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Regulatory Spotlight

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Pharmaceutical companies face the changing future of pharmacovigilance

The pharmaceutical industry is facing a growing threat from safety data on the drugs it produces. The FDA has fostered unprecedented transparency on drug safety data, forcing companies to manage novel challenges from parties already busy mining those data: regulators, the public and data analytics firms. In this climate, pharmaceutical companies have the opportunity to find ways to mitigate risks, unlock savings, make new discoveries and create competitive advantages.

Several changes in particular are increasing stakes for pharmaceutical companies. The FDA has made it easier to report adverse events and is making them public and searchable online. Life sciences companies, insurers and third parties are using this data to transform their businesses and viewpoints. Consumers, too, are using it to inform themselves about medical products.

These changes come as the FDA prepares to use new approaches to approve products more quickly using new types of data. Drug safety data will play an even bigger role in determining which products succeed.

Adverse event reports are growing in number and complexity, increasing companies' costs. As patients embrace social media and other forums of online discussion, assessing these data will prove difficult without investing in new technologies.

The trickle of data is becoming a flood

In 2014, the FDA began requiring companies to submit pharmacovigilance data electronically. The FDA also made it easier to report adverse events through webpages and mobile apps. These changes have made it substantially easier for the FDA to collect, analyze and distribute data on the drugs it oversees.

In recent years the FDA also began receiving more adverse event reports than ever before. From 2009 to 2016, the number of reports the agency received increased 300 percent, with the vast majority submitted by product manufacturers, according to an analysis by PwC's Health Research Institute (HRI). The rise is likely due to a combination of factors, including regulatory enforcement, ease of reporting, increased use of technology to find and report events, and greater public awareness of adverse event reporting (**see Figure 1**).

The collection of that data will likely continue to increase as electronic health records, mobile apps and connected "smart" medical products become more widely used.

More people and organizations are using these data too. Though adverse event data was always subject to Freedom of Information Act requests, agency responses often were slow and expensive, and the data could be difficult to decipher. But in 2014 the FDA launched OpenFDA, which made its adverse event data easily accessible to the public and provided basic analytical tools. Data can be downloaded by anyone for free.

Such easy access has created new risks for companies. The public, able to access and analyze safety data once seen mostly by regulators, can misinterpret and share adverse events, feeding conspiracy theories and dissuading others from taking or using a product that may be safe, such as vaccines.

Specialized data analytics firms also are searching this data to find previously unknown or underestimated safety risks or trends, sometimes making their findings public before the FDA is aware of them. These findings sometimes have been sold to Wall Street traders to help them make investment decisions. Law firms can use analysis of such data to solicit clients for lawsuits alleging that a company failed to adequately label its products with

At a glance

The FDA has made new changes affecting drug safety monitoring, including:

- Increased transparency
- Requiring adverse event reports to be submitted to FDA electronically
- Increasing cooperation with global regulators
- New regulatory authority to approve drugs more quickly

These changes are increasing the stakes for the pharma industry, which is dealing with an influx of data.

Without advanced analytical capabilities, companies may be leaving value on the negotiating table and be at greater risk from regulators, market competitors and third parties.

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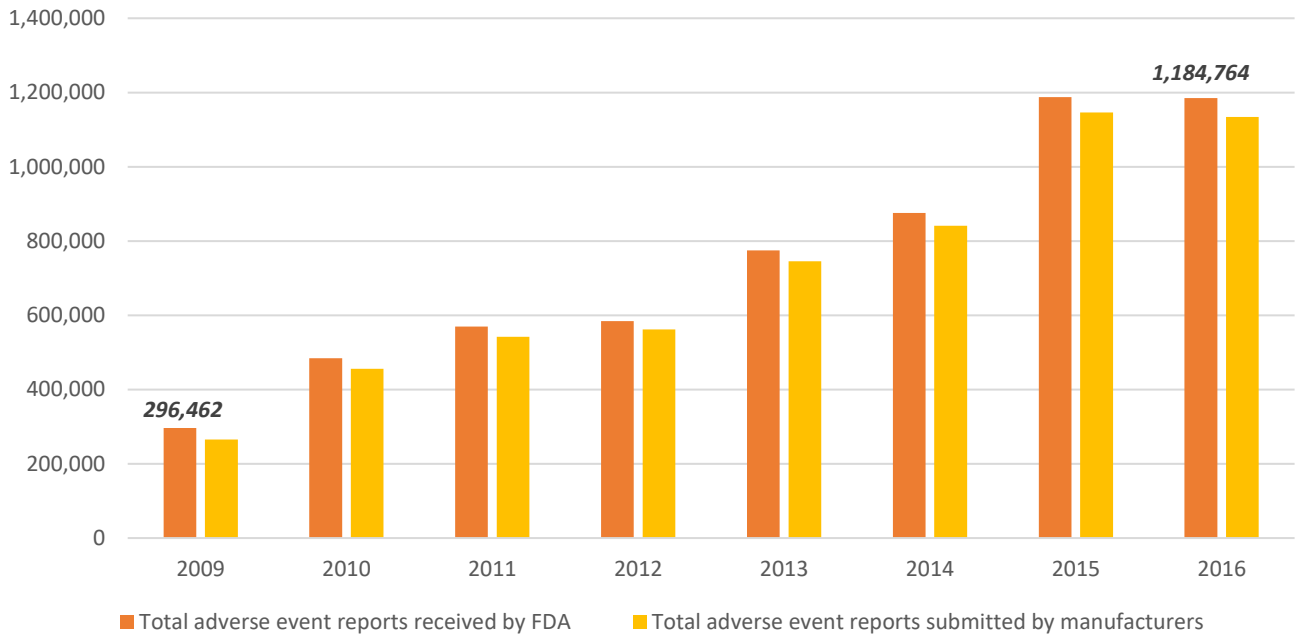
Figure 1. Drug companies are reporting more adverse events to the FDA than ever before
Adverse events received by the FDA, by year and reporting entity



Source: HRI analysis of OpenFDA data

warnings about a particular side effect. Data also have been sold to insurers and pharmacy benefit managers, who use it to inform their pricing decisions and formulary placements.

