

Promotion of Food and Drug Administration-Regulated Medical Products Using the Internet and Social Media Tools: Evaluation of Uncertainties and Challenges for AE Monitoring Using the WatchNet™ Frameworks

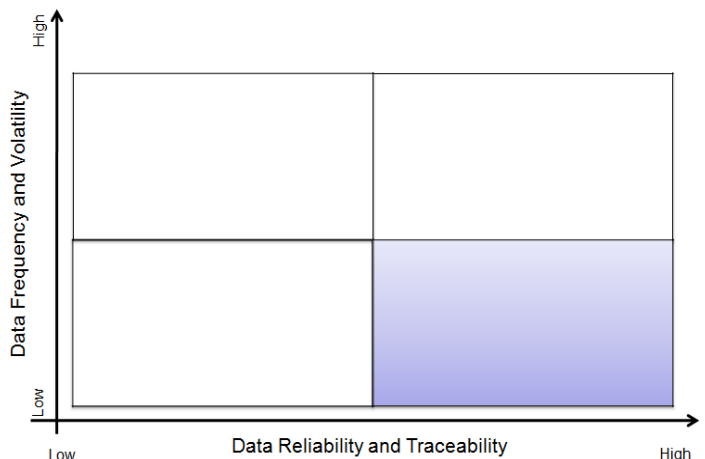
The emergence of social media for communication with regard to pharmacovigilance and drug safety has the potential to dramatically alter the landscape of public health, and not necessarily for the better. For a pharmaceutical company, simply receiving more information is not always better, though receiving more *accurate* information is. How, then, should pharmaceutical companies best proceed with regard to using and monitoring social media?

Through examination of data volatility, frequency, traceability, and reliability, current forms of social media can be categorized to demonstrate the difference between old and new paradigms of communication. Depending upon future regulatory guidance from the FDA, companies can then best understand the implications of the social media forums which they use to communicate.

This paper, then, posits the WatchNet™ frameworks of as-is analysis and further categories which refine the to-be world for action by companies. The FDA regulatory guidance on social media will comprise the crucial piece of information necessary to finalize the frameworks; for now, this paper suggests to the FDA the categories for consideration upon which companies would like to receive guidance.

Adverse Event Reporting Before Emergence of Social Media

Before the emergence of social media, adverse event reporting was primarily characterized by a relatively small number of well-controlled, traceable inputs from individual consumers, health care professionals, or investigators for clinical trials. This remains the dominant paradigm of drug safety reporting and pharmacovigilance processes within drug safety departments in leading pharmaceutical companies. These processes are largely designed for paper-based information channels, and while these processes have been automated in large part by technological advances (including E2B reporting accepted by the FDA), they rely on a one-to-one communication avenue of reporter to company.



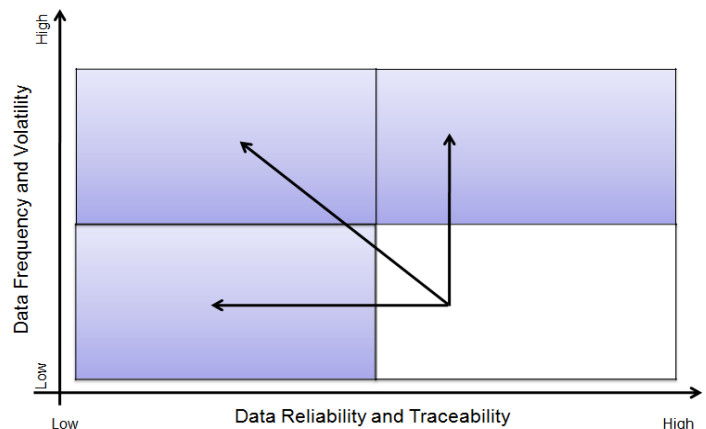
As a result, there is a current strong patient reliance on one-on-one communication with health care providers (HCPs) for information. Adverse event reports which arrive in drug safety departments are usually and relatively more easily traceable than internet reports, and the intent to report is quite clear. This is a key distinction to be explored further later on, but is worth noting the difference in intentionality between a consumer actively calling a pharmaceutical company to express a safety concern or inquiry as contrasted with an internet posting.

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Finally, both the frequency and volume of adverse event follow-up has been controlled by combination of regulation and internal company policies, rather than by consumers.

Adverse Event Reporting with Emergence of Social Media

With the emergence of social media as a reporting medium for adverse events, pharmaceutical companies have suddenly been forced to process large numbers of untrained, poorly traceable, and uncontrolled data sources. As is apparent by this reclassification, pharmaceutical companies must now take processes created by prior ways of reporting and 'fit' social media data into these processes, at least in accordance with guidance as it stands now.



