

FDA Inspection Analysis in the Indian Pharmaceutical Industry



FDA Inspections

FDA inspections play a crucial role in ensuring product quality and safety in the pharmaceutical industry. The pharmaceutical industry is responsible for producing drugs and medications that have a direct impact on public health, and therefore, maintaining high levels of quality, safety, and compliance with regulations is of utmost importance.

FDA inspections mainly assess and ensure the following key aspects:

- 1. Ensuring Regulatory Adherence**
- 2. Safeguarding Patient Well-being**
- 3. Upholding Quality Standards**
- 4. Identifying and Rectifying Deficiencies**
- 5. Preventing Deceptive Practices**
- 6. Ensuring Transparent Supply Chains**
- 7. Good Manufacturing Practices (GMP)**
- 8. Personnel Training**

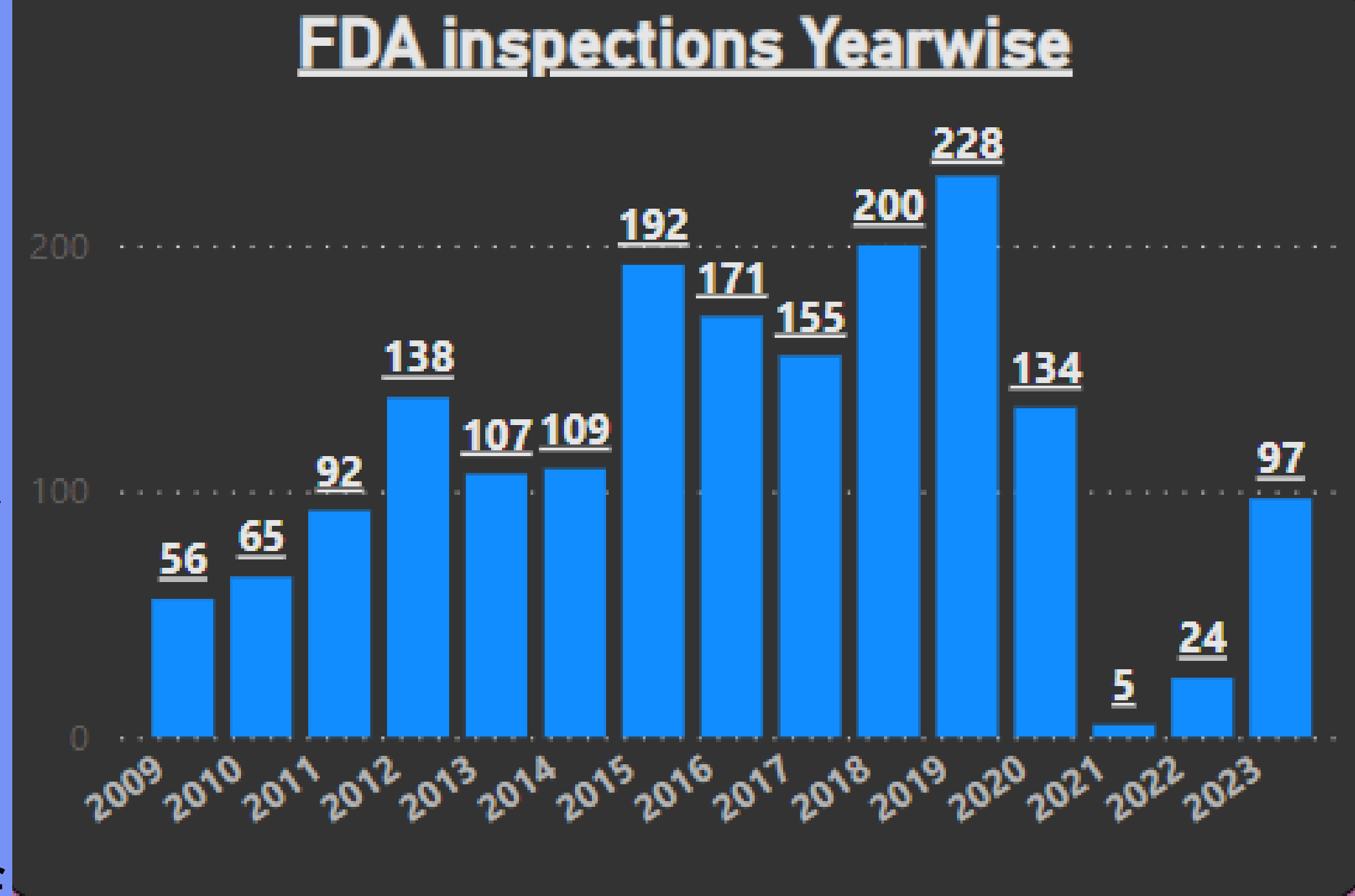
Importance

The importance of FDA inspections is twofold.

