Compliance Matters

The Pendulum Swings

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Under the Bush administration, Food and Drug Administration (FDA) site inspection and enforcement activities were generally acknowledged to have been assigned a lower priority than under the Clinton administration. However, as the Bush administration relaxed FDA enforcement, a number of key Democratic members of Congress publicly criticized this policy and began calling for the FDA to strengthen their oversight of drug manufacturers. With the Democrats back in control, FDA watchers have been waiting to see what position the Obama administration will take regarding regulatory compliance enforcement activities of drug manufacturers.

A number of factors can foretell the potential direction of enforcement policy within a new administration, but a leading indicator is the individual selected to head the FDA. For example, during the 1990s Dr. David Kessler was appointed FDA commissioner. Kessler, both an M.D. and a lawyer, was quick to establish a tough enforcement climate. During his tenure the medical gas industry experienced one of the most unforgiving enforcement climates ever. While a number of the enforcement actions from that era were taken against medical gas firms as a result of unfortunate incidents involving patient fatalities, there is no question that there was also a crackdown mentality at work inside the FDA, which was supported by the White House. The appointment of Dr. Kessler came after enforcement actions had languished under the previous Republican administration. The appointment of Margaret Hamburg, M.D, to head the FDA under this administration appears to support the premise that the compliance pendulum tends to swing from one side to another depending on the philosophy of the party in power at the time.

In May, Dr. Hamburg, was approved by a unanimous vote in the Senate and assumed the responsibilities as the newest FDA commissioner. On August 6th she made her first public speech entitled "*Effective Enforcement and Benefits to Public Health,*" the text of which can be found at http://www.fda.gov/NewsEvents/Speeches/ucm175983.htm. In her speech she emphasizes the need for a strong FDA and the importance of establishing and promoting the agency's credibility with the public. She specifically addressed the FDA's responsibility to be vigilant and visible in identifying problems and *"…using meaningful penalties to send a strong message to discourage future offences."*

In her speech, Dr. Hamburg also noted that that there has been a steep decline in the FDA's enforcement activity over the past several years, and during the same time period many of the enforcement actions that the FDA did undertake were hampered by unreasonable delays. She noted that *"…these delays do not result from a lack of commitment on the part of FDA career staff, but rather that the pathways for enforcement action can be too long and arduous, even when the public's health is in jeopardy."* We see this statement as a very public condemnation of the Bush administration's policy requiring FDA headquarters to review and approve all warning letters before issuance. Implementation of this policy had a direct, immediate, and significant dampening effect on both the speed and the number of FDA enforcement actions issued over the last six years.

SIX NEW FDA ACTIONS

Dr. Hamburg's speech outlined six new actions the FDA is implementing (initially) to improve the effectiveness of enforcement systems.

1. The FDA will set post-inspection deadlines. When the FDA finds that a firm is significantly out of compliance, and issues a form 483 — Notice of Inspectional Findings, they will now expect a prompt response. The firm will generally have no more than 15 working days in which to respond before the FDA moves ahead with a warning letter or enforcement action. Historically, firms have not been required to respond to a 483.
2. The FDA will take steps to speed the issuance of warning letters. A new policy now limits warning letter reviews to significant legal issues only. This will move enforcement letters through FDA in a considerably more streamlined fashion. This new review policy is consistent with the FDA's longstanding historical practice prior to the Bush years. It appears to restore the authority of the FDA districts to pursue enforcement actions, and removes a key roadblock set in place by the Bush administration.
3. The FDA will seek to work more closely with their regulatory partners to develop effective risk control and enforcement strategies. In many food safety cases, for example, local, state, and international officials have more authority to take action quickly than the FDA. When the public health is at risk, the FDA now will reach out to its partners to take rapid action while the agency alerts the public and prepares longer-term responses.
4. The FDA will now prioritize enforcement follow-up. After a warning letter is issued or a major product recall occurs, they will make it a priority to follow up promptly with appropriate action, such as an inspection or additional investigation to assess whether or not a company has made required changes in its practices. Historically, this has been a weak area for the FDA. It is not uncommon for firms to have little or no follow-up from the agency years after having been issued a warning letter.
5. The FDA is now prepared to act swiftly and aggressively to protect the public. The FDA will no longer issue multiple warning letters to noncompliant firms before taking enforcement action. If the FDA finds that it is necessary to move quickly to address significant health concerns or egregious violations, they will consider **immediate** action — even **before** issuing a formal warning letter.

This means that if the FDA finds significant issues at your site you need to move quickly to contact key decision-makers inside the agency. Engage them in meaningful dialogue or things may quickly escalate to a seizure in days, not months.

6. The FDA is developing a formal warning letter "close-out" process. This action differs from the others as it relates to the agency's response to firms **after** they have made necessary corrections.

