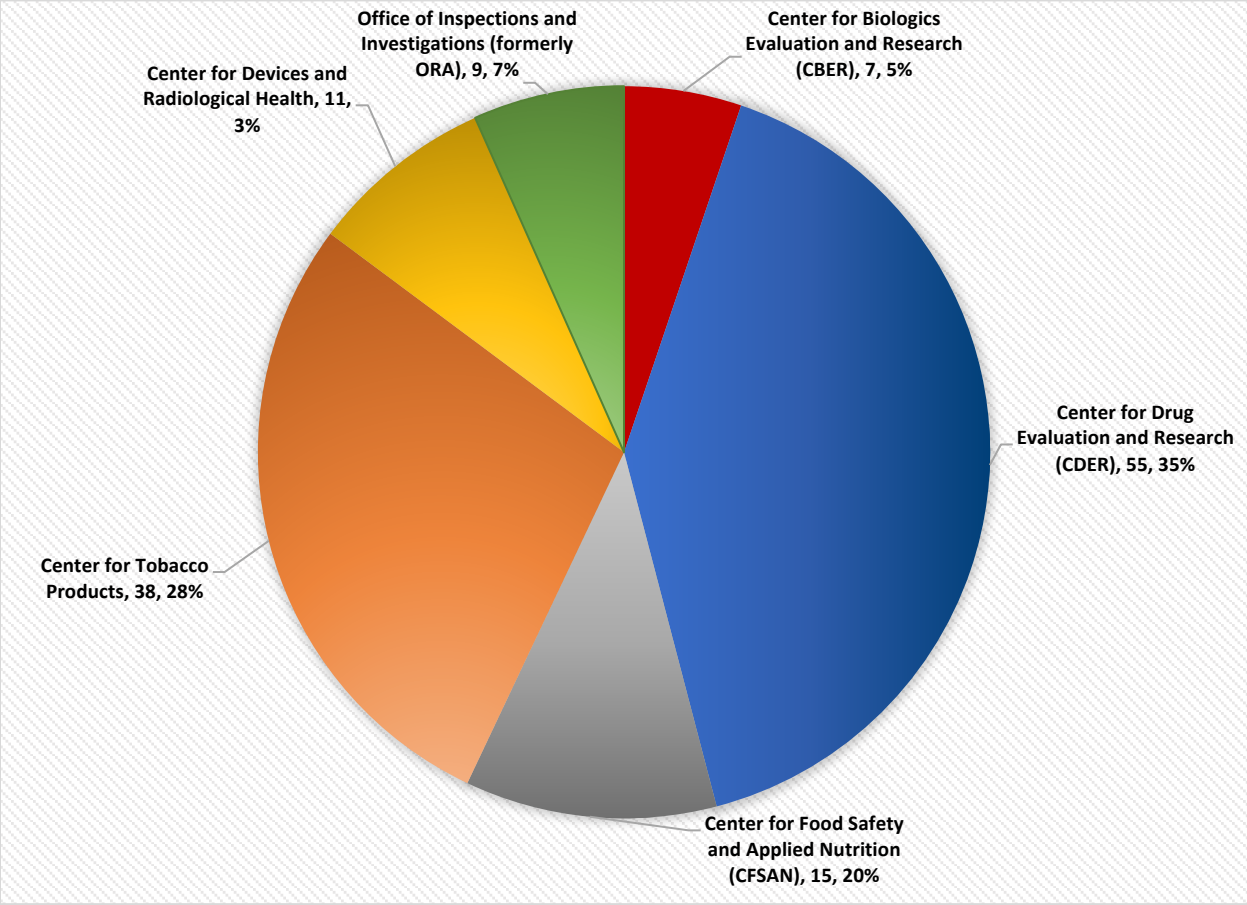
TCG Newsletter

April 2025

FDA Enforcement Trends: Q1 2025

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: 135 WARNING LETTERS ISSUED BY CENTERS[1]



The FDA issued 135 Warning Letters during the first quarter of 2025. The global distribution of Warning Letters is presented below in Table 2, with the United States continuing to have the majority of Warning Letters (107 out of 135) issued followed by China, India, and others.

