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Serialization 101

Fraud is a serious issue for drug manufacturing, and pharmaceutical and medical device regulations using serialization have been mandated to defend against counterfeiting.

By Kim Overstreet

In the realm of pharmaceuticals, there are some concerning statistics according to the Pharmaceutical Research and Manufacturers of America. One in ten medicines worldwide are presumed to be counterfeit, and 95% of internet drug outlets have been found to be out of compliance with federal and state pharmacy laws & practice standards. During one week alone in March of 2020, over 48,000 packages containing counterfeit medicines were seized by Interpol.

Serialization assigns a unique serial number linked to information about the product origin, batch number, and expiration date, to each saleable unit of each prescription drug product. According to a new report by PMMI Business Intelligence, "Pharmaceutical & Medical Devices | Trends & Opportunities in Packaging Operations," regulations vary worldwide.

In the United States, the federal Drug Supply Chain Security Act (DSCSA), enacted in 2013, establishes a system to track and trace prescription drugs throughout the U.S. supply chain. The key purposes of DSCSA are to verify the legitimacy of the drug product identifier down to the package level; to make drug recalls more efficient; and, to enhance detection of illegitimate products in the drug supply chain.

The goal of DSCSA is unit-level traceability by 2023, including aggregation, or being able to trace a single unit to the larger bundle, case or pallet that it came from.

Implementing serialization technology creates challenges beyond compliance at all stages of the packaging process due to the numerous steps involved.

There are specific challenges to

serialization such as noncompliant or unusable bar codes, the potential for lost productivity on production lines, the need for major human and capital investment for new processes and data management, and inventory issues caused by the mismanaged tracking of returned products.

For medical devices, the FDA established the Unique Device Identification (UDI) system in 2014, to improve patient safety by identifying devices sold in the United States beginning with manufacturing and continuing through distribution and patient use. When fully implemented, the labels on most medical devices will include a UDI in both human-readable, and machine-readable form on the device itself. Device labelers must also submit certain information about each device to the FDA's Global Unique Device Identification Database (GUDID).

UDI requirements have been implemented in stages, beginning with Class III devices. Due to the impact of COVID-19, the final stage of implementation – for Class I devices – has been postponed from September 2020 to September 2022.

Data and AI Accelerate Digital Transformation in Pharma

The PDA Annual Meeting emphasized the growing need for pharma manufacturing facilities to become digitalized to improve productivity, open the door to further technologies, and make the most of the 'digitally native' workforce.

By Melissa Griffen

As the name implies, "Pharma 4.0" is Industry 4.0 applied to pharmaceutical manufacturing, which is the addition of cyber-physical systems to computerize manufacturing while focusing on the human element. The concept has been gaining traction in recent years and was a common theme in the 2021 Parenteral Drug Administration (PDA) Annual Meeting.

The four pillars of Pharma 4.0, as explained by Gilad Langer, industry practice lead at Tulip Interfaces, a digital technology provider, are:

- Resources
- Information Systems
- Organization and Processes
- Culture

These pillars focus on digitization, digitalization, and the human element. Here's one company's explanation of digitization vs. digitalization. Further, Pharma 4.0 allows for the democratization of technology. In other words, what once was available only to experts is now available to the general workforce. The shift to this democratization can be eased through the new generations entering the field, who are all but raised on technology, making them what Langer called "digitally native." Yet, the pharmaceutical industry is not taking full advantage of these advancements.

One of the main facets of the Resources pillar is digital transformation which centers on real-time data and information to increase productivity, enable machine operators to do their jobs more efficiently, and further allow the use of predictive technologies, augmented reality (AR) and virtual reality (VR), Big Data, artificial intelligence (AI), and machine learning (ML). It allows for connectivity through integrated systems, equipment, people, and other software systems; real-time visibility into operations; transparency for quicker reaction time; and, at

Adoption of AI in validation and other processes, including data collection and management, can result in valuable predictive qualities within a manufacturing facility.

its highest levels, predictability and self-optimization in that the system can predict the outcome of a batch or machine's performance and self-correct. In this kind of environment, apps, smart sensors, or the Industrial Internet of Things (IIoT) are used as a means of first capturing the data from the floor, which is then transferred to the cloud, available for use.

Replacing documents with data

Thus, a focus of digital transformation is replacing the use of paper as a means of data collection. Paper is cumbersome and time-consuming, placing additional unneeded demands on the workforce, yet factories–and especially those in pharma–still rely heavily on its use. Referencing the Pharma 4.0 pillars, Langer pointed out that digitally native workers come into the workplace only to be brought into a Culture which teaches them to use Organization and Processes that are centered on paper. This is a waste of ability to help transition into the digital era and serves only to create a workforce gap.

At the same time, digital transformation is not one large operational problem to be tackled at once, but rather is made up of a multitude of small changes facilities can make which don't take as large of an investment to fix, according to Langer. The Organization and Processes need to become digitally native, and continuous improvement is at the core of this transformation. Langer envisions this process taking a number of years to fully accomplish, with one foot on each side of "the digital divide." This paradigm shift to digital data will happen gradually, requiring the industry to switch from its current

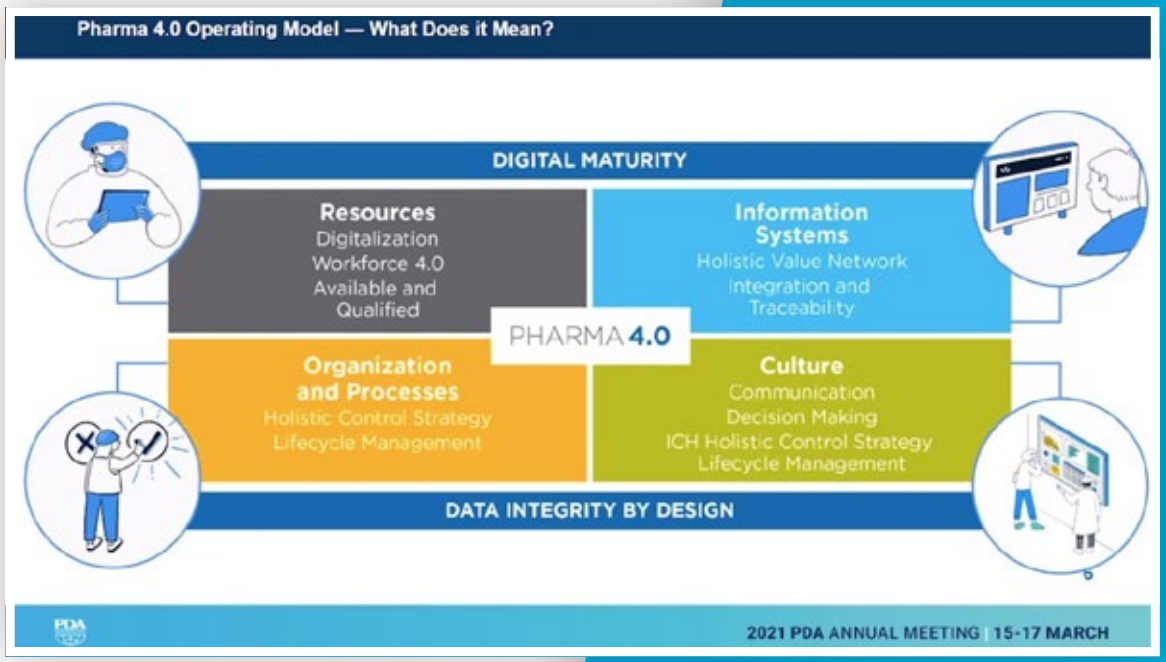
document mindset, and it is never too late to start.

"What we want to do is create digital content that is human-centric for one small problem at a time," said Langer. He went on to explain a few examples applied with a set of technologies called no-code apps or digital content. "Basically, all of your engineers, all those who are within the operational domain of your manufacturing plant, can use something that feels like and looks like a PowerPoint to create these digital sets." They do this by logging events, creating data sets that can then be stored in the cloud in a way that will allow advanced algorithms like AI and ML to use the data.

More sophisticated ways to capture data–such as work order terminals that interact with an ERP to get input on work orders on the floor, and batch processing and recording, capturing batch record data–can be used, though simple checklists on mobile devices, simple deviation/exception recording on a laptop or tablet, and especially digital logbook solutions are also effective.

Digital logbooks run operators through simple screens on interactive apps with built-in quality checks and

These pillars focus on digitization, digitalization, and the human element.



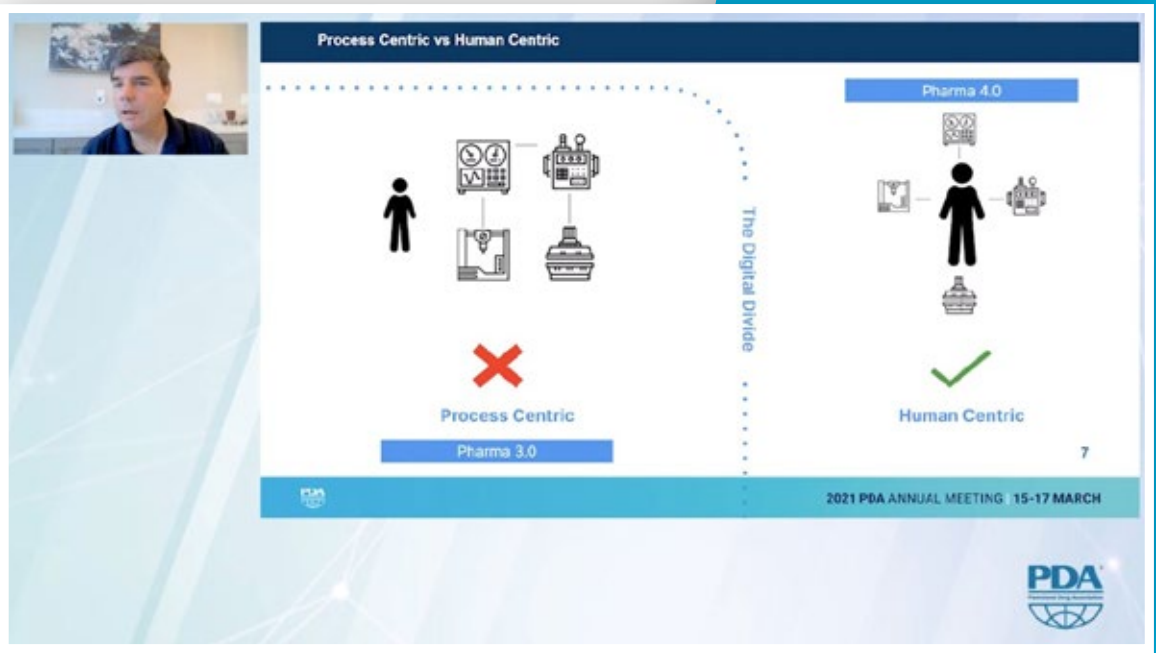
built review-by-exception. Langer suggests incorporating digital logbooks as a simple way to introduce digital transformation to the floor along with batch records. Data entered in is displayed in tables, graphs, charts, and other familiar formats, which are easily consumed by advanced algorithms. This data is simple and transparent and does not require sophisticated databases.

