REGULATORY FOCUS

Proactive Regulatory Intelligence Communication

By Emily Huddle and Kirsten Messmer

This article focuses on regulatory intelligence communication approaches for medium to large companies and highlights the advantages and disadvantages of each.

Introduction

To stay current with the rapidly changing landscape, regulatory affairs professionals must monitor and identify pertinent regulatory information on a continual basis. This information must then be analyzed and interpreted for the application and implications to team projects, the organization and potentially other partners or clients. Generating this intelligence is just the first step. Communication is an important next step to ensure intelligence is implemented, whether to facilitate efficient drug development or a successful regulatory strategy. Communication strategies might depend on the type of information, company size, industry type (e.g., pharmaceutical, biotechnology, contract research organization (CRO), consulting, etc.) and audience size.

Compliance with regulatory requirements is integral to the research, testing, approval and continued ability to market new medicinal products. As regulatory approvals are sought in new markets, the spectrum of regulatory requirements likewise will multiply. The rapid development of new scientific and technological advances has demanded an ever-increasing pace of new regulatory guidance to ensure the development of safe, effective and high quality medicinal products. Additionally, new precedents are established in the form of innovative trial designs, endpoints and statistical analysis to answer scientific and regulatory questions during the drug development process. It is an essential part of a regulatory intelligence (RI) professional's role to follow these updates/trends, analyze the impact to the organization and disseminate the information more broadly.

The RI professional's responsibilities are best summarized within the Drug Information Association Regulatory Intelligence Working Group definition of regulatory intelligence:

"The act of gathering and analyzing publicly available information. This includes communicating the implications of that information and monitoring the regulatory environment for opportunities to shape future regulations, guidance, policy and legislation."[1]

The specific responsibilities of an RI professional will depend on a variety of factors, including business needs, company size and the background and experience of the individual. Assigned RI responsibilities also will depend on whether the person is solely dedicated to the RI role or only devotes a portion of time toward RI. Regardless of whether it's a dedicated or part-time role, it is paramount that pertinent regulatory intelligence be effectively captured and communicated via the appropriate channels in order to reach its intended audience so it can be leveraged for the greatest benefit.

The presentation of RI most likely will depend on the intended audience or customers and the type of information. The term customers can refer to individuals within the same company such as regulatory affairs colleagues or other departments, or may be outside of the company, in the case that services are provided to external clients, partners and collaborators.

The intended use of RI also determines how polished the output from the RI is required. For example, if the RI will be used as part of a larger report or contract proposal, it may be provided in a raw format since it will be shaped by the entire team to fit into the overall presentation. On the other hand, something that will be provided directly to the ultimate customer will need to be extremely polished.

The communication of RI in response to a specific request or ad hoc query is not the subject of this article, but will be addressed in a follow up article. Proactive communication as addressed in this article has to be concise, precise and with actionable RI clearly identified.

Proactive Communication of Regulatory Intelligence

Essential to the role of an RI professional is the proactive communication of changes in legislation, regulations, guidance documents and other pertinent regulatory updates. An effective communication strategy includes dissemination to key stakeholders to ensure implementation of relevant changes, with potential impacts to regulatory compliance, time and cost-effective medicinal product development and/or successful regulatory strategies.

The US Food and Drug Administration (FDA) issued a suite of draft guidance documents to support efficient development of oncology products (e.g., first-in-human-expansion cohorts, master protocols, adaptive clinical trials, etc.). While analyzing the guidance documents, it is essential to highlight key aspects that could provide gains in efficiency or cost-effectiveness through the use of innovative trial designs described within the guidances:

- First-in-human expansion cohorts:[2] A single protocol allows seamless progression from dose-escalation phase to three or more expansion cohorts addressing specific research questions.
- Master protocols:[3] Umbrella, basket and/or platform trial designs allow the assessment of multiple therapeutic products and/or multiple indications or both within one protocol.
- Adaptive clinical trials:[4] Adaptive trial designs allow prospectively planned changes to one or more aspects of trial design based on the data accumulated from patients.

The communication strategy to disseminate RI depends on the size of the company and on the overall impact and relevance of the guidance documents to the company.

This article will focus on communication approaches for medium to large companies (including but not limited to pharmaceutical, medical device, contract manufacturing, contract research companies and consultancies). For small companies (less than 100 employees for the purpose of this article), it may be likely to inform all employees across the company at the same time. The complexity of departments and reporting lines within a larger company may necessitate more defined communication strategies.

