TCG Newsletter

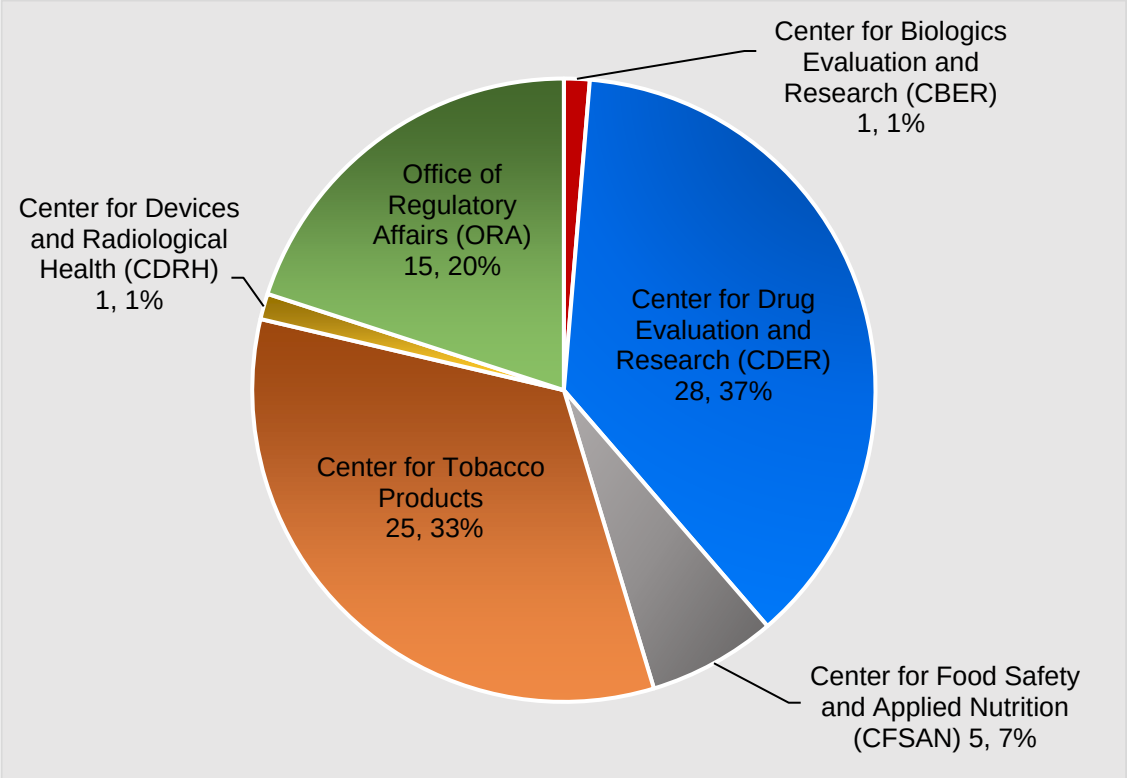
April 2020

FDA Enforcement Trends: Q1 2020

Toscano Consulting Group, Inc. (TCG) provides Quality and Regulatory consulting services to companies within the Pharmaceutical, Biologics, and Medical Device sectors. TCG continuously monitors FDA's Regulatory Enforcement activities to keep abreast of current regulatory enforcement trends. This newsletter provides a summary of Warning Letters issued from the various centers to deliver insight into FDA's active enforcement areas.

We had hoped this newsletter would provide a respite from the nonstop focus on the COVID-19 situation, however; COVID-19 has made its way into the FDA's Q1 2020 Warning Letters. The FDA issued a total of 75 Warning Letters in Q1 of 2020. Many of these are for typical cGMP violations, however there were 12 Warning Letters issued for Unapproved and Misbranded Products related to Coronavirus (COVID-19) also known as: SARS-CoV-2, and/or nCov, 2019 Novel Coronavirus. The distribution by Issuing Centers is provided below in Figure 1.

FIGURE 1: WARNING LETTERS ISSUED BY CENTERS[1]



After assessing the full list we then focused on the 18 Warning Letters (excluding COVID-19) that specifically cited cGMP violations for Pharmaceuticals, Biologics and Medical Device companies; that were primarily issued by CDER, CBER, CDRH or ORA. Out of the 18 Warning Letters the top five reoccurring CFR citations are provided in Table 1 below.

TABLE 1: TOP CFR WARNING LETTER CITATIONS

Top CFR Citations	Description	Number of Citations	Percentage
21 CFR 211.165	Testing and release for distribution.	9	50%
21 CFR 211.22	Responsibilities of quality control unit.	6	33%
21 CFR 211.84	Testing and approval or rejection of components, drug product containers, and closures.	6	33%
21 CFR 211.100	Written procedures; deviations.	5	28%
21 CFR 211.192	Production record review.	5	28%

The United States leads in the number of Warning Letters issued followed closely by India and China (Table 2). The USA leading is not surprising given that the number of domestic inspections far exceeded that of foreign inspections by 4 to 1. In 2019 the FDA conducted 15,393 inspections of which 12,292 were domestic (nearly 80% of all inspections) vs. 3,101 foreign inspections accounting for approximately 20% of inspections.

TABLE 2: Q1 GMP WARNING LETTERS BY COUNTRY

Country	Total Number of GMP WL	Percentage
USA	7	39%
India	5	28%
China	3	17%
Bulgaria	1	6%
Denmark	1	6%
S. Korea	1	6%

SUMMARY OF KEY INSPECTION POINTS

- 9 out of 11 (82%) of the foreign cGMP audits resulted in the FDA putting the inspected company on Import Alert.
- 13 out of 18 (72%) of the Warning Letters had recommendations for the companies to obtain a 3rd party consulting firm to assist with addressing the citations.
- 5 out of 18 (28%) of the Warning Letters had primarily Data Integrity focused citations.
- 7 months was the approximate average lag time between when a site is inspected and when a Warning Letter is issued. In some cases, Warning Letters were issued within a 30-day time period (i.e. companies were cited for Unapproved Products Related to COVID-19), these were excluded from the average.

Through reviewing data and recent notices from the FDA it is readily apparent there has been a significant drop in the number of inspections. On March 10, 2020 the FDA issued a statement[2] indicating that they would be postponing most foreign inspections through April in response to the COVID-19 pandemic. A few days later on March 18, 2020, the FDA issued a second statement[3] indicating that the FDA was temporarily postponing all domestic routine surveillance inspections. We anticipate that these developments will likely result in a continued reduction of Warning Letter issuance throughout 2020. We will continue to monitor FDA enforcement actions and provide another Quarterly update as the 2nd Quarter comes to a close in early July 2020.

Please do not hesitate to contact us here at TCG with any questions you may have. We are always here to provide help and clarity. Wishing you and your family health and safety during these unprecedented times.

Sincerely,

George Toscano, TCG, President

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References:

[1] Note for those Warning Letters issued by certain offices such as the Office of Pharmaceutical Quality, they were grouped by the respective center (CDER).

[2] https://www.fda.gov/news-events/press-announcements/coronavirus-disease-2019-covid-19-update-foreign-inspections

[3] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-focuses-safety-regulated-products-while-scaling-back-domestic