

Law and Order

With all the new regulatory standards currently under development, how is the life sciences industry supposed to know which are most important and prioritise their implementation?

Jim Nichols at Thomson Scientific, Ligent Regulatory Solutions has the answers



Jim Nichols has been at the forefront of the technology industry for over 15 years. As VP of Product Strategy and Marketing of Thomson Scientific's Ligent Regulatory Solutions business, Jim is responsible for product strategy and overseeing the delivery of the complete line of products and services. During his five-year tenure, Jim has driven a number of significant milestones in the company's history namely: defining the market and corporate propositions behind many of its leading publishing and regulatory products; spearheading the company launch into Japan; and managing the company market transition from ESPS to Ligent. Jim garnered much of his management expertise during his time at Intracorp, where he directed project management and software operations. Jim was awarded his degree in Mathematics from the Pennsylvania State University.

First, one must understand the organisations that are developing these standards, and the level of acceptance within the industry and throughout the regulatory agencies. The purpose of this article is to introduce the latest standards and those that may impact your organisation in the next few years.

THE HISTORICAL BACKDROP

Standards development has come a long way in the pharmaceutical industry. By the late 1970s, it became clear that there was an urgent need to harmonise requirements for new drug registrations. The goal of harmonisation was to minimise delays in the approval and marketing of safe and efficacious new therapies for patients at a time when the cost of health care was continually rising.

In the 1980s, harmonisation of regulatory requirements was pioneered by the European Community, and the success that was achieved caused other regions to take notice. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was formed in 1990 at a meeting hosted by the European Federation of Pharmaceutical Industries and Associations (EFPIA) in Brussels. Representatives of industry associations and regulatory bodies from Japan, Europe and the US met to plan an international conference. Through the commitment of all parties to the objectives and outcome of ICH, there has been significant improvement in the efficiency of the process for developing and registering new medicinal products in those regions. ICH however, is not the only standards development organisation that creates standards for the life sciences industry

The Clinical Data Interchange Standards Consortium (CDISC) has been working to establish worldwide industry

standards to support the electronic collection, exchange, submission and archival of clinical trials data and metadata for medical and biopharmaceutical product development. They also want to share in the recognition of creating regulatory submissions that allow for flexibility in scientific content and are easily interpreted, understood and navigated by regulatory reviewers.

Health Level 7 (HL7) was founded in 1987 and was granted ANSI accreditation in 1994 operating in the healthcare area. Many standards organisations focus on requirements for a particular portion of the healthcare space, whereas HL7 focuses on the requirements of the entire healthcare organisation through technical committees and balloting of messages through its membership base. The technical committees are directly responsible for the content of standards. The Regulated Clinical Research Information Management (RCRIM) technical committee is responsible for most of the initiatives affecting the pharmaceutical industry. Structured product labelling (SPL), regulated product submissions (RPS) and structured clinical trial protocol (SCTP) are just a few of the active projects within HL7's RCRIM technical committee.

RECENT SUCCESS OF STANDARDS IMPLEMENTATION

There are many potential roadblocks to standards implementation with regulatory bodies. Local laws, level of

technology advancement or required training can present significant challenges. This typically results in a phased approach to implementation from country to country.

Application Format

Many steps go into creating and receiving support and acceptance of new standards. The most notable success, on a global scale, was the Common Technical Document (CTD). The CTD, an ICH developed standard, harmonised the organisation and structure of a marketing application for a new drug. The CTD standard was finalised by ICH in November of 2000. The regulatory authorities in the three regions quickly moved to adoption, with the EU and Japan requiring all new applications to be submitted in CTD format by July 2003.

In an effort to further streamline processes, and leveraging the success of the electronic new drug application (eNDA) and electronic biologics license application (eBLA) at the FDA in the US, ICH quickly moved to the creation of an electronic delivery standard for the CTD, more commonly known as the electronic common technical document (eCTD). The eCTD was finalised in July 2003. While many regions now accept applications submitted in the eCTD format, the technology investment required by the regulatory bodies and reviewer training requirements has resulted in slower agency adoption than originally anticipated. As a result, the adoption of the eCTD format within life sciences organisations is not yet widespread, and it is unlikely that any regulatory authority will make the eCTD mandatory before 2009.