- **First**, they **ensure the safety and efficacy** of the products manufactured by drug firms. Any violations or deficiencies in the quality and compliance of drug firms could pose a risk to the consumers and harm their health.
- **Second**, they **affect the competitiveness and reputation of drug firms in the global pharmaceutical industry**.
- The FDA is one of the most stringent and influential regulatory agencies in the world, and its inspections, actions have a significant impact on the market access and performance drug firms. Any violations in the quality and compliance of drug firms could result in regulatory actions by the FDA, such as warning letters, injunctions, seizures, import alerts, or bans. These actions could damage the credibility and trustworthiness of drug firms and reduce their market share and profitability.



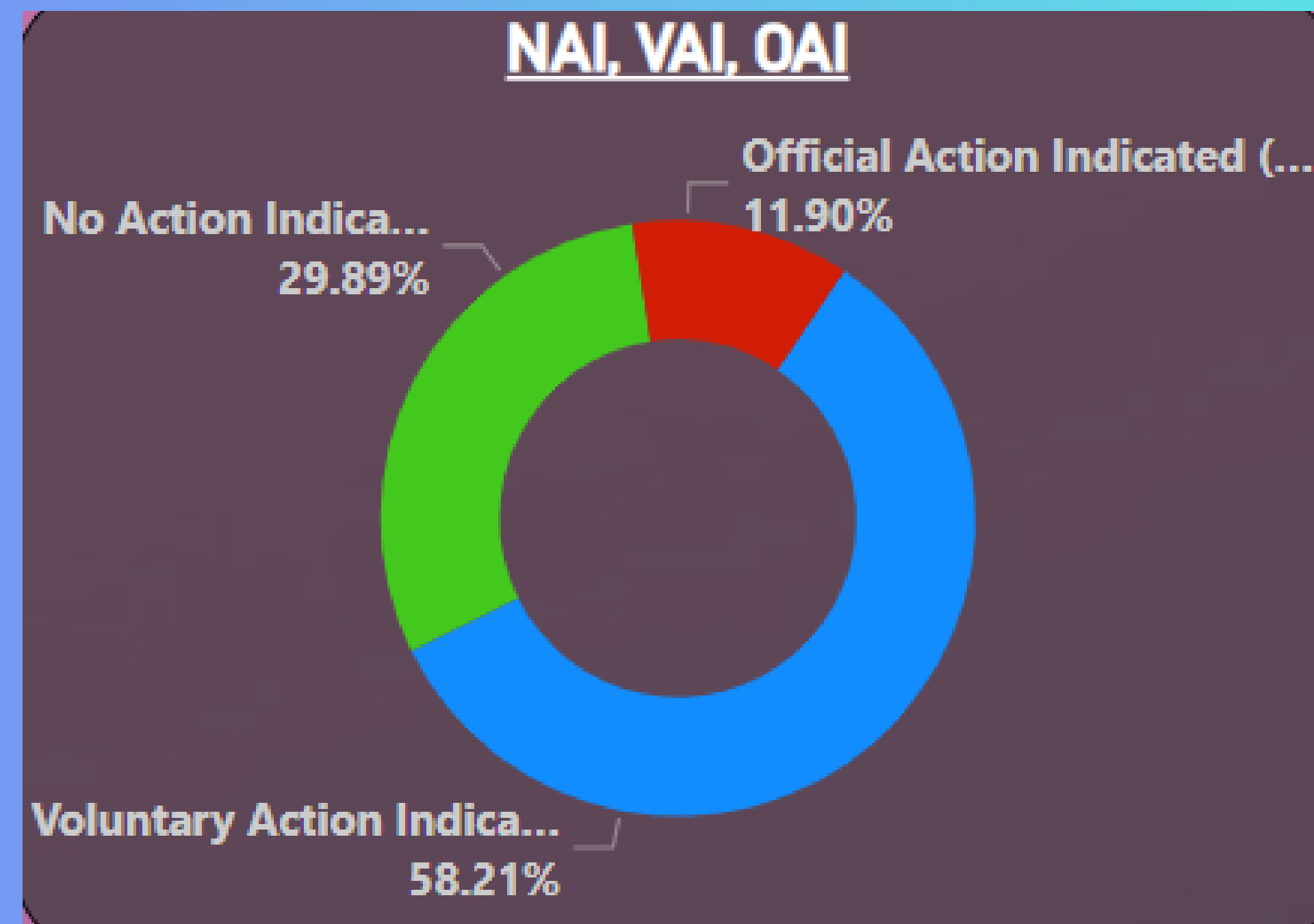
Between 2009 and 2023, the frequency of FDA inspections displayed a gradual upward trajectory, reaching its zenith in 2019. However, a significant and notable decline was observed in the subsequent years. This decline can be attributed to the imposition of COVID-related restrictions, resulting in a reduction in the number of inspections conducted.