Managing your data

Vasu Rangadass, CEO of L7 Informatics (L7), Inc, a software solution provider, agrees with Langer, that starting small is the way to approach digital transformation though the end state needs to be kept in mind. Otherwise, as Rangadass puts it at the PDA event, the process will be like putting together a puzzle without knowing what it should look like in the end, which only wastes time and resources.

Rangadass went on to explain that digital transformation requires a clean set of data. The traditional way of collecting data is to gather it from all sources and put it into one single database as a system of reference. But this creates “digital

Organization and Processes need to become digitally native, and continuous improvement is at the core of this transformation.



silos," which then require validation and as companies merge, are acquired, and receive new products, this leads to complications with outdated data, resulting in high IT expenses as IT maintains various complex, redundant systems. Unified platforms would simplify the collecting and sharing of data between departments and companies and eliminate those complex, aforementioned redundant systems. Unified platforms have common data models, codes, tooling, architecture, and a common business process that spans capabilities across departments and companies in order to provide greater process intelligence all from one system that offers the applications needed.

L7's ESP software solution has taken on concepts from Robotic Process Automation (RPA) composable unified platforms with an FDA regulatory compliant framework, which is applicable to the manufacturing scene. Applying such a digital solution can take anywhere from 3 to 9 months, said Rangadass, depending on the complexity of the process, the quality control (QC) process, and the manufacturing process. When a system has become digitized, the application speed increases. L7 customers tend to start the digitalization process with QC and batch records.

"We want to remove barriers to connectivity. We have connectors to 150 different wire process equipment, environmental monitoring systems, software systems, etc. These connectors play an important part, and we package them as part of the platform to reduce any kind of impedance for customers," said Randagass. "While connectors are very easy and cheap to build, not having them in one place is a challenge, so we package all the connectors so

customers can easily deploy the platform and that gives them contextualized data whether it's environmental or from the wire process equipment."

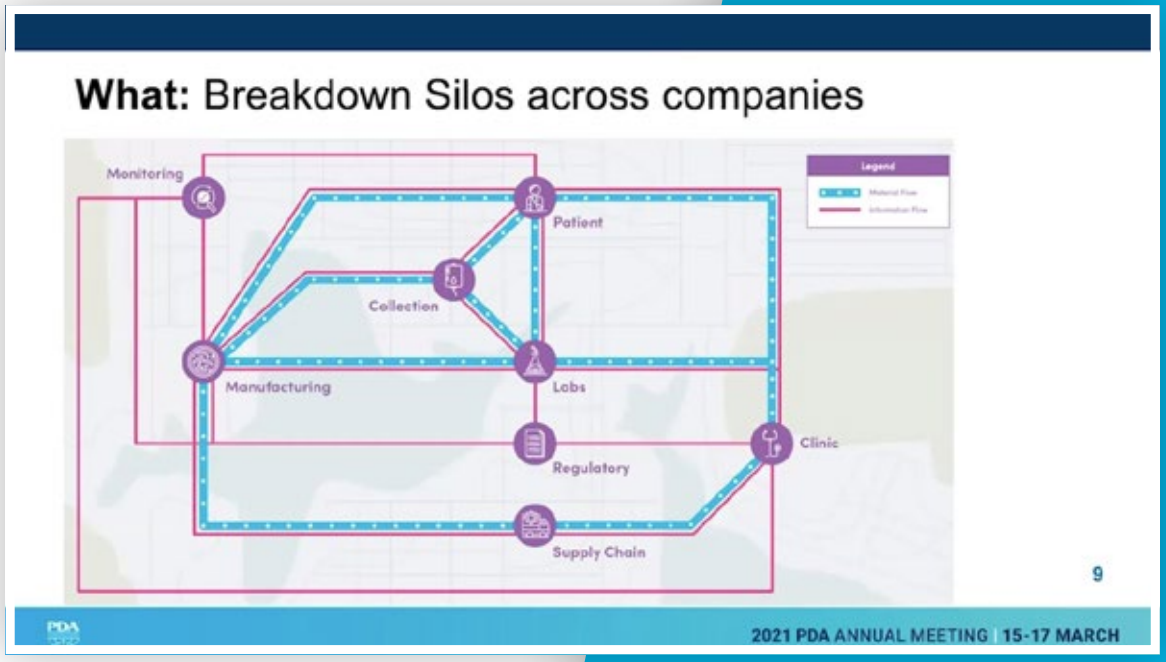
Validation and the regulatory aspect

L7's efforts towards regulatory compliance with ESP span to its creation as a Good Manufacturing Practice (GMP)-compliant platform, which can be up to 80% validated, meaning that customers need only drop in their processing and validate the last 20%.

Langer further pointed out that if companies choose a vendor in the GMP space, their platforms will come pre-validated, and from there they could build on the platform with no-code apps. Validation for no-code is also different from software validation in that it must be validated based on intended use, as in the end:

- the apps are instruments in processes for capturing data
- that data will prove the results, which
- further proves the companies are in control of the data and that they are in compliance.

Unified platforms would simplify the collecting and sharing of data between departments and companies and eliminate complex, redundant systems.



Toni Manzano, CSO and co-founder of Aizon, an AI platform provider, added to this by explaining that the way to validate software with cloud web browsers has completely changed as technology has continued to evolve and we cannot make the assumptions once made about classical software.

"The FDA is even moving from classical computer system validation to computer system assessment where documentation is not the base of the pyramid. Risk assessment is now the base of the pyramid so you can see that everything is changing but you can assess the risk and act accordingly," said Manzano. He explained that principle component analysis (PCA) can be used as a classic algorithm to find relationships between variables within data, but AI must come into the picture in order to make robust real-time processes to keep product manufacturing under statistical control. This involves critical factors that affect processes and which further rely on feedback from the floor, supplying data to run the AI and determine that it is working properly. Adoption of AI in validation and other processes, including data collection and management, can result in valuable predictive qualities within a manufacturing facility.

"Technology has come a long way in the last several years and will dramatically reduce the cost of information technology to use new platforms," said Rangadass. "Digital transformation is necessary to reduce costs and increase the speed of drugs to market."

Blow-Fill-Seal Expands in Aseptic Filling, Vaccines

Live from #PDAannual: Recent developments in the technology have bolstered the use of BFS in aseptic processing, including temperature control and needle addition for pre-filled syringes.

By Keren Sookne

While not a new concept, blow-fill-seal (BFS) technology isn't as prevalent in pharmaceutical aseptic filling operations compared to traditional filling. But in recent years, BFS technology has started to gain more traction in vaccine production, temperature-controlled product filling, and pre-filled syringe manufacturing said Leonard Pauzer, director process technology at IPS-Integrated Project Services at the 2021 PDA Annual Meeting held virtually this week.

With BFS, the reduction in container weight is beneficial from a logistical standpoint, while a reduction in contamination and particulates—filling and closure happen at once—is a value-add for quality. Additionally, a manufacturer can change container shapes (with the cost and several weeks to change a mold) without purchasing a new machine, which offers new delivery options for patients.

While BFS technology offers unique solutions to pharmaceutical manufacturers, it also brings new facility, quality, and process changes he said. Recent advancements include the following.

1. **Pre-fabricated PODs:** "We've seen an increase in the past two years of blow-fill-seal being used," Pauzer noted. "Companies have been looking at and installing BFS into a POD, allowing for rapid deployment and ease of installation."
2. **Temperature control** adds a new element to BFS capacity.
3. **Vaccines:** Not only has there been an uptick of vaccine filling via BFS, but Pauzer has also seen "integration of a syringe needle with a BFS container, which in the past has not been done on a large scale."

For those not familiar with the technology, here's a brief overview for rotary BFS filling. If you're familiar, jump ahead to **BFS vs. traditional filling.**

- The liquid product moves through machine's piping.
- Simultaneously, LDPE pellets are melted and extruded into a continuous ribbon of parison

(melted resin).

- Product and parison are fed into the fill machine. Sterile air is applied to the center to expand the parison so that the new container can enter the mold and form properly.
- Simultaneously containers are formed, filled, and sealed.

As Pauzer explained, "an aseptic BFS machine can utilize technology referred to as 'rotary filling' with a closed parison. Forming, filling, and sealing of containers occurs within a continuous ribbon of parison flowing around the needles." The outside environment will not affect the product as long as the parison is running.

BFS vs. traditional filling

In the closed parison process, BFS machines do not have a traditional air shower like in isolators or RABS, and the filling needles are completely enclosed within the parison so it is not possible to perform continuous viable and non-viable particle monitoring throughout the filling of a batch because you would have to penetrate the parison.

"I reference PDA Technical Report 77 because most of us who are used to an isolator or RABS know that you'll do continuous monitoring for viable and non-viable, and you can also do surface plating either at the end of beginning of the process," he said. The BFS situation is so different that this is not possible—this is a challenge to some quality groups and also changes how brands think

about environmental monitoring for aseptic filling.

While both filling techniques can run at speeds of approximately 300 to 400 containers/min, there are some parameter differences to note. With BFS, the container is plastic instead of glass, and the relatively tiny critical zone is installed within the machine. “The critical zone or environment for a BFS machine is approximately 36 square inches of space that includes the needles. All this monitoring is outside the parison. Compare that to a medium-sized isolator or RABS which has approximately 2,304 square inches of Grade A environment. Where our needles are located in BFS is not considered grade A,” he said.

