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Division of Dockets Management (HFA – 305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852



RE: Docket Number FDA-2009-N-0441 Promotion of Food and Drug Administration-Regulated Medical Products Using the Internet and Social Media Tools; Request for Comments

Merck & Co., Inc. (Merck) is a global healthcare leader who is working to help the world be well. Through our medicines, vaccines, biologic therapies, and consumer and animal products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching programs that donate and deliver our products to the people who need them.

Merck appreciates the opportunity to engage in a dialogue with the Food and Drug Administration (FDA or "the Agency") on this important issue of promotion of FDA-regulated medical products using the Internet and Social Media tools. Merck is committed to providing accurate, balanced, and scientific information about its products to both healthcare professionals and patients and routinely utilizes the Internet and/or other forms of technology to serve that purpose. These online activities can help physicians and other healthcare providers make more informed prescribing decisions for their patients. Merck also uses the Internet to inform and educate patients about diseases that may be relevant to them and therapeutic options they may want to discuss with their physician. The ultimate decision to prescribe a product remains with the physician following discussion with their patient.

Enclosed below are Merck's comments and recommendations on this important matter. Our comments are divided into two sections – the first section captures our general comments while the second section provides responses to selected questions posed by FDA in its *Federal Register* (FR) Notice. Also included in Section 2.A. Internet Promotion Using Tools with Space Limitations are results from Merck's market research that evaluated sponsored links.

For additional information or questions, please feel free to contact me by phone or email per the below contact information.

Sincerely,

A handwritten signature in black ink that reads "Sandra A. Kerr".

Sandra A. Kerr, RPh
Office of Medical/Legal

SECTION 1. GENERAL COMMENTS

The Internet has become an increasingly important source of health information to consumers and has changed the role of the physician as the sole deliverer of medical information. Social media in particular has influenced how patients and consumers obtain medical information and make decisions relating to their healthcare options and treatments. Consumers are posting explicit medical information about themselves and are receiving feedback on suggested courses of action via the Internet. Additionally, it is estimated that over 111 million Americans rely on the Internet to find health information.¹ There are over 2.67 billion searches worldwide per day, 183 billion emails per day or roughly 2 million every second, and 15 hours of video uploaded to YouTube per minute². These statistics reflect total volume and do not include web-based health related postings through user-generated video, audio, text or multimedia that are published and shared in a social environment, such as a blog, wiki or video hosting site.

Further, a recent survey by the Pew Research Center found that 61% of American adults look online for health information and about a third of adults have sought information about a prescription or OTC drug on the Internet.³ The Internet continues to advance at a rapid pace (e.g. Web 3.0), ahead of guidance from FDA. Given the importance of the Internet as a resource for disease and product information that serves both healthcare professionals and consumers, Merck believes that the mission of the FDA is best advanced, and the interests of the public and industry are served best, through issuance of policies and standards along with prospective and proactive dialogue among FDA and its stakeholders.

Merck supports FDA's efforts to evaluate how the statutory provisions, regulations, and policies concerning advertising and promotional labeling should be applied to product-related information on the Internet and new technologies. Merck also supports the Agency's desire to understand the issues involving the reporting of adverse event (AE) data revealed through social media platforms. Merck commends FDA for recognizing the continually evolving nature of the Internet, including Web 2.0 and social media tools (such as wikis, blogs, Facebook, Twitter, etc) and the need for additional guidance on how the regulations should be applied to the special characteristics of these and other emerging technologies. Merck encourages the Agency to provide policies and standards that will help ensure that information about FDA-regulated medical products promoted on the Internet and other social media tools to both health care professionals and consumers is truthful, non-misleading, and balanced.

Merck strongly believes that policies and standards on the use of the Internet as a tool to promote FDA-regulated products are needed. However, we recognize and appreciate that

¹ Belliveau MA, Cowan A. A Proposal for Sponsored Links: Connecting Consumers to Important Health Information. Slides presented at: FDA public hearing on Promotion of FDA-Regulated Medical Products Using the Internet and Social Media Tools; November 12-13, 2009; Washington, DC.

² id.