The pandemic-induced limitations had a discernible impact on the regularity of inspections during these later years.

- The FDA classifies inspections into three categories based on the findings and outcomes of the inspections:

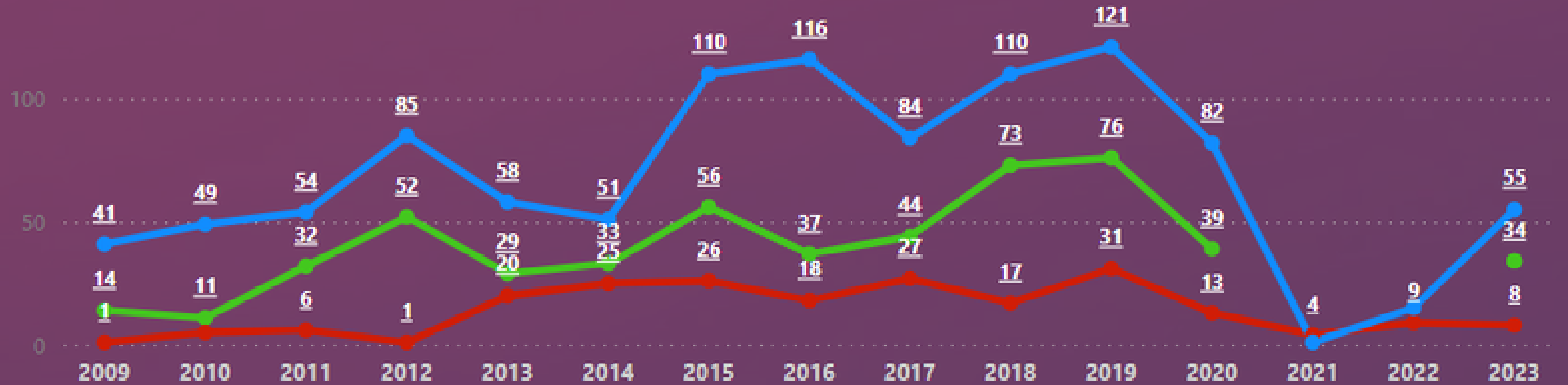
- No Action Indicated (NAI): No objectionable conditions or practices were found during the inspection.
- Voluntary Action Indicated (VAI): VAI is a classification used when the FDA has identified minor violations of regulations during an inspection. It indicates that while some issues were observed, they are not significant enough to warrant official enforcement actions.
- Official Action Indicated (OAI): OAI is a classification given when significant violations of regulations or non-compliance are identified during an inspection.



- During the period of 2009-2023,
- 58% of the inspections resulted in VAI,
 - 29% of inspections are NAI,
 - Only a small fraction of the inspections resulted in OAI

