The Impact and Use of Social Media in Pharmacovigilance

⬡ Unlocking Social Media's Value Into Your Company's Strategy

> Pharmacovigilance practice has evolved and grown more complex over the past 5 to 10 years due to higher data volumes, evolving regulations, increased influence of emerging markets and the emergence of social media and innovative technological advances.

The phenomenal reach of the internet and social media over the last few years has led to a revolutionary shift in how people are communicating with one another today. Social media platforms and applications are fast becoming the go-to form of communication in the era of Web 2.0.

Digital media is used by biopharmaceutical companies for communication with patients to create awareness about diseases and treatments, clinical trial enrollments and patient support programs. However, unlike other areas in healthcare, use of the internet and social media has progressed slower in Product safety/Product Vigilance (PV). This presents the life science and service provider industry with multiple exciting, yet overwhelming, opportunities for appropriate and effective use of social media to drive innovative and meaningful changes in PV and how we communicate with patients and healthcare practitioners around the world.

This whitepaper examines how the influence and reach of the internet and social media can be harnessed to drive valuable outcomes for the PV industry. In this paper, we look at available regulatory guidelines, current state and future considerations for use of social media in PV, possible areas of influence, expected challenges, potential solutions and next steps.

Considerations for Using Social Media in PV

Social media websites and applications allow for the exchange of user-generated content where people talk, share information, participate and network. Within the last decade, social media has become one of the most powerful sources for news updates, viral marketing, online collaboration, networking and entertainment.

The key question that needs to be answered is: Can the use of social media help drive consequential and valuable changes in PV? The simple answer is "Yes" – at a minimum.

Social media presents new channels and methods that can enable companies to move away from traditional PV systems and safety reporting methods towards more patient-centric models for reporting, analyzing and monitoring of safety data. These channels have the capability to allow swift and open communication between companies and the consumers/patients and healthcare providers using the medicinal products,

thereby helping foster transparency and build public trust.

Social media monitoring will likely become a standard practice in PV in the future. However, before that, careful evaluation and assessment of the use of social media as a PV tool needs to be done; both in terms of meaningfulness and impact on outcomes. Further, evaluation of regulations and laws required for effective use, practicality of the use of big data obtained via social media channels, cost of use and overall cost-benefit analysis needs to be done.

Regulatory Guidance on Use of Internet and Social Media in PV

Today, biopharmaceutical companies operating in the social media space have a responsibility to document and follow-up on any potential adverse outcomes communicated through these forums in compliance with the applicable regulatory guidance.

Companies must comply with all applicable legislations. In Europe, two pieces of legislation underpin PV expectations: Regulation 726/2004 (as amended by Regulation 1235/2010) and Directive 2001/83/EC (as amended by Directive 2010/84/EU)[1]. Operational aspects, including the Commission Implementing Regulation 520/2012, are detailed in the associated GVP guidance[2]. Pharmaceutical companies in UK also need to comply with requirements in the "Association of the British Pharmaceutical Industry" (ABPI) Code of

Practice for Pharmaceutical Industry[3] and informal guidance on digital communications, given by the Prescription Medicines Code of Practice Authority (PMCPA)[4].

GVP Module VI states[5] that marketing authorization holders (MAH) should regularly screen the internet and/or digital media under their management and responsibility, for potential reports of suspected adverse reactions. In this aspect, digital media is considered to be company sponsored if it is owned,

paid for and/or controlled by the MAH. The frequency of the screening should allow for potential valid individual case safety reports (ICSRs) to be reported to the competent authorities within the appropriate reporting timeframe based on the date the information was posted on the internet site/digital medium. MAHs may also consider utilizing their websites to facilitate the collection of reports of suspected adverse reactions (VI.C.2.2.1).

If a MAH becomes aware of a report of suspected adverse reaction described in any non-company sponsored digital medium, the report should be assessed to determine whether it qualifies for reporting. Unsolicited cases of suspected adverse reactions from the internet or digital media should be handled as spontaneous reports. The same reporting time frames as for spontaneous reports should be applied (VI.B.7).