Labelling

The hottest topic for the past 18 months surrounding standards development has been the new extensible markup language (XML) based labelling standards; the HL7 standard structured product labelling (SPL) for the US, and Europe's product information management (PIM) standard. While these standards provide significant benefit to the regulatory agencies in terms of review of labelling changes and consistent dissemination of information, it presented an entirely new authoring paradigm for those individuals that produce labelling content. The shift to XML required adoption of new technology

and a much better understanding of the content, and potential reuse of the content, across labelling types.

PIM was the first XML-based labelling standard to be proposed. The project started in 1999 with the goal of streamlining the submission and review of product information in Europe. The first PIM submission to the European Agency for the Evaluation of Medicinal Products (EMEA) was due in June of this year. It is expected that this format will become mandatory for all submissions utilising the centralised procedure in 2007.

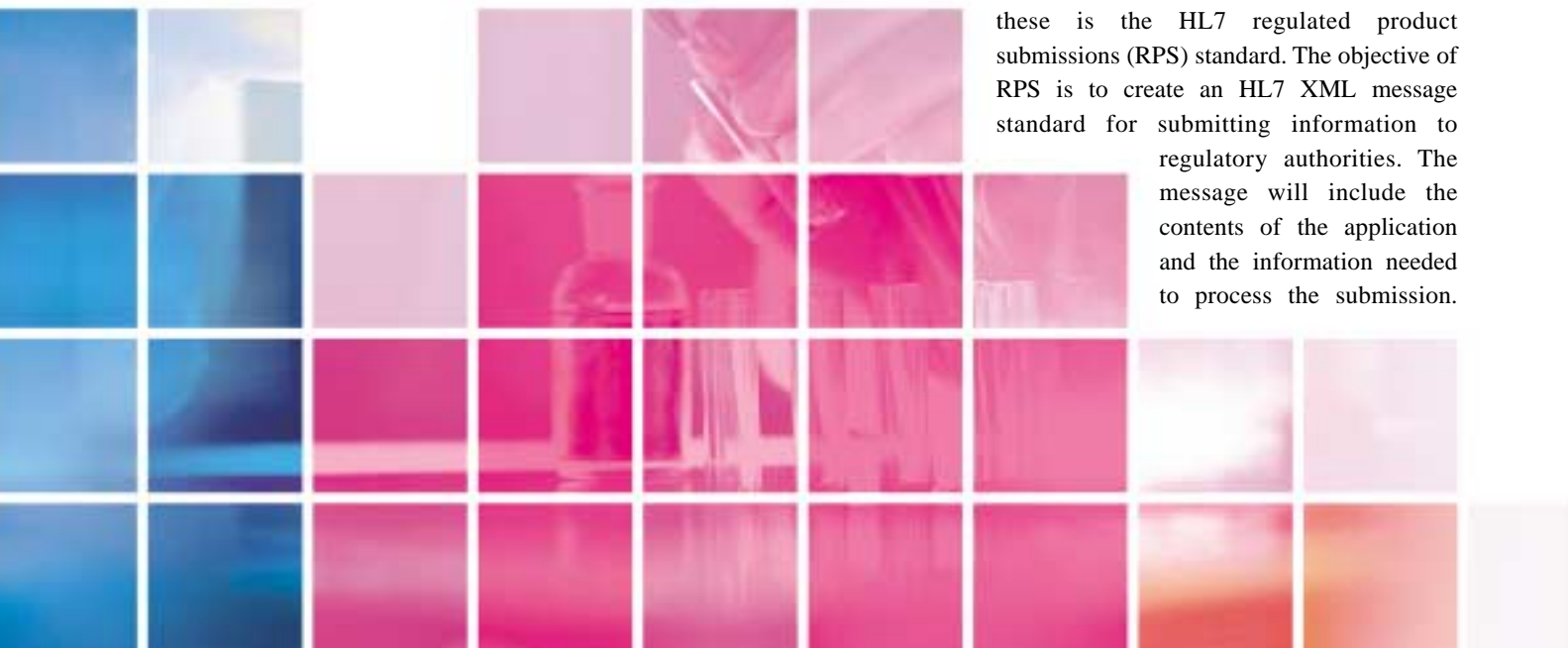
The SPL initiative aims to make patient safety a priority, with electronic prescribing and health records management on the horizon this will be imperative. The SPL standard was the most quickly adopted electronic submission standard in US history. Since November 2005, the US FDA has required that labelling information for new drugs be submitted according to the SPL standard. The SPL standard is continually evolving as well, which makes implementation even more challenging. In June 2006, with the addition of the physicians labelling rule (PLR) to SPL, the pertinent labelling information is at the top so that consumers of the information will be able to easily determine the important aspects of the use of the drug.