Inspections classification by Fiscal Year

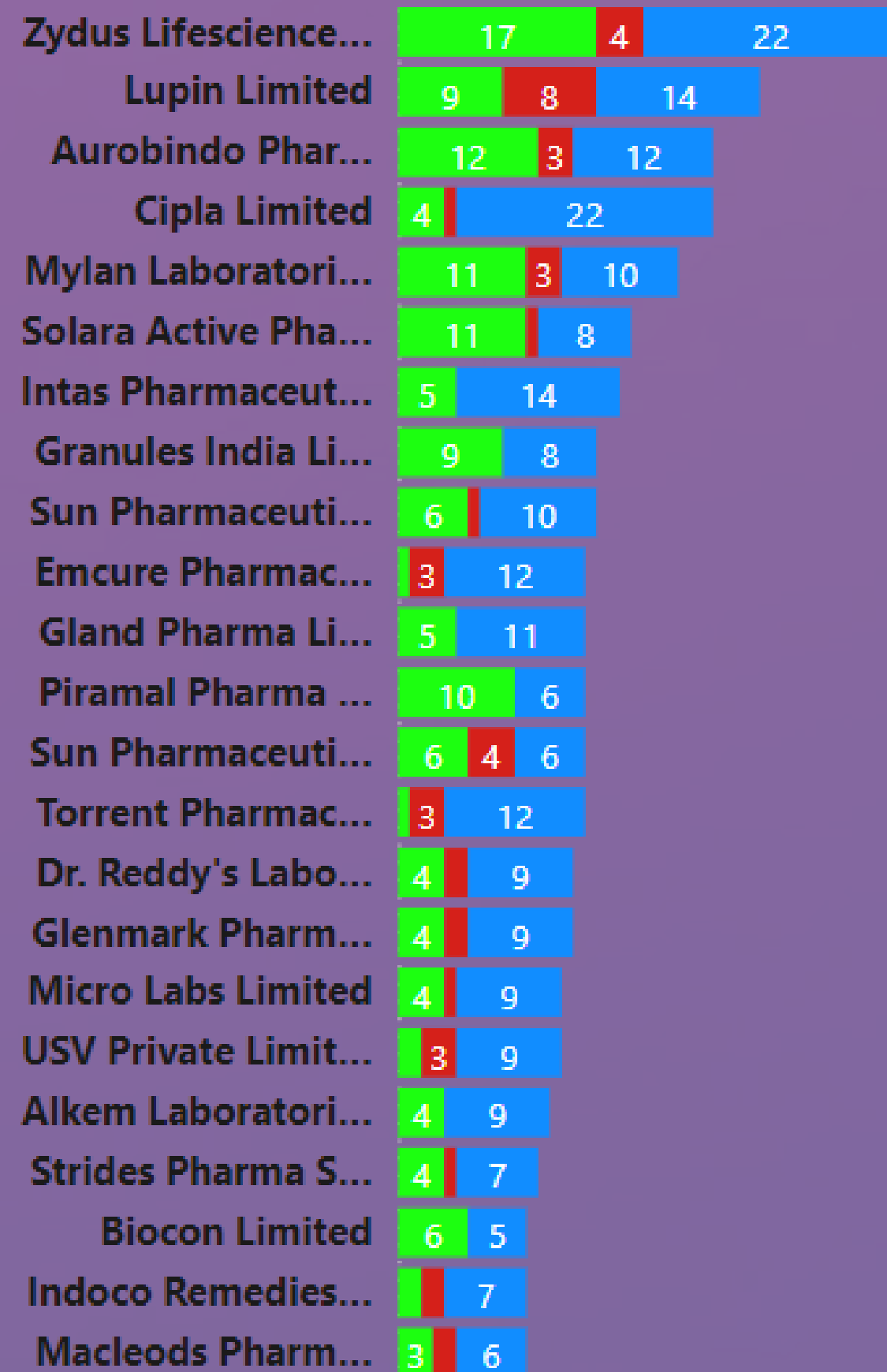
Classification ● No Action Indicated (NAI) ● Official Action Indicated (OAI) ● Voluntary Action Indicated (VAI)



- The number of VAI inspections increased significantly in 2015-2016, and in 2019
- The number of NAI inspections fluctuated over the years, with a peak in 2018-2019 and a low after 2020,
- The number of OAI inspections increased sharply in 2013 onwards

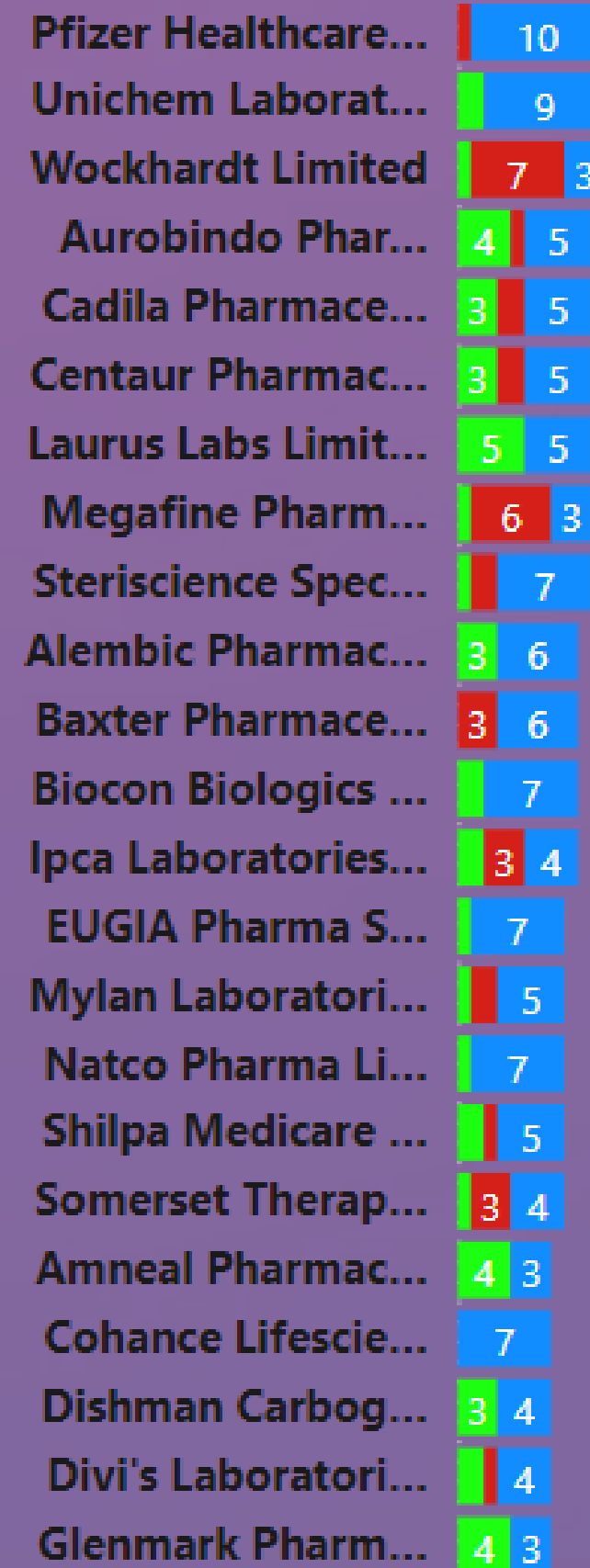
Classification by Legal Name and Classification