In the case of large companies with multiple oncology products at different stages of development the suite of oncology guidance documents likely has a major impact on planning of future oncology clinical trials. Therefore, the information will need to be communicated in various ways to ensure all applicable stakeholders are informed.

Horizontal Communication

Horizontal communication can be described as "flat" and involves disseminating information across a team, for instance a RI professional's regulatory affairs colleagues involved in oncology clinical trials. In turn, these colleagues would engage the appropriate stakeholders in order to discuss the new guidance documents and to implement a regulatory agency's recommendations to support their medicinal product development programs and regulatory strategies. However, this horizontal communication only would address projects already under way or are upcoming. A guidance of significant impact also should be leveraged in communication with future customers, i.e., business development.

Using the example of the oncology guidance documents, multiple scenarios come to mind. Two of them are:

1. When communicating with a future potential customer at a very early stage of development, the first in-human expansion cohort guidance could be explored for applicability to that customer's program. Highlighting the applicability of the guidance and how it could be applied to the program based on the presenting company's experience likely would instill confidence in the potential client that the presenter is well-positioned to support the early stage program cost and time efficiently.
2. In the second scenario, the business development department is talking to a later stage client with a product that might be used in multiple indications. Here, to showcase the presenting company's expertise, the implementation master protocol guidance and internal experience can be leveraged to demonstrate an efficient drug development program to the potential client.

   The necessity of communicating regulatory changes beyond a single department or team can be determined by a triage team in order to escalate the new information to a broader audience or what would be considered vertical communication.

Vertical Communication

Due to the broad impact of the suite of oncology guidance documents and implications outside of the regulatory affairs department, their release also should be communicated vertically, that is upward to senior leadership and across to the impacted functional areas or departments. Depending on the company size and choice of communication strategy will dictate whether the communications are initiated by a single person or a team, such as a cross-functional committee. A single person could communicate the potential impact to other department heads who then would be responsible for further dissemination of the information among their respective teams. Likewise, a cross-functional team comprised of pertinent members from various departments could determine the impact and then disseminate the information across their respective teams.

Companywide Communication

Information that will affect the operations of multiple departments within a large company necessitates a communication channel that will reach a wide audience in order to educate internal stakeholders on the pertinent changes as well as overall impacts to the organization. The format used to distribute information on a company wide level depends

on the content to be provided and audience expectations. Some examples of formats are email alerts or blasts, bulletins and newsletters.

Email alerts or blasts generally should contain high-level, easy-to-understand information and timely distribution is paramount. An effective email alert or blast, although an informal way to distribute RI to a large audience, should be focused and concise, concentrating on key details describing the change, the impact to the organization and any pertinent deadlines or timelines.

For less time-sensitive news, it may be more logical to compile numerous regulatory news items together in a bulletin, newsletter or digest—each of which serves a slightly different purpose. The RI professional should consider these forms of wider communication, taking into account the definitions and aims of each. From the Merriam Webster Dictionary, the definitions are as follows:

Bulletin: "A brief notice issuing usually from an authoritative source."[5]

Newsletter: "A small publication (such as a leaflet or newspaper) containing news of interest chiefly to a special group."[6]

Digest: "A summation or condensation of a body of information …," "a product of digestion."[7]

Each of these publication forms serve a specific purpose and based on the definition of RI presented earlier in the article, "The act of gathering and analyzing publicly available information …" a newsletter or digest likely would be the most appropriate communication tool. Independent of how the type of format is used to communicate information at a companywide level, it is critical to include references and/or links to the original sources of information and/or further information.

A bulletin generally is a compilation of news with high-level updates. It can serve to keep a special interest group updated and/or to inform other stakeholders of updates in a certain area. A bulletin also can cover a wide array of topics, providing information in short summaries. However, within a bulletin, these summaries only convey very limited information without the provision of any type of further analysis. Often, the bulletin summaries are based on a single news release or published paper. A bulletin strictly serves to inform of events and left to the readers to draw their own conclusions or analysis.

A newsletter, according to the Merriam Webster Dictionary is a small publication conveying information to a special interest group, such as a regulatory affairs department. Newsletters and the articles within them come in all shapes and sizes. Similar to a local daily newspaper, depending on the topic and author, the analysis and depth of information will vary. The distinction between a newsletter and digest may be somewhat blurry, but a digest implies some digestion or interpretation of the information, in this case, into actionable RI. Independent of the name, a recurring RI publication should be: timely, addressing topics important to the company's and/or client's business needs; supported by references; informative; and concise.

The issue of timeliness can be subjective and can vary from company to company. The pertinent question to consider is: "When does news become old news for the company?"

