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Labeling Pharma "Green"

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This article presents arguments for the implementation of an electronic labeling system in the life science industries. These systems are capable of generating significant Return on Investment (ROI), while at the same time reducing waste, improving efficiency, and delivering on regulatory compliance requirements.

Introduction

Sustainable manufacturing issues have come to the forefront of current news with the idea of "green" driving many new initiatives. There are many ways to reduce a company's carbon footprint and function in a more environmentally friendly way. These "green" issues, such as recycling, energy and cost reduction, and increased efficiency are not only concerns in industries, such as automobile manufacturing and power plants, but in all industries, pharmaceuticals included.

In pharmaceutical manufacturing, there are many processes that produce large amounts of waste, expend excess energy, increase costs, are inefficient, and can introduce a greater level of risk than necessary. While many processes can become more environmentally responsible and economical, one process that could be improved with minor changes to operating methods is the design, approval, control, printing, and application of product labels. Implementing an Electronic Label Management System (ELMS) can deliver significant improvements that can make a company more "green." Other areas may require significant investment in new facilities, equipment, and systems, but labeling can translate with little relative cost and effort.

It once was true that a regulatory compliant third-party ELMS solution was not available as a Commercial Off-The-Shelf (COTS) product. That is no longer the case and today a pharmaceutical company's IT organization need not develop and maintain compliance add-ons because today the required functionality is built into the product.

Implementation of an ELMS affords many benefits including: waste reduction, cost reduction, decreased risks, and increased efficiency, all of which make a company more productive, sustainable, and "green."

Common Existing Practices versus ELMS

Manual System Summary

The following describes a simplified typical scenario where there is no ELMS in place:

In many if not most pharmaceutical manufacturing facilities today, the typical process begins with a label template being developed within a label design software application. The template creation process normally requires printing many hard-copy examples before the objective appearance is achieved. Once this point has been reached, the label is routed through a manual approval process for review and red-lining. This may take several weeks to complete depending on the circumstances. Finally, a template for the label is approved for printing and application to products - *Figure 1.*

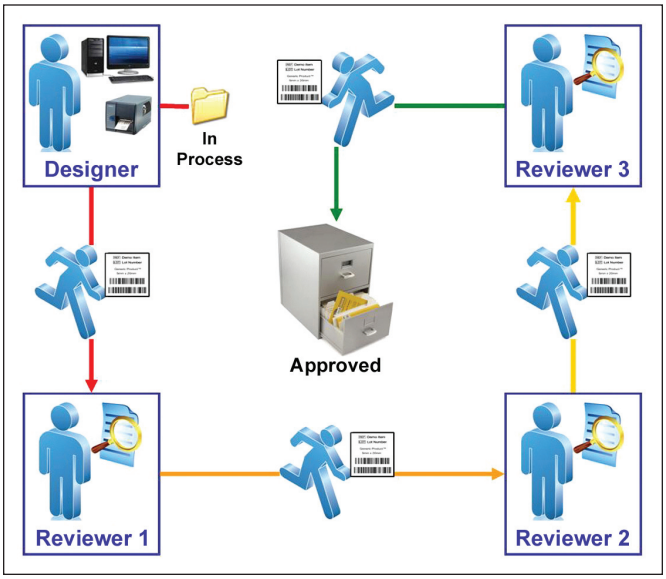

Figure 1. Typical process flow in a manual label review/approval routing process.

When it is time to print, the approved template is merged with variable lot/product data. This is normally a manual process that takes place in advance of the packaging operation in a label printing room, and so requires management,

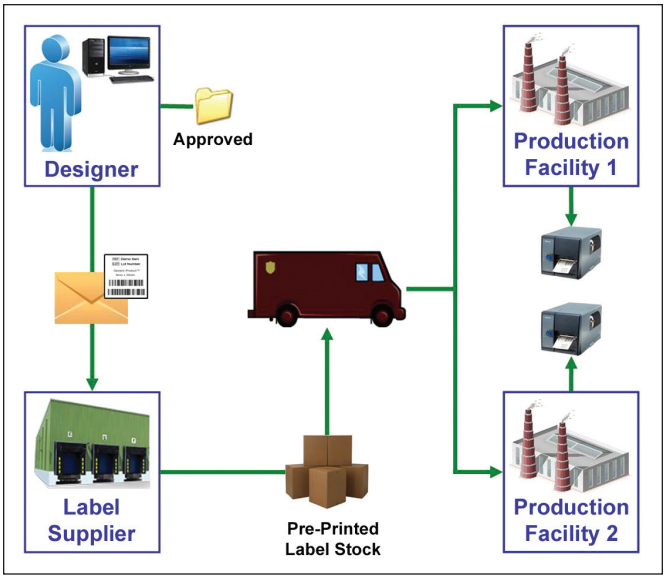

Figure 2. Traditional flow of labels in the pharmaceutical manufacturing supply chain with labels from third party suppliers.

