER catalog with respect to whether or not they are listed in an approved application.

Agenda

- RSPQ Background
- RSPQ FY2020
  - Manufacturing Site Demographics
  - Impacts of COVID-19
  - Manufacturing Site Compliance
  - Drug Product Quality
- OPQ's Commitment to Quality
- RSPQ FY2021

Background – Office of Quality Surveillance

- OQS continuously monitors and provides the state of quality for all regulated sites and products. The availability of quality medicines is assured through signal detection, data analysis, review of the state of quality, and proactive stakeholder engagement.
- OQS created the annual RSPQ to support OPQ's mission and vision and to provide useful information for the public.

Background – RSPQ

- The RSPQ characterizes the state of pharmaceutical quality for human drugs legally marketed in the U.S. for each fiscal year.
  - Identifies indicators, or elements, of quality based on analysis of available FDA data for site compliance, post-market reporting, and product testing.
  - Provide insights and trends that can be inferred about site quality and product quality.

RSPQ – First Three Years

[FY2018 RSPQ]

[FY2019 RSPQ]

[FY2020 RSPQ]

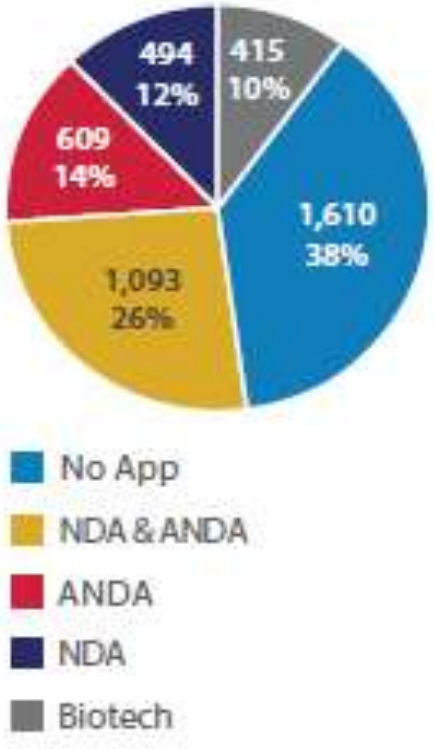
FY2020 RSPQ

- The RSPQ has several sections, including
  - Manufacturing Site Demographics
  - Impacts of COVID-19
  - Manufacturing Site Compliance
  - Drug Product Quality

- The report also provides other findings including innovative data analyses (e.g., cluster analysis, statistically significant trending, machine learning models).

Manufacturing Site Demographics – Industry Sectors

- Sites[1] in the CDER Site Catalog[2] are categorized through a hierarchy of industry sectors:
  - 10% of all sites are listed in at least one Biologics License Application (BLA)
  - Of the remaining sites listed in approved FDA applications:
    - 12% of sites are listed in at least one New Drug Application (but no ANDAs or BLAs)
    - 14% of sites are listed in at least one Abbreviated New Drug Application (but no NDAs or BLAs)
    - 26% of all sites are listed in both ANDAs and NDAs
  - The remaining 38% of sites are not listed in any approved FDA applications (e.g., OTC monograph, unapproved products, homeopathic)



- **62% of all catalog sites are listed in application products.**
- **38% of all catalog sites manufacture non-application products.**

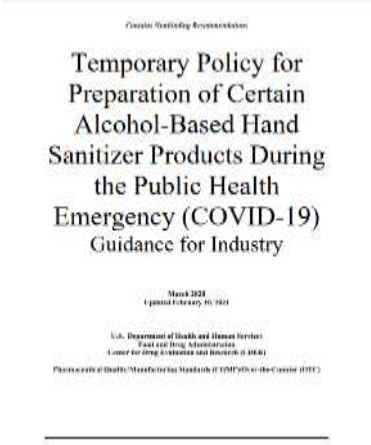
[1] Medical gas and newly-registered hand sanitizer manufacturers are not included
[2] Site Catalog as of November 2020

