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Engage with confidence: Managing online adverse event reporting

Ensuring digital pharma engagement with customers fulfils the regulatory requirements

The pharmaceutical industry is waking up to the enormous potential offered by social media and other online data sources for informing better decisions around drug development and commercialization.

Finding pharma's needle in the electronic haystack

Social media may be the digital revolution causing pharma executives to have sleepless nights about online adverse events, but the phenomenon actually predates the Facebook generation by some time. "Adverse events have been reported by people on the internet ever since there were chat rooms or an ability to post online," says Joy Liu, a partner at law firm Ropes & Gray, suggesting the issue first reared its head in the early 1990s.

So how big a problem is it for pharma? Initially, the regulatory risk from direct two-way online dialogue was clear. "There was recognition that if pharma companies let people leave comments on one of their pages they may report adverse events, leading to obligations from the company to act," elaborates Liu, resulting in early online pharma activities being mostly didactic one-way communication.

As the digital space has developed, pharma gradually ventured further into online dialogue, with forums and Facebook pages offering an opportunity to build connectivity with prescribers and patients. In 2011, however, Facebook removed the ability for companies to turn off comments on their pages, leading to several retrenching from the channel completely. Slowly and uncertainly they have returned but it is to an environment where the reporting of online adverse effects remains challenging, despite the FDA publishing draft guidance in January 2014 on 'Fulfilling regulatory requirements for post-marketing submissions of interactive promotional media'.[1]

Recognizing that the industry faces a number of difficulties around taking a responsible and compliant approach towards tracking online adverse events, Siva Nadarajah, General Manager, Social Media at IMS Health , started working to identify solutions to two main challenges. Firstly, the high volume of comments from online channels potentially makes screening and tracking of adverse events difficult. Secondly, adverse events from such unstructured data are not always obvious, with Nadarajah highlighting that "identifying these adverse events and a lack of clarity on those cases where you cannot identify the patient" can cause problems.

It is something the regulators are grappling with too. Whilst the easy answer might be to simply apply existing adverse event reporting guidelines to online activities, in practice this is ambiguous. For example, guidelines from the US regulators state that four criteria must be met for a reportable adverse event:[2]

1. An identifiable patient
2. An identifiable reporter
3. A suspect drug or biological product
4. An adverse experience or fatal outcome suspected to be due to the suspect drug or biological product

> In the absence of specific and clear guidance pharma has had to learn best practice the hard way – by trial and error

In reality, only some of these criteria may be met with online comments. For example, an anonymous forum poster would not fulfil criteria (1) or (2), even with a clearly reported side effect and drug. Some companies take a proactive stance and actively seek the missing information, but data protection can be an issue here. "If a patient has purposefully commented from a closed profile we have to careful not to infringe privacy", says Nadarajah. As a result, Liu notes that pharma companies prefer to manage these issues offline and "would much rather have someone call the hotline so that the person answering the phone can ask them all the relevant questions".

Case studies shaping the approach for pharma

After years of waiting for the FDA to provide some clarity on the subject, the recent draft guidance is helpful in that it says that companies are only responsible for the content that they produce or sponsor on behalf of their brands. However, this doesn't resolve the issue of how to run effective and compliant post-marketing surveillance activities on the online content they are responsible for.

As in the past, pharma will have to learn best practice the hard way – by trial and error. A good example of this was illustrated by the Sanofi-Aventis VOICES Facebook page, which was used by a disgruntled patient to post side effects she experienced after taking one of its cancer drugs, Taxotere. After a sustained commenting campaign led by the patient and involving numerous other patients, the company had to close the page.[3]

The problem arose for Sanofi-Aventis due to lack of a clear policy around responding to adverse events reported via comments. As a result, the current Sanofi Facebook page has clear 'Rules of Engagement'[4] for users, which specify appropriate channels for adverse event reporting, no doubt reinforced by robust behind-the-scenes processes.

Experiences like Sanofi's may have helped pharma companies develop the right approach for managing their web presence, especially where user comments are involved. And many CEOs will be breathing a sigh of relief that the regulator is not demanding that pharma also monitor popular third-party online sites for drug side effects.