storage, movement, and control of the labels.

At packaging time, the pre-printed labels must be picked and moved to the packaging line. Once at the line, the labels must be verified prior to use. Samples are applied to the batch record and the line is approved for the packaging operation to begin. In many cases, labels are pre-printed by third-party suppliers adding yet another layer of complexity with its associated time, cost, quality, and control considerations - *Figure 2.*

Electronic Label Management System Summary

By contrast, when there is a validated ELMS in place, once a label has been designed, the approval process sends the image as an attachment through a workflow simultaneously to all reviewers - *Figure 3.*

The system architecture can allow for a global approval process. In this case, the company's Wide Area Network (WAN) is used to facilitate communication among the reviewers who can share comments and document feedback electronically in real-time in order to dramatically improve the overall label template approval process - *Figure 4.*

Once the approval workflow is complete, the label template version is approved with its effective begin and end dates. The template may then be assigned to product(s) lot(s) at the time of packaging.

The approved label image is then ready to accept variable lot data. The ELMS may have been interfaced with a validated ERP or other database(s) so that the variable information such as lot number and expiration date are available for merging into the template at print time. Labels are then printed on demand and applied to containers, cartons, shippers, bundles, and pallets during the packaging process for a fully automated print-and-apply process. The need for pre-printing and all of the related costs, lead times, and controls have been eliminated.

Benefits of an ELMS

Regulatory Compliance

Are there significant efficiency improvements and waste reduction benefits from implementing an ELMS? Yes, definitely. However, in today's regulatory environment, for many companies, the primary driver for implementing an ELMS is compliance. According to one source, heavily regulated industries are now spending more than 40% of their IT budget on compliance.[1]

Many companies might have recognized the benefits of automation and jumped to implement electronic systems for labeling, perhaps a bit too soon. Most systems available until only recently were not developed with regulatory compliance in mind. So, somewhat ironically, replacing a manual system with a more efficient electronic system might have been a perceived hurdle that many companies did not care to jump

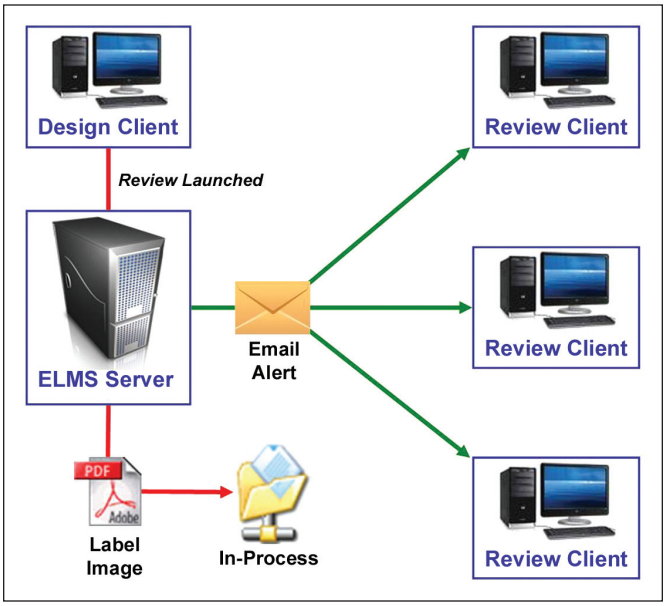

Figure 3. New or updated label review notification process via email using an Electronic Label Management System (ELMS).

