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Race to Comply with FDA ESG Guidelines

By James Brown

For life sciences companies, paper-based commercial material submissions do not cut it anymore, not only when it comes to automating processes for improved efficiency, but also in the face of rapidly approaching new regulatory guidelines on electronic submissions from FDA. This article discusses the urgency as well as the findings of a 2015 global commercial content management study.

Each year, life sciences companies send more than 80,000 promotional material submissions to the US Food and Drug Administration (FDA) for approval. Most of the submissions are done manually – paper documents are saved onto disks and are mailed to FDA. Before long, that will change. FDA has set a deadline of May 2017 for companies to start sending NDA, ANDA, BLA and master file submissions as eCTDs via the Electronic Submissions Gateway (ESG), a central transmissions point that automatically routes submissions to the proper FDA office for review. Commercial IND submissions also must be submitted in the same format and mechanism beginning 5 May 2018.[1] The good news is FDA will be able to process Form 2253 submissions in higher volumes and at a quicker pace, but it also means life sciences companies will need to change their internal processes and possibly, their technologies, and do so quickly to beat the buzzer.

A handful of life sciences companies, seeing this as an opportunity to go paperless and improve efficiency, have made strides with this transition. However, too many others lag behind as confirmed by Veeva Systems' global, industry-wide survey.[2]

Electronic submissions to FDA are not new. In fact, the number of electronic submissions increased 35-fold between 2006 (58,664 submissions) and 2014 (2,100,772 submissions), and continues to climb. However, these submissions have been mostly for New Drug Applications (NDAs), updates on product safety codes and new indications resulting from clinical studies. Those submissions are sizeable and document trials with long timeframes − from six months to

several years for a large clinical study. Hundreds, if not thousands, of documents compile those submissions.

FDA submissions for commercial materials are smaller in size, but similarly intense due to the faster pace of commercial content development and huge number of promotional pieces a typical life sciences company produces. A submission to the governing health authority is required for every single piece of marketing content, including brochures, ads, website copy plus less traditional, but increasingly crucial, digital promotions such as patient or healthcare professional apps and iPad presentations.

Inefficient Processes Pervade

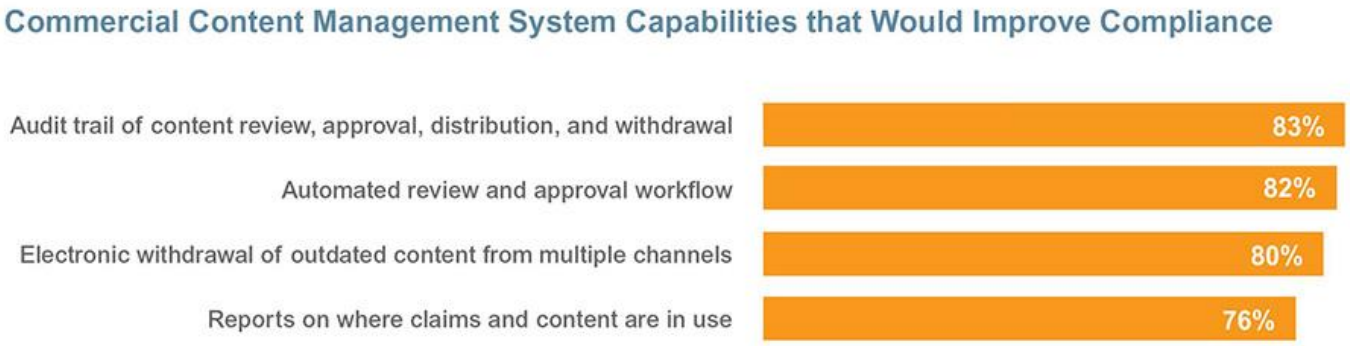
Historically, submissions have been printed on paper and mailed to FDA. In recent years, these submissions have been saved electronically as PDFs, burned onto disks and then mailed, but it's still largely a slow manual process, difficult to track and cumbersome.

The problem is exacerbated by explosion of content today – life sciences companies spent $4.5 billion on marketing prescription drugs in 2014, up from $3.5 billion in 2012, according to research by Kantar Media.[3] Combine this volume with the growing number and complexity of digital channels actively used to distribute promotions worldwide, and it is clear companies are exposed to an alarmingly large risk of error along with all of the associated regulatory and business consequences.