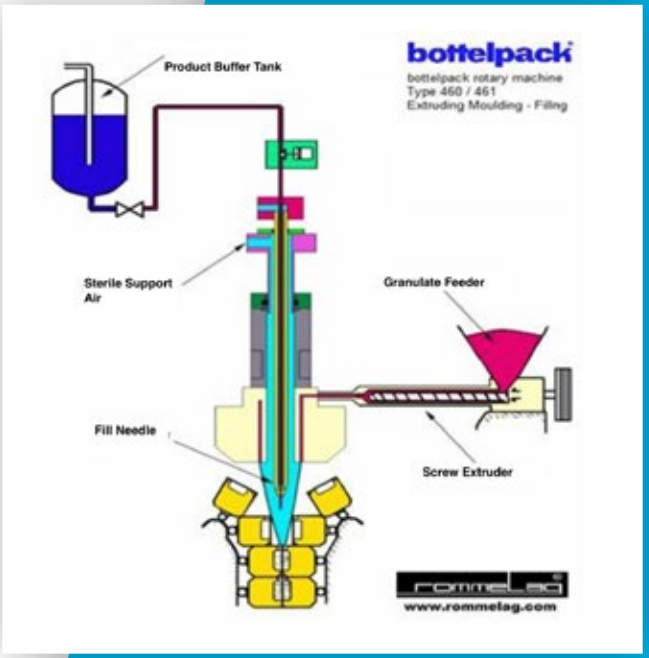
Controlling temperature

Vaccines bring temperature challenges, but they can be overcome with careful BFS design. Most vaccines are heat sensitive, and can be out of refrigeration anywhere from 10 hours up to 30 or 70 hours—depending on the product—with a typical target temperature of 2 to 8°C.

Pauzer said BFS technology has advanced to the point where you can refrigerate or control throughout the product filling. “At the point of dosing, you’re merging with a warm parison. The molds are cooled, but you do have to take that into account when you design your facility. Today, you can bring the product right to the point of dosing at a specific temperature.”

Most vaccines require a range of 2 to 8°C, but this may depend on

While product runs through the system, resin pellets are melted and extruded into a continuous ribbon of parison (melted resin). (Image: IPS)



the product and viscosity. He said most companies try to target 4°C because it allows for variation while staying in the 2 to 8°C window.

One design he highlighted includes a double-walled piping system with cooling media circulating through it, which is a fairly new development. Cooling media will depend on the site and country as the U.S. and Europe, for example, differ on which type of glycol is accepted. He offered the following temperature control considerations:

- Maintain the product temperature in the buffer tank. This improves dosing accuracy.
- Consider a dedicated chilling system. Any reduction in temperature variation reduces risk. "Many companies have a house glycol unit but there's quite a bit of variation in that. What we've learned is if you dedicate a very detailed, designed unit for your blow-fill-seal, it gives you the best results," Pauzer said. He described a tiered cooling concept with multiple temperature control units, each with a consecutively tighter range to increase control as they stepped down. Three units were individual circuits on the BFS machine, one covering the product tank, one for product piping, and another for the molds.
- Determine how you will evacuate the glycol out of the piping when you need to clean in place (CIP) and steam in place (SIP).
- Consider where safety relief devices within the cooling will be placed. "This is very small tubing… and now you have a jacket on top of it or another pipe around it. We have to get safety devices in because we are now running steam through the inner pipe, radiant energy goes out to the glycol, and it expands the glycol. Again, we're dealing with a process that was not previously done so this was a first of its kind for us working with a vendor to

create this," he said.

- Pauzer explained they ran into some challenges with piping radiuses, ultimately opting for a complex fabrication process: "Our risk assessment looked at what would happen to the product if it sat for a minute, two minutes, and then what happens to product temperature on continuous flow."
- In the example he highlighted, valves were not cooled like the tank and long runs of the piping were. They insulated the loop as much as possible, which helps maintaining temperature.

Other challenges when making the switch

Automated inspection brings considerations, particularly because BFS containers are opaque (See sidebar below). "We have industry standards for glass vials and syringes. Even plastic vials are used in automated inspection machines. Inspection standards and criteria will be compared to vials and syringes for comparable products. It's a different way of thinking," he said.

The container has the benefit of being flexible, but if it is secondary packaged at a different location, then a tray and rigid container are needed for shipment.

Companies must establish of a viral boundary. "Closed parison gives you your first level of containment for viral boundary. Now this can be discussed with the quality group, but many companies believe that it is your first level," he explained. "Then you think about aligning the technology with existing technology—some companies will introduce this technology into a facility that already has a traditional vial and syringe filling line. And you're going to have contrasts on

how the viral boundary is managed. For BSL-1 products, this is not too challenging, but as you increase in your biosafety levels you have to take this into account and understand how you're going to manage it." Finally, most vaccines require a chemical or heat inactivation step. Both are possible because a BFS machine has an integrated CIP and SIP system within it. Pauzer noted, "Some products need a specific chemical. So rather than a cleaning step, you need a true inactivation step before opening the machine up and before going to drain with your product."

Designing for a POD

A POD is a prefabricated clean room which can be transported to a facility, using a truck, plane or ship. The room is completely built in a factory, with wall panels, doors, and even some equipment and furniture, then loaded and shipped. One critical factor not to be overlooked is the sheer weight of a BFS system. The base or foundation has to be strong to support it. "When you combine all the equipment within a POD, it's 31,000 pounds—the filler itself is 28,000 pounds. We're talking about a unit that's nominally 14 feet high, 10 feet wide, and 20 feet

The height of the BFS system for the highlighted project required IPS to use a double stacked POD, referred to as a "high hat" configuration. (Image: IPS)

long," he said. "The challenge also is that is just your filling machine. You have to include in any air handling, ductwork, lighting and structure above it."

The height of the BFS system for the highlighted project required IPS to use a double stacked POD, referred to as a "high hat" configuration to accommodate the two levels. (They only extended the second level where the BFS was.) The location of the BFS machine within the POD needed to be strategically chosen because it had to be moved into place.

Adding a needle

Dealing with COVID-19, the industry as a whole has been figuring out on the fly how to get mass doses out to the public. "For years, the industry has been moving away from multi-dose containers. Vaccines used to be distributed 10 doses per vial and the doctor's office would draw out one container. There has been a push to go to single-dose prefilled syringes—it reduces the doctor making that manipulation and multiple entries into one container," he said.

Using BFS technology, the syringe barrel is a multi-chamber container that's fabricated immediately, and a company can attach the needle right then—the concept is a BFS container, a connector and a needle. "You can fill, form, and assemble in one process step. Because we're using BFS containers, it reduces the weight and if you can remove a processing step, you can get to the market quicker," he said. With COVID-19, every week or month matters, but for any vaccine or life-saving medication, speeding output means getting to patients in need faster.

From Drug Supply to Staffing, the Benefits of RFID Integrated into Vial Labels

In this Q&A, a manager of pharmacy operations explains why RFID-embedded vial labels just may change the world of inventory management and dispensing.

By Keren Sookne

Automated inventory management solutions are used for a variety of different products, including medications and equipment. Their popularity continues to grow in tracking drugs for efficiency benefits across health systems.

We talked with Eric Schaefer, PharmD, manager of pharmacy operations at Allegheny Health Network, about how using label systems from Kit Check and CCL Healthcare has opened doors, increased efficiency, and more.

Before we get into the benefits—and Schaefer explains there are many—we'll go over the technology that makes this possible. Kit Check and CCL Healthcare have partnered to deliver labels embedded with RFID tags to pharmaceutical manufacturers.

RFID inlay for small vials

Until recently, flag labels with RFID tags were manually applied to individual vials at the hospital system. The labels could not be applied at the manufacturer due to the time-consuming nature of the process. “Additionally, pharmaceutical companies use specific adhesives which are tested against migration and anything that can affect the drug,” says Karl Hoelper, director of marketing at CCL.

CCL has integrated the RFID inlay into the existing vial label that they print for the manufacturer. Vials then arrive at the hospital pre-tagged, eliminating the flag-application workflow at the hospital.

“Because we’re producing the label already, we can take a transfer tape and match that adhesive so there are no qualification issues for the pharmaceutical company, which is a pretty big hurdle—it could be a year or two years to qualify,” explains Hoelper. “This mitigates the risks of any chemical migrating off the label and into the drug.”

Glass, liquid, and small vial/syringe sizes—including the traditional 2 mL vial—all pose challenges for RFID functionality. In addition to these challenges, the RFID inlay needs to be rotated 90 degrees in order for the antenna to fit properly on the 2 mL vial.

With the CCL/Kit Check partnership, manufacturers receive labels with RFID inlay that appear identical to their existing label—and don’t require artwork changes and new FDA approval—and do not affect packaging lines.

To make integrated RFID labels a reality on small vials, CCL custom-built a machine to orient inlays so that manufacturers wouldn't have to change any aspects of their label artwork. The machinery allows them to remove each RFID inlay from the reel, pick it up, rotate it, and space it properly.

The process requires extreme precision with multiple sensors and camera systems on the line to ensure the tag fits behind the label. The labels undergo numerous quality checks before they are released.

The result is that manufacturers receive labels with RFID inlay that appear identical to their existing label—and don't require artwork changes and new FDA approval—and do not affect packaging lines. "We're working within the constraint of the current label, which is key for that 2 mL vial," says Hoelper. "We wanted to make sure we made this work with their current adhesive and current label so that adding RFID is as painless as possible."

DoseID

With the goal of ensuring the quality, performance, and interoperability of RFID tagged drug products as they move through the supply chain, DoseID launched in August 2020. CCL and Kit Check are founding members of this self-governing consortium established to unify the industry around an approach to serialized, RFID-tagged pharmaceutical products. "Creating pharma specific RFID labels is irrelevant unless there is an interoperable supply chain that sees the value of RFID. DoseID substantiates that value," says the consortium.

They report that they take serialization beyond DSCSA, from the unit of sale to the unit of use. DoseID uniquely serializes every dose, container, or device to track every action taken upon it during its entire lifecycle.

The consortium takes a practical approach to ensure that the system works in the rigors of the real world. DoseID drugs and hardware devices are compliant with existing standards like RAIN and GS1. They are tested to ensure (1) performance (the best inlay is chosen for the application), (2) interoperability so that the drug will read in real-world scenarios, and (3) complete and accurate data in which the evolving record of a drug's attributes and event history is stored in the cloud and accessible to all parties.