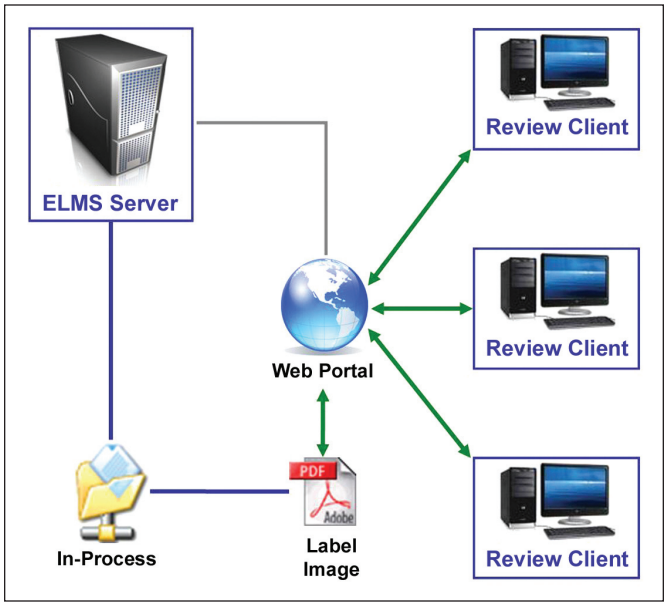

Figure 4. New or updated label design review via the internet in an Electronic Label Management System (ELMS).

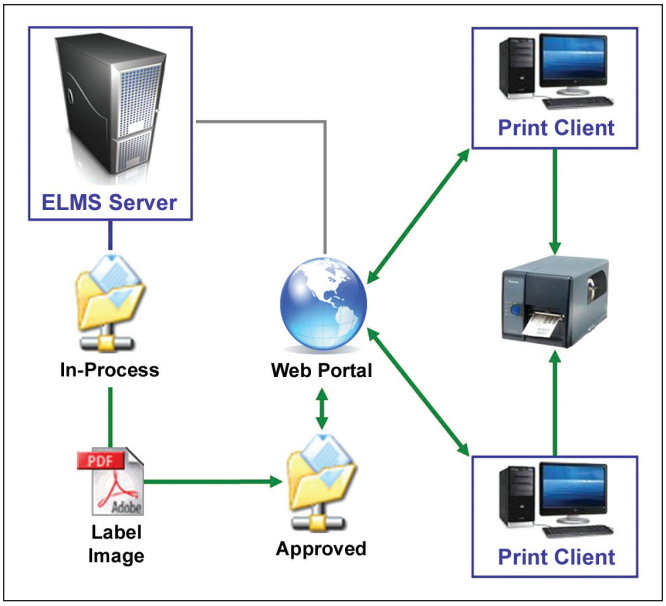

Figure 5. Printing process via Web client print portal in an Electronic Label Management System (ELMS).

over until it was seen as an absolute need. That is no longer the case, because today compliant ELMS solutions are readily available in the marketplace.

FDA's regulation 21 CFR Part 11 section 11.1 paragraph (e) states "Computer systems (including hardware and software), controls, and attendant documentation maintained under this part shall be readily available for, and subject to, FDA inspection." As computer systems have become more prevalent in industry, electronic labeling has evolved and is now being developed around the specific needs of pharmaceutical companies and the regulations that guide them. ELMS capable of complying with 21 CFR Part 11, Annex 11, and other regulations are now available.

Many of the regulations and requirements of the industry have changed to include specifics about electronic data and record keeping. With a more concrete picture of what is required, manufacturers as well as solution providers have been enabled to shift from manual to electronic systems within the manufacturing environment because the requirements no longer fall into a grey area. Provided that these specific guidelines and regulations are met, many companies have been able to realize the benefits of moving into an electronic labeling process.

Risk management also plays a large role in the sustainability of a given manufacturing plant. High risk processes and procedures can lead to costly losses. A regulatory compliant ELMS can assist companies in label management matters that are considered high risk.

Without an ELMS, paper files and paper documentation are kept in order to satisfy, among other things, audit requirements enforced by various regulatory agencies and internal audit groups. These requirements force companies into keeping traceable records of each label, from design to printing and all of the steps in between. When providing this information in paper form, the ability to quickly and accurately retrieve and present the data can be a daunting task. Loss of any paperwork through the shuffling of hard copy documents is a real risk and can negatively impact a company's audit trail. This in turn can create major problems with the agencies if and when requested documents cannot be produced. If all label-related documents can be kept in electronic form, there is never a question of whether the data can be produced. An ELMS keeps files from being misplaced or shuffled into stacks of papers. The risk of losing important audit information is minimal with an ELMS. Also, the speed at which data can be located is typically much faster than with a manual paper system.