³ Fox, Susannah, Jones, Sydney, The Social Life of Health Information, Pew Internet & American Life Project, June 2009, <http://www.pewinternet.org/Reports/2009/8-The-Social-Life-of-Health-Information.aspx?r=1>

FDA will be constantly challenged to provide guidance that addresses the rapidly evolving technologies and web-based forums, along with issues raised by this rapidly dynamic medium. Merck encourages the Agency to maintain a dialogue with industry, third-party providers, trade associations, and other groups to stay abreast of new technologies as well as the challenges and issues with Internet promotion. This dialogue and continued learning could be accomplished in several ways, including public workshops.

Since the Internet and associated tools are ever changing, FDA should consider the establishment of an Advisory Committee comprised of key experts (including consumer advocates, representatives from the medical community, technical experts, and industry representatives) to review issues periodically that involve the communication of product information over the Internet and via social media tools. Such a committee could exist as a sub-committee to the FDA Science Board or the Risk Communication Advisory Committee.

Another approach for FDA to consider is the use of existing regulations regarding administrative procedures for advisory opinions that provide a means for an interested person(s) to request an advisory opinion on a general issue or matter related to the promotion of FDA-regulated medical products on the Internet and in social media. FDA could also consider developing a voluntary process for making public, at the request of an advertiser (sponsor), advisory comments on promotion and advertisements submitted to FDA for comment under 21 CFR 202.1.(j)(4). Other Federal Agencies have established voluntary public advisory opinion processes, including HHS's Office of Inspector General and the Centers for Medicare & Medicaid Services^{4,5}. While the constituencies and responsibilities of these agencies are different than those of FDA, their advisory opinion processes may be useful in considering a process for FDA.

⁴ U.S. Department of Health and Human Services, Office of Inspector General Advisory Opinions <http://oig.hhs.gov/fraud/advisoryopinions.asp>.

⁵ U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services Advisory Opinions, http://www.cms.hhs.gov/physiciansselfreferral/07_advisory_opinions.asp

SECTION 2. RESPONSES TO SELECTED QUESTIONS IN FR NOTICE

A. Internet Promotion Using Tools with Space Limitations

The Internet continues to grow as a source of health information. According to the Manhattan Research ePharma Consumer study, over the past five years, the number of Americans who have used the internet to research prescription drug information has tripled to about 95 million, which represents 41% of the adult U.S. population.⁶ Data from the 2009 Pew Online Health Search report indicates that the health information found on the Internet affects how consumers make health decisions, including how they treat an illness or condition and how they approach maintaining their health or the health of someone they care for.⁷ Because of the significant role of the Internet as a source for health and treatment information, it is critical that medical product manufacturers, as the product experts and innovators, be allowed to provide medically accurate, non-misleading, and balanced information about their products and the diseases they prevent or treat on the internet. This provision of information via the many tools available on internet will necessarily include digital media that have space or formatting limitations, such as banner advertising, mobile applications, text messaging and sponsored advertisements in search engines. While pharmaceutical manufacturers do not have control over the space limitations inherent to this media, they are in a position to provide scientifically accurate and balanced information about the product that can help educate consumers and provide access to credible medical information.

Search engines, the most utilized limited space technology, are the primary tool used to search for health information on the Internet⁸. Consumers are most likely to use search engines to research symptoms for a condition, followed by searches for pharmaceutical and health information, particularly after they receive a diagnosis and before they begin taking a new prescription.⁹ Between October and December of 2007, there were 4.6 billion searches on health keywords and 111 million individuals searched for information using health keywords.¹⁰ Search engines are designed to help individuals find web pages of interest on the Internet. The search results are not designed or intended to include all of the information from the relevant web pages. When performing searches, users scan dozens of links, descriptions, and words within seconds. If a searcher is interested in learning more, they know to click the search result listing, without further prompting.

Most search engine web sites allow for paid advertisements or listings, also known as "Sponsored Links", "Sponsored Sites" or "Sponsored Results" to appear next to the natural search results. All search engines have formatting standards for sponsored links that limit the number of characters per line and the formatting of the ad text. Because the

⁶ Manhattan Research, LLC, ePharma Consumer® v8.0, "Reaching Today's ePharma Consumer: How Consumers are Using Online Channels for Pharma Product Information." 2009, http://www.manhattanresearch.com/files/White_Papers/Reaching_Today_s_ePharma_Consumer.pdf Accessed February 5, 2010.