In the meantime, Nadarajah believes there is value in companies taking a more proactive approach to social media listening with regards to drug side effects, particularly with regards to the big social channels. In the long run, it could help provide early warning of new adverse events, or other clinical information that directs product development and avoids downstream litigation. Drawing parallels with the recent brake issues carmaker Toyota experienced, Nadarajah points out that "if Toyota had listened to social media they might have caught these brake issues much earlier".

Calculating a true risk-benefit profile

Lack of clear regulations is not, however, the major concern for the pharma industry – it is the perceived overwhelming volume of adverse event reports online that causes the anxiety.

So while monitoring online brand mentions can provide useful information to pharma companies, Nadarajah describes how the "benefit-to-risk ratio of gathering information from online sources, then using it for marketing intelligence, is perceived to be high on the risk side".

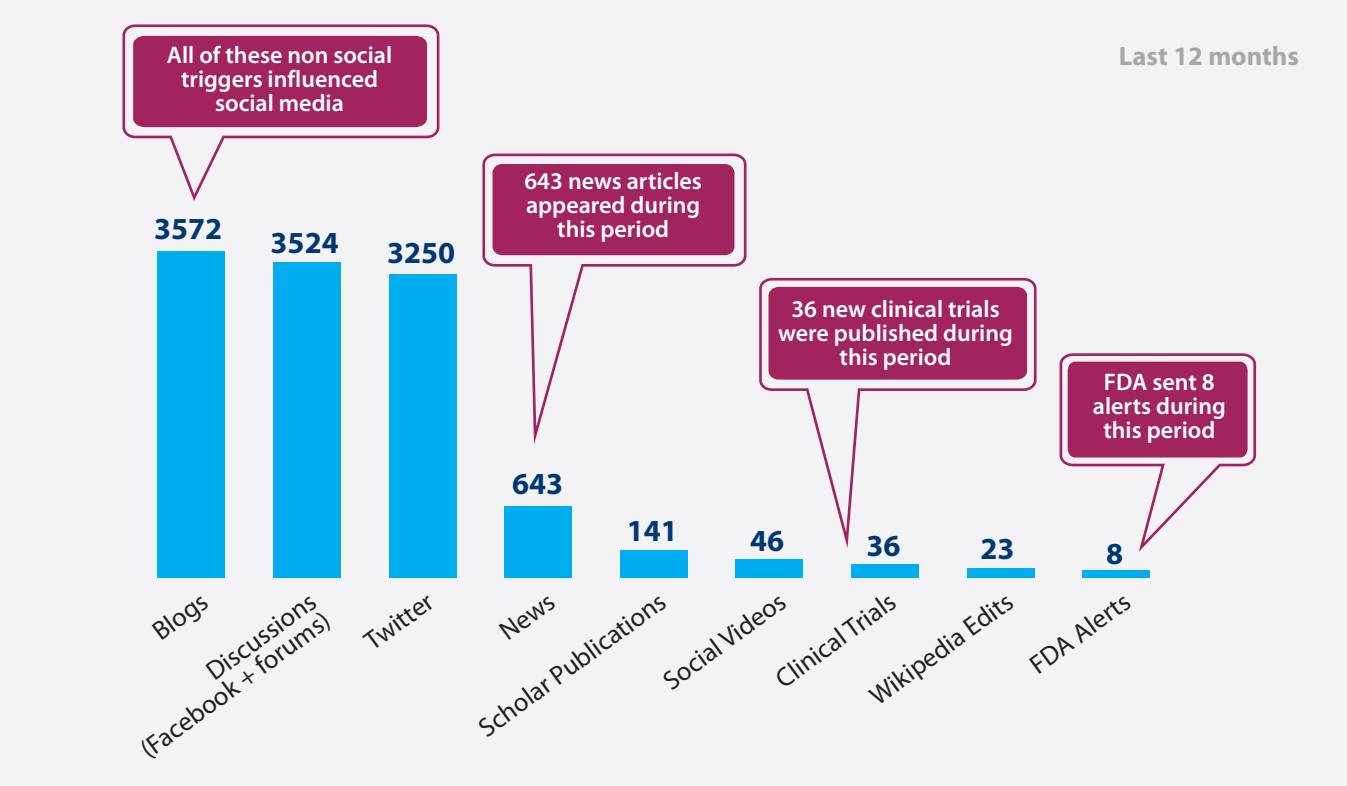
In order to test the real scale of online adverse event reporting and challenge this perception, he was involved in a study tracking posts relating to a leading type-II diabetes drug over a 12-month period.[4]