In relation to cases from the internet or digital media, the "identifiability" of the reporter refers to the existence of a real person, that is, it is possible to verify the contact details of the reporter (e.g., an email address under a valid format has been provided). If the country of the primary source is missing, the country where the information was received, or where the review took place, should be used as the "primary source country"[5].

Section II d (p.55) of Current Challenges in Pharmacovigilance: Pragmatic Approaches, (Report of CIOMS Working Group V)[6] states: A procedure should be in place to ensure daily screening by a designated person(s) of the website(s) in order to identify potential safety case reports. The working group does not believe it necessary for regulators or companies routinely to 'surf' the internet beyond their own sites for individual spontaneous reports.

Thus far, the US Food and Drug Administration (FDA) has published 3 documents about product promotion on social media and the Internet by pharmaceutical and medical device companies[7-9]. The first FDA draft guidance addressed how pharmaceutical companies should respond to off-label inquiries, including inquiries originating from digital platforms[7]. The second FDA draft guidance for industry addressed how pharmaceutical and device companies provide benefit and risk information on Internet and social media platforms with character space limitations (e.g. Twitter)[8]. The third FDA draft guidance is about how companies should address misinformation about their products on the Internet and social media websites[9].

Another long-awaited draft guidance with non-binding recommendations, issued by FDA in January 2014[10], provides pharmaceutical drug and biologics manufacturers with the FDA's current thinking on how to fulfill their post-marketing regulatory requirements for submission of "interactive promotional media" as it relates to their FDA-approved products. "Interactive promotional media" means technology that permits real-time communication and interaction with users which pharmaceutical drug manufacturers use to promote their products. According to the Guidance, examples of interactive promotional media include blogs, microblogs, social networking sites, online communities and live podcasts. The Guidance provides pharmaceutical drug manufacturers with direction about whether they should report product communications that utilize interactive technologies to the FDA to fulfill their post-marketing submission requirements. It also addresses the practical considerations that these manufacturers face with regard to submitting real-time information that is constantly increasing in volume and changing as it is posted online and shared by users.

Today, most guidance from EMA and FDA, is focused around screening of company owned/monitored websites, forums and other social media channels to enable and ensure maximal safety reporting. Additional specific guidance is required in terms of confirmation of validity of safety data, obtained via social media (within the norms of data privacy), protocols to guide further retrieval, analysis and integration of such data with other standard safety data (obtained from standard PV sources) and also effective use of social media for risk management and communication.

These regulatory guidelines have helped clarify to a certain extent, the thinking and approach of regulatory authorities towards evaluating content shared on internet and social media platforms and serve as an important first step towards providing guidance for companies to develop and implement their social media strategies for PV.

Current Status of Social Media in PV

> Social media activities for PV by companies fall into three broad categories, listening (safety data reporting), engaging (follow-up) and broadcasting (risk communication), each with varying degrees of complexity, associated issues and requirements.

Today, most of the regulatory guidance and hence PV activities involving social media and internet are primarily focused around screening of social media sites and follow-up of reported safety data, as detailed further in this section. However, their impact and use in other areas of PV like retrieval, integration and analysis of safety data and as potential tools for risk communication and management, is either minimal or absent.

Companies rely on multiple AE reporting channels such as email correspondences, company websites and physician hotline resources. Further to the regulatory guidance from EMA and FDA[1-10], today many companies in both EU and US, already show responsibility for their own online content. This is evident, based on data from several surveyed companies, wherein social media serves as one of the adverse event-reporting channel (32%) in these companies[11].

The internet represents an excellent means of collecting drug and device AEs primarily from healthcare providers. Adverse events can be directly reported to the FDA MedWatch in US, to Health Canada MedEffect in Canada as well as to the "Yellow Card Scheme" in the UK and in Australia. Social media has already impacted the community of medical practitioners (www.sermo.com), community of patients (www.patientslikeme.com), community of medical education and community of medical care facilities (Mayo Clinic). These sites have proven that appropriate messages posted on social media platforms and channels can have meaningful and rapid impact.