Impacts of COVID-19

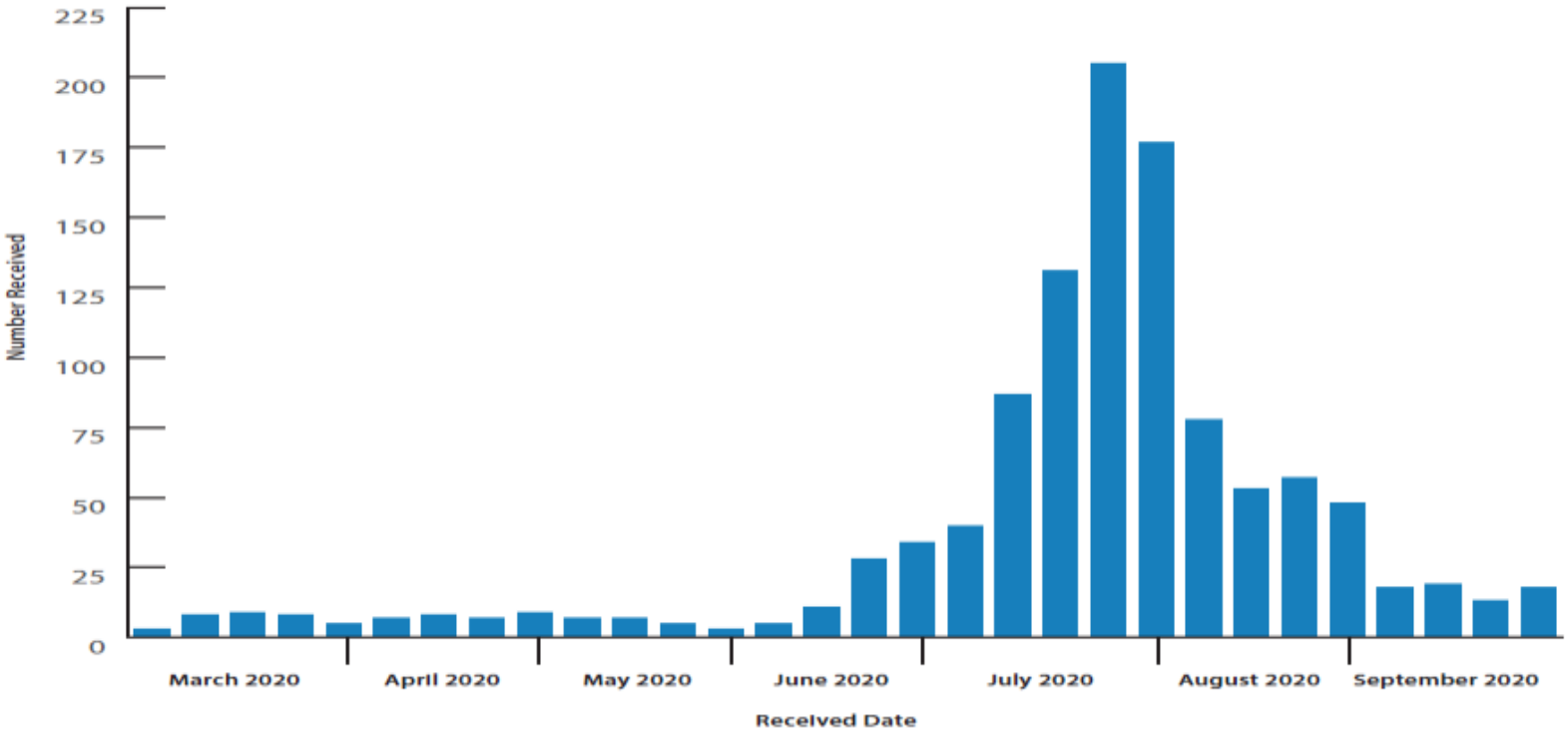
- Postponement of non-mission-critical inspections
  - FDA applied and innovated strategies from existing authorities to assess regulatory submissions that would typically have needed a pre-approval inspection (PAI) or pre-license inspection (PLI).
    - ➢ Surveillance history
    - ➢ Requests for records and information under §704(a)(4) of the FD&C Act
    - ➢ Inspection reports obtained from MRA partners, including 3rd country reports
  - CDER completed facility assessments to meet User Fee dates over 90% of the time and reduced the need for PAIs and PLIs.