The agency believes these procedural changes will help them ensure that violations are taken seriously by drug manufacturers and that warning letters and enforcement actions occur quickly. It also gives the FDA the ability to implement steps to protect consumers in cases where immediate enforcement action is not possible. This includes issues where the FDA may not have clear jurisdiction, or where they need to ask Congress for legislation granting them additional authority.

THE NEW CLOSE-OUT PROCESS

Regarding the sixth action noted above, the FDA is developing, at the direction of the Commissioner, a formal warning letter "close-out" process. The FDA will determine if a firm has fully corrected the violations raised in a warning letter based on a re-inspection. If satisfied, the FDA will provide a "close-out" letter indicating that the issues in the warning letter have been successfully addressed and will publish that notice on their website.

The close-out letter process is a significant change to enforcement as the FDA has historically never required firms to obtain this type of written agency approval of remedial actions. Based on our 30 years of experience with FDA enforcement actions and agency inspectors, we expect obtaining a close-out letter to potentially be an arduous process. It appears that once you believe you are ready to obtain a close-out letter, you will have to ask the agency for a re-inspection. Alternatively, the FDA may simply decide to re-inspect once they believe you **should** have completed all remediation activities. Since warning letters typically do not list all non-conformances, only the major ones, it is possible the re-inspection process could find new items that must also be addressed. This implies that a firm could go through several cycles of the re-inspection process before passing the finish line and getting its close-out letter from the FDA. In our opinion, any medical gas firm receiving a warning letter in the future should IMMEDIATELY have a compliance expert do a complete gap assessment to identify any potential problems, and do so prior to committing any remediation timelines to the FDA.

A COMMITMENT TO COMPLIANCE

The FDA commissioner closed her speech with the following admonition to industry: *"Ultimately, the FDA's success should be measured not by the number of warning letters or injunctions or seizures … but by our impact on the health and welfare of the public. Enforcement of the law is not simply an end in itself… enforcement is critical to the agency's public health mission. This connection between the law and public health is as true for industry as it is for the FDA. When you fail to meet the standards that the FDA has set to prevent harm… then you are putting the public at risk. You are also jeopardizing the public's confidence in your industry. The solution is a commitment to compliance backed by a strong compliance program. Now is a good time to reassess whether you have such an effort in place."*

We interpret this as meaning it will take the FDA some time to get the new tools and policies in place, so industry should use that time wisely and get their house in order if they know, or suspect, they have potential compliance issues.

So, what can be learned or inferred from this speech, and what actions should medical gas firms be considering over the next 6–12 months? We believe it is very significant that the first public speech given by the new Obama era FDA Commissioner focused on strengthening and speeding up their enforcement activities. This is consistent with what key Democratic Congressional members have been calling for over the last five years. We do not believe the gases industry is in FDA's enforcement cross hairs, however. Many of the marginal companies that caused a number of the problems that caught the FDA's attention in the 90s no longer exist. Therefore, barring the future occurrence of another medical gas issue involving patient fatalities, we do not expect to see a massive enforcement blitz in our industry like we did in the 90s.

We also believe that FDA now recognizes that medical gases are somewhat lower risk pharmaceutical compounds, with some unique properties that help assure patient safety. On the flip side of that coin, however, the agency is also keenly aware that there are still many small companies involved in medical gases, and key agency compliance officials have historically expressed concern that these companies may not have adequate resources to manage effective compliance programs. So the FDA is not likely to ignore our industry completely either.

Most significant to our industry is Dr. Hamburg's discussion of *meaningful penalties*. Companies that run afoul of the FDA in the future could find it significantly more expensive to get out of trouble than they have in the past. With the new close-out letter requirement, companies that receive warning letters will find it harder and more time consuming to clear their name. With this change in enforcement policy, investing in compliance before problems arise is a smart and prudent fiscal move.

The FDA is prepared to once again "take the gloves off," at least to a greater degree than they have in the last five years. In the next six to eight months, it will become more apparent how intent the FDA is on stepping up enforcement in the gases industry. After that timeframe, FDA inspections will begin to reflect the agency's new enforcement direction and any new compliance surprises and/or changes to regulations for the gases industry will emerge. Firms that have had warning letters in the past could see the FDA come to re-inspect in the near future. We strongly advise firms, especially those that have not seen an FDA inspection in some time, to take steps to understand where they may have potential compliance gaps through either a mock FDA audit or with a compliance gap assessment.

At B&R Compliance we have our finger on the pulse of medical gas compliance activities and will be providing updates in this column as the direction of the new FDA enforcement policies unfold. In the meantime, if you would like to better understand where your potential compliance gaps might be, or just have some general medical gas questions, please give us a call.

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