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Monitoring Adverse Events in Pharma's Patient Support Programs

Executive Summary

As effective patient engagement becomes pivotal to success for the pharmaceutical industry, so does its ability to remain compliant in these interactions. Effective detection and reporting of adverse events is therefore critical to conducting such activities without breaching industry regulations. The reality, as public audits reveal, is that pharmaceutical industry reporting of drug side-effects is far from optimal, exposing companies to unnecessary risk as the regulators start to scrutinize this area more closely and impose penalties on those failing to meet established standards. In this white paper, we outline the scale of the challenge and how technology can be deployed to support compliance in adverse event reporting across the various modes of patient engagement.

The need for engagement

The value of patient engagement to pharma cannot be overstated. Use of search engines, social media and mobile apps for information gathering and sharing has given patients the means to move from passive bystander in their health to active participant. Moreover, that participation is now strongly encouraged by healthcare providers and payers because engaged patients have been shown repeatedly to incur lower healthcare costs.

A Health Policy Brief by US journal Health Affairs, which reported an analysis of 30,000 patients at Fairview Health Services in Minnesota, provides just one example.[1] This showed that those with the least skills and confidence to actively engage in their own healthcare incurred up to 21% greater costs than patients with the highest levels, after adjusting for health status and other factors (see Figure 1). Patient activation scores were also shown to be significant predictors of healthcare costs.

Incentives embedded in the 2010 Affordable Care Act, otherwise known as Obamacare, have accelerated efforts by all healthcare stakeholders to deepen their engagement with patients in line with the "triple aim" framework of the Act: delivering a better experience, improving clinical outcomes and reducing the total cost of care.

Pharmaceutical companies have a wealth of opportunities to contribute to these new value-based structures via patient support programs while, at the same time, enhancing their own patient-centric credentials and positioning themselves as true partners for healthcare systems, physicians and patients.

Figure 1: Predicted per capita costs of patients by patient activation level, where level 1 is the lowest measure of engagement and level 4 the highest

2010 patient activation level	Predicted per capita billed costs ($)
Level 1	**966**
Level 2	**840**
Level 3	**783**
Level 4	**799**

Source: Hibbard, JH et al. Patients with lower activation associated with higher costs: Delivery systems should know their patients' scores. Health Affairs 32. No.2 (2013): 216–22.

Companies now deploy a range of solutions that can help patients self-monitor and receive support between physician visits. Novartis CEO Joseph Jimenez was reported in Forbes recently highlighting a common theme within the industry today, that pharma's vision beyond simply producing pills is the logical and inevitable path forward. Jimenez says this consists of "creating value by embedding products into a holistic offering with the aim to improve patient outcomes and provide tangible competitive advantages.[2]"

Patient engagement tools can be the new differentiators of products. Boehringer Ingelheim's OFEV® (nintedanib) and Roche's Esbriet® (pirfenidone) are two competing drugs to treat idiopathic pulmonary fibrosis that were approved on the same day in November 2014. They are priced at similar levels and

[1] (February 2013) James, J. Health Policy Brief. Retrieved at: http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_86.pdf (accessed April 21, 2015)

[2] (August 2014) Bloomberg, J. Digital transformation moves pharma 'beyond the pill'. Retrieved at: http://www.forbes.com/sites/jason-bloomberg/2014/08/15/digital-transformation-moves-pharma-beyond-the-pill/ (accessed April 21, 2015).

both have patient support programs with 24/7 access to nurses, financial resources and ongoing education. Boehringer Ingelheim's US CEO Paul Fonteyne says, "The support services we provide around the product and how effectively we present the product to physicians and patients will be the driving force in terms of what eventually results from a market share perspective."

But any relationship developed around a prescription medication imposes at the same time an obligation for the company to report all suspected adverse events from that medication to the regulators.