⁷ Fox 2009.

⁸ iCrossing, "How America Searches: Health and Wellness" conducted by Opinion Research Corporation, January 14, 2008.

⁹ Manhattan Research 2009

¹⁰ Belliveau 2009

vast majority of Internet users searching for health information use one of the many available search engines, Merck utilizes sponsored links as an important communication tool to provide access to relevant, credible and balanced information about our products.

Due to the space limitations of sponsored advertisements and FDA regulatory requirements (any promotional communication that makes claims about a medical product must include certain required disclosures such as the approved indication as well as a fair and balanced presentation of the risk information), medical product companies are restricted to two types of search engine sponsored advertisements: brand reminder advertisements and "help-seeking" advertisements. Brand reminder ads are precluded from making any representations or suggestions about the product and therefore are generally only effective when there is a certain level of brand awareness amongst the Internet target audience or when health information seekers are searching for a specific brand or generic name.

"Help-seeking" ads contain unbranded content and are used to "redirect" health information seekers to a product web site through a disease or help-seeking link. Although help-seeking ads are not regulated by the FDA, they may lack transparency. An individual searching for information on depression, for example, may view a sponsored help-seeking ad as confusing or worse, potentially deceptive, if the link provided redirects to a company-sponsored product web site instead of a disease-specific web site. In the 2007 Prevention DTC Survey, 50% of respondents found the information in help-seeking ads not useful and just another way pharmaceutical companies are trying to sell their products.¹¹

Merck believes that the current formats for medical product advertisements in limited space digital media are not serving the needs of individuals who are seeking accurate and credible health information on the Internet. Therefore, Merck encourages FDA to issue policies that provide medical product companies with an acceptable method for providing accurate and balanced information about the benefits and risks of their products in digital media that have space or formatting limitations, such as search engine sponsored advertisements. Similar to FDA's policy to fulfill regulatory requirements for Direct-to-Consumer TV ads by means of adequate provision of the approved product labeling, FDA should issue policies that acknowledge the unique characteristics and space limitations of certain digital media. FDA should also look to FTC's guidance on disclosures in online advertisements. The FTC guidance acknowledges that hyperlinking to a disclosure may be useful for lengthy disclosures as is the case with the required disclosure of indication and risk information for medical product-claim advertisements¹².

To support FDA's development of these much needed policies, Merck conducted market research to evaluate the effectiveness of search engine sponsored advertisements. The research evaluated 5 different sponsored ads for a migraine medication to evaluate their impact (positive or negative) on searcher experience, content transparency and the appropriateness of using hyperlinks to access benefit and risk disclosures.

¹¹ Rodale, Inc., "Prevention 10th Annual DTC Study." 2007.

¹² Dot Com Disclosures: Information About Online Advertising, Federal Trade Commission, issued May 2000, available at <http://www.ftc.gov/bcp/edu/pubs/business/ecommerce/bus41.pdf>

The following ads were tested:

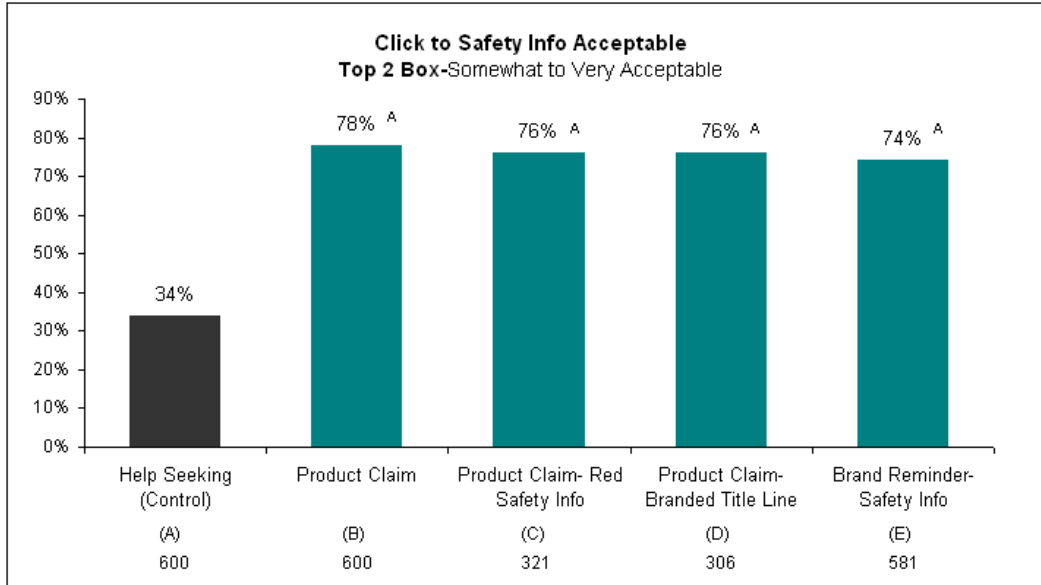
Info Seeking (Control) (A)	Get Migraines? Migraine-Pain-Support.com Use This Discussion Guide to Talk With Your Doctor About Treatment.
Product Claim (B)	Get Migraines? brandx.com BRAND X (generic) Talk With Your Doctor About Migraines. Learn about safety and product information, find out if this product is right for you. Read More
Product Claim- Red Safety Info (C)	Get Migraines? brandx.com BRAND X (generic) Talk With Your Doctor About Migraines. Learn about safety and product information, find out if this product is right for you. <u>Read More</u>
Product Claim- Branded Title Line (D)	BRAND X brandx.com BRAND X (generic) Talk With Your Doctor About Migraines. Learn about safety and product information, find out if this product is right for you. Read More
Brand Reminder- Safety Info (E)	BRAND X brandx.com BRAND X (generic) Talk With Your Doctor About Treatment. Learn about safety and product information, find out if this product is right for you. Read More

Participants in the research were males and females, ages 35+, diagnosed with migraines that were either treated or untreated with medication. Participants were presented with a scenario of performing a search for information on migraine and then asked a series of questions about the search results as well as expectations as to the type of content that might be presented if the test ad was clicked.

The key findings from our research show that:

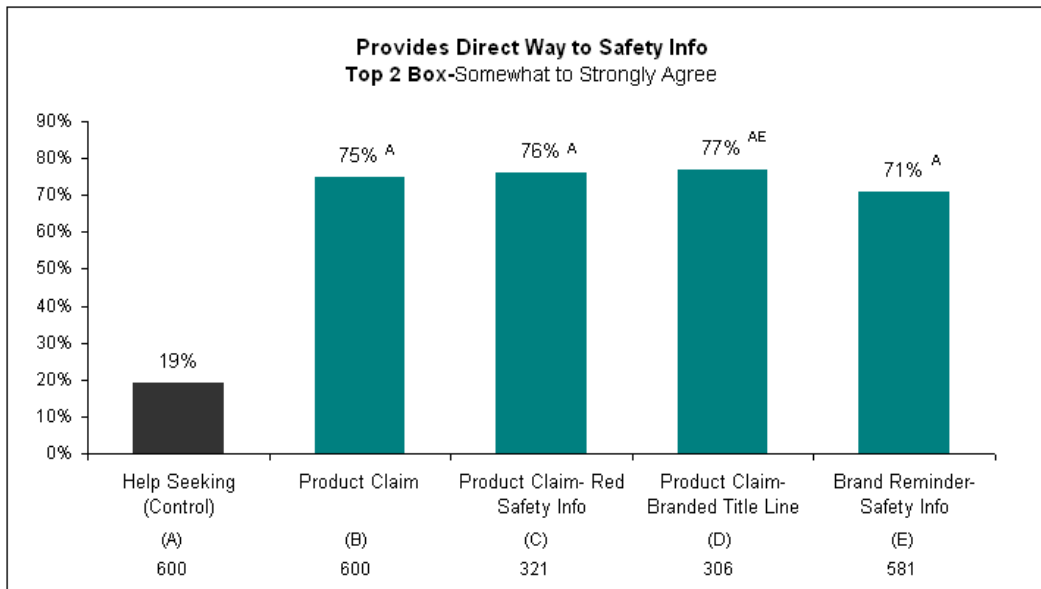
- 1. Consumers were comfortable with clicking on a hyperlink to access product safety information. Hyperlinks provided a direct way to access safety information.**

In the ad formats that provided a hyperlink to more product and safety information, the majority of participants felt that clicking to access safety information was acceptable. There were no significant differences in impact or opinion across the various hyperlink formats.



