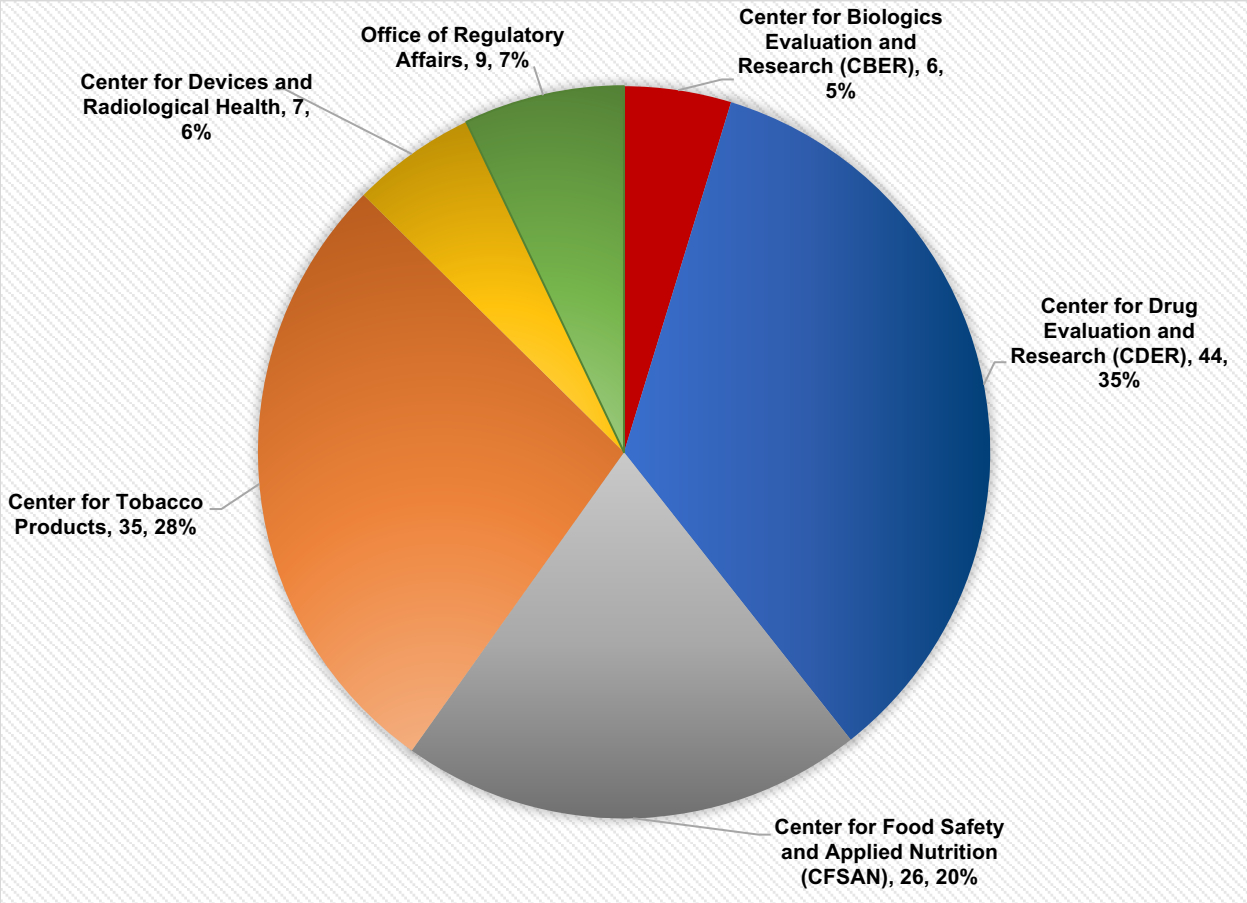
TCG Newsletter

January 2025

FDA Enforcement Trends: Q4 2024

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 provide insight into FDA's active enforcement areas. The distribution of Warning Letters by Issuing Centers is provided below in Figure 1.

FIGURE 1: 127 WARNING LETTERS ISSUED BY CENTERS[1]