Modes of engagement

Opportunities for patient support have expanded massively in terms of educating the patient, helping them adopt healthier behaviors and facilitating better communication between patient and physician. Such services are in addition to more conventional engagement such as patient assistance programs whereby financial help is offered, or the general information services provided by call centers. Examples of current patient-engagement programs now include the provision of:

- Product and disease information
- Telehealth services
- Wellness programs
- Chronic disease management programs
- Adherence support
- Call center support
- Disease management mobile apps
- Sponsored communities in social media

Support programs are not only increasing in importance and scope but their delivery methods are also changing to reflect the widespread use of digital media. This has vastly increased the amount of unstructured data companies are obliged to monitor if they are to identify potential adverse effects. It has been estimated that around 80% of customer engagement programs contain unstructured data in, for example, emails, social media, websites, databases and document management systems.[4]

More broadly, engagement initiatives that contain unstructured data likely to contain adverse events include:

- Call centers

[3] (November 2014) Helfand, C. Boehringer one step closer to challenging Roche in Europe with EMA IPF nod. Retrieved at: http://www.fiercepharma.com/story/boehringer-one-step-closer-challenging-roche-europe-ema-ipf-nod/2014-11-21 (accessed April 21, 2015).

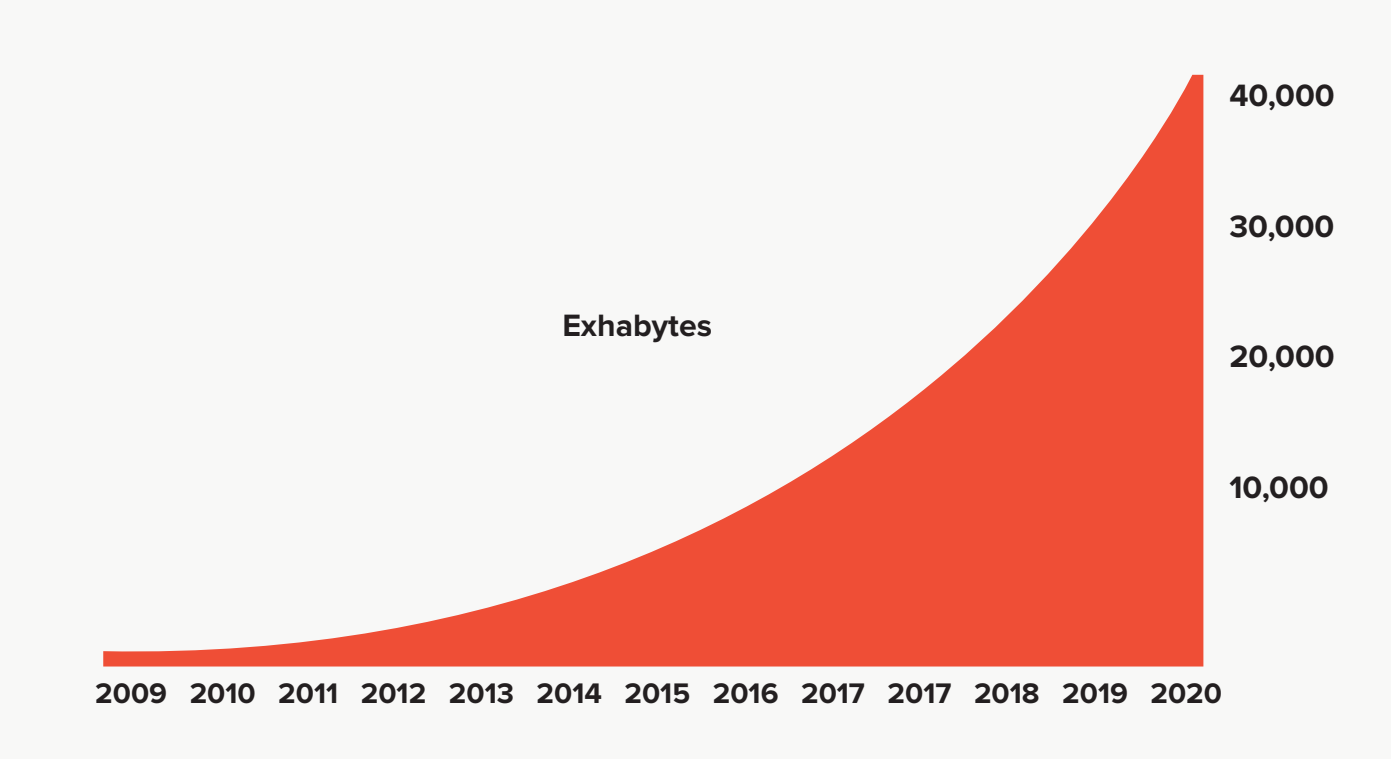
[4] (March 2015) EMA/MHRA Audits on Patient Support Programs. IMS Health PowerPoint presentation.