Classification ● No Action Indic... ● Official Acti... ● Voluntary ...



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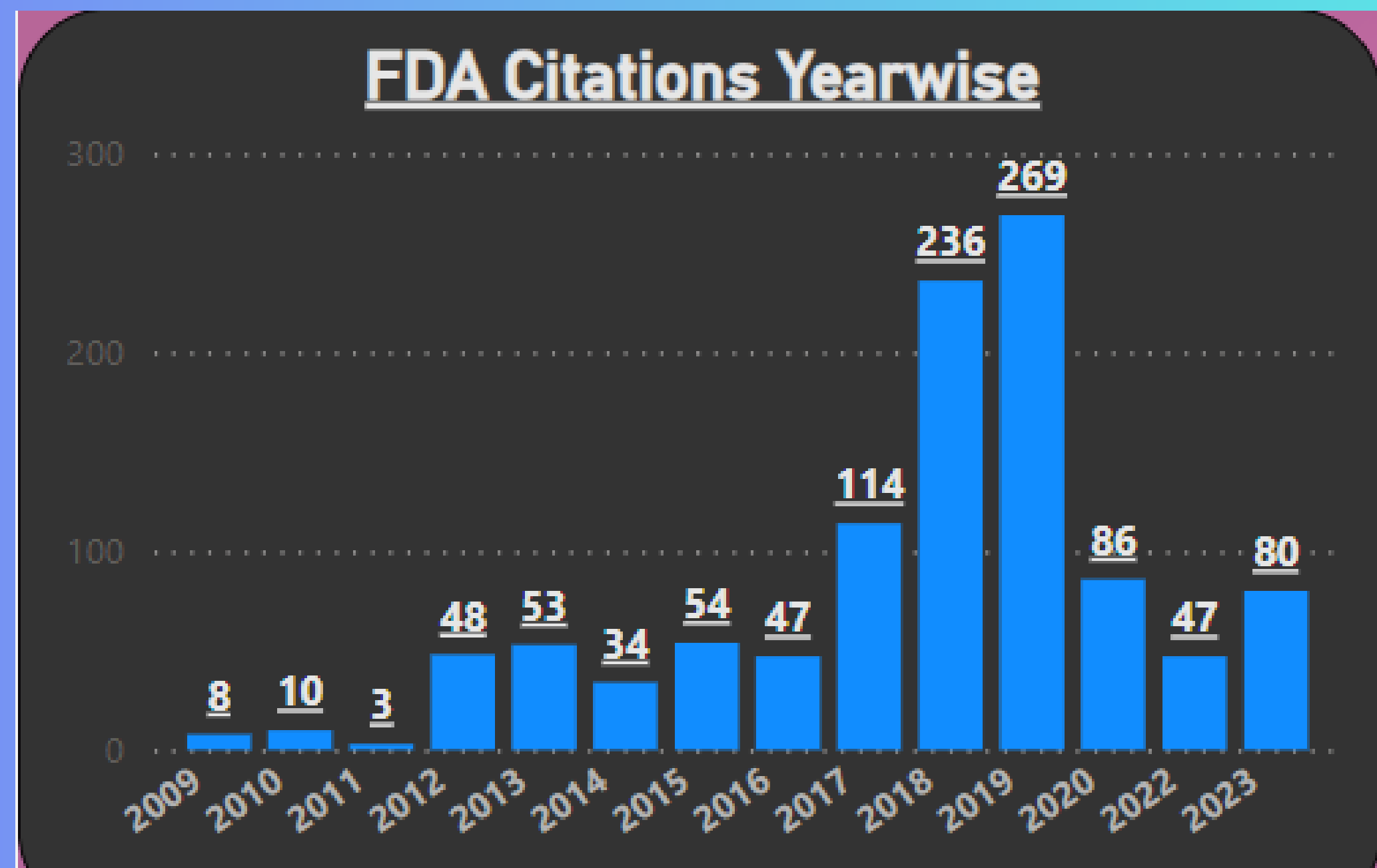