There are now multiple sites and applications for patient and consumer reports on computers and smartphones. One such tool is the MedWatcher, a free tool that allows

patients and physicians to submit adverse event reports to the FDA via smartphone or tablet (MedWatcher.org). The primary purpose of such tools is to give patients or health care professionals (HCPs) information on drugs, devices, interactions and other pharmaceutical information while some also allow reporting of AEs. It is likely that these tools will proliferate and will further become smarter (user-interactive) and sophisticated and help both sponsors and regulators to listen to the voice of patients and consumers directly.

Today, more and more medical and consumer health companies are realizing the importance of having appropriate and sufficient controls over social media sites to avoid potential gaps/risks in the areas of reporting, identification and monitoring of AE data.

Companies are now actively engaged to identify and understand the value drivers for adopting a comprehensive PV social media strategy, which encompasses proactively creating social media platforms to solicit/capture AE data to enable an organization's social media monitoring and reporting activities as they relate to AE compliance (rather than monitoring and reporting what comes in passively on existing company sites) and further examine the successes and challenges of the different types of social media platforms being used.
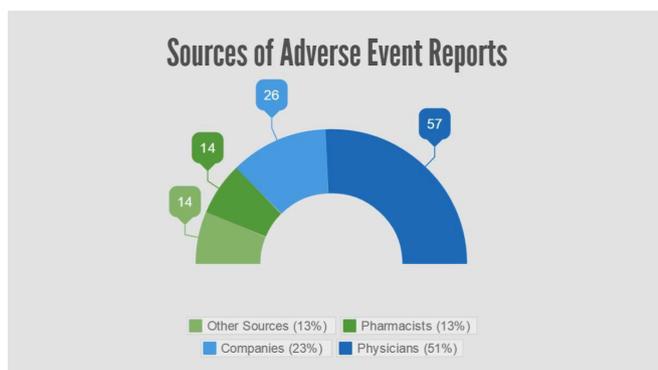
Companies are now also providing their employees with social media guidance and best practices to facilitate effective safety reporting via social media. Employees are encouraged to be a scout for reporting safety issues/adverse events that they come across on social media sites, wherein side-effects are mentioned after having taken one of the client products drugs in a credible and identifiable way[12].

Future Impact and Potential Areas to Leverage Social Media in PV

Social media for safety data reporting and follow-up

Users in an online community often share a wide variety of personal medical experiences. For many reasons, patients often share health experiences with each other rather than in a clinical research study or with their physician[13]. One study, led by Knezevic et al in 2011, describes how a Facebook group was created as an Adverse Event (AE) channel and its effectiveness was tracked. The group found that it was able to connect with 1,000 Facebook users and received 21 adverse reactions within the course of seven months[14].

Social data offers some advantages over traditional AE reporting data or data mined from health and reimbursement records. Social reports are rapid, closer to real-time data (occurring in close proximity to the event) and potentially richer sources than reports filtered through HCPs (coming directly from the patients).

Sources of Adverse Event Reports

26

14

14

57

Other Sources (13%)   Pharmacists (13%)
Companies (23%)   Physicians (51%)

Companies receive, on an average, just above a quarter of AE reports (26%) from patients while the remaining AE reports are received from physicians (57%), pharmacists (14%) and other sources (14%)[11]. Social media channels have the potential to act as a significant source of AEs as well as data on off label use and impact of treatments on quality of life.

The ability of companies to leverage social media can transform these platforms into strategic PV tools. One of the key areas of influence is therefore to establish social media as an AE reporting channel by expanding its existing use and unlocking its potential as a value-add for companies' PV strategies.

Social media platforms, by design, can work to increase connections between companies and healthcare consumers and thereby allow and encourage safety reporting through direct patient and consumer engagement. This gives companies an opportunity to connect, engage and encourage patients and consumers to report more, helping address the concern of adverse events, going unreported.

However, for companies used to processing drug safety data, confirmed by physicians and other healthcare professionals, verifying safety data obtained via social media may prove challenging, given the issue of confirming the "identifiability" of both reporter and patient. Also, adverse events received through social media may contain less information and require additional follow-up.