- Data collected during market research, for example:
    - PowerPoint decks
    - Transcripts
    - Videos
    - Excel spreadsheets
- Open-ended and structured questions in surveys
- Rep-entered notes in customer relationship management (CRM) systems
- Company-sponsored social media assets
- Mobile app store comments

Sheer volume of unstructured data

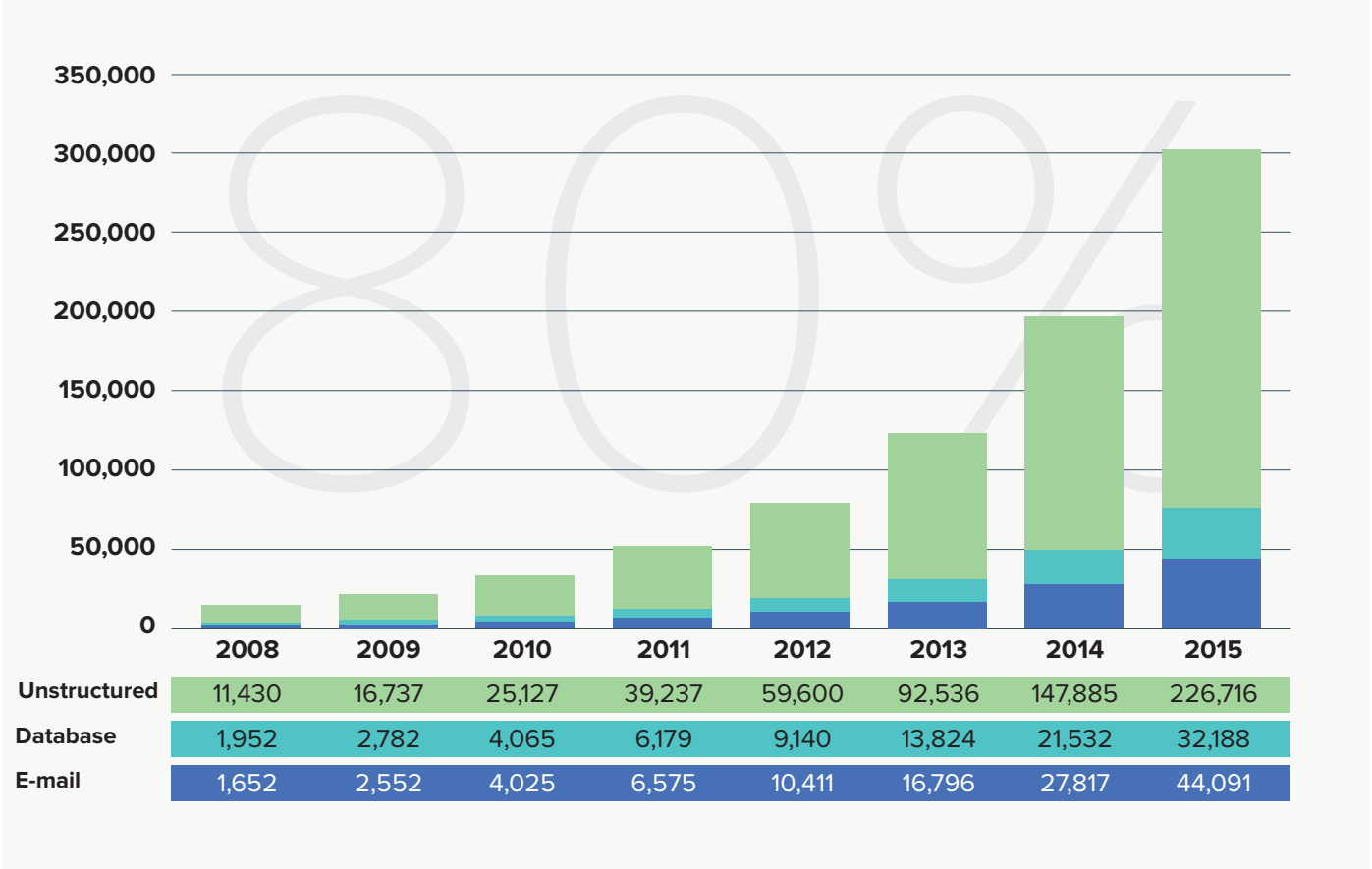
Finding data on adverse events in an unstructured digital environment is a formidable challenge, especially as the volume of digital data is expected to double every two years (see Figure 2). Furthermore, 80% of this growth is expected to come from unstructured data, as shown in Figure 3. In this scenario, a technology-powered approach becomes the only viable way to manage the adverse event tracking process effectively.