During this time, 11,246 posts were picked up that mentioned the specific drug, which were spread across a variety of sources (see Figure 1), including blogs, forums, social channels and news alerts. Over the 12 months there were 36 new clinical trials published and eight alerts issued by the FDA. And the volume of reportable adverse events identified from these posts?

Two hundred and eleven – just 1.8 percent of the total posts. It is a figure that is representative of other studies, says Nadarajah. "You see about 2 percent of the conversations will have reportable adverse events, pretty much across all disease states". Even if you look for reports that do not meet all criteria, the figure is still relatively low, with typically 7-8 percent of posts falling into this category that should be tracked but not reported.

The real challenge, Nadarajah explains, is not therefore the total volume of adverse events, but being able to quickly identify the relatively small number of adverse events from large amounts of data.
"The problem for pharma companies has been knowing out of these 10,000 or 100,000 posts which are adverse events. Without the proper technology, someone has to look at all these posts," he says.
An unenviable job for anyone!

FIGURE 1: TOTAL POSTS MENTIONING A SPECIFIC TYPE-II DIABETES DRUG OVER A 12-MONTH PERIOD AND BREAKDOWN BY CHANNELS. [4]



The role for technology in managing online adverse events

The solution, Nadarajah believes, lies in using the right technology to quickly and efficiently sift through this enormous volume of data to identify and report adverse events that meet some or all of the regulatory criteria. In order to do this, any technological solution must be able to:

- Interrogate different sources and formats of potentially unstructured data;
- Know what language/key terms to look for when searching for adverse events;
- Allow users to efficiently review the outputs and form links between associated data pieces that individually might not constitute a reportable adverse event.

Whilst there are numerous tools that can rapidly screen online data for specific terms and present the outputs in a user-friendly format, the most complex aspect relates to the second point – knowing exactly what language to look for when searching for adverse events. "Here, technology plays a very important role," says Nadarajah. "You need a new set of taxonomies, a new set of ontologies, which can understand how a patient describes a side effect on Facebook, for example. This requires historical data collection, and a very rich dataset that can catch every single description of an adverse event, every single variation of it, misspellings and abbreviations, that people use in social media."

Without this rich background data library, derived from historically studying how people talk about side effects online, it is like looking for a needle in a haystack without knowing what the needle looks like. It is here that most 'non-pharma' technologies fall down and it is a problem Nadarajah has spent three years focusing on; slowly developing a 'side effects lexicon' for each disease state by observing the conversations of patients, doctors and pharmacists. With this piece in place, the rest flows seamlessly. Without it, the downstream process may appear seamless but, like a slick forecasting model with bad data inputs, it is fundamentally flawed.

What is interesting is that the language-driven technology can be applied to 'offline' data too, such as market research reports or representative data from a CRM system. "As long as you can process one unstructured dataset you can process any unstructured dataset," Nadarajah explains.

> You need a new set of taxonomies, a new set of ontologies, which can understand how a patient describes a side effect on Facebook

Can adverse event monitoring be totally automated?

Nadarajah is unequivocal in his response. "No. Eighty percent of the work is done by the machine and 20 percent by the human; we are not going to eliminate the human factor." Even with the best natural language processing dictionary and the smartest technology, the process is not perfect. What is important is that the technology is not missing any potential adverse events, but is being overcautious, so human intervention is still needed to review the outputs.

"The human's job is to eliminate false positives, because the machine is always going to give you some, and ensure the pharmacovigilance department is not being bombarded with too much data. But the machine ensures no genuine positives are missed," he explains. So this synergy of adverse-event language-trained machine and medically trained human allows for an efficient and compliant process that is not overwhelming.