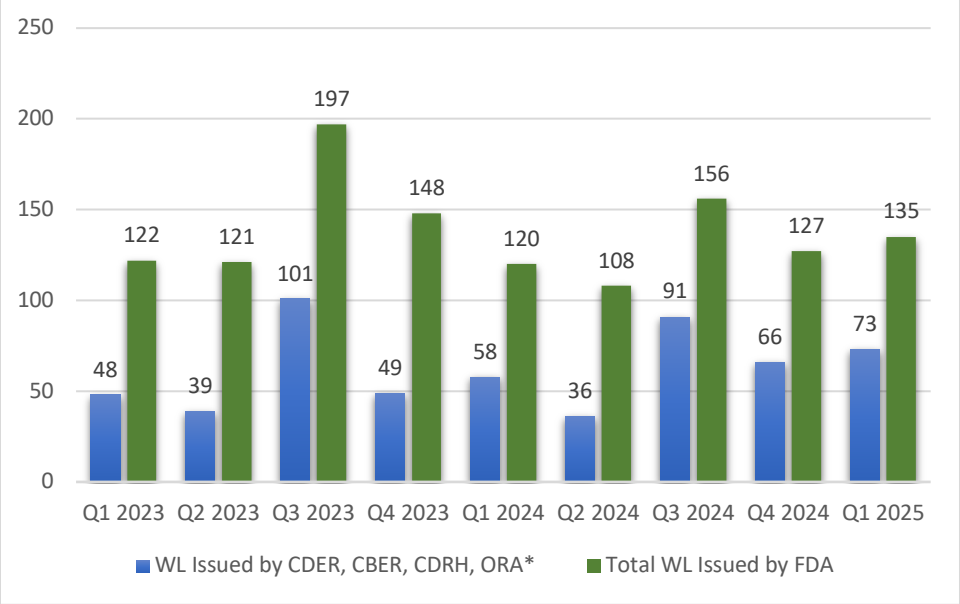
TABLE 1: Q1 WARNING LETTERS BY COUNTRY

Country	Total Number of WL	Percentage
US	107	79%
China	8	6%
India	7	5%
S. Africa	2	1%
Turkey	2	1%
Bulgaria	1	1%
Canada	1	1%
France	1	1%
Japan	1	1%
Nicaragua	1	1%
Portugal	1	1%
Thailand	1	1%
United Kingdom	1	1%
Vietnam	1	1%

The amount of Warning Letters issued by quarter since 2023 is presented in Figure 2. The amount of Warning Letters issued by CDER, CBER, and CDRH Warning Letters that obtained GMP related findings issued in Q1 2025 is slightly higher than it has been in both Q1 2023 and Q2 2024. This trend will likely be tested with the recent Reductions in Force (RIF) that have been occurring at the FDA. The Department of Health and Human Services (HHS) will be laying off approximately 10,000 workers. About 170 employees were cut from the FDA's Office of Inspections and Investigations (formerly ORA). Although these cuts are not of FDA inspectors or investigators; much of the administrative support has been reduced.

As the FDA comes to grips with these cuts, they will need to react to new ways of working with a streamlined workforce. It is likely that this adjustment period may lead to a reduction in the number of surveillance inspections and may impact FDA's ability to review New Drug/Biologic/Device submissions within regulatory timeframes. Lastly, this is in addition to an already existing backlog of deferred inspections due to the pandemic which may impact enforcement actions due to reduced FDA inspections.

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 Office of Inspections and Investigations (formerly 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 73 Warning Letters.

SUMMARY OF KEY INSPECTION POINTS FOR GMP WARNING LETTERS

- Of the 73 Warning Letters issued, 23 were for foreign inspections, and 13 of these inspections resulted in the FDA placing the inspected company on Import Alert 66-40.
- 20 out of 73 (27%) 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 saw the smallest percentage yet of Data Integrity focused citations accounting for only 1% (1 of 73) of the assessed Warning Letters.
- 7 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 37 Warning Letters. Out of the 37 Warning Letters the top 5 reoccurring CFR citations are provided in Table 3 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	13	35%
21 CFR 820.30	Design controls	13	35%
21 CFR 211.84	Testing and approval or rejection of components, drug product containers, and closures	12	32%
21 CFR 211.192	Production record review	8	22%
21 CFR 211.42	Design and construction features	7	19%

Q1 2025, marks the first quarter over the last several years where Medical Device Quality System Regulations are at the top of the list citing Design Controls (21 CFR 820.30) as a top finding. This may show a heightened focus of FDA investigators in this area. Design Controls relate to the development of primarily Class 2 and 3 Devices and the supporting steps to realize these devices including: design and development planning, design input/output, design review, verification, validation and design history files (DHF).

In summary we are undergoing a period of rapid changes in the US with widespread changes across the government landscape. At TCG our clients are asking many questions regarding the impact of some of these changes. We understand that many changes done so quickly cause uncertainty, but are confident that in time things will settle and some level of predictability will return. We may be operating in a different landscape than before, but we are reminded of one constant and that is change.

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,

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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).