Figure 2: Digital data is expected to grow 50-fold from start of 2010 to end of 2020



Source: IDC

Figure 3: Total archived capacity by content type, worldwide, 2008–2015 (petabytes)



	2008	2009	2010	2011	2012	2013	2014	2015
Unstructured	11,430	16,737	25,127	39,237	59,600	92,536	147,885	226,716
Database	1,952	2,782	4,065	6,179	9,140	13,824	21,532	32,188
E-mail	1,652	2,552	4,025	6,575	10,411	16,796	27,817	44,091

Source: Enterprise Strategy Group

The human factor

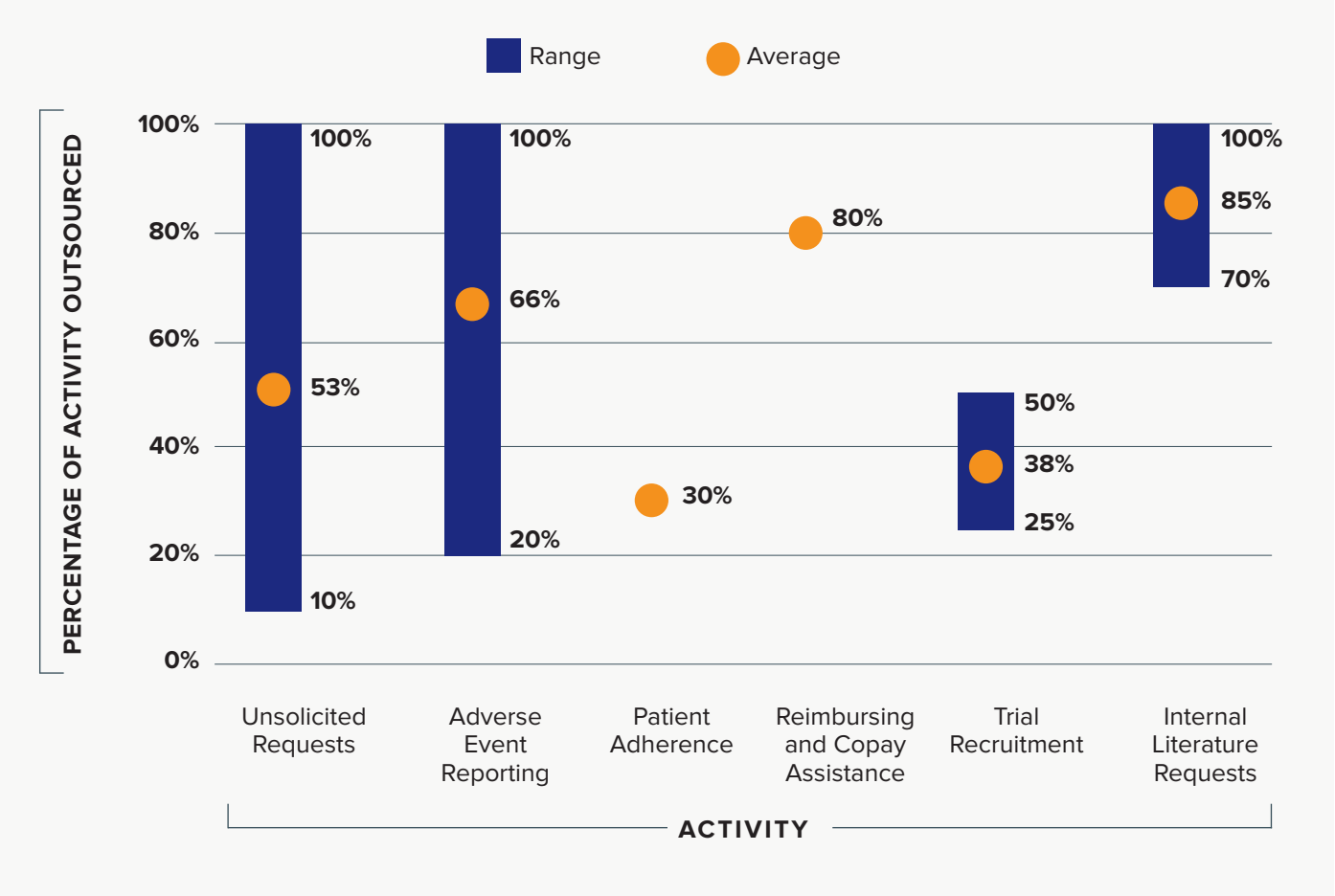
One of the main risk factors in failing to report adverse events lies in the traditional, or human-mediated, routes for engagement such as call centers or in the calls entered by reps and medical science liaisons (MSLs) into CRM systems.