Companies have had to dedicate resources to understanding the SPL and PLR requirements, and to determine the best methodology for migrating their package inserts to the new format. Due to a lack of experience internally, many companies decided to outsource the conversion of their labels. As software vendors were learning about the standard at the time it was being developed, few have offered off-the-shelf software products that can be utilised to produce SPL. In fact, few organisations have adopted this technology in the hope of implementing a single solution that can be utilised to produce both PIM and SPL/PLR compliant output.

STANDARDS TO WATCH

Regulated Product Submission

There are a couple of standards in development that could make a significant impact on the life sciences industry and its electronic information exchange. One of these is the HL7 regulated product submissions (RPS) standard. The objective of RPS is to create an HL7 XML message standard for submitting information to regulatory authorities. The message will include the contents of the application and the information needed to process the submission.



RPS is intended to apply to submissions for human and animal drug products and medical devices. The primary goal of the RPS standard is to make re-use of documents and document components a priority for ease of use resulting in a seamless transition from an investigational new drug application (IND) to a marketing application. This standard will represent a significant shift in document handling and submission to the FDA. With this model, the industry should be able to achieve a real 'submit once, use many' approach for documentation submitted to the FDA in support of clinical trial and marketing applications.

This standard has been progressing through the HL7 process, and was recently approved as a draft standard for trial use. Over the next six to eight months, the RPS team will be testing the message and determining the necessary harmonisable artefacts for sending to the Biomedical Research Integrated Domain Group (BRIDG) team. It is expected that this standard will be adopted by the FDA shortly after being accepted as an HL7 standard.

Biomedical Research Integrated Domain Group

BRIDG was formed with the goal of developing standards for the exchange of clinical trial information – basically a bridge between different models of clinical trial information. The BRIDG model is based on shared semantics of regulated clinical trial research. It is also the foundation for application

and message development for HL7, the Cancer Biomedical Informatics Grid (caBIG) and CDISC. The RCRIM technical committee adopted BRIDG as their domain analysis model in 2005. BRIDG has active subprojects on topics such as trial design, statistical design, electronic data capture, clinical registries and adverse events. It is expected to have a significant impact in the collection and sharing of clinical trial information.

CONCLUSION

All in all, standards in the life sciences industry have made significant progress in the last 15 years, with both industry and regulatory bodies acknowledging the benefits. It can only be anticipated that these standards will continue to evolve and new standards will be proposed. As regulatory professionals, we have been asked to broaden our horizons and embrace the changes before us – acknowledging that information technology will be a much more prevalent in our daily interactions with agencies. These new standards that we must come to terms with are designed with one ultimate goal – providing safe and effective healthcare to patients. As we are thrust forward into the age of electronic records and information exchange, we should embrace this opportunity to grow professionally. ♦

*The author can be contacted at
james.nichols@thomson.com*