The topic selection to be covered by each issue of the newsletter/digest will be guided by the importance to the company's business, e.g., a device company will be less interested in updates to guidance and legislation addressing pharmaceuticals unless some its products are combination products. Similarly, if the company or clients are operating in a very specific market, news outside of that market will be less important unless the market may be a future target market.

In the example of the suite of FDA oncology draft guidance documents, it would be outside the scope of a newsletter/digest to go into significant detail for each of the guidance. Providing high-level summaries, relevance for ongoing and future projects, providing

links and/or reference to the guidance document or any other source of information provided would be an appropriate amount of detail to include within a newsletter or digest article.

As a general rule, any news article should be well written, free of grammatical and spelling mistakes and easy to understand. Summaries, bullet points and call-out boxes could effectively highlight the main points of a longer article. This article will not address issues of confidentiality since it assumes information would be drawn from publicly available sources.

The composition of the newsletter/digest and length of individual articles depends on various factors that may include:

- Is the topic being addressed very focused (e.g., specific guidance – short article) or has a long history or complex ramifications (e.g., larger ethical issue – longer article)
- Number of updates or guidance documents released within the time period covered (e.g., the suite of oncology guidance documents, gene therapy guidance documents)
- Number of countries covered within the newsletter/digest (in the case of cross-country collaboration)

As noted earlier, it's critically important to include references to information obtained from other sources so as to avoid the act of plagiarism, which is, by definition, passing off someone else's work as one's own. Plagiarism is a significant issue and sometimes copying as few as five consecutive words in the same order can be considered plagiarism and carries the charge of literal fraud. However, there is no fast and safe rule.[8] Citing sources of information appropriately will clearly indicate where the information came from and how conclusions were drawn.

Copyright infringement, which is the unauthorized use of a work protected by copyright law, is also an important potential issue to avoid. The RI professional responsible for issuing any information that contains copyrighted works must first ensure that proper authorization has been secured from the copyright holder for the intended use, republication, etc., of such a protected work. If the RI professional is uncertain about compliance with copyright law, advice of legal counsel should be sought, particularly as copyright law varies between jurisdictions. Further, the use rights authorized by individual copyright holders varies widely as well.

For example, looking at FDA and the European Medicines Agency (EMA) only, the authorizations granted and conditions required by each entity for use of content made available on their respective websites are handled very differently:

FDA: FDA's website cites that "unless otherwise noted, the contents of the FDA website (www.fda.gov)—both text and graphics—are not copyrighted. They are in the public domain and may be republished, reprinted and otherwise used freely by anyone without the need to obtain permission from FDA. Credit to the US Food and Drug Administration as the source is appreciated but not required."[9]

EMA: EMA's website states that "in particular, unless otherwise stated, the Agency, according to current European Union and international legislation, is the owner of copyright and other intellectual property rights for documents and other content published on this website."

"Information and documents made available on the Agency's webpages are public and may be reproduced and/or distributed, totally or in part, irrespective of the means and/or the formats used, for non-commercial and commercial purposes, provided that the Agency is always acknowledged as the source of the material. Such acknowledgement must be included in each copy of the material."

"Citations may be made from such material without prior permission, provided the source is always acknowledged."

"The above-mentioned permissions do not apply to content supplied by third parties. Therefore, for documents where the copyright vests in a third party, permission for reproduction must be obtained from this copyright holder."[10]

Another consideration is the layout of the finished publication. Newsletters/digests usually contain multiple pages of text with imagery and other features to enhance readability. Can a busy executive grasp the main updates from quickly looking over the article? Choosing appropriate vehicles to highlight pertinent information and conclusions is paramount to inform the busy reader with little time. The full article text always will be available for further information.

Summary

New regulations, guidance documents and other regulatory information are issued from multiple agencies on a daily basis. The RI professional is responsible for identifying information relevant to their company and/or client and also evaluating its impact. A communication strategy for identified regulatory intelligence is a critical next step. Either a horizontal, vertical and/or companywide communication flow could be considered, depending on the essential stakeholders that need to be notified. There are a variety of formats that can be employed to communicate RI, such as email blasts or alerts, bulletins, newsletters or digests. Depending on factors such as time sensitivity, topic complexity and number of updates to be communicated, one format may be more advantageous over another.

Utilization of features such as call-out boxes, bullet points, pictures and graphical representations of data may help with the readability and comprehension of the information. While making sure RI summaries are well-written, consideration also must be paid to appropriately referencing sources and legal restrictions regarding copyrighted information.

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