Call centers

Call centers are an area of high potential risk for pharma companies as their whole purpose is for patients, physicians and pharmacists to ask questions about drugs, including the adverse events they are experiencing. And despite companies having strict protocols in place for capturing adverse events, lapses in collection and reporting can and do occur.

Adhering to protocols becomes more of a challenge when the medical information function is outsourced to external call centers (see Figure 4) and companies have less direct control over 1) identifying what is an adverse event and 2) reporting it.

Figure 4: Activities outsourced at US call centers



Source: *Cutting Edge Information report: Medical Information and Call Center Performance*

CRM reporting

As sales reps and MSLs talk about their products, inevitably adverse events are mentioned and recorded. This presents significant risks for pharma, with one recent audit by IMS Health for a pharmaceutical client identifying 15% of records found in a CRM database containing adverse events that were never reported to the company's drug safety personnel.

Increasing regulatory audits of adverse event reporting

In all three major pharma markets – the UK, the EU and Japan – there is evidence that the regulators are looking more closely at how pharma companies report adverse events. In early 2012, the UK regulator, the Medicines and Healthcare products Regulatory Agency (MHRA) carried out a routine pharmacovigilance inspection on a leading global pharmaceutical company. It found 80,000 uninvestigated adverse reaction reports for medicines marketed in the US that had been collected

through a sponsored patient-support program. These included more than 15,000 reports of deaths, 23,000 suspected adverse drug reactions and 600 clinical trial-related adverse effects.[5,6] , While a subsequent investigation by the European Medicines Agency (EMA) found these events did not "substantially impact the benefit–risk assessment" of the 19 medicines involved, the potential penalties in such a situation can be severe. They can include fines of up to 5% of a company's preceding year's revenues and, in the event of continued non-compliance, an ongoing periodic fine of 2.5% of daily revenues until compliance is assured.[7]

In another example, the Japan business unit of a top 10 pharma company was threatened with suspension for 15 days in February 2015 after failing to report adverse events properly. In May the previous year, Japan's Health, Labour and Welfare Ministry had started investigating charges that the company had collected information on 3,000 Japanese patients taking one of its products but failed to disclose all 30 cases of side-effects within a month as is required by law.[8]

The lessons of these two examples are that without the right systems in place human error is almost certain given the incredibly high volume of interactions, whether they are managed in-house or externally.

Meanwhile, in the US, a report published in February 2015 has found pharma companies seriously lacking in their adverse event reporting.[9] The report, published by the Institute for Safe Medication Practices (ISMP), looked at the effectiveness of the FDA's Adverse Event Reporting System (FAERS), the government's primary safety surveillance system. Its conclusion was that the system was in need of modernization on two counts. One is that companies are not entering sufficient information on the adverse events and the other is that the reporting system does not reflect the post-reform environment. "It suffers from a flood of low quality reports from drug manufacturers and has not yet been updated for the changing environment in which drugs are marketed to health professionals and consumers."[10]

Specifically, the report looked at 847,000 reports made during the 12 months that ended on March 31, 2013 and found that while pharma companies account for 96% of the reports, less than half are considered complete. This compares with FDA-collected reports, which are complete 85% of the time.

It should be stressed that this report only considered *known* adverse events. It has been estimated that 90% are not reported back to the regulator. Reasons for this include the fact that surveillance systems on both sides of the Atlantic require patients and physicians to provide information voluntarily and there is no incentive for them to do so. It can take 45 minutes for physicians to fill out the Yellow Cards used by the MHRA in the EU or the FAERS forms in the US. There are no fines if they do not fill in the forms so the regulators must rely on spontaneous reporting.

