TCG Newsletter

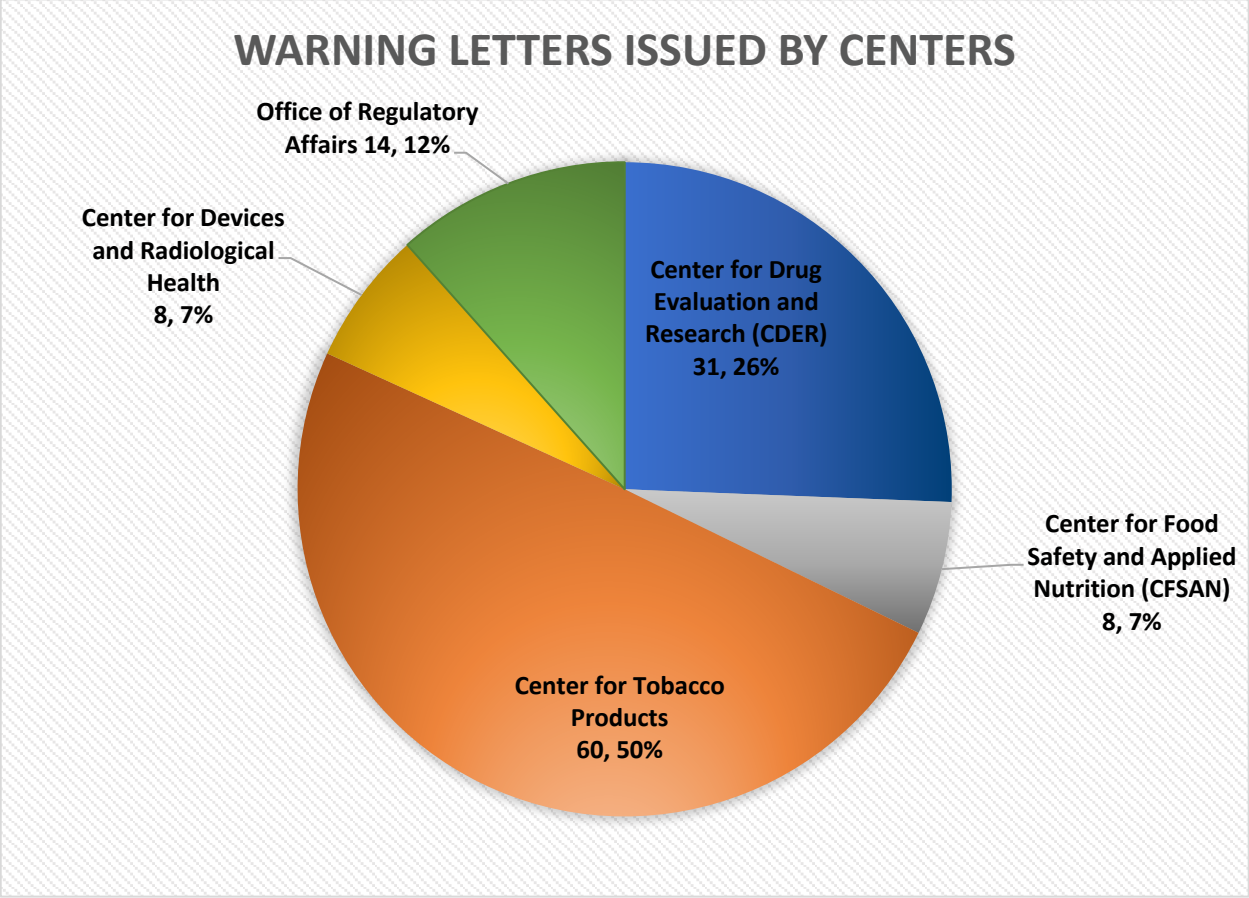
July 2023

FDA Enforcement Trends: Q2 2023

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.

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

FIGURE 1: 121 WARNING LETTERS ISSUED BY CENTERS[1]



After assessing the full list of 121 Warning Letters issued this quarter, TCG removed Warning Letters issued by CFSAN, ORA, and Center for Tobacco Products to focus on those issued by CDER, CBER, and CDRH which resulted in a total of 39 Warning Letters. ORA was removed again from the assessment this quarter as the subject matter this last quarter was primarily focused on the Division of Human and Animal Food Operations, and this newsletter focuses on Pharmaceutical, Biologics and Medical Devices for human use.

Consistent with past Newsletters the United States led in the number of Warning Letters (32 out of 39) issued followed by India, UK, Egypt, Mexico, China and Canada. (Table 2).

TABLE 2: Q2 2023 GMP WARNING LETTERS BY COUNTRY

Country	Total Number of GMP WL	Percentage
US	32	82%
India	2	5%
UK	1	3%
Egypt	1	3%
Mexico	1	3%
China	1	3%
Canada	1	3%

SUMMARY OF KEY INSPECTION POINTS

- Of the 39 Warning Letters issued, 7 were for foreign inspections, and only 2 of these inspections resulted in the FDA putting the inspected company on Import Alert 66-40 for companies India and Egypt.
- 8 out of 39 (21%) Warning Letters had recommendations for the company to obtain a 3rd party consulting firm qualified as set forth in 21 CFR 211.34 to assist with addressing the citations.
- Data Integrity focused citations were 3%, representing a small percentage of the Warning Letters reviewed this quarter.
- Approximately 4 months was the approximate average lag time between when a site is inspected and when a Warning Letter is issued. This represents a shortened timeframe relative to past quarters.

TCG further analyzed the Warning Letters with cGMP violations specifically for 21 CFR 210/211 (Pharmaceuticals), 21 CFR 820/803 (Devices), 21 CFR 312 (INDs) and 21 CFR 56 (Clinical Investigations) resulting in 22 Warning Letters. Out of the 22 Warning Letters the top six 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 211.84	Testing and approval or rejection of components, drug product containers, and closures.	8	36%
21 CFR 211.22	Responsibilities of QC unit	8	36%
21 CFR 820.30	Design controls	6	27%
21 CFR 211.192	Production record review	6	27%
21 CFR 211.100	Written procedures; deviation	6	27%

21 CFR 820.75	Process validation	6	27%

Citations related to 21 CFR 211.84 continue to be the top item consistent with last quarter's Newsletter. It is interesting as this item was not often cited in years past. A closer look at these Warning letters indicate that the FDA is focusing on two items specifically companies that did not test glycerin for the limit of Diethylene Glycol (DEG) and Ethylene glycol (EG) prior to their use in manufacturing and companies not testing Ethanol and Isopropyl Alcohol for the presence of Methanol. The FDA has provided the industry with Guidance documents for both of these items, they are listed below for reference.

Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID-19) Guidance for Industry, January 2021
https://www.fda.gov/media/145262/download

Testing of Glycerin, Propylene Glycol, Maltitol Solution, Hydrogenated Starch Hydrolysate, Sorbitol Solution, and other High-Risk Drug Components for Diethylene Glycol and Ethylene Glycol Guidance for Industry, May 2023 https://www.fda.gov/media/167974/download

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.

Sincerely,

George Toscano, TCG, President

E: gtoscano@thetcg.org

P: (786) 201-3663

References:

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