"If all label related documents can be kept in electronic form, there is never a question of whether the data can be produced."

No matter what process a company uses, there is always risk when creating, approving, and maintaining labels. In a process that is paper-driven, there is risk to loss of data simply by the required movement of documents in the label approval process. There is risk to missing pieces of an audit trail and there are risks surrounding a formal audit when all required documents are in hard copy paper form.

That's not to say there aren't risks involved in electronic labeling. Often, a lack of understanding and preparedness surrounding computer systems creates anxiety about having a paperless system. Computer malfunction is a concern, but with disaster recovery plans and sufficient backup policies and procedures in place, loss of data is a non-issue relative to an electronic labeling system. To ensure that data loss does not occur, it's important to have a backup system in place. Generally, backing up the database and associated label folders, i.e., image folders and approval documentation folders to a place other than the main server once daily will keep data safe. Many manufacturing sites will choose to backup more frequently if possible, and some may additionally send copies of their databases to an offsite third-party in case of system failure within the network.

In order to be efficient, a plant needs to be able to print around the clock. There is risk in an electronic system that connectivity may be lost and/or the network may become inaccessible due to power outages or other unforeseen circumstances. In this case, it's important to have another point of access to all data in the form of a cache or database backup on workstations. In the event of connectivity issues, a cache file may allow a plant to continue the manufacturing process as normal. Having another database copy on an off-site server also may provide a second layer of access should a site's internal network become inaccessible. This process may or may not be desirable, but is certainly an option with today's technology. Pharmaceutical Information Technology and manufacturing organizations are now very familiar with the requirements for business resumption and disaster recovery. It is probably safe to say that all companies in the life sciences industry now have formal methods and procedures in place and that they are tested routinely.

Another concern surrounding a fully electronic ELMS is data corruption. Should the network or a workstation

become exposed to malware or other viruses, or should an outage happen during a process that causes a saved file to be corrupted or inaccessible, backups can restore the database and subsequent label printing system back to its most recent uncorrupted state.

Although it does not represent the level of concern it once did, system validation is still a major undertaking and should not be considered lightly. Today, using a risk-based approach, the burden of validation and computer system life cycle (CSLC) maintenance is well understood and more reasonably addressed than in the past. An application that is assessed to be in the COTS 4 category (configurable software) can be "validated" with much less effort than in the past using a practical approach and leveraging the supplier's documentation and compliance awareness.

Environmental Benefits of an ELMS

Eliminating Waste

Electronic labeling makes the pharmaceutical labeling process more environmentally friendly and proficient. When creating labels electronically, there is less waste due to:

- fewer printed approval documents
- fewer printed audit documents
- fewer required test prints

Typically, a pharmaceutical manufacturing company will generate significant paper waste in the labeling process. Much of this is from test labels and other forms of paper. A good method of reducing paper waste is by turning much of the paper into electronic form – both of sample labels as well as approval and audit documentation. Many forms of waste can and should be recycled; however, creating less waste in the first place has an even more significant environmental impact. With an ELMS, paper waste can be significantly reduced.

When creating a label, the look and feel of the label is a high priority. Often, to be sure that a label looks the way it is supposed to look, a test label will be printed multiple times to ensure that the data prints correctly. Changes are made frequently based on the outcome of test prints, and then the updated labels are again tested to ensure quality, readability, and alignment. With an ELMS, the need for this paper waste is significantly reduced, because a user is able to design a label and preview it in the system, using data from any item entry in the database. A program that can construct a label's exact size and color will be able to give a nearly 100% accurate representation of what will physically print. If a data object does not fit properly, is the wrong size, or wrong font, it can be caught through an onscreen preview reducing the number of printed samples.

Waste is also reduced when the label approval process is made electronic. An average approval cycle for a label creates a large paper file containing various types of documentation for an audit trail. Often, there is a printed label sample, along with supporting documentation breaking down the label layout and design. These documents are placed in a file folder which is then routed amongst the various departments required to sign off on the approval. Within the file, more documentation is added as the label sample moves from department to department. Documents containing reviewer comments, approval forms, and other supporting materials may be added along the way. Electronic label approval can remove the paper from each step of the process. There is no need to print a label sample to be routed; instead, a preview image can be created in the electronic labeling system, and routed as an electronic image. To get this image to the correct reviewers in the various departments, electronic routing makes the image and all additional documentation available to the correct departments all at the same time.