"In recent years a variety of different RFID solutions have come into the healthcare market to track drug products, instruments, and supplies without any industry-wide standards having been established to ensure quality, performance, and interoperability between them," says the consortium. "With industry-wide support of a comprehensive set of RFID standards for healthcare, players along the pharmaceutical supply chain can work together to solve these issues proactively rather than reactively."

With that explanation in mind, we sat down with Dr. Schaefer to hear about how the end users at heath systems have gained efficiency from RFID solutions adopted by pharmaceutical manufacturers.

From Drug Supply to Staffing, the Benefits of RFID Integrated into Vial Labels

Healthcare Packaging (HCP): To start, how are you using automated inventory management for drugs at your facility? I understand companies are transitioning away from flags into seamless systems with embedded tags.

Eric Schaefer: What we choose to tag is going to depend on where we're utilizing this technology. When you look at how people select automated inventory management, there's one mindset of "I'm going to use it to check this tray or this kit."

Then there's also the mindset of "I'm going use this to check those items and reduce the time it takes to check or use pharmacy time. However, I also see the other benefits that are available: the analytics, the inventory pieces, the recall pieces, and shortage management options with the tray."

At my prior facility, I did a major implementation for two systems. We converted part of the facility to Kit Check for crash cart trays and for anesthesia trays where they do a tray drop, in which they take the used tray out, place a new tray into that drawer, and then it's 100% stocked. Those are going to be items that are usually higher value vials—they lend

themselves well to this use.

Most facilities that implement this are probably going to start with a crash cart because turnover in that cart isn't daily, so it's something where if you have an option to know electronically where stock is, and what's expiring, you're able to manage those and rotate those out rather than opening every cart every month.

That was the case here at Allegheny General Hospital, and at the previous facility I worked at. We started with crash cars and then expanded into other areas, but really you're looking at those kitted items for emergency kits, trays, and operating room (OR) based items.

HCP: What is the importance of the ability to scan vials without a direct line of sight?

ES: There's a big time difference between scanning RFID versus 2D codes. If I needed a line of sight to scan a 2D barcode for a box or a bagged kit of drugs, if the label is on the side, I have to stand all those vials up or twist them so that the barcode is showing.

With Kit Check the nice thing is that I'm confirming that this drug is inside using RFID, without necessarily having the line of sight. I can use it to scan trays and scan boxes, such as radiology reaction boxes, without physically having to look at each item.

With 2D barcoding, I'm still going to have to physically look at every vial in that area. Many places will spend about one day every six months doing

outdates and pulling drugs for the next six months. With an RFID system, I can now scan my bins once a week, or it may even be more frequent. I can eliminate scenarios where I have six months of a drug in limbo that I could be using up.

The 2D barcode is usually going to end up being on the vial cap. What I had found is when they pop that off, it's still attached and the lid will sometimes fall back down, so it looks like it's an unopened vial. Whereas with RFID, the tag is attached to the side and I can tell when that top is off or when it's used.

HCP: Why did you end up selecting the Kit Check as opposed to other competitors?

ES: I am in the camp that the capabilities of Kit Check allow for a broader use of the system.

Speaking from my pharmacy manager experience in my previous facility, I looked at the options available. As I mentioned previously, there are the subset that look at it as a way to scan a tray, then there are the groups that look at it for fuller functionality.

When you're going to implement any technology, you have to pitch the benefits to the people who are going to be providing you the funds. If you're going in and you're saying, "I scan a tray" and you don't explain the benefits, they're probably going to want to lean towards the cheaper route.

However, I saw that as technology advances, there would be opportunities to use RFID to scan the products for inventory.

From Drug Supply to Staffing, the Benefits of RFID Integrated into Vial Labels

In the past, we would make medication kits for the OR nurses with a 2D barcoding system. Their kit functionality was a laptop with a handheld scanner and scanning each vial. That takes more time than me putting a kit into a scanner and reading in seconds compared minutes.

When I used 2D versus Kit Check, the scan times vary greatly because you have a camera trying to assess the location of those barcodes. So it's something where being able to place it into the reader, have it recognized, not having to stand all the vials up to make sure that perfect make it up there in there with kind of that savings.

And for me, I don't necessarily assume it as a time savings in the aspect of cutting people or hours. It's about what can I now do that's more value-added with that pharmacist hour. How can I elevate a technician's level of involvement to helping with the dispensing portion rather than just filling the tray and waiting for a pharmacist to check.

Even for pharmacists, other than having them check each of the hundred items that are in a tray manually for expiration, I can have

To make integrated RFID labels a reality on small vials, CCL custom-built a machine to orient inlays so that manufacturers wouldn't have to change any aspects of their label artwork.

a technician dispatch it, and I can now use that pharmacist's time for providing clinical information, interacting more with the provider, and being more involved in patient care versus them having to check a tray for 10 minutes at 40 trays per day.

HCP: One feature is that information associated with an RFID tag isn't static. Can you provide an example of additional or updated information being sent to RFID tags?

ES: We have a prime example of syringe shortages. For several years, there's been an ongoing shortage of emergency syringes and even FDA updates to their expiration dates. The nice thing is I can validate that information on the FDA website, log into the system, and update the expiration on that lot number.

I can see the history of the tracking. I can see that for some of the syringes, I had to update the lot numbers two or three times because they were performing testing and allowing extended dating due to shortage. We can update expiration dates automatically without having to replace the tag.

HCP: So it's both a patient benefit, a cost benefit, and a sustainability benefit because you're not necessarily getting rid of something that's already in short supply? If an expiration date has been updated, then somebody isn't mistakenly thinking it's expired and tossing it?

ES: Right. So a user looking at the vial doesn't see the old expiration printed on the tag (maybe they do on the carton) but we know that when we're releasing that drug, it has had an updated expiration in the system.

Fresenius Kabi Goes Above and Beyond DSCSA Requirements

With the support and standards of GS1 US, the pharmaceutical manufacturer fulfills customer needs for an additional system to ensure safe use of medication on a unit-of-use level.

By Melissa Griffen

The U.S. Food and Drug Administration (FDA) put into effect the Drug Supply Chain Security Act (DSCSA), which was enacted by Congress in November of 2013, in order to outline the steps necessary for the industry to build an electronic, interoperable system by 2023 to identify and trace–through the packaging and homogenous cases of products–certain prescription drugs as they are distributed throughout the United States. This is meant to develop and enhance drug supply chain security and includes product tracing requirements which went into effect in 2015 for manufacturers, repackagers, wholesale distributors, and dispensers such as pharmacies.

The DSCSA requires that manufacturers and repackagers affix or imprint to each package and homogenous case of product a product identifier, which includes:

- The product's standardized numerical identifier–composed of the National Drug Code (NDC) and a unique alphanumeric serial number

- The lot number
- The expiration date

This information must be included in a 2-dimensional (2D) data matrix barcode for packages and either a linear barcode or 2D matrix data barcode for homogenous cases which complies with current good manufacturing practice (cGMP).

GS1 US, a not-for-profit information standards organization, provides a system of standards for identifying products, locations, and logistic units, thus enabling manufacturers and repackagers to meet the DSCSA requirements. This allows pharmaceuticals in packages and homogenous cases to be tracked and traced from manufacturers to the receiving docks of healthcare providers at the unit of sale level. However, the management of medicines throughout hospitals—from receipt to administration, or at the unit of use level—is not within the scope of DSCSA.

GS1 US member company, Fresenius Kabi–a healthcare company that specializes in lifesaving medicines and technologies for infusion, transfusion and clinical nutrition–was approached three years ago by many of its customers (hospitals and pharmacies) about implementing RFID tracking on medication inventory, which they had been adding manually–a time-consuming and tedious process. Fresenius Kabi's customers had found RFID tracking to be more accurate than barcodes, allowing them to scan many drugs at once, more easily track expiry dates, and better maintain

tighter inventory levels. Healthcare Packaging's two-part series on RFID implementation at Allegheny Health Network goes into further depth of the interest in RFID from a distributor perspective.

Implementing RFID

So, the company began research into RFID that took up the majority of a year. Considering the lack of mature RFID system vendors available, Fresenius Kabi turned to eAgile, a vendor that supplies both RFID-enabled labels and RFID equipment, and spent the next year on the initial equipment design and implementation. In early 2020, the company began implementation of its +RFID system at its Sweden facility, which Jeanne Sirovatka, senior director for packaging design and technical projects at Fresenius Kabi, as well as analytical chemist, explains ran into a few snags when the COVID-19 pandemic hit. Implementation was slowed as countries went into lockdown and the company could no longer send in its U.S. team that had conducted the research in person

Photo credited to Fresenius Kabi.

and resorted to using many virtual conferences instead. “Ultimately, we got it done and it all worked out, but I would have preferred not to do this during a pandemic,” Sirovatka says. So, in the Fall of 2020, Fresenius Kabi became the first pharmaceutical manufacturer to embed medication identification data into an RFID tag, relying on GS1 Standards to permit full interoperability and compatibility.

In Fresenius Kabi’s research, customers responded that they wanted the NDC, lot number, expiry date, and serial number provided in the RFID tags. The company has been using these tags on specified products, including glass and plastic vials and syringes, which were commonly tagged by its customers in anesthesia and similar fields.

Each RFID tag is embedded into the existing label so it can run on the company’s existing packaging lines and this makes the process fairly invisible to the packaging line operators with no physical interaction at the packaging point. The tags are pre-encoded with the Global Trade Item Number (GTIN), and a unique serial number at the eAgile facility. They are encoded with the lot number and expiry date on the Fresenius Kabi packaging line via antennas that interact with the tags through radio frequency. Tags that are unreadable or with incorrect information encoded are rejected from the line.

The RFID antennas, interrogation equipment, and at some facilities the reject equipment (depending on the configuration of the line) were purchased primarily from eAgile. “This gives us a universal solution,” says Sirovatka.

Pros and cons

While testing its RFID system on a syringe plant, Fresenius Kabi learned the hard way that the environment can interfere with the antennas, such as the placement of a metal ladder too close to the antenna, or the presence of water. “Subtleties like that in the environment really had a much greater effect on the equipment than anyone who is new to this technology would have expected,” says Sirovatka.