Not all data are easy for companies or regulators to make sense of, however. Increasingly, data are found in unstructured ways such as on social media and web forums, and in medical journals and news reports. An adverse event seen by a company in a medical journal report can be just as important as one sent to it by a doctor.

These data can be more difficult to sort through and require more follow-up to assess. Luckily, advances in machine learning and artificial intelligence (AI) are making these types of data accessible in new ways, opening opportunities for companies.

What is pharmacovigilance?

Pharmacovigilance refers to the monitoring of a pharmaceutical or biological product's safety both before and after it has been approved by regulators.

Pharmacovigilance efforts ensure that safety risks that were observed during clinical testing and after market approval are known to regulators, that long-term safety risks are better understood, and that any risks that occur at an unexpectedly high rate can be assessed.

Under FDA regulations, companies are required to submit reports of adverse events that they receive – such as from patients or doctors – to federal regulators, generally within 15 days of being made aware of the event. The report must include information about the patient, the adverse event and the product suspected of causing the event. Companies must submit similar information when they become aware of events through the scientific literature, on the internet and social media, or from postmarketing studies. Other entities, such as healthcare providers and insurers, are not required to report adverse events and do so voluntarily.

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More to come

While the 21st Century Cures Act of 2016 could result in drugs being approved more quickly and reliably, it also shifts the burdens of proof to the post-approval setting. If pharmacovigilance data show that a drug is less safe than originally believed, the FDA may rely more on that data to determine whether a drug should be taken off the market, since the original safety data from the clinical trials are based on a relatively small sample or short timeframe.

Companies, then, may find themselves in a precarious position. Without evidence from large clinical trials to substantiate traditionally approved products' safety and efficacy, these expeditiously-approved products are more vulnerable to the FDA's concerns. The products also could be more vulnerable to attempts by the public, competitors or third parties to find safety issues with a drug where none exist.

The fact that the FDA shares data with its global counterparts, such as the European Medicines Agency, also raises the stakes of pharmacovigilance. Problems discovered in the US can result in products being taken off the market in multiple regions—and vice versa. Without global capabilities to receive, analyze and process adverse event reports, companies can miss information that is important to them—and their competitors.

But data also present opportunities. As the FDA opens the door for greater use of real-world evidence, companies that can determine that their drugs are safer than shown in premarket clinical trials, or result in other positive outcomes, can use that data to seek label changes and potentially expand markets and revenues.

HRI impact analysis

Use data competitively: Companies can use these data to gain competitive advantage, including finding new uses and indications for drugs, predicting safety issues in other products, designing better clinical trials and assessing drugs' economic impacts. Preliminary data from clinical trials can help companies target their products to appropriate patient populations and avoid populations unlikely to benefit. Pharmacovigilance data should be a key part of all companies' launch strategy, especially as insurers and pharmacy benefit managers begin to place greater emphasis on paying for the value of outcomes and total cost of care. Of pharmaceutical executives surveyed by HRI, 25 percent reported their company engages in value-based contracting. In 58 percent of those contracts, negotiations began after a product's approval, when postmarket pharmacovigilance data could inform those negotiations. A drug that is safer than its competitors in real world settings has more value.

Automation and AI can help: Companies are being asked to analyze increasing volumes of structured and unstructured adverse event data more rapidly. To cope with these new challenges, companies will benefit from investments in AI that can help them automate their adverse event intake, preliminary processing and analysis and following up on incomplete reports. For example, AI can be used to translate adverse event reports in foreign languages, search medical literature to find unstructured reports of adverse events, and automatically follow-up with entities that file reports—faster than a team of humans could, and with the ability to work around the clock. These capabilities can help companies increase the speed of companies' pharmacovigilance functions and reduce their costs, allowing existing staff and resources to do more strategic and scientific safety work, such as risk/benefit analysis.

Use data to manage risk and become a value-producing safety organization: Pharmacovigilance is evolving from its traditional and reactive focus on regulatory compliance ("what happened") to a proactive function managing risk and creating opportunity ("why it happened" and "what will happen"). Speed-to-insights is crucial. If companies aren't the first to obtain insights on their products, their competitors, third parties, or regulators will be, placing manufacturers at a distinct disadvantage. Public reports that a drug is unsafe—in absolute terms or relative to a competitor—take time to analyze and dispel. Companies that have the capability to quickly and proactively analyze issues will be able to manage these problems as they arise and respond accordingly, including asking regulators to update a product label, accelerating product development, voluntarily removing a product from the market when necessary, or vigorously defending the safety of their product. Analytical capability can help companies anticipate adverse events, understand their causes and give regulators in-depth answers. These capabilities are crucial for making sense of voluminous adverse event data, filtering out the signal from the noise. Without those capabilities, companies may be overwhelmed by data. They can also help companies beyond pharmacovigilance, including analyzing real-world outcomes data and improving the chances of successful research and development.

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