TCG Newsletter

January 2021

FDA Enforcement Trends: Q4 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 saw a continued decrease of Warning Letters related to COVID-19 issued during Q4 2020, with 28 issued. While COVID-19 Warning Letters were at an all-time low for the year, we did see a new Warning Letter subject emerge. This new subject was in regard to Finished Pharmaceuticals/Unapproved New Drug/Misbranded/Adulterated hand sanitizer products being manufactured and distributed from Mexico. A number of firms recently registered as human drug manufacturers with the FDA and 13 of these firms were given a Warning Letter in Q4. The FDA conducted laboratory testing of the hand sanitizer products and as a result they were found to have adulteration and misbranding violations within the meaning of section 501(d)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act), 21 U.S.C. 351(d)(2). For example, the product label claimed to have 70% of the active ingredient ethyl alcohol (ethanol). However, the FDA laboratory testing found that the product contained an average of <0.25% ethanol and an average of 70% methanol volume/volume. Additionally, a number of the hand sanitizer products were unapproved new drugs introduced or delivered for introduction into interstate commerce. As a result the products were detained and refused admission at the US border.

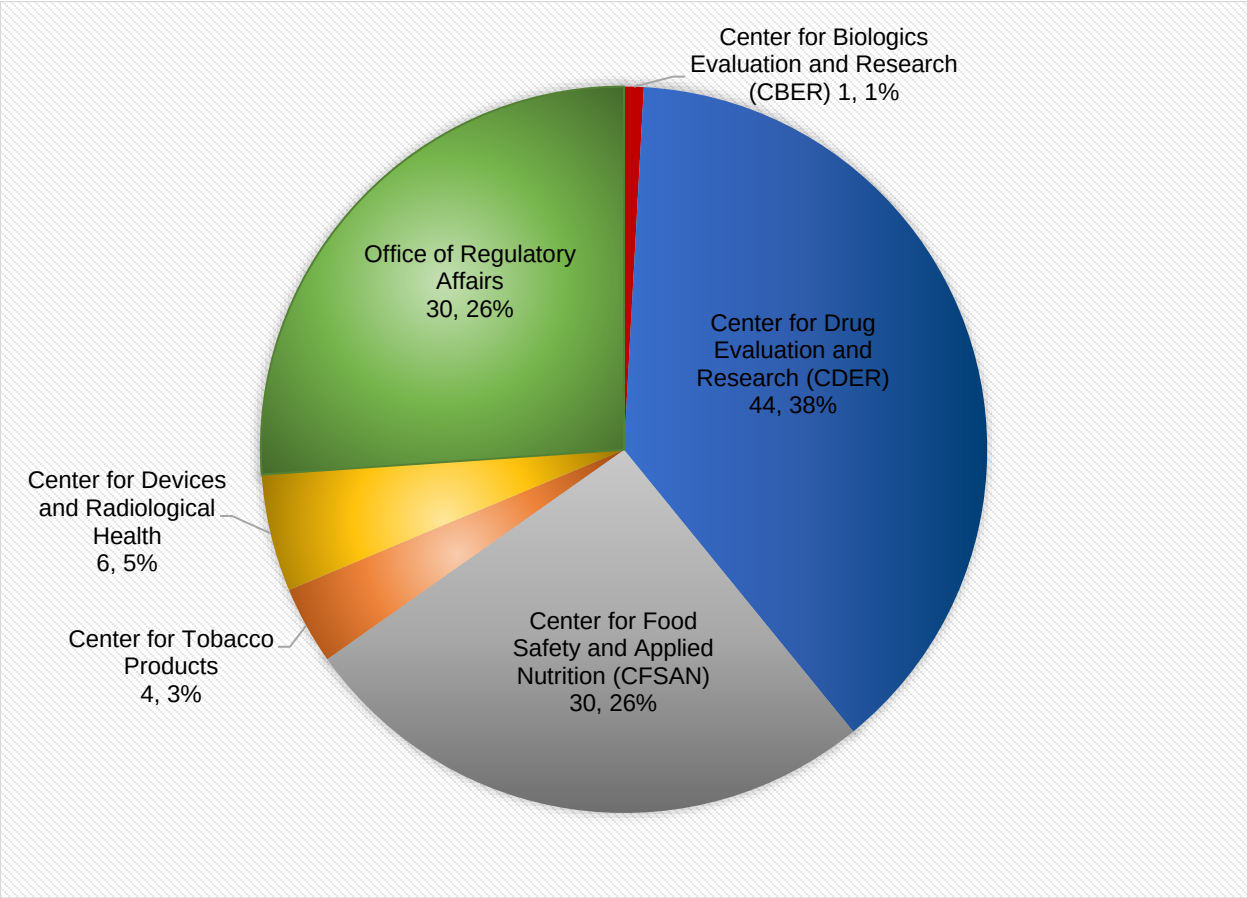
This quarter we saw an overall decrease in the amount of Warning Letters issued resulting in only 115 letters total. A summary of Warning Letters issued per Quarter for 2020 is provided in Table 1.