-2023

Firm wise classification of inspections carried out from 2009

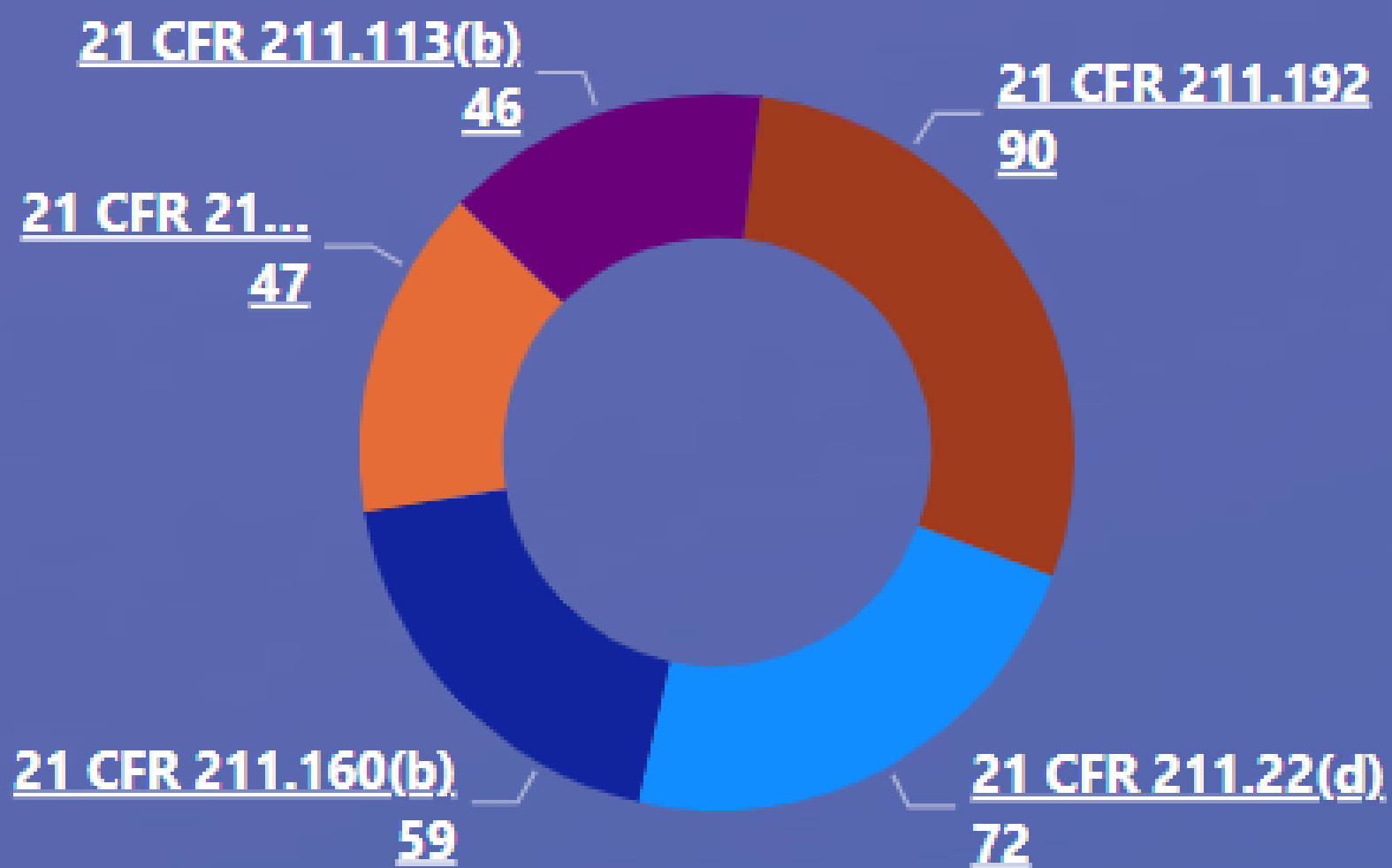


There has been a consistent upward trend in the number of citations issued, reaching its highest point in both 2018, 2019. However, the landscape changed significantly during the subsequent years due to the unprecedented impact of the COVID-19 pandemic. With a decrease in the frequency of inspections carried out during 2020, 2021, and 2022, the number of citations correspondingly reduced.