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[5] (June 2012) Palmer, E. Roche, Genentech overlook 80,000 adverse reaction complaints. FiercePharma. Retrieved at: http://www.fiercepharma.com/story/roche-overlooks-80000-adverse-reaction-complaints/2012-06-21 (accessed April 21, 2015).

[6] (November 2013) Gaffney, A. EMA investigation into Roche Adverse Event reporting failures finds no new risks. Retrieved at: http://www.raps.org/regulatoryDetail.aspx?id=9670 (accessed April 21, 2015).

[7] Under Article 16.2 of EC No 658/2007.

[8] (July 2014) Weintraub, A. Novartis apologizes for lax business practices in Japan as side-effect scandal widens. FiercePharma. Retrieved at: http://www.fiercepharma.com/story/novartis-apologizes-lax-business-practices-japan-side-effects-scandal-widen/2014-07-31 (accessed April 21, 2015).

[9] Report

[10] (January 2015) Sukkar, E. Searching social networks to detect adverse reactions. Pharmaceutical Journal. Retrieved at: http://www.pharmaceutical-journal.com/news-and-analysis/features/searching-social-networks-to-detect-adverse-reactions/20067624.article (accessed April 21, 2015).

New EU framework for detecting adverse events

In response to the under-reporting of adverse events, the EU's Innovative Medicines Initiative (IMI) is funding a €2.3 million consortium to develop a framework for detecting adverse events mentioned on social media. The stated goals of this public-private healthcare partnership, which started in September 2014 and is known as Web-RADR (Recognising Adverse Drug Reactions), are to:[11]

- Develop a mobile application that healthcare professionals and patients can use to report suspected adverse drug reactions to medicines regulators in the European Economic Association (EEA).
- Assess the possibility for medicines regulators to provide accurate, timely and up to date information on medicines to patients, consumers, healthcare professionals and caregivers through the mobile app.
- Explore the identification of potential safety issues with medicines from user comments in social media, taking into account compliance with personal data protection legislation.
- Develop recommendations as basis for a policy framework for the use of mobile technologies and social media in the context of pharmacovigilance and the monitoring of the safety of medicines.

Why a tracking solution is needed

As regulators in the major pharmaceutical markets start to address the inefficiencies of their surveillance processes, companies are exposed to significant risks unless they have systems in place that can ensure they are identifying, and reporting, all the adverse events mentioned in relation to their products.

Partial solutions involving company-owned social media properties have been to simply lay down a clear set of rules on what can and cannot be said. "We let patients know what the rules are, that they cannot mention a drug by name, or create adverse event comments," Clement Chan, director of digital marketing at Janssen in Canada, told *eyeforpharma* recently.[12]

This is all very well, but such an approach still does not take account of adverse events mentioned in call center conversations, reports in CRM systems and in market research. There is also a case for companies to know what adverse events are being discussed even in non-company sponsored social media properties, where there is no obligation to report them, as these are now being trawled in publicly funded projects such as the EU's Web-RADR and equivalents elsewhere.

Only an electronic technology solution can give companies the confidence they are identifying all adverse events, irrespective of media type or location, when conducting essential patient support programs. Specifically, a company should look for a system that is built for the life sciences industry, with statistically valid processes, can take in a wide range of unstructured data, has human support to validate the automated results, and can easily link to its own adverse event reporting processes.

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[11] (January 2015) First IMI WEB-RADR Workshop. WEB-RADR. Retrieved at: http://web-radr.eu/2015/01/05/first-innovative-medicines-initiative-web-radr-workshop-mobile-technologies-and-social-media-as-new-tools-in-pharmacovigilance/ (accessed April 21, 2015).

[12] (2013) Steele, B. The future of patient engagement. Eyeforpharma. Retrieved at: http://social.eyeforpharma.com/patients/future-patient-engagement#sthash.c8J8Q00A.dpuf (access April 21, 2015).

