TCG Newsletter

October 2020

FDA Enforcement Trends: Q3 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.

While COVID-19 continues to make its presences known to the FDA we have seen a decrease of Warning Letters issued during Q3 2020, going from over 70 in Q2 to just 37 in Q3. This quarter we also saw a decrease in the amount of Warning Letters issued topping in at 176 total with a heavy focus in letter responses. The FDA also conducted 14 remote/virtual Foreign Supplier Verification Program (FSVP) inspections this quarter. We saw a familiar topic on the news make a presence for the first time this year, "Unlawful Sale of Unapproved and Misbranded Opioids to United States Consumers Over the Internet" with over 15 letters being issued by CDER. A number of internet pharmaceutical distributors were identified as selling unapproved and/or misbranded opioid drug products. The FDA explicitly states that, *"Opioid addiction and abuse have created an immense public health crisis, and the death toll is staggering. Given the severity of the opioid epidemic, the easy availability of opioids via the Internet poses significant risks to U.S. consumers."*

For example, a pharmaceutical manufacturer was found to be marketing and selling Oxycodone with an off-brand name, identifying it as a "painkiller" and claiming that it is used "to cure moderate to severe pain". While there are a number of approved generic versions of Oxycodone the FDA identified that this company's marketed off-brand name is not one of them and there are currently no ANDAs that have been filed for it. Approved Opioids such as Oxycodone and Tramadol require the strongest FDA warning a "black box warning". This warning indicates that the drug can pose "significant risk of serious or even life-threatening adverse effects".

The distribution by Issuing Centers is provided below in Figure 1.

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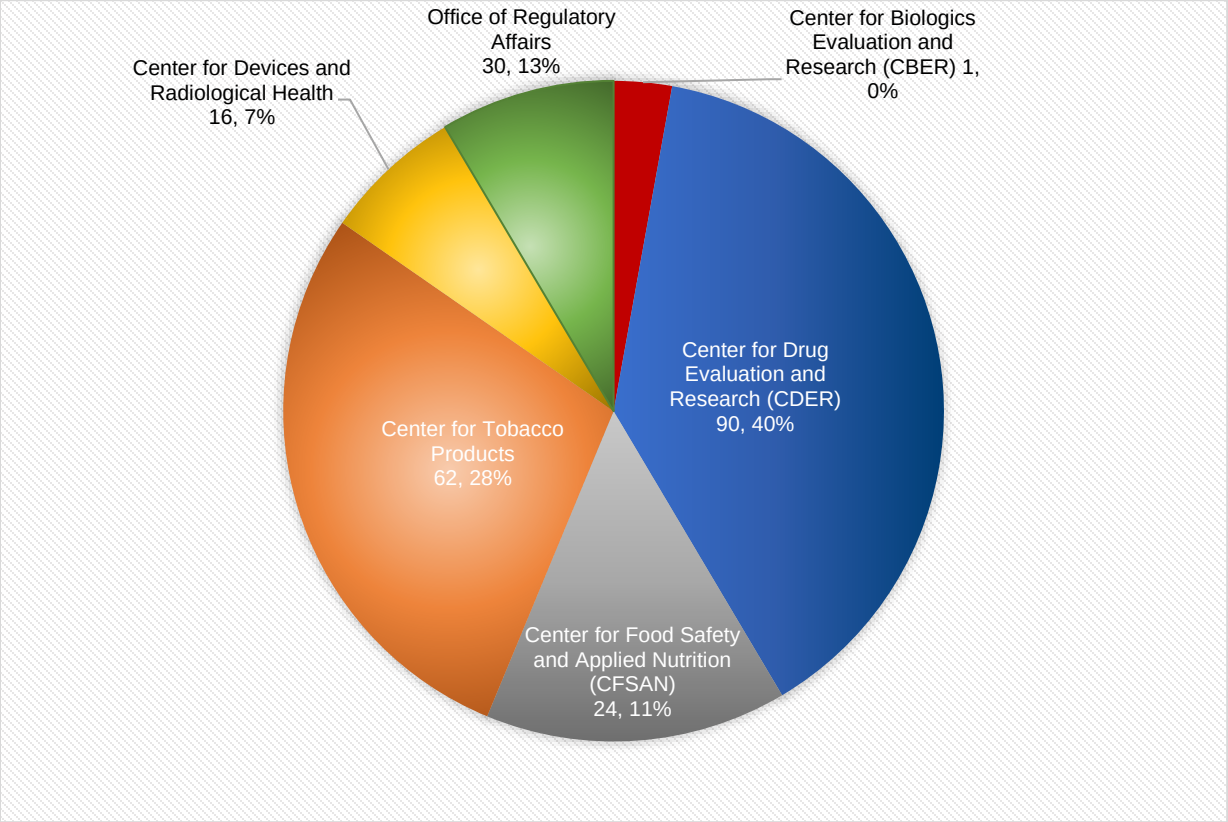
FIGURE 1: 176 WARNING LETTERS ISSUED BY CENTERS[1]



After assessing the full list of 176 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 67 Warning Letters. For the third time in a row the United States continues to maintain the lead in the number of Warning Letters (out of 67) issued followed by China, India, Mexico. Not listed in the table are Indonesia, Iceland, New Zealand, Pakistan, Canada and Puerto Rico each which had one Warning Letter (Table 1).

TABLE 1: Q2 GMP WARNING LETTERS BY COUNTRY

Country	Total Number of GMP WL	Percentage
USA	51	76%
China	5	7%
India	3	4%
Mexico	2	3%

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SUMMARY OF KEY INSPECTION POINTS

- Of the 67 Warning Letters issued, 16 were for foreign inspections, 8 of which resulted in the FDA putting the inspected company on Import Alert.
- 13 out of 67 (19%) of the Warning Letters had recommendations for the companies to obtain a 3rd party consulting firm to assist with addressing the citations.
- 7 out of 67 (10%) of the Warning Letters had primarily Data Integrity focused citations.
- Approximately 4.5 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 an average 30-day time period (i.e. companies were cited for Unapproved Products Related to COVID-19), these 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 19 Warning Letters. Out of the 19 Warning Letters the top five reoccurring CFR citations are provided in Table 2 below.

TABLE 2: TOP CFR WARNING LETTER CITATIONS

Top CFR Citations	Description	Number of Citations	Percentage
21 CFR 211.165	Testing and Release for Distribution	9	47%
21 CFR 211.22	Responsibilities of Quality Control Unit	8	42%
21 CFR 211.166	Stability Testing	6	32%
21 CFR 211.42	Design and Construction Features	6	32%
21 CFR 211.192	Production Record Review	6	32%

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

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