Such an approach is unsustainable and in fact counterintuitive to good pharmacovigilance. The aim of pharmacovigilance is to develop accurate and timely safety profiles of products to safeguard the public health. A key aspect of safety data or queries currently obtained by customers is that they are largely willingly reported by consumers or health care professionals in a manner which, by obligation or strong feeling, reach out to a pharmaceutical company. This is a completely different intentionality than posts based on 'gut feel' rather than empirical evidence, particularly from consumers. Individuals posting on social media sites may be driven by a variety of motivating factors that must be taken into account such as the need to connect with communities larger than themselves, the need to sympathize with others, or the need to relay information that is commonly in the discourse of adverse events associated with that product.¹

In the experiences observed with current pharmaceutical companies as they attempt to monitor social media and manage the ambiguity associated with current expectations for monitoring, significant amount of PV resource time (approximately = 80 hours/month) is being expended to monitor people's chats with:

- *no changes* to safety profiles and no significant new findings
- *no further understanding or enhancements* to known safety profile, and
- increased *challenges* of poor case quality follow-up

Such results demonstrate that, when analyzed in the context of what pharmacovigilance is intended to do for the patient, monitoring websites to comply with prior notions of 'initial', 'follow-up', and

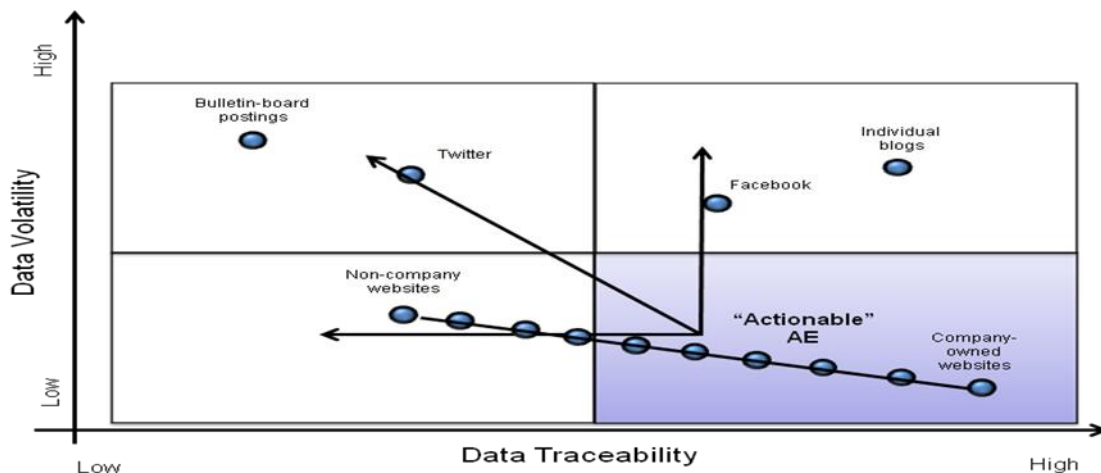
¹ See also "Complaint Box: Online Insults," *New York Times*, February 4, 2010. The author recounts the invisibility of the people behind the screen names of those who post derisive comments online.

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associated information becomes a spurious course of action on the part of pharmacovigilance personnel. Rather, pharmacovigilance personnel should focus on nuanced safety profile analysis for products which includes accurate aggregate report data and also signal detection and management. For example, the addition of such a large volume of non-serious cases to the safety database may *negatively* impact the ability to identify important new signals using signal detection tools (i.e. a potential diluting effect).

The WatchNet™ Frameworks: Conceptualizing Social Media for Actionable AEs

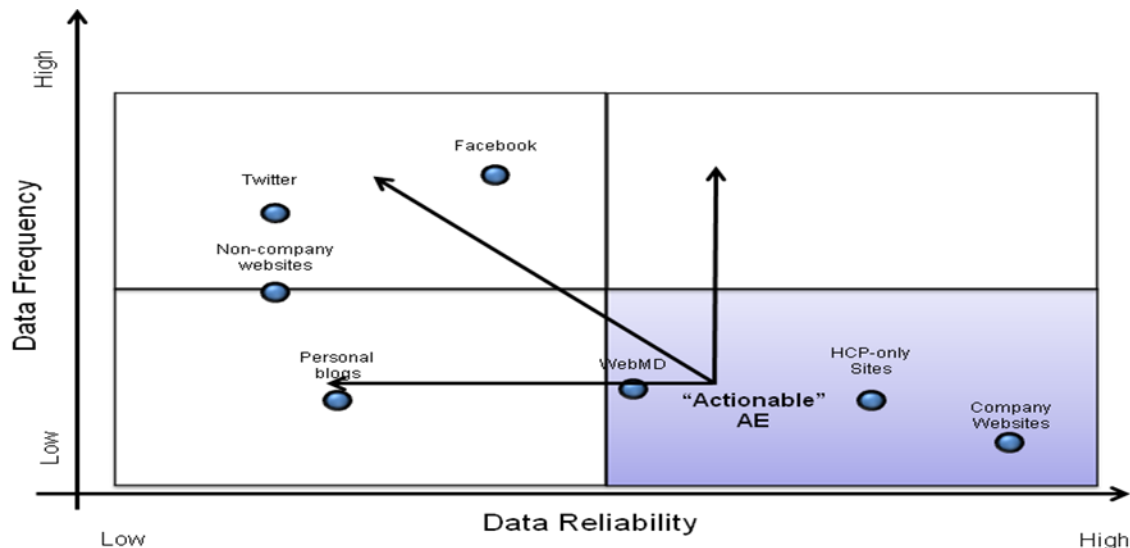
The emerging forms of social media can be categorized in relation to data volatility and traceability (Fig X), as well as data frequency and reliability (Fig X):



As observed in this framework, the emergent forms of social media lie outside the current 'Actionable' Adverse Event for which companies have established processes.