New guidance to ensure appropriate validation of the reported safety data and recommendations to help address data privacy issues in safety data obtained via social media is required. GVP module VI, Section VI.B.2, page 12[5] states: When collecting reports of suspected adverse reactions via the internet or digital media, the term "identifiable" refers to the possibility of verification of the existence of a reporter and a patient (see VI.B.1.1.4).

The "identifiability" of the reporter refers to the existence of a real person, that is, it is possible to verify the contact details of the reporter (e.g., an email address under a valid format has been provided). If the country of the primary source is missing, the country where the information was received, or where the review took place, should be used as the "primary source country".

In a social media setting, patients are likely to be reporters themselves, without any confirmation of data from HCPs. Credibility and origin of these self-generated reports are key issues. Also, social media with no appropriate checks on provenance can open the avenue to unscrupulous attacks from "pseudo-reporters". Allowing posts only after registration and record of basic user data on company monitored websites helps verify the minimal criteria for confirming case validity (identifiable patient, identifiable reporter, suspect product and adverse event/reaction) and allows follow up with any additional questions.

Safety data obtained via social media often contains personal data related to the patient (subject of the case) and the reporter (patient's healthcare provider, family member or the patient themselves). Companies need to process personal data in compliance with the applicable data protection laws, supported by transparent and robust processes to ensure personal data protection. Data protection notice on company-sponsored sites should detail how user-generated information (deemed to be an AE/PC) is collected by company to meet legal obligations, why such information is beneficial for the protection of public health and that company may follow-up directly with the reporter. Regular training in data protection requirements is recommended for all company staff involved in PV activities[15].

Another area of uncertainty, around the use of social media for safety reporting is about the scope and scale of monitoring of both company and non-company sponsored digital media. Companies will need to prioritize monitoring social media and other forums for which they are directly responsible to better manage time and financial resources, in line with the guidance outlined in GVP Module VI and also the report of CIOMS Working Group V[5, 6]. Concentrating on company-managed social media websites can keep PV teams' workloads manageable and also potentially help decrease chances of receiving duplicate adverse event reports from different online reporting channels. Furthermore, this can help companies maintain the reliability of incoming data.

Retrieval, interpretation and integration of safety data obtained via social media

Social media is a promising source for new safety data and potential emergent safety signals. Yet, it is important to keep in mind that this data is essentially unstructured data; obtained via uncontrolled and ungoverned processes in a non-regulated environment and is neither driven by data quality standards nor by specific business area orientation. The large amount and variety of information obtained via social media as well as its rapidly changing nature, makes it a typical big data problem. Consequently, companies may struggle to integrate adverse event reports received through social media with reports received from more standard sources like email correspondence or physician hotlines.

The retrieval and analysis of safety data, obtained via social media channels entails extra workload and additional resources, given the sheer size and success of social media and networks. There is a vast amount of information on drug safety matters, available on social media and networks, some of it useful and some not, depending on the perspective and needs of the user/reviewer.

Another concern is the potential bias introduced by the "reporter population" and thereby accurate representation of the reported safety data. Of the large number of social media users, only a small percentage (1%) are actually commenting and reporting AEs while most others are only occasional contributors or simply observers/readers. Also, many elderly individuals do not use social media and this is important because it creates a strong user bias for PV as this demographic is a large user of prescription medications.

There are a number of additional technical challenges to be addressed including:

1. Identification of duplicate safety information with respect to data originating from digital media i.e. the same ADR may be reported by the same or a different user on multiple digital media platforms, requiring robust methods for the evaluation of data provenance.

2. Multiple languages and how data collected in different languages maps to standard ADR.

3. Data privacy and personal data protection issues surrounding such mining and discovery also need special attention.

4. Data curation and cleaning would also be required to mitigate the risk of spreading rumors/false safety concerns. On top of all this, is the global diversity that is represented by social media and networking. The challenges here are manifold and not just confined to linguistic issues and translation, but relate to social structures, practices and intangibles[16].