Sirovatka also explains that with vial sizes and RFID reflectivity being unique and dependent on vial material, the RFID tag antenna must have the capability to be customized so that the tags have the signal strength required in the hospital systems.

In addition, with aggregation needs and cost of the RFID system, this solution is not meant to be a DSCSA replacement but rather an addition to 2D data matrix barcodes. This makes RFID tags an added layer of protection for pharmaceutical integrity for the sake of patients, while saving healthcare providers time and providing precise inventory control throughout hospitals.

Fresenius Kabi’s customers have responded positively to +RFID, appreciating these pre-tagged, ready-to-read products that are of high quality and reliability. Gwen Volpe, director of medication technology for Fresenius Kabi and trained pharmacist, says, “Currently, RFID is in its infancy and gaining momentum in the United States. Eleven percent of hospitals are now using this technology and the numbers are growing every day.”

Other benefits of using an RFID system include strengthening the DSCSA

serialization regulations through the combination of the GTIN, serial number, and tag ID being embedded into the label, which further virtually eliminates the threat of counterfeiting.

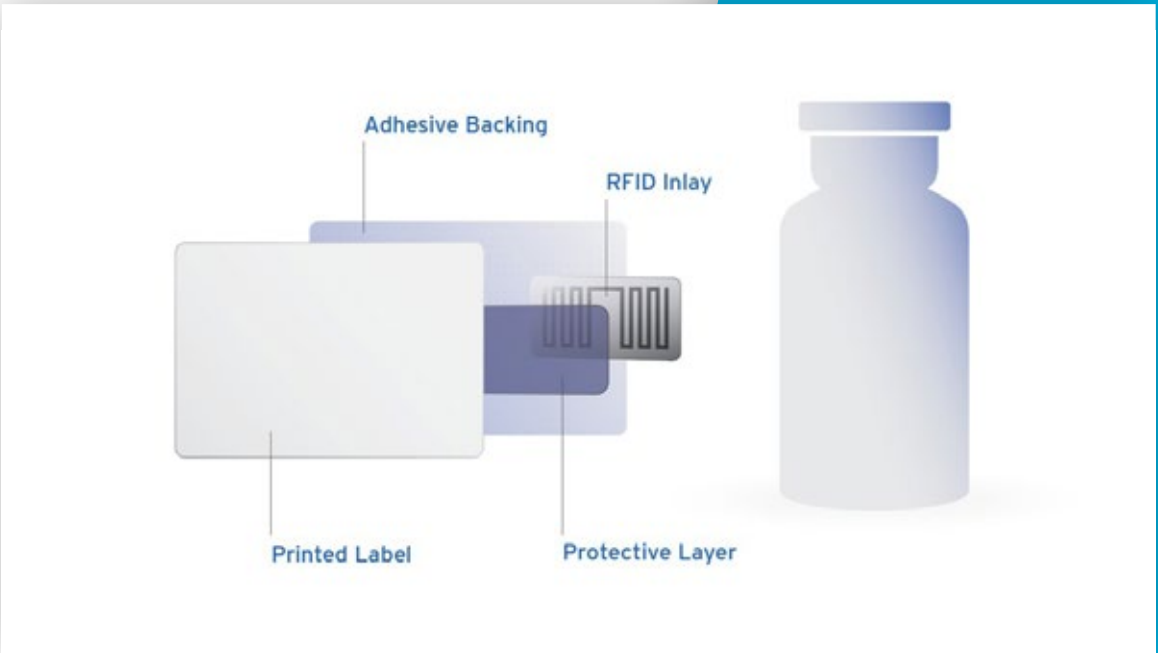
In the event of a recall, the serialized RFID tags allow items to be identified and pinpointed down to the expiration date, and lot number, as well as other related manufacturing details. RFID-tagged medication can also reduce inadvertent entry error changes to a medication's product data at the hospital and other points along the supply chain.

GS1 US involvement

Using GS1 Standards makes the RFID tags readable anywhere, allowing the industry consistency and delivering on interoperability. "The vast majority of the vendors we asked were adamant that we follow GS1 Standards," says Volpe.

According to the company, "GS1 Standards enable any supply chain participant across the globe to read data with the proper RFID equipment, including hospitals and pharmacies that comprise Fresenius

The company began implementation of its +RFID system at its Sweden facility. Photo credited to Fresenius Kabi.



Kabi's primary customer base. By tagging each dose of medication, the healthcare provider and patient have an additional serialized measure of unique product identification." This further allows Fresenius Kabi the potential to work with all of their customers' RFID tracking system vendors, thus enabling the customers to choose the system that's right for them.

GS1 US played a supporting role throughout, beyond spreading the word about RFID benefits. They worked closely with Volpe, Sirovatka, and other Fresenius Kabi employees who were involved in creating the company's RFID system, +RFID, to publish a case study and create a white paper at the end of 2020, to help other companies embarking on the RFID path. GS1 US also provided its RFID specialist to guide and collaborate with Fresenius Kabi to confirm the company was taking the correct approach, consistent with GS1 Standards.

"GS1 US approached us about the case study to guide others who are going to be going down this path and we're happy to help. It's not always easy being the first, but you can use the experience to assist others as they join you. Using GS1 Standards ensures customers have a consistent experience with our pharmaceutical products and ensures the most important data attributes are always at our customers' fingertips," says Volpe.

Med Device Market Shifting Business Models to Automation and Technology

Four out of five medical device companies interviewed for a new PMMI white paper believe automation and other technological advances are one of the biggest changes to manufacturing in recent years.

By Kim Overstreet

According to "Pharmaceutical & Medical Devices | Trends & Opportunities in Packaging Operations," medical device companies are streamlining processes and adding more flexible solutions to their operations - with a continued focus on ROI, cutting costs, reducing waste, and investing in machinery that can meet several needs at the same time.

Connecting with customers and patients through a variety of different services and technologies has reinvented how the medical device market operates, while also giving some companies a competitive advantage in the market.

New technologies are creating efficiencies throughout the supply chain, and technologies such as wearables, smart devices, IoT, and cloud-based analytics are all becoming more widely used in the industry, requiring medical device

companies to adapt. Said one Director of Packaging Engineering, "We continue to invest in capital, plus we see growth in our business. We hit thresholds where automation has good ROI and challenges the industry."

According to the report, competitive technology advantages in the US include:

- Microelectronics (very small electronic designs and components, typically made from semiconductor materials)
- Telecommunications
- Instrumentation
- Biotechnology (genetic manipulation of microorganisms for the production of vaccines, antibiotics, hormones, etc.)
- IoT (network of physical objects that are embedded with sensors, software, and other technologies to connect and exchange data with other devices and systems over the Internet)
- Software Development

There are also specific trends and opportunities that the report identifies for development in the medical device market:

- Increased need for diagnostic testing kits
- Increased use of plastic packaging (polycarbonate)
- Need for longer shelf-life packaging
- Increased need for sterile medical packaging
- Supply chain disruptions due to COVID-19

COVID has, of course, impacted the market in the last year.* Research and development has seen delays to clinical trials and new product development, while some future R&D has been left in limbo due to budget-driven constraints or reduced productivity due to work-from-home orders.

Manufacturing and the supply chain have also been impacted by lockdowns, social distancing, and work-from-home orders, as well as delays due to diversion of resources or limited movement of freight, and travel restrictions. These issues - supply chain challenges, shorter lead times, and staffing issues related to COVID-19 - highlight the need for more automation and connectivity in the market. Said one Associate Director of Equipment Engineering, “There’s a greater demand for certain commodities, but some are not manufactured at the rate you need, or you can’t scale up. For example, we need more syringe barrels, more glass, more aluminum for caps, and more corrugate.”

There is also a declining demand for devices in non-COVID segments of healthcare, as well as a decrease in healthcare spending on non-COVD treatments, and a decrease by more than 50% for elective surgeries.

Key Changes Due to COVID-19

Almost two-thirds of medical device companies who responded to the report say that new equipment will be the largest investment in packaging and processing due to COVID-19. “We’ve seen huge upticks in demand in areas such as PPE, syringes, swabs, and diagnostics. In some cases, all of a sudden, we need more capacity and can justify more automation with those. Everything pushes us in that direction in driving higher output at lower cost,” said one Director of Packaging Engineering.

Although some operations have been delayed, most manufacturing facilities have been granted exemptions for their critical systems. Dealing with challenges related to restrictions for on-site staffing have affected plant operations, however, particularly those that require on-site evaluations. Said one Packaging Engineer, “Some of our new product development projects have slowed down because of restrictions. When we try to get a new product line up at the plant, if we are not there in person to evaluate the plant situation, it makes it harder. We have a virtual meeting, which is not always ideal, or we can’t go there unless it gets approved by higher management levels.”

Modular: The Modern Way of Manufacturing Injectables

Flexibility allows manufactures to meet the needs of the growing and versatile injectables market.

By Placeholder

Modular manufacturing is on the rise in the pharmaceutical industry. The last few years have shown an increase of interest in modular solutions for a variety of uses and Stevanato Group–a provider of integrated systems for pharma and healthcare–projects that this tendancy will only continue, especially in injectables.

This popularity is due to the flexibility offered by modular manufacturing, allowing pharmaceutical processors to produce a range of products in a single facility with faster changeovers and improved overall equipment effectiveness (OEE). Modular manufacturing breaks down a system into discrete component “modules” that perform specific roles and can be integrated into or removed from the overall structure at will.

The following factors are driving this movement in the injectables market:

- Many treatments are moving from hospital to home, reducing costs for healthcare providers and increasing patient comfort, requiring the need

for user-friendly injectable devices, which has been further exacerabated by the COVID-19 pandemic

- The demand for auto-injectors and pen injectors is skyrocketing as life-style related diseases, such as diabetes, become more widespread in both developed and developing countries and as the niche of targeted small batch and personalized medicines, including oncological formulations and certain biologics, grows, driving the need for more mobile, less intrusive, and simpler solutions that remain cost-effective, which in turn demands flexibility on the manufacturing side

These self-administered options allow patients to treat themselves more independently and autonomously than ever in a safe manner. As editor Aaron Hand says in Burgeoning Auto-Injector Market Demands Flexible Production Options, “Auto-injectors help avoid common risks associated with self-administration via syringes, such as incorrect dosages and misuse, serious injuries and discontinuation of treatment.”