Ultimately, the way in which Nadarajah views managing adverse event reports can be compared to the way in which doctors manage their patients. The number one rule for a doctor is 'do no harm', which equates to the number one rule for Nadarajah to 'not miss any adverse events'. Beyond that, it is about optimizing the process of managing adverse-event reporting, which allows pharma to do the constructive work it wants to do online, without fear of a call from the regulators.

Social media listening gets pharma talking

But is online adverse event monitoring purely about mediating risk or could it have a more significant impact on pharma?

Nadarajah sees the potential here but is philosophical about where the industry is right now and the time it will take to steer a course into less reactive work. "Pharma is mainly using this technology as a compliance necessity around product or disease promotional campaigns or market research activities," he explains. "I have not seen a lot of companies proactively looking for adverse events in social media as an early warning of problems because they have not been sure about the guidelines".

However, beyond the walls of corporate pharma, other healthcare and regulatory bodies are quickly moving into such forward-looking activities such as the Innovative Medicines Initiative (IMI), which includes efforts to 'leverage emerging technologies for pharmacovigilance'.[5]

Within pharma, the benefits of broader social media activities, including listening to customers in relation to specific products, are being embraced mostly by companies with a strong over-the-counter (OTC) presence, Nadarajah says. One large OTC company invested considerably in a Facebook page that became a case study at a recent Facebook conference on how a regulated company used its site and saw a ten percent uptake in sales.

As he points out, OTC brands are regulated very much like prescription drugs, with stringent requirements around reporting side effects and off-label usage, but the companies see the benefits of being closer to their customers as outweighing the risks from engaging.

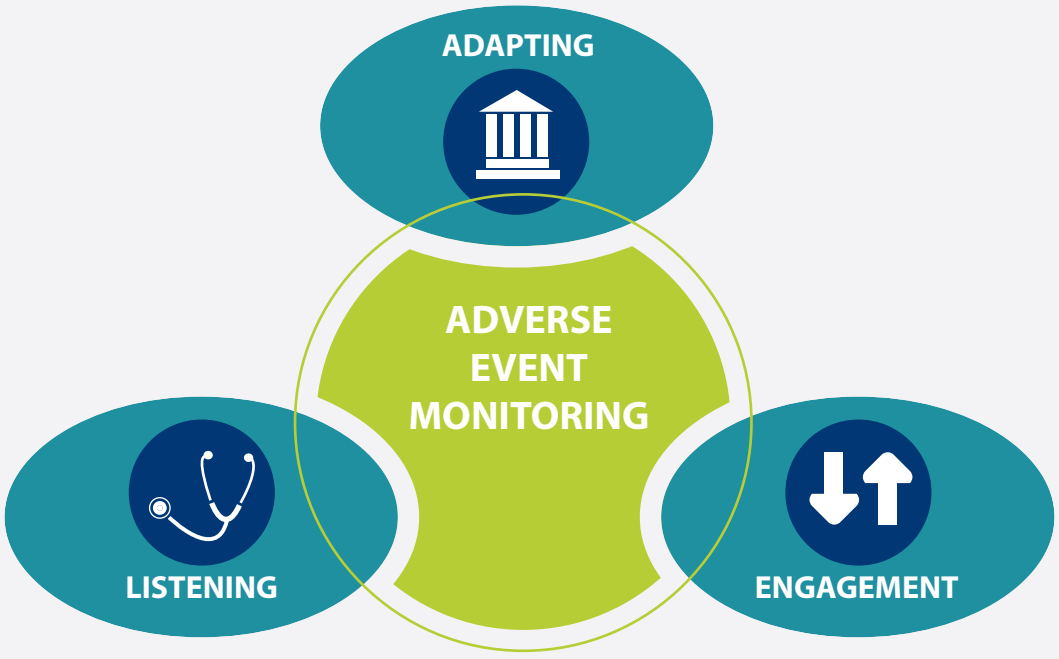
Listening leads to talking

The old adage of having 'two ears and one mouth' certainly applies to the pharma industry with regards to social media. Most companies are, at least, monitoring some online dialogue relevant to their brands even where they are not proactively engaging, Nadarajah observes. But he also sees this inevitably leading to more dialogue, which could dramatically change pharma's relationships with patients and providers for the better.