Overcoming these social media hurdles for validation and consolidation of incoming data thus poses a great challenge, requiring the concerted efforts of PV teams. Life sciences companies along with regulators now recognize the benefit of adapting automated tools (text-based or concept-based searches and data mining techniques) for big data analytics to help manage and differentiate between signals received from social media platforms and any accompanying noise.

Google Insights for Search is a tool that allows one to look at any public concerns, as measured by web traffic, which can also include drugs and disease (adverse effect) terms and browsing possible associations, but without much precision. Using this tool is fascinating, but it has a long way to go before it can be used for the purpose of pharmacovigilance to derive possible associations between adverse events and companies' products and thereby may help companies prioritize among an influx of incoming social media signals[16].

The FDA is currently actively exploring a number of such social media-based strategies, including Google search tools towards optimizing data gathering from content communities and collaborative sites. Another prototype, created within the framework of the European research Project TrendMiner, helps analyze the comments on social media by using natural language processing techniques (NLP), whereby patients' colloquial descriptions are "translated" into manageable data, allowing identification of safety patterns and trends.

Another interesting project called the WEBAE project (Web Adverse Events) aims to form a specialist public private consortium between the EFPIA (European Federation of Pharmaceutical Industries and Associations) and the Applicant Consortium to undertake research into the appropriate policy and technology solutions to leverage web based media mining and crowd-sourcing technologies in pharmacovigilance to strengthen the protection of public health[17].

The primary objectives of this project are to develop a technical and policy framework for mining publicly available (and licensed) web and social media content and adopt methodologies and data mining algorithms applicable to social media content (forums, blogs, tweets, public posting, etc.) in order to find emerging, self-reported medical insights such as adverse events associated with medicines and medical devices. This program also intends to enable direct reporting of suspected ADRs to national competent authorities via EudraVigilance, with required applications (free of charge) available to all users of tablets, smartphones, and the mobile web, for all major platforms as well as social networking sites like Facebook.

It is indeed an interesting time for PV teams across the globe, as the latest technological advances hold the promise to transform the future of PV practice. How PV teams and stakeholders collaborate with regulators to derive meaningful results from the big social data deluge remains to be seen.

Risk management and communication to patients and healthcare providers via social media

There are multiple ways in which industry can positively engage consumers and providers while remaining within the draft FDA social media guidance[7-9]. The first step is switching from a mindset of simple risk communication to one of listening, educating, building trust, increasing safety awareness, and improving health outcomes. Some meaningful ways that PV teams can use social media to engage and improve awareness about the safety of a product and provide more value to patients and healthcare professionals (Figure 1).