Citations are statements of specific conditions observed during an inspection that violate the laws, regulations or Acts enforced by the FDA. Citations are listed on a Form 483, which is a document that communicates the inspection findings to the inspected facility.

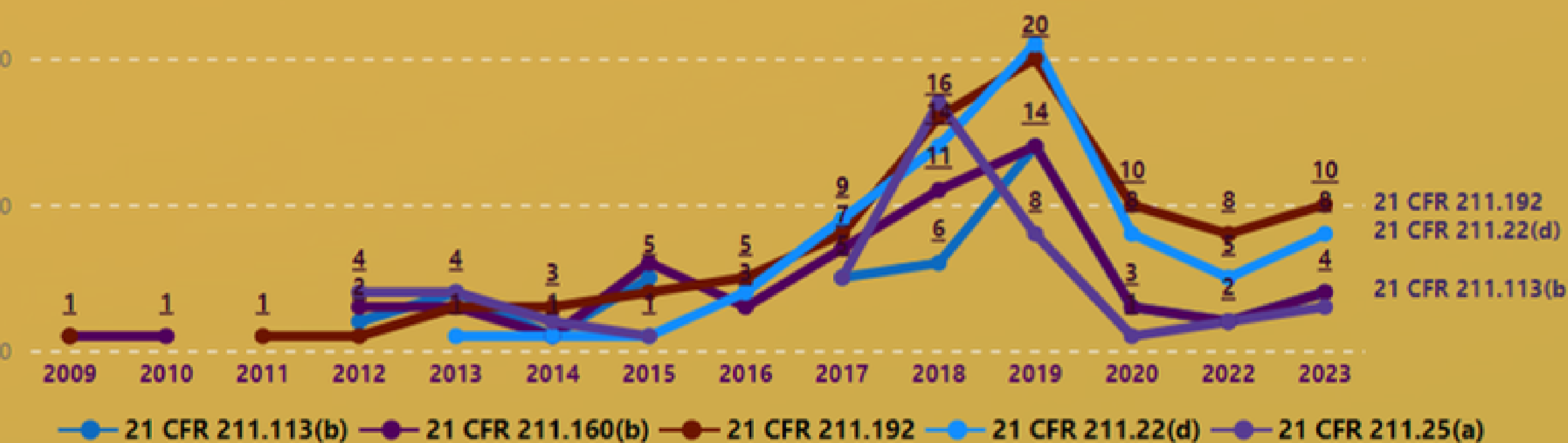
Top 5 Observations



Observations are statements of specific conditions observed during an inspection that violate the regulations or Acts enforced by the FDA. The labels for the segments are references to the Code of Federal Regulations (CFR) Title 21, which contains the rules for drugs regulated by the FDA.

A select set of five particular observations are listed, these are the most frequently encountered. These include instances tied to specific regulatory references: (21 CFR 211.113(b)), (21 CFR 211.192), (21 CFR 211.22(d)), and (21 CFR 211.25(a)).

TOP 5 Observations yearwise



The prominence of these top five observations reached its pinnacle during the years 2017-2019. This escalation in observations directly correlated with the surge in inspection activities during those years.

Top citations and Observations

Act/CFR Number	Short Description	Count of Act/CFR Number
21 CFR 211.22(d)	Procedures not in writing, fully followed	72
21 CFR 211.160(b)	Scientifically sound laboratory controls	59
21 CFR 211.192	Investigations of discrepancies, failures	50
21 CFR 211.113(b)	Procedures for sterile drug products	34
21 CFR 211.25(a)	Training , Education , Experience overall	29
21 CFR 211.192	Written record of investigation incomplete	22
21 CFR 211.25(a)	Training--operations, GMPs, written procedures	14
21 CFR 211.192	Extent of discrepancy, failure investigations	13
21 CFR 211.113(b)	Validation lacking for sterile drug products	12
21 CFR 211.25(a)	GMP Training Frequency	4
21 CFR 211.192	Quality control unit review of records	3
21 CFR 211.192	No written record of investigation	2
Total		314