Q: How do you feel about having to click on the link to gain access to the product safety information?
 Letters indicate statistically significant differences at 90% confidence versus other cells.

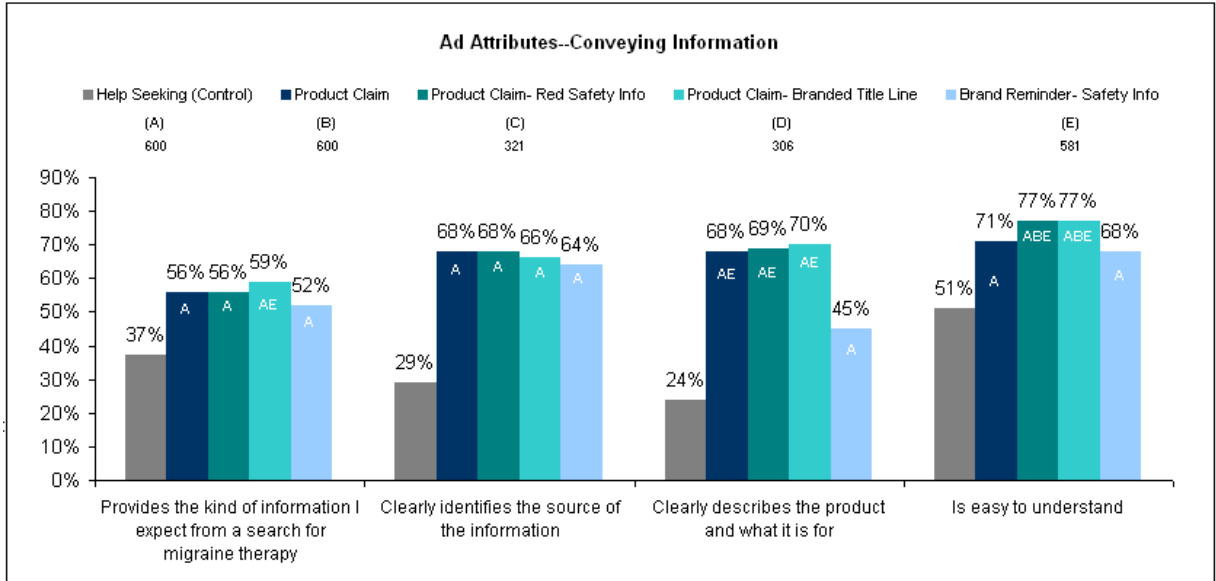
Additionally up to 77% of participants felt the product claim and brand reminder formats provided a direct way to safety information.



Q: How much do you agree or disagree that this sponsored search result provides you with a direct way to get to product safety information on the medication?
 Letters indicate statistically significant differences at 90% confidence versus other cells.

2. Product claim and brand reminder ads were the most effective at conveying information and providing information that meets searcher expectations.

While the other formats performed similarly, the product claim with branded title showed a trend of slightly better ability to provide expected information and understandability.