The benefits for healthcare providers and patients are clear. As injectables continue to become more customized and self-administered, manufacturers will need to modify the design, engineering, and production of their assembly line equipment to meet these and future demands. This will in turn benefit manufacturers–contractors and service providers in particular, who will need to prove adaptable–as the industry will continue to evolve with varying shapes, sizes, and materials of injectables as well as in product volumes, demand, and

sub-categorical issues like target audience differentiation. Production processes will need to be time-efficient and customizable.

A Pharmaceutical Networking article, Defining ideal modular design for effective pharma packaging, seconds this perspective and explains that the modular design must be adapted to the existing development process and embedded into ongoing operations during implementation in order to minimize adaptation demands which will surely come.

Automation and Pharma 4.0

Stevanato Group outlines characteristics that modular manufacturing has that assembly machinery needs in order to keep up with the needs of modern combination products: fast format changeover to reduce costly downtime, flexibility to allow reduced CAPEX investments and achieve shorter time to market, and scalability for additional modules to meet increased volumes.

Another factor Stevanato Group emphasizes is automation. Though

Placeholder

lower volumes of product are typically required with auto- and pen-injector production, efficiently switching to wider-scale production efforts can be necessary. Automating processes can also reduce human intervention and further decrease production downtime.

The company explains that automation becomes valuable through its reliability, precision, repeatability, and process optimization. The greatest benefits come from incorporating automation into the very beginning stages of the development process, offering an alternative to the prototyping phase with a benchtop through a semi-automatic pilot line. This offers inherent scale-up advantages, allows early de-bugging, and mitigates future risks as the technologies used from pilot line to large-scale, fully automated line are the same.

Says Stevanato Group, “Involving equipment partners with modularity experience from the early stages offers a distinct advantage, since they’ve seen for themselves how initial development work is crucial for establishing early proof of principle and validating the assembly process.”

Looking at containment systems and automation scale-up early on are key, in part due to injectables’ product-specific complexity.

In Industry 4.0 with a Pharma Focus, Pat Reynolds covered the efforts of the Marchesini Group in the life science space, noting, “…once processes are digitized, it opens the door to other exciting possibilities such as machine learning, condition monitoring, remote-access monitoring, and, ultimately, the smart factory. In the smart factory, operations are carried out with

minimal manual intervention, high reliability, and maximum flexibility. The automated workflows, synchronization of assets, and improved tracking and scheduling in the smart factory lead to increased yield and quality along with reduced cost and waste.

"Predictably enough, the pharmaceutical industry is anything but immune to the impact of IoT and Industry 4.0, trends that are transforming pharma manufacturing at a rapid pace."

This is echoed in the Pharmaceutical Networking article which further builds on the potential for Industry 4.0 concepts in modular manufacturing in pharma, such as shared data, artificial intelligence (AI), and increased connectivity enabled through the Internet of Things (IoT).

Systems incorporating these concepts and created by collaborative efforts from Dividella–a supplier of cartoners and secondary packaging machines for the pharmaceutical and biotech industry–and Medipak Systems–a system provider for the pharmaceutical industry–also use the "Plug & Produce concept of vertical integration that imposes a standardized interface between machines in production and the production control system." This allows modules and production lines to be connected or disconnected through plugging a drive into a computer via a USB interface.

This setup has further allowed Medipak Systems to create advanced systems that include smart packaging, Enterprise Manufacturing Intelligence (EMI), smart devices, and condition monitoring and predictive analytics. These advancements improve end-user experience, user-friendliness for operators, and allow superior decision-making by producers.

Benefits of the modular format

There is a range of benefits that come from modular manufacturing, beyond adapting to market demands, fast changeovers, improved OEE, and up scaling options with automation and plug and play expansions. Modularity can also:

- Deliver standardization–as modules are simplified, produced more economically, and made reusable–and customization by tailoring systems to individual and specialized demands.
- Reduce costs in both implementation and operation
- Ensure faster production and delivery, and when machine utilization rates are high, offer high return on investment within a short timeframe
- Allow manufacturers to meet the need to deploy manufacturing regionally, reduce the cost of goods sold (COGS), increase capacity utilization and speed-to-market, and fulfill multi-product campaigns requiring different production schedules
- Encourage engineering and production teams, through its synergy-centric nature, to collaborate by planning–in parallel–for near-term and longer-range scaling needs

Softbox Supports Pfizer in the Global Cold Chain Distribution of COVID-19 Vaccines

When correctly managed, the ULT Shipper can be used to store vaccines in excess of 30 days. Through "Re-Icing," the dry ice in the Softbox ULT Shipper can be topped up ensuring maximum thermal protection of the highly temperature sensitive mRNA vaccines.

Softbox, a global provider of passive temperature control packaging solutions for the pharmaceutical, life science, and cold chain logistics industries, is proud to support Pfizer in the distribution of COVID-19 vaccines through the supply of a high-performance temperature-controlled parcel shipper developed specifically for ultra-low temperature applications.

Softbox supported Pfizer with the development of the specialized and reusable ultra-low temperature (ULT) shipper to help them on the distribution of ultra-low temperature vaccines and storing them at Point of Use (POU) sites. Ultra-Low Temperature vaccines, such as that developed by Pfizer–BioNTech, uses mRNA (messenger RNA) technology and must be stored at temperatures between -90°C to -60°C to ensure that the vaccine's quality and efficacy is maintained.

Softbox Supports Pfizer in the Global Cold Chain Distribution of COVID-19 Vaccines

The ULT shipper is capable of maintaining the required temperature during shipping of COVID-19 vaccines between -90°C to -60°C for at least 10 days unopened.The innovative shipper utilizes high performance insulation materials, incorporated in a robust and reusable construction, in conjunction with dry ice, to ensure long term ultra-low temperature control. Based on current guidelines, the Softbox ULT Shipper can be opened twice a day, for up to three minutes at a time. This allows clinicians at Point of Use (POU) sites to access the vaccine vials required for each day's immunization clinics without exposing the remaining vaccine stored within the shipper to ambient temperatures, thus ensuring integrity of the vaccine is maintained.

When correctly managed, the ULT Shipper can be used to store vaccines for in excess of 30 days. Through a process called "Re-Icing" the dry ice in the Softbox ULT Shipper can be topped up ensuring maximum thermal protection of the highly temperature sensitive mRNA vaccines.

"Softbox's extensive knowledge and experience in temperature control packaging solutions and the cold chain industry was the right choice for us. They immediately understood

The innovative shipper utilizes high performance insulation materials, incorporated in a robust and reusable construction, in conjunction with dry ice, to ensure long term ultra-low temperature control.

the unprecedented task at hand that was in front of us with the distribution of the vaccine, and quickly started to work with us to develop a unique packaging system that does not waste any precious vaccine and creates a seamless experience for customers." said Tanya Alcorn, Vice President, Biopharma Global Supply Chain for Pfizer. "Their technical capabilities and innovative approach helped us achieve an excellent result in a very short period of time."

Kevin Valentine, CEO of Softbox, said: "We are immensely proud to be playing such an important role in the fight against COVID-19. We worked extremely hard during 2020 to help Pfizer develop this highly innovative ULT shipper; establishing one of the world's largest fleets of reusable temperature-controlled parcel shippers in the process and setting up two world-class service centers to support ULT shipper refurbishment."

"It's a huge honor to have the opportunity to support the distribution of these vital vaccines at the right temperature, maintain their integrity and help save millions of lives," he added.

Based on current guidelines, the Softbox ULT Shipper can be opened twice a day, for up to three minutes at a time.

Consequences of Supply Chain Blind Spots and Solutions in New Survey

Companies lose millions due to spoilage; improved tracking methods increase end-to-end visibility and mitigate loss.

By Melissa Griffen

Cloudleaf–a provider of supply chain improvement systems–partnered with Sapio Research–a market research agency–to survey 210 U.S. supply chain decision makers in the pharmaceutical and food & beverage industries over a month's span. The report is meant to highlight critical blind spots in today's supply chains and highlight what's needed to improve supply chain effectiveness in the future.

According to the survey results, most manufacturers do not 100% trust data for tracking product, as methods are historically outdated and lack the efficiency needed to achieve true end-to-end visibility; thus 99% of respondents in the pharmaceutical industry use some sort of manual processes to achieve supply chain visibility. Yet, the report shows that on average, these respondents still lose $95 million annually in medical inventory due to spoilage resulting from cold chain failures. This number

also jumps to $179 million for companies with 1,000 or more employees.

Due to the complex global network companies in the life sciences industry rely on to get product to end users, as well as the strict requirements on the industry, life science companies need a granular view of the flow of products traveling through the supply chain, from the initial supplier all the way to the patient. However, these companies are often lagging in digital transformation initiatives when compared to other industries. The overwhelming majority (79%) of these respondents also say they do not have 100% visibility into the condition of products in their supply chain during the last mile of delivery.

The survey offers up the following suggestions to mitigate losses in the supply chain:

- Track hard attributes such as location, temperature, vibration, and humidity
- Track soft attributes in the business process context such as purchase orders and payment terms, and in the environmental context such as weather, and traffic conditions
- Enable visibility and tracking by creating a digital model of the various supply chain components to perform real-time analysis
- Install an enterprise-wide messaging system to track soft handoffs through soft attributes within the organization and across companies. Using this method should also remove blind spots in tracking hard handoffs.

Metered Dose Inhaler Line Centralizes Control from Canisters Through Pallets

A deep dive into a "one machine" concept for a metered dose inhaler line, with system integration for 18 pieces of machinery and components from a variety of OEMs.

By Keren Sookne

"Digital disruption has reached the healthcare sector, and with it comes an imperative for life-science companies to retool core technology to remain competitive," says McKinsey and Company about the changes underway in healthcare automation.

One manufacturer taking this to heart is Kindeva Drug Delivery ("Kindeva"), with their recent endeavor to implement 18 machines and components into a "one machine concept" for their new metered dose inhaler (MDI) line developed by MGS Machine.

The project began in November 2018, and Kindeva was established as a standalone company in 2020. Kindeva's business model persists as a contract development and manufacturing organization (CDMO) that

develops and manufactures complex drug and combination products for pharmaceutical and biotechnology companies.