Trend Analysis

1. The number of FDA inspections increased sharply from 2015 to 2018, reaching a peak of 228 in 2019.
2. The number of inspections categorized as "No Action Indicated (NAI)" remained relatively stable over the years, with some fluctuations.
3. "Voluntary Action Indicated (VAI)" inspections show variations but generally increased until 2019 and then slightly decreased in 2020.
4. "Official Action Indicated (OAI)" inspections display a varying pattern, with higher values in 2014, 2015, and 2019.
5. "VAI" inspections generally increased over the years, which could suggest heightened scrutiny and growing concerns about compliance matters.
6. - There is a correlation between increased inspection activity and the number of "OAI" and "VAI" inspections. This suggests that as the number of inspections increased, a higher number of observations or violations were noted.
7. The decline in "OAI" inspections in 2020 might be linked to the COVID-19 pandemic, which led to reduced inspection activities and a focus on critical matters.
8. The reduction in "OAI" inspections in later years could indicate a successful response by companies to address issues, resulting in improvements and fewer major violations.

Root Cause Analysis

The root cause of the top 5 citations can be attributed to a number of factors, including:

- Lack of training and education on GMPs: Many drug manufacturers in India do not have adequate training on GMPs. This can lead to non-compliance with GMP requirements, such as not having all procedures in writing or not following them consistently.
- Inadequate quality control systems: Many drug manufacturers in India do not have adequate quality control systems in place. This can lead to the production of unsafe or ineffective drugs.
- Lack of resources to implement GMPs: Implementing GMPs can be expensive and time-consuming. This can be a barrier for some drug manufacturers in India, especially smaller companies.

Recommendations and Actionable Insights

- **Education and Training:** ✓

- **Recommendation:** Implement comprehensive training programs focused on Good Manufacturing Practices (GMPs) for all employees involved in the manufacturing process.
- **Action:** Develop training modules covering GMP principles, regulatory requirements, and the importance of consistent adherence to procedures. Regularly update training materials to reflect the latest regulations.

- **Resource Allocation:** ✓

- **Recommendation:** Allocate resources for the effective implementation of GMPs, recognizing their significance in ensuring product quality and safety.
- **Action:** Conduct a cost-benefit analysis to demonstrate the long-term benefits of GMP compliance. Consider investing in technology and infrastructure that facilitate adherence to GMPs.

- **Management Commitment:** ✓

- **Recommendation:** Foster a culture of strong management commitment to GMP compliance and quality assurance.
- **Action:** Leadership should actively communicate the importance of GMPs throughout the organization. Set clear expectations for GMP adherence and allocate sufficient resources to support compliance efforts.

Recommendations and Actionable Insights

- **Quality Control Enhancement:** ✓
 - **Recommendation:** Strengthen quality control systems to identify and address discrepancies, failures, and deviations effectively.
 - **Action:** Implement robust quality control measures, including scientifically sound laboratory controls, to ensure the accuracy and reliability of testing results. Regularly review and update these systems to align with evolving industry standards.
- **Documentation and Procedures:** ✓
 - **Recommendation:** Emphasize the importance of maintaining written procedures and consistently following them.
 - **Action:** Develop a comprehensive documentation management system that centralizes all procedures, making them easily accessible to employees. Implement a process for regular review and revision of procedures as necessary.
- **Regulatory Compliance Oversight:** ✓
 - **Recommendation:** Establish a dedicated regulatory compliance team responsible for monitoring and ensuring adherence to all relevant regulations.
 - **Action:** Create a cross-functional team comprising regulatory experts, quality assurance professionals, and manufacturing personnel. Regularly conduct internal audits to identify and rectify any gaps in compliance.

Recommendations and Actionable Insights

Collaboration and Knowledge Sharing: ✓

- **Recommendation:** Foster collaboration and knowledge sharing within the industry.
- **Action:** Participate in industry associations, workshops, and seminars focused on GMPs and regulatory compliance. Collaborate with peers to share best practices and lessons learned.

Continuous Improvement: ✓

- **Recommendation:** Adopt a continuous improvement mindset to address root causes of non-compliance.
- **Action:** Implement corrective and preventive actions (CAPAs) to address root causes of citations. Regularly review CAPAs and assess their effectiveness in preventing recurrence.
- By implementing these recommendations, Indian drug firms can enhance their GMP compliance, improve product quality and safety, and strengthen their standing in the global pharmaceutical industry. It's essential for companies to prioritize compliance, invest in training and resources, and consistently uphold the highest standards of manufacturing practices.

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Thank you



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