"The sheer quantity of promotional materials that has to be reviewed and approved internally, then submitted to the FDA, is mind-numbing and the demand for accuracy has never been more stringent," said Stephanie Bova, head of Europe and Canada, at Takeda Digital Accelerator Group. "Performing these tasks manually is a slow, inefficient process and because materials go through the hands of so many people, the chance for errors is relatively high."

Veeva's 2015 study, which looked at the impact of changing from paper-based to digital content management processes, revealed startling obstacles across the digital supply chain – from content creation and review to expiration and withdrawal. Roughly half (52%) of respondents in the global study report automating review and approval, but most say they're missing some, if not all, capabilities that are essential for compliance. The vast majority (81%) of respondents, for instance, cannot report on where claims and content are in use. Almost half (49%) do not have primary systems that provide a full audit trail to manage commercial content throughout its lifecycle, yet most report that this capability would improve compliance - **Figure 1, below**.

Figure 1



In addition, most of the companies surveyed in the Veeva study (88%) said their content management function is scattered among many systems and methods, suggesting serious break points in existing processes that breed inefficiency and risk of noncompliance. In fact, respondents said that, on average, they use four different systems for commercial materials management with 31% reporting to use between five and 20 systems. Life sciences companies with different systems for different regions, as an example, often end up creating similar product marketing materials for their regions concurrently, duplicating efforts that could be streamlined with a single, centralized solution that provides global access to core content. Sanofi Pasteur MSD recently adopted a new, end-to-end commercial content management solution to centralize content production while providing local regions with the ability to adapt core content to meet specific regulatory or cultural needs. And, because the solution is in the cloud, its global agencies have easy access to promotional assets…further streamlining development. Medical/Legal/Regulatory (MLR) reviews of content also are streamlined when all stakeholders have access to a single source of truth in a global, end-to-end system. In the first year of system use, Sanofi Pasteur MSD projects will reduce the number of hours spent conducting MLR reviews from 795 to 494 – a 38% reduction. And in years two through five, the company forecasts that number will improve to a 50% reduction annually.

"With a single promotional content master library that local product managers can quickly access, search, and find what they need quickly. The gain is amazing. We expect a return on investment in less than six months due to content reuse alone," said Alexandre Gultzgoff, deputy director of IT at Sanofi Pasteur MSD "As important, we can see what asset is being used where, when and for what purpose for greater control."

However, one of the most pressing compliance concerns among life sciences companies is preventing regulatory citations from health authorities by ensuring outdated content is retired wherever it is used. Yet, 78% of survey respondents said they are unable to electronically withdraw content from multiple channels using their primary system. When asked about the principal method used to verify that content has been withdrawn from the market, most (76%) say they do not perform any verification, manually or with the help of third parties.

Globalization Compounds the Problem

Life sciences companies that manage massive amounts of commercial content via paper-based processes are not just saddled with widespread inefficiency; discrepancies also arise when brand teams in many departments on several continents have different versions of a promotional piece. The results of the Veeva study show how pervasive these problems are today: 81% of companies surveyed expressed a need for automated review and approval workflow for commercial content, and 71% said they would benefit from global digital asset management that provides centralized access to all content. With this type of access, global team members can review and revise the most current, updated version of commercial materials. Further, regional affiliates can save time and resources by reusing approved content from a central, authoritative digital asset library.

Without these capabilities, a warning letter from FDA instructing a company to remove all claims from promotional materials for a given product can seem harrowing. Last year, nine companies received letters from FDA's Office of Prescription Drug Promotion – a record low.[4] While this is down from 10 in 2014, the price of noncompliance remains high. According to the US Department of Justice, drug firms agreed to pay $13 billion between 2009 and 2013 for fraudulent marketing practices.[5] Then again, government fines are just one price to pay and do not encompass the expenses from lost productivity, delays to market, and damaged reputations.

Most respondents to Veeva's 2015 survey (81%) are unable to report specifically where claims and content are used globally. To locate and remove a single claim, a company might have no choice but to pull an entire campaign, which leads to lost promotion time as many multichannel assets are stripped of usable, approved content and wastes valuable marketing resources. It also drains the regulatory department and slows the review and approval of other promotional materials in the queue that are not affected by that regulatory warning. According to data compiled from Veeva clients, life sciences companies reduce the potential productivity of their review team by about 25% due to unnecessary rework.