Figure 1
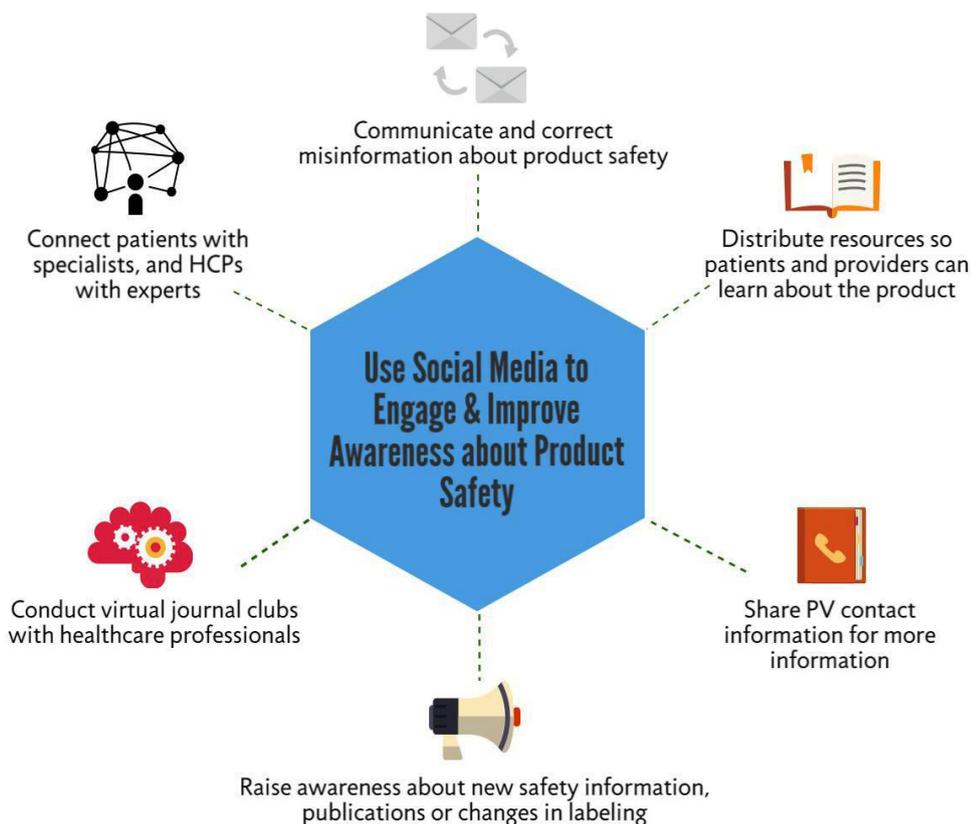
Next Steps and Conclusions

The fundamentals of social media (listening, broadcasting, engaging) are well-aligned with the principles of PV practice, thus social media offers a potentially transformative AE reporting channel and an overall strategic tool to drive better PV outcomes in the future.

The use and monitoring of social media sites and channels for safety reporting has increased in recent years. At the same time, legislation to ensure appropriate pharmacovigilance and regulate the safe use of medicine continues to become more stringent. However, unlike many other areas in the healthcare industry, the internet and social media do not yet play a major role in drug safety and PV.

The GVP and CIOMS guidelines and recently issued US FDA guidelines provide guidance to the pharmaceutical and medical device industries for screening internet or digital media under their management or responsibility for potential reports of suspected adverse reactions,

posting informationon social media networks and also correcting misinformation posted by others. The FDA guidance also requires companies to post both the benefits and the main risks associated with a product, potentially with a hyperlink taking the reader directly to a more detailed list of risks. These guidelines are an important first step towards providing guidance for companies towards development and implementation of their social media strategies for PV.

Appropriate engagement of consumers and healthcare providers through social media by PV teams, certainly holds the promise of better outcomes (Figure 2).

Figure 2

Social Media Promises Better Outcomes

- Better educated consumers and HCPs
- Quicker reporting and communication of new safety concerns/issues
- Increased insight for product benefit-risk evaluation
- Enhanced risk evaluation and mitigation strategies
- Improved communication of updated safety information, back to stakeholders
- Improved relationship between companies and the community

Appropriate use of the internet and social media can prove to be a significant catalyst in the transformation of the PV practice in the not so distant future. However, there is no magic pill or solution to the various challenges facing the PV industry today. New regulatory paradigms are needed and many questions need to be answered, like:

- What is the limit of the industry's responsibility in collecting and reviewing social media data?

- What new tools and methods could be used to capture spontaneous reports from social media or mobile apps and provide emerging safety signals through a process of real time data mining?

- How can PV teams confirm the "identifiability" of the reporter and patient in safety data obtained via social media and establish safeguards against faulty adverse event reporting?

- What will be acceptable practices for following up on potential signals within the context of data privacy?

- What are the protocols for big data integration, analysis and interpretation, and reporting of follow-up results?

These and many such questions will need to be addressed before industry can be comfortable with the use of social data for drug safety surveillance. Traditional PV methods will certainly prevail, yet social media has the potential to become an added new-age tool to monitor data in real-time, making it an early indicator of potential safety issues for further investigation.

Further, this would enable companies to generate more robust product safety profiles by leveraging the additional social media information.

Overall, the benefits of social media engagement for PV seem to significantly outweigh perceived risks. The time is now right to elevate social media's role within the PV organization to a more strategic level and drive better PV outcomes through appropriate and effective use of social media within the evolving regulatory framework.

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