

FDA's Increased Information Transparency

Leveraging information and your need to know.

As a government entity, the U.S. Food and Drug Administration (FDA) has an obligation to provide transparency in its operations, which it does through its FDA Transparency Initiative.¹ The goal is to enhance the understanding of stakeholders in FDA's actions to achieve its mission to protect and promote human and animal health. Better, more frequent communication and new and more user-friendly tools ensure that stakeholders have the information necessary to successfully navigate a global and ever-changing regulatory and compliance environment.

Data, data, data

If you like to crunch data or get the general sense of the enforcement landscape, FDA has provided the opportunity to examine a variety of data points through the Inspections Database, FOIA Reading Room, posted Warning Letters and enforcement statistics within the Enforcement report, including recall, market withdrawal and safety alerts. Recently, the FDA took an additional step to enhance the data stakeholders may examine to understand the enforcement of the Federal Food, Drug, and Cosmetic Act and associated regulations. This updated dashboard can be found at <https://datadashboard.fda.gov/ora/index.htm>.

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While the data within the dashboard is only updated semi-annually, there is a vast amount of information available now in a much friendlier format to digest. However, the limitations of the data must be understood. For example, FDA continues to withhold pending compliance actions such as Warning Letters, seizures and injunctions until those actions are executed. Of greatest interest is the ability to grasp sources of information quickly, across varying statistics in inspection numbers and trends, import operations and enforcement actions.

It is not uncommon for those regulated by the FDA to fail to consider the misfortune of others operating in the same sphere. For example, the FDA has consistently issued FDA-483s for observations related to data integrity; yet, the same mistakes continue to be made, or fail to be self-identified and voluntarily corrected by competing firms. Additionally, the global nature of our supply chain necessarily implicates import operations as a key factor to any foreign manufacturer's success. How frequently does a manufacturer consider the ramifications of compliance actions against their competition and when does a foreign supplier pay attention to trends and enforcement activities extending beyond the standard cGMP Untitled or Warning Letter?

The data dashboard can provide quick access to information such that the manufacturer's internal resources can understand and prepare for what may be afoot in their own organizations. Here are some examples of information that can help players gain an appreciation for the FDA's global operations.

A quick filtering of enforcement and compliance data support the increase in Warning Letter actions against foreign



operators. The dashboard now allows a quick view of those warning letters issued to foreign manufacturers.

Dates of inspections and actions are clearly identified and provide for an expedited deeper dive into the details of those actions. By researching those profiles that are similar to their own, companies can gain deep insight into the problems that may be plaguing the competition.

Additionally, and unlike the inspection database or the Warning Letter database, the new dashboard allows you to easily select by foreign or domestic, country, state and product type. Now, information on any company and its FDA interactions is clearer than ever.

Import information has been traditionally difficult to extract from the FDA dashboard and databases. It is now possible to understand which products are being refused, and from what region of the world. For example, import refusals for drug and biologics was filtered for fiscal year 2016, however, filtering further, we discovered that only 25 of the 3,455 product lines imported for drugs and biologics were ever physically sampled and refused. Almost exclusively, imported

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drug and biologic products are refused as already on import alert—detain without examination—or as unapproved, misbranded or adulterated drugs, based solely on document review.

Examination of the refusal data can be telling if you understand how FDA import operations work. For example, refusals associated with 8,883 drug and biologics refusals in fiscal years 2014-2016, shows which products were sampled and which were not. Products refused without sampling are generally associated with the following: unapproved supplier, new drug or biologic not approved for U.S. distribution, misbranding, or the product or supplier is on import alert. The majority of these products are “detain without examination,” meaning that the declaration of the product at the border is enough to detain it for examination. Examination is not the same as sampling. Sampling involves physical samples for analysis. Examination involves physically examining the product or examination of the declaration to determine the status of the product or supplier.

U.S. Customs and Border Protection established an imports management system called ACE, or automated commercial environment. ACE allows 46 agencies to work together in one platform for review of imported materials.² This cooperative environment means that fewer things slip through the cracks or have an opportunity to fly under the radar. Although FDA still only reviews on average of 1% of all import lines, the reviews are being productive. It may be no coincidence then that in 2016, the year ACE went into effect, the number of refusals increased by 3,530.

Finally, access to recall information has improved. The dashboard allows recall information to be quickly searched by fiscal year, class and product. It is interesting to observe that recalls for drug products have decreased over the last two fiscal years. However, when looking at the total number of on-going recalls, you see a

steep increase in the numbers. This is an indication that the recalls are complex and are taking an extended amount of time to bring to closure.

Data can be further isolated by fiscal year and class of recall. As has been the trend, class II recalls are the most common. Isolating the data to fiscal year 2017, class II recalls for drug products, allows a table to be generated with direct links to the recall notice from the enforcement report where the reason for the recall is readily available.

Old is not necessarily bad

The enhancement of the data dashboard does not mean the traditional tools of transparency have lost their value. For example, FDA has recently decided that recall information should be more readily available. Anyone who has had to issue a difficult recall understands it can take FDA months to render a classification. In the interim, consumers do not have the information on the recall available to them. The weekly enforcement report will now have a category for “not-yet-classified.” This will allow information regarding the product and the reason for the recall to be communicated while the recall classification is pending FDA review. This is not only good for the consumer, but also for the industry, by allowing early awareness of problems that may be afflicting a particular commodity.

The Warning Letter database³ continues to provide information on the specific observations most concerning both FDA and industry and, the Inspections database⁴ has also been improved. The database is now updated on a monthly basis instead of quarterly. This database allows one to search the most recent inspectional outcome for an entity, helping users understand the current compliance status as well as the historical.

Finally, the Inspections Observations link⁵ trends in specific 483 observations. Comparing those trends to those observations being cited in specific Warning Letter violations helps provide an un-

derstanding of what FDA finds to be of greater significance. A snapshot of 2017 FDA: 483 observations for drugs shows the prevalence of the data integrity observation, noted 124 times in approximately 694 FDA-483s issued in the drug program.

Why does it matter?

FDA has been very clear with regard to its on-going initiatives to help drug and medical device manufacturers bring new products to the market more quickly. This is often referred to as being the “kinder and gentler” FDA. However, the desire of FDA to focus on the part of the mission to “promote” public health, does not mean that they have forgotten about the “protection” role.

It is no longer possible to reasonably argue that one did not know the expectations. Aside from the very overt notice of a Warning Letter, there are limitless resources available to consumers and to industry. Remaining “current,” within the meaning of CGMP, means putting forth the effort to remain current. That means not only in technology and process improvements, but also in ensuring an understanding of the Agency’s concerns, focus and expectations.

FDA’s increased transparency brings with it industry’s responsibility to remain current and knowledgeable. It also brings the opportunity for industry to leverage this information for proactive quality system improvement at a much lower cost than remediation. **CP**

References

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