All Along the Audit Trail

Where is your commercial content? What department is editing? What countries have the latest claims? Most companies cannot answer these crucial questions because they lack a reliable, complete audit trail. Almost half (49%) of Veeva survey respondents conceded that while they don't have primary systems that provide a full audit trail, having that capability would improve compliance.

With a full audit trail, outdated materials or claims can be pulled, revised, and redistributed quickly – mitigating the risk of noncompliance and saving both marketing and regulatory teams the chore of manually searching for every instance of a claim or asset. Overhead costs for the review, rework, and distribution of materials plummet. Indeed, even marginal cost savings across the many stages of the digital supply chain can result in significant savings. Likewise, a digital system with a full audit trail and digital asset management frees up regulatory department resources by streamlining approval, re-use, distribution, and withdrawal of materials to global company sites.

Digital Content – No News Is *NOT* Good News

The number of warning letters from the FDA is slightly less than previous years, which sounds like a good thing, but for life sciences companies trying to hone in on the FDA's standards for commercial materials, no news isn't necessarily good news and could actually increase risk long-term when it comes to non-traditional content. Of the nine letters issued by OPDP in 2015, nearly half involved digital promotional materials.[6] "If the agency is silent through the guidance process and silent through the enforcement process, it leaves a large swath of uncharted and unknown territory, not just for companies, but also for patients seeking health information through digital platforms," says Mark Senak in his blog, *Eye on FDA.*[7]

"By automating the distribution, withdrawal and update of marketing claims and content, pharmaceutical companies gain more compliance control as well as speed time to market," noted Erik Larsen, head of global content management at Accenture.

With electronic submissions, companies have increased compliance tracking, which allows them to manage the submission process within whatever compliance tools they have already in place. Systems can be designed to automatically enforce FDA submission guidelines are followed by all stakeholders. This leads to a more fluid and uninterrupted submissions process. In fact, 100% of companies using content management systems that support the digital supply chain report satisfaction with their ability to adhere to regulatory standards across channels and 88% are satisfied with their ability to electronically withdraw outdated content.

Time to Get Moving

The life sciences industry is midstream in its transition from paper/manual processes to a digital approach to commercial content management. Over the past decade, more and more companies have automated a portion of the process through the adoption of commercial content review and approval systems. However, continued reliance upon supplemental manual processes or external systems shows that, despite some progress, gaps remain. Most companies cannot compliantly manage all of the crucial commercial content in the digital supply chain using their primary system – especially as new content channels emerge, driving the quantity of content skyward.

Equally important, the industry is racing the clock. With less than 18 months to meet the ESG initial requirements, companies stuck with paper-based claims inventories face the immense task of going digital and transferring their records to fit the new standardized submission forms. A next-generation technology with digital asset management capabilities supporting the full digital supply chain enables compliance while speeding commercial content development, approval, and distribution.

Certainly, the transition to electronic submissions will require process and technology changes. However, the result will not only improve compliance, but also overall efficiency and productivity that extends beyond just the commercial operations team. Since the regulatory department must collaborate with commercial and other operations, the switch to electronic will help improve their productivity and broaden their scope.

Buzzer beaters may make for exciting basketball games, but there is a lot more at stake when it comes to commercial content management today like compliance and heavy fines. As important, there is also a lot to gain including major jumps in productivity, global harmonization and faster time to market.

"Life sciences companies should have a sense of urgency about making the change to electronic submissions," concluded Bova. "Even companies that are well-prepared for the transition should expect the process to take 12 months. Further, the best path forward includes engaging external vendors, determining their strategies for technology and change management and staying informed of the evolving guidance from FDA. Companies have a lot to do on this issue and they do not have a lot of time to get it done, but the end result has the potential to be highly rewarding."

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About the Author

James Brown is vice president and general manager of commercial content at Veeva Systems. He graduated with a degree in biochemistry from Nottingham University in 1992. Brown spent nine years at Merck & Co in sales and marketing roles before leaving in 2001 to start Zinc Ahead. Under his guidance, Zinc Ahead's flagship product, Zinc MAPS was implemented by the world's top 20 pharmaceutical companies for promotional materials management, including medical/legal/regulatory review processes. The solution became established with more than 50,000 users in more than 160 countries, leading to the acquisition by Veeva in 2015. He can be contacted at James.brown@veeva.com.

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