Impacts of COVID-19

- Hand Sanitizer
  - Starting in March 2020, FDA issued guidance detailing temporary policy for alcohol-based hand sanitizers
    - Allowed firms to register and manufacture hand sanitizer without being subject to routine surveillance inspections.
    - More than 5,000 firms, including distilleries and other industrial manufacturers, registered.
    - After FDA outreach to confirm registrants and their products, about two-thirds de-registered.
    - Currently there are ~1,500 newly registered hand sanitizer manufacturers.
  - Sampling and testing of imported and domestic hand sanitizer – providing an estimate of the quality of newly registered firms
  - For-cause sampling based on complaints
  - FDA “Should Not Use List”
  - FDA “country-wide import alert” for hand sanitizer from Mexico.


Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)
Guidance for Industry

Hand Sanitizer Complaints, FY 2020

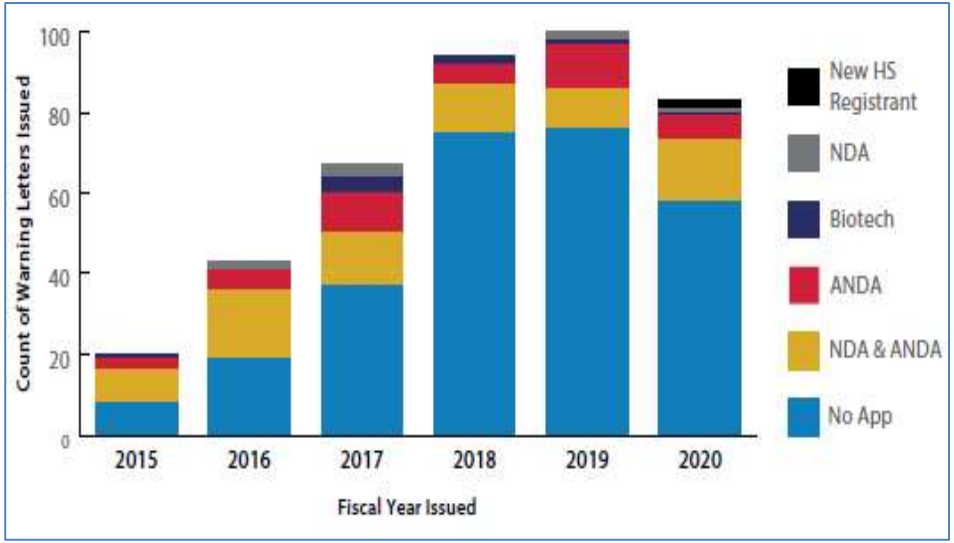


Manufacturing Site Compliance

- Due to COVID-19 the postponement of all non-mission-critical inspections began in March 2020.
  - Nevertheless, FDA still performed 562 drug quality assurance inspections in FY2020 (mostly before the public health emergency).
  - Mutual Recognition Agreement (MRA) was used to assess 183 sites.
  - In total, only 745 sites (18% of the CDER Site Catalog) received surveillance inspection coverage.
  - By comparison, during FY2019, 1,367 sites (32% of the CDER Site Catalog) received surveillance inspection coverage.

Warning Letters – Industry Sectors

- CGMP violations that are observed either through an inspection, violative evidence collected from a record request, or failing analytical sampling and testing, may result in a regulatory action including Warning Letters (WL).
- The number of WLs issued in FY2020 was slightly lower than in FY2018 or FY2019, but still over four times higher than FY2015.
- As in past years, most WLs were issued to sites manufacturing exclusively non-application products (No App sector).