"With the OTC example on Facebook, the company's call center volume significantly dropped because patients are using the site to ask questions or report adverse events. It is about customer service as the relationship between the pharma company and patient is changing," Nadarajah explains.

Looking further ahead, he believes such activities could even help the pharma industry refine the positioning of its products, something other industries, such as fast-moving consumer goods, have wholeheartedly embraced using social media for customer feedback. "This could open up the whole business model, as pharma companies realize they can find out much earlier about the real-world efficacy of a drug, or adherence issues in how it is being used by patients, in addition to much earlier knowledge of potential incidents related to the drug," Nadarajah says. The pathway from listening, will lead to more engagement and adaptation of pharma's research and commercial activities (see Figure 2).

FIGURE 2: THERE ARE BENEFITS TO PHARMA IN MOVING BEYOND LISTENING FOR ADVERSE EVENTS AND INTO DEEPER ENGAGEMENT WITH CUSTOMERS, LEADING TO ADAPTATION.



> Other healthcare and regulatory bodies are quickly moving into such forward-looking activities

Certainly, the offline activities of the pharma industry have shifted to reflect a more patient-centric approach of recognizing the value of input, at both the research and commercialization stages of development, in delivering products that work, so the same benefits could be amplified by taking these discussions online.

The risks for pharma of standing back

The other, perhaps more cautionary, aspect of this is the fact that key stakeholders for the pharma industry, such as the regulators and payers, are most definitely starting to monitor social media for their own research. They see that online discussions can be a great resource for not only monitoring the side effects of drugs, but also for real, on the ground, dialogue around their efficacy and quality plus, critically, the real-world outcomes that are defining market access for all pharmaceutical products.

As Nadarajah elaborates, "the regulators are trying to find out about adverse events popping up from social media, which either the pharma company knows about or is ignoring". Even if the pharma company (genuinely) pleads ignorance, the downstream impact could be significant. One could imagine, he goes on to say, a situation where further investigation is triggered.

"The regulator could act on an online signal to say 'let's go and look at all your market research programs' and potentially identify market research vendors who did surveys showing a new side effect that was not reported."

From a commercial perspective, it certainly makes sense for pharma to stay at least in line with the regulators and payers, if not one step ahead. Investors do not like unpleasant surprises!

In conclusion, Nadarajah is keen to reinforce that it is easy to see the digital world, particularly with regards to social media, as a separate realm. However, the benefits and risks outlined above apply to all kinds of engagement between the pharma industry and its customers, as does the technology.

"Adverse event monitoring is not just about social media; the technology can be applied to any unstructured data that pharma companies are using – offline or online," he explains.

So the technology behind online adverse event monitoring is not just about mitigating the risk of digital activities. It is about changing the way the pharma industry interacts with its customers in the much broader space.

The risks have been clearly documented by many and experienced by an unfortunate few, but the benefits are only just starting to be realized. And with an efficient process for highlighting those adverse-event needles in the haystack, pharma companies can not only start to really engage with its end-user customers but also feed their research and commercial activities from the wealth of patient and prescriber data that exists online.

This white paper was adapted from a series of interviews with Siva Nadarajah of IMS Health by Paul Tunnah of pharmaphorum, first published in September 2013.

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Siva Nadarajah is General Manager, Social Media at IMS Health and joined the organization through the acquisition of Semantelli, which he co-founded and grew to be an industry recognized leader in social analytics for pharma. Prior to founding Semantelli, Siva was responsible for global CRM and compliance solutions with Cegedim. Siva is a voting member of the Wikimedia Foundation and has spoken worldwide about adverse events management in social media and the impact of Wikipedia in healthcare. He was recognized for uncovering two major security holes in Microsoft Hotmail in the early days of the Internet, which forever changed the security design of internet based email systems.

IMS Health would like to acknowledge the contribution of Joy Liu, a Washington-based life sciences partner with Ropes & Gray. She represents pharmaceutical, biotechnology, and medical device companies on a broad range of FDA regulatory issues.

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