TABLE 1: TOTAL 2020 WARNING LETTERS BY QUARTER

2020 Quarter	Total Warning Letters
Q1	75
Q2	222
Q3	176
Q4	115

The FDA also continued to conduct remote/virtual Foreign Supplier Verification Program (FSVP) inspections this quarter. A trend we saw peak this quarter was that of FDA website review resulting in Warning Letter issuance. The FDA not only reviewed the company website domain, but they also assessed Amazon storefronts and social media sites (i.e. Facebook, Instagram, Etsy etc.). This resulted in 60 Warning Letters which is over 50% of the total letters issued this quarter.

FIGURE 1: 115 WARNING LETTERS ISSUED BY CENTERS[1]



After assessing the full list of 115 Warning Letters issued this quarter, TCG removed Warning Letters issued by CFSAN, Center for Tobacco Products and related to COVID-19 to focus on those primarily issued by CDER, CBER, CDRH or ORA which resulted in a total of 65 Warning Letters. The United States continued to maintain the lead in the number of Warning Letters (49 out of 65) issued followed by Mexico, India, and Canada (Table 2).

TABLE 2: Q4 GMP WARNING LETTERS BY COUNTRY

Country	Total Number of GMP WL	Percentage
USA	49	74%
Mexico	13	20%
India	2	3%
Canada	1	2%

SUMMARY OF KEY INSPECTION POINTS

- Of the 65 Warning Letters issued, 16 were for foreign inspections, 13 of which resulted in the FDA putting the inspected company on Import Alert.
- 20 out of 65 (32%) Warning Letters had recommendations for the company to obtain a 3rd party consulting firm qualified as set for in 21 CFR 211.34 to assist with addressing the citations.
- For the first time in 2020 we did not see any Data Integrity focused citations in the Warning Letters issued in Q4.
- Approximately 4.7 months was the approximate average lag time between when a site is inspected and when a Warning Letter is issued. This includes Warning Letters issued from FDA Lab Testing and Website reviews in addition to onsite audits which skews the issuance time to a shorter duration. Warning Letters issued related to COVID-19 tend to be issued within 30 days, therefore they were excluded from the average.

TCG then proceeded to further analyze the Warning Letters with cGMP violations specifically for 21 CFR 210/211 (Pharmaceuticals), 21 CFR 820 (Devices) and 21 CFR 600 (Biologics) resulting in 23 Warning Letters. Out of the 23 Warning Letters the top five reoccurring CFR citations are provided in Table 3 below.

TABLE 3: TOP CFR WARNING LETTER CITATIONS

Top CFR Citations	Description	Number of Citations	Percentage
21 CFR 211.100	Written Procedures; Deviations	5	22%
21 CFR 211.67	Equipment Cleaning and Maintenance	4	17%
21 CFR 211.192	Product Record Review	3	13%
21 CFR 211.22	Responsibilities of Quality Control Unit	3	13%
21 CFR 211.166	Stability Testing	3	13%

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 happiness during the new year!

Sincerely,

George Toscano, TCG, President

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References:

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