Drug Product Quality

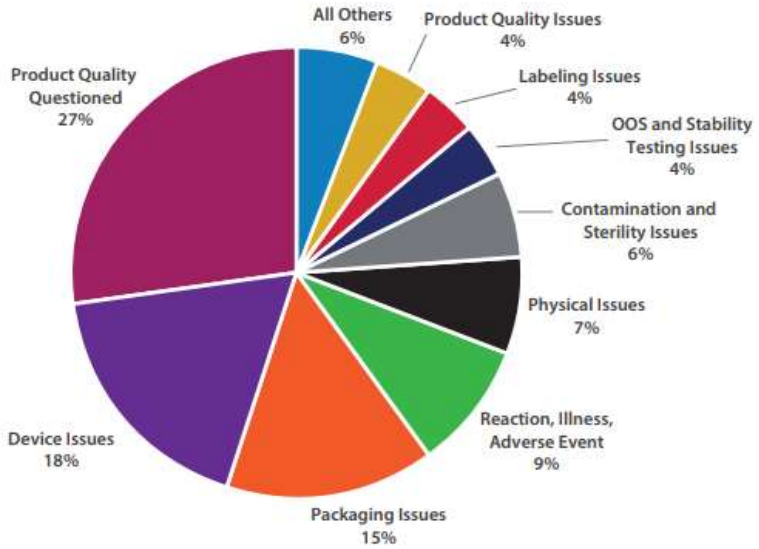
- The FDA receives feedback from industry, healthcare providers, patients, and consumers on product quality via Product Quality Defect (PQD) reports.

- These include:
  - Field Alert Reports (FARs)
  - MedWatch Reports (MWs)
  - Biological Product Deviation Reports (BPDRs)
  - Consumer Complaints (CC)

Product Quality Defects (PQD)

- The FDA collects PQD reports, assesses defect severity, and looks for trends and ways to mitigate issues.
- During FY2020, FDA received PQD reports:
  - 11,932 MedWatch reports
  - 4,308 FARs
  - 263 BPDRs
  - 253 Consumer Complaints
- These PQD reports are grouped into 20 defect categories.
  - Over the past five years, three categories: Product Quality Questioned, Device Issues, and Packaging Issues accounted for more than 60% of all PQDs.

Top Defect Types, PQD Total FY2016–2020



Recall Analysis

- In recent years, major recalls have been associated with microbial or chemical contamination/impurities. This suggests a focus area for industry to improve quality and for FDA to increase oversight.
  - FY2017 – microbial contamination → recall of antibacterial products (e.g., povidone-iodine antiseptic pads and oral care solutions)
  - FY2018 & FY2019 – nitrosamine impurities → recalls of several cardiovascular products
  - FY2020 – nitrosamine impurities → recalls of gastrointestinal products

RSPQ FY2021

- Under development
- Identifying relevant questions that will be of value to the public and FDA.
- Will likely reflect the unique nature of FY2021
  - Postponed inspections
  - Alternate tools for quality surveillance, e.g., §704(a)(4) of the FD&C Act
  - Discussion on the quality of hand sanitizer products

Summary: OPQ's Commitment to Quality

- The RSPQ annual report summarizes various measures of the pharmaceutical manufacturing industry's ability to deliver quality drug products to U.S. patients and consumers.
- In doing so, it enables the public to understand the pharmaceutical industry and how FDA acts proactively to address potential pharmaceutical quality issues before patients and consumers are impacted.

Challenge Question #1

True or False: FDA's Temporary Policy for alcohol-based hand sanitizer manufacturers allows firms to manufacture hand sanitizer products without being subject to Good Manufacturing Practices (GMPs).

A. True

B. False

Challenge Question #2

Which of the following is NOT a type of Product Quality Defect (PQD) report used by FDA?

A. MedWatch Reports

B. Ebay Customer Ratings

C. Field Alert Reports (FARs)

D. Biological Product Defect Reports (BPDRs)

E. Consumer Complaints

Challenge Question #3

When did consumer complaints about hand sanitizer products peak?

A. May and June 2020

B. July and August 2020

C. January and February 2021

D. June and July 2021

Closing Thought

U.S. patients and consumers deserve confidence in their next dose of medicine.

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Thank you, questions?

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