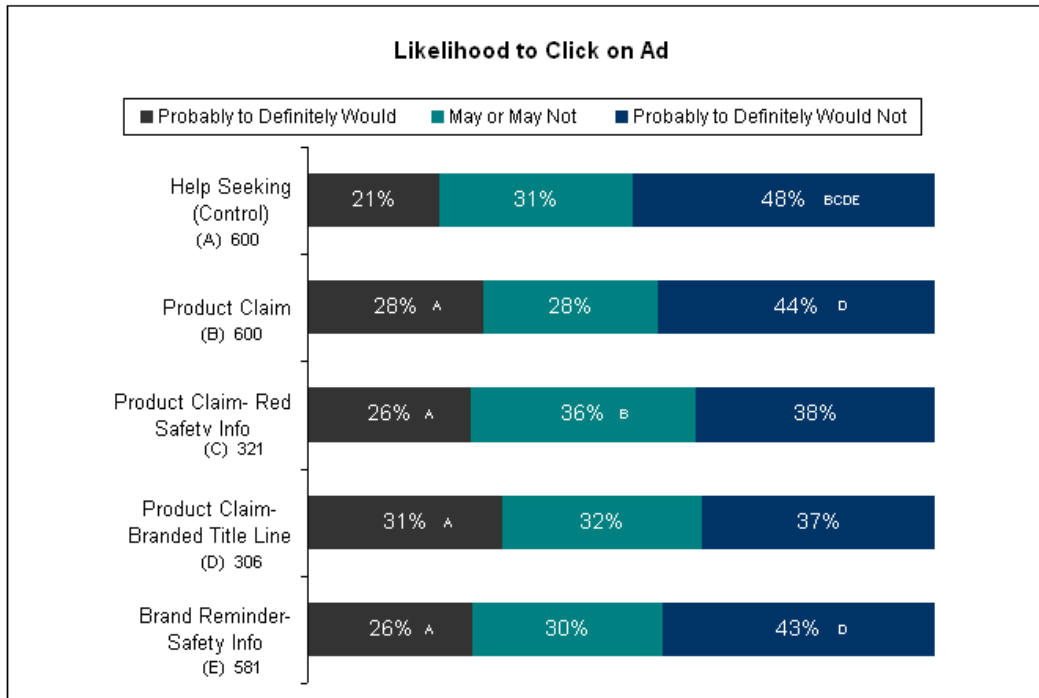
Q: Below is a list of comments other people have said about the ad or sponsored result you just saw. How much do you agree or disagree with each statement?

Letters indicate statistically significant differences at 90% confidence versus other cells.

There were similar results for the credibility and reputability of the information provided in the branded ads. In both cases, the product claim and brand reminder ads were 3-4 times more effective at achieving an opinion that the information in the ad was credible or reliable.

3. The help-seeking format was the least effective in conveying the purpose of the sponsored search result.

Approximately 21% of participants indicated they probably to definitely would click on the help-seeking format—not substantially lower than the other formats that garnered 26% to 31% click intent.



Q: How likely or unlikely would you be to click on this sponsored search result if you were searching for information on migraines?

Letters indicate statistically significant differences at 90% confidence versus other cells.

The striking result is in the post-click expectation. Only 6% of participants expected to land on a product web site upon clicking—7 times lower than the expected landing experience for the other formats (43% to 47%).

This mirrors Merck's in-market tracking results when sponsored search ads were revised to the help-seeking format in March 2009 in response to DDMAC's enforcement letters on sponsored links. Across several brands, we observed an increase in click-thru rates with the unbranded, help-seeking format indicating that the format may have attracted more users seeking condition-specific information. However, the number of landing (product) site pages consumed after the click-thru consistently declined. For one brand, the number of page views by the searcher dropped by nearly 50%. This decrease in content consumption could indicate a lack of transparency between the advertisement and the linked to content. The sum of these results suggests current unbranded, help-seeking sponsored links do not meet the needs of health information seekers using Internet search engines.

Based on our research results and in-market experience, Merck asserts that branded product-claim sponsored links are the most effective at meeting the needs of individuals who are seeking accurate and credible health information on the Internet. Merck believes that the use of hyperlinks is an appropriate and effective way to disclose product use and safety information in limited space formats. FDA should adopt standards to be consistent with FTC guidelines and allow hyperlinks to fulfill the regulatory requirements for product use and safety information disclosures in digital media with space limitations,

including but not limited to, banner advertising, mobile applications, text messaging and sponsored advertisements in search engines.

B. Adverse Event Reporting and the Internet & Social Media

Merck recognizes the responsibility for monitoring websites under our management for adverse drug reaction (ADR) reports. However, with respect to ADR postings within all of social media, there are significant challenges not seen in traditional spontaneous adverse event reporting. Examples of these challenges include the following:

- Anonymous nature of the internet
- Inability to verify the existence of an identifiable reporter and/or identifiable patient
- Inability to contact reporters to collect more detailed adverse event information
- Distortion of information through hearsay
- Case duplication
- Limited role of the physician/healthcare provider
- Multimedia postings
- Vastness of the internet

It is hypothesized that the addition of a large volume of cases from the Internet that cannot be validated may negatively impact the ability to identify important new signals using signal detection tools (i.e. a potential diluting effect) or to generate false positive signals. Using diabetes as an example, for a search conducted in December 2009, there are:

- More than 354,000,000 results from a Google search
- More than 34,000 diabetes YouTube channels
- More than 3000 diabetes groups on Yahoo!
- Over 41,000 photos tagged as diabetes in Flickr
- More than 4,000,000 diabetes forum discussions
- More than 4,000 views per day (on average) of the Wikipedia diabetes page
- Nearly 50,000 resolved questions about diabetes in Yahoo! Answers
- 1,000's of diabetes related groups in Facebook

The amount of information from these sources is too vast, reiterative and ever expanding to be processed for ADR reporting meaningfully and economically. The rapid, indiscriminate dissemination that occurs via social media could cause a single adverse event to be reported exponentially with enough serial distortion that would render the determination of duplicity impossible. This then provides the very real potential for signal dilution and false positive signal generation.

Case verification of any events garnered via the internet has proven very difficult because the quality of information is poor, the reporter refuses to disclose their contact information, and screening is difficult due to lengthy and reiterative chats between a

myriad of people. Direct reporting of confirmed serious adverse events typically does not occur through social media. Instead, these are most often reported through traditional routes where the patient's clear intention was to report a serious ADR. The majority of serious adverse events seen on social media outlets are hearsay reports that cannot be confirmed. There have also been many instances where persons have deliberately spread misinformation about adverse events because of their personal beliefs, desire for notoriety, or even because they hope to benefit financially.

Additionally, important information that is relevant to evaluating cases is frequently not available - for example, age and gender of the patient, time to onset and outcome of the event, dose of the medication in question, concomitant medications, confounding factors and background disease, duration of exposure and action taken. The case reports have been sparse in the level of detail provided and therefore insufficient for any meaningful assessment, presumably because the patient had not intended to report an ADR. Lastly, the effort and resources used for follow-up and confirmation of these reports consume resources that compete with those that are currently used to identify bona fide signals.

The reliability, quality, and utility of these reports must be carefully considered within the context of the impact this exponential volume may have on existing pharmacovigilance systems and safety surveillance efforts. This could result in the potential to significantly and adversely affect public health by generating the appearance of more adverse events than really exists. Generation of false positive signals or dilution of important signals has the potential to impact public health negatively and falsely change the benefit-risk profile of a medicinal product. This has the downstream effect of prescribers and patients making medical decisions on inaccurate information. Future pharmacovigilance guidances need to be creative in meeting the challenges of new information technology in a more efficient and effective way without detracting attention from real safety issues.

Merck advocates that the responsibility for web-based adverse event management should be dependent on the level of company intentional involvement in the site. In addition, any standards or policies developed by FDA should recognize the distinction between a communication with the intent to report (e.g., patient or other reporter contacts the manufacturer or FDA through toll-free telephone number or the filling out of an ADR form made available on a company website) versus a communication that is a general discussion with other consumers with no first hand knowledge of the report (e.g., consumer chats with other consumers about an event they heard in the news).

We have presented below several recommendations that seek to mitigate and/or resolve the above issues.

1. For company-sponsored web-based media within the sponsor's control, we propose:
 - A. Sponsors should screen areas of websites under their control for identification of suspected ADRs.

- B. To identify any pattern related to the safety of the product from chats entered on a message board on a company controlled website, a periodic review of the message board (monthly or quarterly) should be conducted as part of the company routine signal detection process, but this information would be considered non-validated until the event can be confirmed through contact with the reporter. The definition of identifiable reporter should be “an individual that is privately contactable” (e.g. provides associated email address).
 - C. Reports from social media should be managed and assessed separately from other sources of data (e.g., randomized controlled trials, observational data, scientific literature, and spontaneous data) obtained through traditional reporting mechanisms.
2. For web-based media not under the sponsors’ control, we propose:
- A. Sponsors should not be required to monitor any web-based media not within its control.
 - B. Any safety data discovered by the sponsor during review of independent web-based media should be considered non-validated until the event can be confirmed through contact with the reporter. The definition of identifiable reporter for independent sites should be “an individual that is privately contactable” (e.g. provides associated email address).
 - C. During review of independent web-based media, sponsors should not be required to screen video or audio postings for adverse event reporting purposes. If the source of the video or audio posting is privately contactable (e.g., meets the definition of an identifiable reporter) then the sponsor should follow-up with the reporter and provide a toll-free telephone number and an ADR form for the relevant adverse event information to be reported.