Case study: Tracking adverse events in CRM systems and online

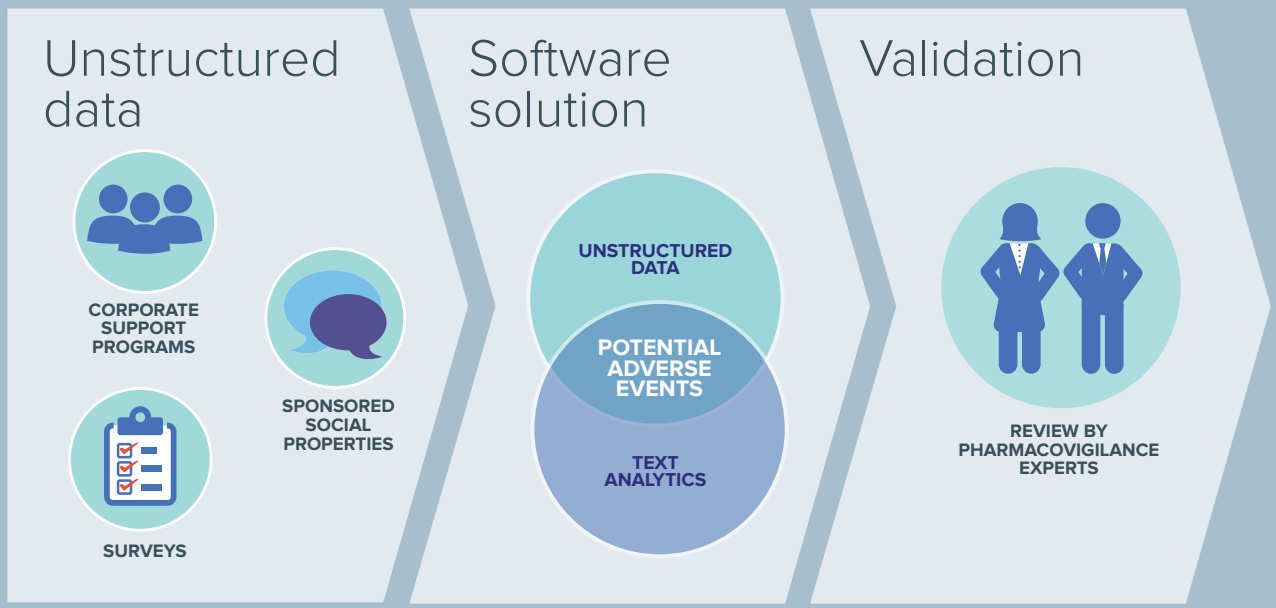
Given the sheer scale of data that must be collected and analyzed, some pharma companies are taking a proactive approach by deploying an electronic tracking system to detect potential adverse events, which are then scrutinized manually for those which must be reported. A sense of the scale of the challenge can be seen from the deployment of IMS Health's automated monitoring technology, AETracker, to analyze one product for a top-20 pharmaceutical company. It searched across:

- 232,989 records in the CRM system
- 281,971 posts in social media, collected by the company for market research broken down by channel:
  - Twitter: 143,588
  - Facebook: 71,674
  - Blogs: 52,840
  - Wikipedia: 1,352
  - Forums: 10,397
  - Pinterest: 956
  - Google Plus: 243
  - YouTube: 921

Of the CRM records, 28% (66,196) were flagged by the AETracker as including potential adverse events. Of these, 11%, or 26,192 records, were confirmed by pharmacovigilance experts as containing actual adverse events. Of the social media posts, 15% (42,898) were flagged as potential adverse events electronically, of which 1.7%, or 4,893, were later confirmed.

The technological solution (see Figure 5) is not only quicker and more accurate than a manual approach; it is also most cost-effective with IMS Health estimating potential savings in the order of 72% and 85% for CRM records and social media respectively.[13]

Figure 5: The automated approach to adverse event detection



Source: IMS Health

[13] Detecting Adverse Events in Social Media and Unstructured Data. IMS Health presentation to Digital Pharma East 2014.

Conclusions

There is now clear evidence that the under-reporting of adverse events is being closely scrutinized by regulators in the three major pharma markets: the US, the EU and Japan. There is also clear evidence that pharmaceutical companies are not always fully aware of the sheer volume of adverse events relating to their products mentioned in places such as social media, call center conversations, CRM systems and market research materials.

As healthcare trends mandate that they move to integrate more closely with their customers – and specifically the patient – it is a matter of some urgency that the industry deploys effective technology to tackle this pharmacovigilance challenge, especially in view of the inevitable human error inherent in manual processes. Identifying and monitoring the adverse events in patient support programs can, in this sense, be seen as a basic requirement in the current information age and one that companies ignore at their peril.

Learn more

To learn more about Nexxus Social's Adverse Event Tracker, visit **www.imshealth.com/nexxus** or contact us at **nexxus@imshealth.com**

About the author

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.

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