Kindeva wanted the one machine concept, taking bulk inhaler canisters all the way through multiple layers of packaging, case packing, and palletizing. With so much to focus on bringing a new inhaler to market, they wanted to collaborate with a company that could deliver the entire packaging line as one.

Their vision was that any operator that walked up to the line would have one common interface, with a cohesive look between each piece of the system including the same buttons, stack lights, programming, messaging, and startup/shutdown procedures. From an operator standpoint, they wanted all 18 machines to "feel" the same.

Selecting a partner

Heading the project was Jeff Annesley, U.S. Engineering Manager at Kindeva, who previously worked at 3M for 15 years as a project engineer for multiple divisions. Annesley says, "This is a very large line that's very complex. We sent a relatively high-level RFI with product characteristics and process requirements, casting a pretty wide

Depalletized canisters are oriented for automated processing.

net." Not only did they need to ensure that the vendor they chose was capable of building this system, but they wanted a level of interest and enthusiasm which helped to narrow it down.

Jeff was introduced to MGS Machine by a colleague who was working on a project with the OEM that was roughly the same size and order of magnitude as the MDI line. "Within a week, I was up there with my manager and that was the first time I met Russell [Kostreba, of MGS]. He had built the machine and asked if we wanted to see it run. He ran the whole line himself by touching one button," says Annesley. "At that point, I looked over at my manager and said, 'I think we may have found the vendor.' Of course there was a lot of due diligence that we went through to get to securing the deal with MGS."

Having a technical expert at the outset who understood the details of such a complex line (and that it could be done) helped solidify the decision. Annesley notes, "One thing that really puts MGS in a unique position is that in addition to a salesperson, they also have an application engineer to interact with during the RFP."

After they were awarded the contract, the magnitude of the project led MGS to create a role for a project technical lead, which Russell Kostreba ended up filling.

Once selected, MGS provided a shop tour to walk through some of the ways that they could integrate smaller projects. "There was a variety of projects out on the shop floor to show different types of capabilities and we introduced people on our team to help Kindeva understand how we would shepherd a project like this. There's an entire team of people that it takes to make something like this happen, so during that visit, we tried to expose the team from Kindeva to who those people would be, what those technologies might be, and our capabilities," says Josh Pangier, Director of Project Management at MGS.

OEM sourcing and purchasing

With 18 machines to consider, sourcing was a critical part of the journey. MGS took responsibility for most OEM sourcing, purchasing, installation, and controls. See it in action at the integrated MDI packaging line's video here or scroll below.

"There were some OEMs that we specified—in particular Brooks Machine and Design for the tray unloading station," explains Annesley. "Coming off of the fill line we have a canister that gets placed into trays, so a strategic decision was made early on to have the same vendor provide the design of the tray loading station on the end of the fill line and the unloading station at the beginning of the packaging line because the common piece there is the trays storing the canisters. We wanted to make sure that there was clear communication and machine design compatibility between the end of the fill line and the beginning of the packaging line."

Pangier says, "In any type of automation process, no matter where it is on a packaging line, it's not just about building the machine but about how it interfaces with the commodity and the end users'

The Brooks Machine and Design Spray Testing Module primes and tests each individual canister for proper discharge.

processes. We learned all kinds of details between Kindeva, MGS, and Brooks and it took collaboration amongst all the parties to make that part really successful."

Ultimately, the line combines 18 machines and components from over 10 suppliers into that one machine concept, starting with bulk canisters and ending with aggregation of cases to pallets:

1. Depalletizing & Tray Unloading Module

Purpose: The Depalletizing & Tray Unloading System from Brooks Machine and Design automatically takes bulk canisters stored in trays on pallets and singulates them onto a conveyor.

Details: A vision guided Fanuc robot with MGS programming locates the tray, picks it up, places it onto a conveyor, and inspects to ensure all canisters are present. Once the inspection is valid, the tray enters an inverter where it is rotated 180 degrees to orient the canisters for automated processing. Empty trays are returned to a pallet utilizing the same vision guided robot.

2. Spray Testing Module

Purpose: The Brooks Spray Testing Module automatically tests each individual canister for proper discharge.

Details: Individual canisters are passed through priming stations and are then tested to ensure proper discharge. Canisters that do not fire (No fire) or continuously discharge (Continuous fire) are rejected. Valid canisters are sent downstream.

3. Canister Checkweigher

Purpose: The Mettler Toledo Canister Checkweigher weighs canisters to ensure that there is an appropriate amount of product to provide patients with a full quantity of doses.

Details: Canisters are passed over a precision weigh cell—underweight and overweight canisters are rejected. Valid canisters are sent downstream.

4. Canister Labeling Module

Purpose: The Accraply Canister Labeling Module applies labels with product information onto each canister.

Details: Each label is printed with a lot code and expiration date. Proper printing is verified using an integrated Optel vision inspection system. Labels with an invalid lot or date are rejected while valid canisters are sent downstream. Labels are wrapped around the canister and a vision system inspects each canister to ensure the label is present and properly applied. Canisters that do not have a properly applied label are rejected. Valid canisters are sent downstream.

Linear servos insert the canisters into the actuators when the components are properly aligned in the starwheels.

5. Inhaler Assembly Module

Purpose: The MGS Inhaler Assembly module assembles individual components into the final inhaler and verifies proper assembly.

Details: Bulk Actuators are dumped into a hopper; a centrifugal bowl is utilized to singulate and orient them. Labels are dispensed and applied to each actuator and placed into a starwheel. A vision system is used to verify label placement and actuator cap presence. Actuators without a cap or proper label do not receive a canister. Canisters from the Mettler Toledo Canister Checkweigher are singulated and placed into a starwheel. A linear servo inserts the canisters into the actuators when the components are properly aligned in the starwheels. The fully assembled inhaler is inspected by a vision system to ensure the dose counter on the actuator has the correct number of doses displayed. Fully assembled inhalers that have passed all inspections are picked up by a robot and placed into the Flow Wrapping Module.

6. Flow Wrapping Module

Purpose: This Campbell Wrapper Flow Wrapping module wraps the assembled inhaler in a sealed foil package that also contains a desiccant pack.

Details: A desiccant feeder dispenses a desiccant pouch and combines it with a fully assembled inhaler. The foil for the pouch is printed with a lot and date code that is inspected by an integrated Optel Vision system. The desiccant and fully assembled inhaler are wrapped and heat sealed into a pouch.

7. Leak Detection Module

Purpose: The Bonfiglioli Leak Detection Module verifies the integrity of the pouch.

Details: Pouches are loaded into a vacuum chamber where a vacuum leak down test is performed. Any pouches that fail the leak down test are rejected, while good pouches are sent downstream.

8. Pouch Checkweigher

Purpose: The Mettler Toledo Pouch Checkweigher weighs pouches to ensure all components are present inside the pouch.

Details: Pouches are passed over a precision weigh cell—underweight and overweight pouches are rejected. Valid pouches are sent downstream.

9. Pouch Accumulation Module

Purpose: The Ambaflex Pouch Accumulation Module provides a buffer of material to absorb the imbalance in product flow that would otherwise impact overall production.

Details: A vertical spiral conveyor is used to provide approximately four minutes of product accumulation.

10. Stealth CT Cartoning Module

Purpose: The MGS Stealth CT Cartoning module automatically loads the finished pouches and two pieces of literature into a carton that is then weighed and serialized.

Details: Two pieces of literature are picked, inspected, and then placed into a

conveyor. Finished pouches enter a vision guided Fanuc robotic infeed where they are picked and placed onto the previously placed literature. Cartons are automatically fed, opened, loaded with pouches and literature, glued, and closed. Cartons are then weighed via a Mettler Toledo system to ensure all components are present. Overweight and underweight cartons are rejected. Valid cartons are printed and inspected by a printer and camera controlled by an integrated Optel Serialization system. Cartons that fail the vision inspection are rejected and valid cartons are sent downstream.

11. Stretch Banding Module

Purpose: The Omega Stretch Banding Module combines serialized cartons into one stretch wrapped bundle.

Details: Product enters the module where they are upstacked into a product matrix. The product matrix is discharged through a stretch wrap film and the film is heat sealed to create a completed bundle.

12. MatriX Case Packing and Palletizing Module

Purpose: The MGS Stealth MatriX Case Packing and Palletizing module

Ambaflex Pouch Accumulation Module provides a buffer of material to absorb the imbalance in product flow.

combines stretch wrapped bundles into groups and loads them into a case. Cases are closed, labeled, serialized, and automatically placed onto a pallet.

Details: Stretch wrapped bundles are inspected by an integrated Optel camera that aggregates cartons into bundles. Stretch wrapped bundles are upstacked and organized into a specific matrix. Cases are automatically opened and fed to a load station where the specified matrix is inspected by an Optel camera that aggregates the bundles into a case. The fully loaded case is closed and discharged to a labeling station. The integrated Label-aire labeler dispenses and applies a serialized case label that is subsequently inspected by another integrated Optel Camera. An MGS palletizer robot picks up the cases and positions it in front of another Optel Camera for final aggregation of the case to the pallet.

13. Central Control System with Marquee Monitoring

Purpose: True to its name, the MGS Central Control System provides a central control and monitoring station for the entire line as well as final integration of the Optel Serialization System.

Details: The MGS Central Control System allows a single person to control the entire system if local module control is not desired. Functionality includes the ability to start/stop, monitoring production and maintenance data, set and change recipes, initiate product integrity challenges, and perform final pallet labeling and aggregation. The Central Control System also controls the Marquee Display Monitors that allow operators to see real time data for the entire system.

System integration

The original plan was to design and build the MGS portion of the line "in parallel with sourcing a number of components from OEMs and then integrating them all together at one time. That looked good on paper—and then reality hits and you end up working through issues," Pangier says.

Some product and process development went on concurrently according to Annesley, with MGS playing a key role in some instances. For example, the original pouch didn't fit into its carton so they couldn't get started on system design until that was sorted. "We may not be experts at trying to fit products in cartons, but MGS is and that's a key strength," he notes.

"Meanwhile, we're off sourcing other parts of the project that were solid. I think we did nine or 10 revisions of the schedule over that two-year period," says Pangier. "It's all about hitting the end user's market window—if they're not successful, we're not successful. We spent a lot of time collaborating on schedule adjustments or pivots. Throw in the global pandemic and it was even more challenging. The leak tester and the front-end Brooks components ended up being the last pieces in that were most affected by the pandemic."