"Electronic label approval can remove the paper from each step of the process."

PROCESS	Manual System	ELMS	Comment
Label Design	Design Errors	Chance of error reduced up to 80%	Labels are designed as templates and not one for one. The likelihood of errors in a manual system is increased due to the added volume.
Label Approval	Approval Errors	Chance of error reduced up to 80%	Same as above.
Storage and Control	Control Errors	None	Management of physical inventory inherently introduces known error rates for accuracy.
Printing	Data Entry Errors. 6∂ Study shows .5% of all batches impacted.	None assuming integration with validated systems.	Manual keying of data introduces known error rates.

Table A. Opportunities for error reduction from Electronic Label Management System (ELMS).

Reducing Space and Equipment Requirements

Paper label control systems can require significant in-house storage space as well as increased supply costs due to high volumes of printed label documentation.

Manufacturers in the pharmaceutical industry also must keep many years of audit material on hand. With a paper system, more space and equipment is required to store records. The cost for storage of important paper files is exacerbated by the need for fire-proof and climate-controlled conditions. Access and other administrative controls and procedures also must be in place to accommodate a paper/manual method. An electronic file system saves time, facilities, equipment, and supplies. With an ELMS, these considerations have already been built into the required architectural design for computer systems management.

With documentation in electronic form, storage is consolidated onto file servers. This saves money on the cabinets and required facility floor space and manual filing and control activities. In this regard, the ELMS can have a positive impact throughout the enterprise because an electronic labeling sys-

tem will allow access to the stored data across sites without having to keep multiple copies of documents in geographically separate locations. Also, if the ELMS can be centralized, rather than purchasing separate servers for each manufacturing location, all sites can share data on one server environment. If the ELMS is internet-capable (i.e., available through a web browser) it helps contain costs because the requirement for a separate software license for each machine that will be used for printing or designing labels may be reduced. Instead, perhaps only one license purchase is needed and all connected workstations can work off the application server.

Other Cost and Efficiency Benefits of an ELMS

Simplification of the Review and Approval Process

With different departments working concurrently rather than in an ordered line, employees are more efficient and the elapsed time to complete the routing process can be significantly reduced. An electronic review and approval process not only reduces paper and office supply costs by omitting the need for paper and hard copy files, but it also simplifies and speeds up the process while reducing the chance of errors and omissions.

When everything was documented in files and on paper, the original file could only be in the possession of one business group or one person at a time. With an electronic label routing system, a copy of the label and its documentation can be available concurrently to all involved departments. A process that was once linear now becomes parallel through electronic routing. This saves time by eliminating the need to move a physical file from place to place, and it makes the process more efficient by allowing all parties to view the documents and make comments without having to leave their desks or wait for another department to complete their work.

"A process that was once linear now becomes parallel through electronic routing. This saves time by eliminating the need to move a physical file from place to place…"

Risk and Error Reduction

The ability to reduce or remove human intervention from a process invariably reduces risk by improving accuracy. Think of all the places in the process where human intervention takes place where errors can be introduced. Table A shows how replacing manual with electronic methods in the labeling process can result in error reduction.

Determining ROI for ELMS

The primary driver for ELMS is usually to meet compliance needs. However, Return On Investment (ROI) can and should always be factored into any significant investment.

Table B is a tool that may be used to help identify the value of an ELMS investment.

A Case Study of an ELMS

This section presents a case study of a recent implementation of an ELMS. The project was intended to replace a semi-

Item	Current System	ELMS	Benefit	Calculated Saving
Design	One-to-One Label	One-to-Many	Stored approved templates reduced by up to 80%	
Approval	File Transportation	Electronic Process	Movement of paper from place to place	
Printing				
Pre-package Handling	SOPs, storage, and inventory control costs	N/A	Electronic system requires no inventory management and related costs	
Pre-package Control	SOPs, Planning/Scheduling	N/A	No inventory means no need to plan and schedule	
Pre-package Movement	SOPs, material handling operations	N/A	No need to move pre-printed labels from storage to the packaging area at time of packaging	
Pre-package Approval	SOPs, QA Review and Release	N/A	Use of validated systems precludes the need for active approval at of labels at time of packaging	
Other Add other items as they apply. Do not overlook the fact that there may be multiple sites benefitting				
Cost of Non-Compliance				
Cost of current and future systems(s) – Total cost of Ownership (TCO)				
Opportunity Costs				
TOTAL				

Table B. Quantifying potential return on investment from an Electronic Label Management System (ELMS).

electronic label design and approval system to improve the label development process from design to print.