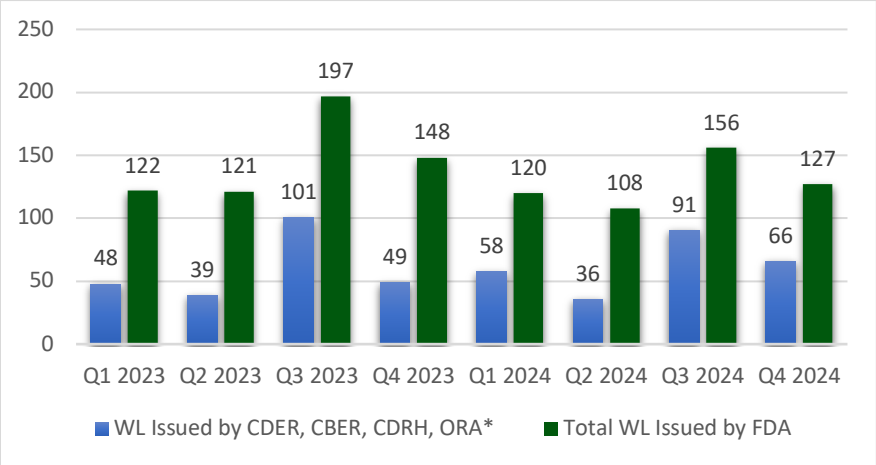


The FDA issued 127 Warning Letters during the fourth quarter of 2024. The global distribution of Warning Letters is presented below in Table 2, with the United States continuing to have the majority of Warning Letters (87 out of 127) issued followed by China, India, and others.

TABLE 1: Q4 WARNING LETTERS BY COUNTRY

Country	Total Number of WL	Percentage
US	87	69%
China	7	6%
India	7	6%
Venezuela	3	2%
Canada	2	2%
Italy	2	2%
S Korea	2	2%
Australia	1	1%
Denmark	1	1%
France	1	1%
Greece	1	1%
Hungary	1	1%
Japan	1	1%
Malaysia	1	1%
Mexico	1	1%
New Zealand	1	1%
S Africa	1	1%
Slovenia	1	1%
Spain	1	1%
Taiwan	1	1%
Thailand	1	1%
Turkey	1	1%
UK	1	1%
Vietnam	1	1%

FIGURE 2: WARNING LETTERS ISSUED BY QUARTER



TCG focuses on FDA enforcement activity for Pharmaceutical, Biologics and Medical Devices for human use, therefore we filtered out Warning Letters issued by CFSAN, Center for Tobacco Products, and ORA (based on finding type) to focus on those issued by CDER, CBER, and CDRH warning letters that obtained GMP related findings which resulted in a total of 57 Warning Letters.

SUMMARY OF KEY INSPECTION POINTS FOR GMP WARNING LETTERS

- Of the 57 Warning Letters issued, 40 (70%) were for foreign inspections, and 19 of these inspections resulted in the FDA placing the inspected company on Import Alert 66-40.
- 25 out of 57 (44%) 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.
- We continued to see a small percentage of Data Integrity focused citations accounting for 11% (6 of 57) of the assessed Warning Letters.
- 7.1 months was the average lag time between when a site is inspected and when a Warning Letter is issued.

TCG then evaluated 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 49 Warning Letters. Out of the 49 Warning Letters the top 5 CFR citations are provided in Table 2 below.

TABLE 2: TOP WARNING LETTER CITATIONS

Top CFR Citations	Description	Number of Citations	Percentage
21 CFR 211.22	The quality control unit shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another	21	37%
21 CFR 211.84	Testing and approval or rejection of components, drug product containers, and closures	17	30%
21 CFR 211.165	Testing and release for distribution	14	25%
21 CFR 211.100	Written procedures and deviations	14	25%
21 CFR 211.166	Stability Testing	7	12%

Citations related to 21 CFR 211.84 and 21 CFR 211.22 continue to be the top items, consistent with TCG's previous newsletters for 2024. These 2 citations are cited together 67% of the time in the Warning letters issued this quarter. The issues related to these observations remain consistent with those reported for over a year now, indicating that companies across the industry have not learned from the past years FDA enforcement actions.

Data Integrity still remains a significant issue, although the number of Warning letters with Data Integrity issues has declined from its peak, companies are still being cited for the same issues that have persisted for decades. Notably one warning letter indicated that analysts documented both the testing process and results, however based on a review of biometric access records, they were not physically present at the facility during testing.

This issue can arise for several reasons both intentional and unintentional. One example that I have often seen is the sharing of badges to allow someone else access into the facility. In this case someone lends their badge to another coworker who forgot their badge and now the worker who is utilizing the badge performs work in the building but they system has no record of them being in the building.

Other examples include 'piggie backing' or 'tagging-along' where someone scans their card to allow access to a building and lets others come in behind them (who do not scan) inside the building. The attendance system now does not recognize this person as being in the building, however testing records that are completed will indicate that the analyst was present, creating a conflict between the testing record and the attendance record. In other cases, the situation can be indicative of more serious issues such as falsification or backdating records.

This type observation erodes the trust between FDA (investigator) and the company as the inspection detected this issue, but there may be many others that were not identified during the inspection. The company now faces a long road to rebuilding trust with the agency to demonstrate that they are responsible actors.

At TCG we have assisted many companies with both Data Integriy issues as well as GMP issues. 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).