Similarly, in Figure (X) below, social media sites propagate an increasing amount of information for companies, yet the reliability of this data is less than 'traditional' forms of web-based communication such as web sites that are completely owned by a company:

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As pharmaceutical companies begin to rely more and more on 'viral' forms of marketing such as through product pages on Facebook or Twitter, they face exponentially increasing challenges of monitoring such sites and determining the boundaries of an individual adverse event report. Similarly, the emergence of personal blogs, which often are founded by individuals who have had a particularly bad experience with a particular product or who have a particular motive in hosting a blog, poses new challenges for follow-up adverse event information gathering.

Recommendations for FDA Guidance

To minimize future uncertainty with regard to adverse handling monitoring responsibilities, it is recommended that the FDA provide specific guidance to companies with regard to both data quality and operational considerations for future adverse event processing.

With regard to data quality, pharmaceutical companies would need to receive specific guidance on treatment of information for initial versus follow-up cases. Within an interactive web site or discussion board with multiple threads and multiple users, how are companies to distinguish between initial and follow-up case information, particularly if a discussion thread receives multiple posts over multiple days? When does an initial report end and the follow-up begin, and for how long shall follow-up be monitored? Furthermore, if a third party posts information into an ongoing discussion thread, is that to be considered a new report or an addendum to an existing case? How are companies to interpret parent/child relationships between temporally or contextually related postings?

In addition, questions surrounding data materiality have emerged. Will the four currently-required minimum criteria for a reportable adverse event change? In addition, how are companies to handle a passing or vague remark that may be made on a blog without mentioning explicit assumed or implied



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causality? One alternative proposed by some industry counterparts has been that social media cases be treated as solicited cases, which would help to resolve the intent to report questions.


A key question requiring regulatory guidance is the notion of reporter authentication. Is an email address or username considered authenticable? How would a pharmaceutical company determine that the identity of the poster is the true identity, and not a false use of the information? Should the pharmaceutical company be required to email each reporter for confirmation?

With regard to operational considerations, companies need guidance on both reporting frequency and scope. How often should pharmaceutical companies be required to scan social media sites for adverse events? One recommendation for consideration would be to allow pharmaceutical companies to use selected automated scanning technologies to assist them in website monitoring and reporting. Industry groups should gather and create an 'industry standard' list of terms to use in scanning, inclusive of requirements for keyword proximity to a product name. Furthermore, industry groups should determine a comprehensive list of social media sites which are in scope for this monitoring. In this way, companies receive the full benefit of awareness of comments in the social media space, yet maintain their ability to conduct good pharmacovigilance practices based on the data retrieved via the searches, so that this data does not affect the accuracy of a product's safety profile. The role of the FDA would mandate processing of company-sponsored blogs run through the technology tool and accept the results, or perhaps offer a list of approved information mining tools to develop consistency in evaluating safety information.

Finally, how will regulatory guidance handle localization or internationalization issues? As pharmaceutical companies are global entities, regulators should define the language scope for adverse events from multiple geographies and the translation requirements for postings on social media sites in languages other than English. If technology is suggested or encouraged by regulators, companies would then need to evaluate the impact on keyword placement rules for different languages.

Overall, then, the data quality and operational considerations faced by the FDA can be aided by looking to prior models for success such as collaboration between the public and private sector. The government has leveraged technological solutions to aid the mining of vast amounts of information in the public sphere. Similarly, the FDA could encourage companies to leverage information mining tools or approved internationally-distributable variance of those developed for other governmental agencies.

Another proposed regulatory change would be to allow companies to post a simple adverse event form on company-sponsored websites with a 'blog' or 'chat' feature to enable a report from a website visitor. The marketing authorization holder could then be required to monitor website monthly or quarterly as part of Signal Detection efforts.



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Conclusions

In summary, the issue of social media regulation has specific implications for adverse event handling. The FDA is encouraged to issue specific guidance on recommended social media monitoring practices for the benefit of pharmaceutical companies and ultimately the public health with regard to both data quality and operational considerations. It is specifically recommended that, because the social media is directly proportional to the leveraging of technology as a communication driver, a technological solution for the monitoring of social media sites be acceptable. In this way, pharmaceutical companies can maximize the information gathered while maintaining the ability to focus their personnel on the key aspects of pharmacovigilance such as signal detection and management for further and vital analysis on product safety profiles.