The original label management system allowed for label design work to be done electronically, specifically on a one to one basis. Electronic sampling was in use in the original system with test prints being done for all labels for the review and approval process. Once the label was designed and printed, it was sent around to the necessary departments in a linear flow. On average, four to five employees were part of the label approval process and the movement of the paperwork from one to the next required that the first person's approval be given before the file was sent to the next person.

While lost documentation wasn't a major issue at any time, frequently paper files would end up in a pile of other documents and forgotten until the due date approached, causing the process of approval to lag. Documents were then scanned into electronic files to be stored. The paper files also were maintained and stored.

In implementing the fully electronic label management system, there were improvements seen in many areas of the label design and approval process. The approval procedure saw the greatest improvement with parallel routing allowing for each of the four or five employees in the approval process to review and approve or reject labels at the same time without delay. Instant notification alerted each individual to the need for label approval and expedited action on that approval.

Another benefit was the ability to create templates for use with multiple products. There was about an 80% reduction in the number of labels requiring control since templates could be approved for use with a number of products.

Not only were label approvals being routed, but the label routing system was also put to use to route other label-related items; image updates, new requirements documentation, etc. This also created a decrease in waste and paper usage by making the majority of label-related tasks paperless.

Perhaps the most obvious improvement from the ELMS is the ability to address rush items. With a one hundred percent electronic system, expedited items can get through the entire routing and approval system within hours due to the ability to access the system from anywhere at any time. This elevated efficiency and cut down on costs since a courier was no longer needed to transport paper files across various sites. Overall, high priority items are taken care of quickly and man hours are reduced in getting things through the approval process. All documents are automatically placed in the proper electronic folders when finished without employees needing to worry about placing them there.

Part 11 compliance was also important. The original system was not compliant with the regulations; therefore, many changes were made to procedures to ensure compliance. The electronic system with routing capabilities also allows for complete audit control, making the system compliant with all regulatory requirements. The ELMS has been in place for almost four years now and auditors are happy with the system's compliance features and no system-related citations have been issued to date. Audit trails are intact and compliance is ensured.

Conclusion

Electronic label management systems capable of meeting challenging regulatory requirements using current technology standards are available to pharmaceutical companies today. Although not typically viewed as a high-impact cost-reduction opportunity, the hidden costs of staying the course with older technologies incapable of complying with regulations such as 21CFR Part 11, Annex 11, and others may be viewed as prohibitive or unwise. We know that labeling has traditionally been a hot button item for auditors and that labeling errors have historically been the most common cause of product recalls. Today, there are commercially available systems that offer compliance, cost, and "green" advantages that had not been available only a few short years ago and they should be considered by companies looking to improve in the label design, approval, control, and print areas.

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About the Authors

Dana Buker joined Innovatum in April 2002. During his tenure, he has established and administered Innovatum's operational procedures. Also, having been employed in the pharmaceutical industry for more than 20 years, he has provided training and guidance to company personnel to facilitate knowledge and understanding of FDA regulations. This translates to the implementation of practices that provide for the compliance needs of Innovatum's customers. Prior to joining Innovatum, Buker held a variety of staff and management positions in the pharmaceutical industry. He has been a purchasing officer, planning supervisor, production supervisor, MRP consultant, business systems manager, and manufacturing systems project leader. His most recent position as an employee in the industry was information management project team leader at Bristol-Myers Squibb Company. Buker was instrumental in the highly successful implementation of several validated ERP systems. His last project included implementation of a Manufacturing Execution Systems (MES) aimed at improving manufacturing data control and processes in a pharmaceutical setting using real-time data collection for weigh and dispense operations. Buker has written or contributed to several published articles on the improvement of business processes through technology. Buker has served as an officer of several industry groups, including a term as president of SSA's Pharmaceutical User Group. Buker holds an Associate Degree in computer science, a BS in business

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