MGS helped OEMs integrate requirements into their machines so the operators would have the aforementioned similar feel to each component. In cases where MGS saw that an OEM wasn't solving an issue, they took on the challenge internally. Some pieces of equipment were thought to be turnkey, but as the team found gaps, MGS made their own alterations to ensure a better result.

Part of the success came from personnel at Kindeva. Kostreba says, “Jeff is excellent at project management, and management of people and meetings. Everything’s informative and the people he selected were great at their jobs. So from our standpoint, I felt like we had an army of Kindeva experts to keep us on our toes because they would help to find gaps and then we would fill the gaps with our own little army of experts. Probably the best part of the project is the number of experts doing their job well, working like we were one team instead of two companies.”

Central control

The central control system (CCS) operates, as the name implies, as a master control system while every machine operates in the background as its own machine. The programming for the modules remains in the modules themselves.

The CCS monitors what each machine is doing and communicates back and forth. Kostreba explains, “Machines upstream and downstream communicate with each other individually for stop or wait

The Omega Stretch Banding Module combines serialized cartons into one stretch wrapped bundle.

commands, and the central control system can also start and stop machines, go to dispatch configuration, half speed, full speed, etc. Then it reports all of that information for everybody in the room to know what's going on."

Annesley says, "A requirement from the beginning was that these equipment modules all have to operate as a single unit. In order to do that, you have to have an orchestrator so there can be that level of coordination between each module. That was something that I would say uniquely positioned MGS because they understood that from the very beginning. This wasn't necessarily the case with all vendors—there are different ways you can approach this. MGS also had very capable technical employees, their control staff had a great understanding of the standards that needed to be put into place and communicated to each one of these OEMs so that they can speak the same language and be coordinated by a single central control station."

Operators can start and stop the system from the CCS or locally at the machine. MGS had to develop programming to ensure that this is done safely. Local maintenance can be done on one module without stopping the entire system.

As was mentioned above, a key goal of the project was to have each OEMs' technology shine in its particular role, while still ensuring that an operator at Kindeva could walk up to a machine and see the basic control was the same as for other machines. Each machine has its own HMI. MGS did not ask OEMs to change their HMIs—their core standards are the foundation of their equipment—but messaging and content look the same to make the operator experience as easy as possible.

"We were adamant that it had to have a certain kind of button layout, and very standardized controls when it came to basic start and stop functions. Then laid over the top of that was the central control system, which gives visibility to the whole line," Pangier explains.

OEMs have different ways of interfacing with the CCS. "From a technical standpoint, we had to translate that. We designed an interface box and sent it to the OEMs and said, 'Put this box in and interface in this way, and give us this information and we'll handle the rest.' Everything uses Ethernet for communication. We had to lay out that expectation, otherwise I think that each of the OEMs would have provided what they provide through their own lens," says Pangier.

Not every OEM was as understanding, so in some cases, MGS stepped in and fixed a system's programming themselves instead of debating about scope. With such a large system and a set deadline, the project team would hold status meetings with OEMs. If an issue was difficult to resolve, MGS would say, "Let's work on it for this long and if we can't break through, here's the stop point" in which the MGS controls department would take over to remain on schedule, according to Pangier.

Case in point: Nearing the deadline, there was an error in handling emergency stops with bad product in process. The source of the issue was a conveyor running through the checkweigher, which came from an outside supplier. "We found an error in that could let bad product downstream. This required pulling in that supplier's engineering team in Europe to get them

to understand what we wanted, but their solution was that we needed to expand everything by about four feet. Of course, there wasn't room to expand that much with walls on both sides," says Kostreba. "It was already built on our shop floor when this was happening. So our controls people used the CCS to monitor the safety network. We installed mechanisms to make sure that bad product never made it through. So we solved the problem because their solution was going to take months and our solution took days."

Ultimately, MGS absorbed all the delays and challenges and delivered the machine a week early, during COVID-19.

Monitors save millions

Adding strategically placed monitors on the line may sound like a small add-on. But Kostreba estimates that the TV/monitor information display system they installed for another customer saves $26 to $52 million per year, based on the product running and time saved.

In a larger system, operators are working in various locations and don't necessarily have visibility into other areas. There can be

The MGS Central Control System offers central control and monitoring for the entire line as well as final integration of the Optel Serialization System.

considerable downtime caused by an operator who's stopped and assumes they're waiting on someone else when the issue is actually at their part of the system. Diagnosing takes time, too, in realizing there's a problem, and walking back and forth between HMIs and machines. Says Kostreba, "If you go in real operator speeds trying to figure out what's going on—not being an expert—it can take a minute and a half. We timed this just watching operators at a different facility. Every problem is different, of course. But when you take that one minute or a minute and a half saved on one stop, all you have to do is save five minutes an hour to get those millions saved on that specific customer's process. Five minutes per hour saved is pretty realistic. When you start having big machines, long distances to walk, and complicated mechanisms where you forget what's going on, or people stand and stare at something thinking it's not their problem, five minutes an hour is really easy to save."

The monitors give a line-level view of everything that's happening—machine data, errors—so operators can just look up. They are located in such a way that from almost anywhere in the room, they can see a monitor and know what's happening in other parts of the line. Saving even seconds on each error means big savings annually.

"So they naturally, by looking at the monitors, can kind of check each other. Every customer has a goal that they're trying to produce a certain amount of product and our information display system helps them without having to walk around to know where they need to go in the system," says Pangier. After a while, when the machine stops, everybody

looks up and immediately knows what to do.

Many people may not understand the value of such monitors right away. “I knew that it was something that would be of benefit, but I didn’t realize how useful it would be and how the operators would respond to it,” says Annesley. “Once the operators saw that it would allow them to understand about the other areas of the line, it just became the line that everybody wants to work on because they’re informed, and the machine functions in a way that they can understand. That makes everybody’s job that much more enjoyable because they’re not confused and frustrated when they’re working on a machine. That was when it clicked for me, even though this was a scope change and added cost, I realized this is really going to help these operators.”

If people feel like they’re productive and able to address issues— rather than being confused and frustrated— the end result is going to be higher productivity, which is the ultimate goal. (On a project for another customer, MGS had installed the carefully placed monitors on a second line. Operators clamored to work on that line, so much so that the customer retrofitted monitors on their first line as well.)

Marquee Display Monitors allow operators to see real-time data for the entire system.

Collaboration for problem solving in real-time

Kindeva benefitted from MGS' collaborative approach to projects where engineering, sales, and machine builders all work hand-in-hand. Less emphasis was placed on titles—it was more about everyone at both companies working together to get the project done.

"When we had a couple of commodity problems such as getting materials into the facility, I dealt with a lot of people I wouldn't expect to in the procurement process. I texted somebody that worked at the factory to get a measurement for me—that was three minutes instead of three weeks of emails," Kostreba notes. "I met with one of Jeff's employees and the manufacturer of the labels about the adhesive. I was directly in contact with their vendor to handle label issues."

From an operator to a packaging engineer to someone responsible for the adhesive on the MDI labels, everyone had a seat at the table rather than having to have everything flow through Annesley, Kostreba, and Pangier to get distributed. Says Pangier, "Things get lost that way, so it would have taken much longer under a different format especially with a project of this magnitude. A lot of it hinges on how teams are structured and whether you've got that level of collaboration. It's not just about the equipment—it's the equipment, the process, and the people—and then putting that all together."

Care Kits Supplement Telehealth for Medicare Patients and More

57% of Americans with chronic conditions delayed healthcare and experienced a gap in care due to COVID-19, per a recent study. Aetna and other companies are shipping kits with specially curated products to offer self-care or supplement telehealth visits.

By Keren Sookne

Telehealth and e-commerce both experienced major boosts during the pandemic, driven by the desire or need to stay at home and reduce exposure. While swapping a trip to the grocery store for an online order may feel easy, healthcare can require extra tools to accommodate the switch to remote options. Delayed healthcare services during the pandemic can be dangerous for those with chronic or serious conditions.

R.R. Donnelley & Sons Company (RRD) launched Care Kits to help healthcare companies adapt to industry changes and demonstrate their commitment to member and patient wellness. Kits are offered in a wide range of treatment areas including telemedicine prep, COVID-19, diabetes management, asthma, social isolation, and more.

RRD reported that in a recent Wellframe study, 57% of Americans with chronic

conditions delayed healthcare services and experienced a gap in care due to the pandemic. Care kits can positively impact a patient's impression of a provider according to the 2021 Medicare Shopping and Switching Study, with 59% of Medicare Advantage members noting that receiving COVID-19 or flu kits improved their opinion of an insurer.

Nicole Williams, vice president of go-to-market strategy, RRD Healthcare Solutions, explained in a recent release that "healthcare organizations find themselves in completely new territory, looking for new ways to deliver care to members from a distance. Healthcare payers and providers can now supplement in-person healthcare services and keep patients and members healthy by delivering tools and resources to their homes."

Aetna, a CVS Health company, is shipping "Caring For You" kits with specially curated, over-the-counter items to all its Medicare Advantage members across the country. The idea is to support members with "simple self-care at home," and kits include a thermometer, hand sanitizer and two Aetna-branded face masks, among other items.

RRD launched Care Kits for patients and to help healthcare companies adapt to industry changes and demonstrate their commitment to member and patient wellness.

"During this challenging time when many of our most vulnerable members are home, we wanted to provide them with some convenient items to help them stay healthy," said Christopher Ciano, president of Aetna Medicare. "We know that something as basic as an oral thermometer can make a big difference during telehealth visits. Sending these types of important items to our members at no cost was simply the right thing to do."

RRD's design process

The end-to-end solution encompasses kit ideation, design, item procurement, packaging, fulfillment and communications—both inside and outside of the box.

Because each kit will hold different products depending on the treatment areas, RRD works closely with customers to determine the goal of the kit and design, then they break it down by products. Each customized kit contains products that are carefully sourced and evaluated for quality, meeting the needs of an individual patient or member.

One kit offered is the "Healthy Mom

Kit," which includes prenatal vitamins, nausea treatment, a pregnancy journal, belly butter, antacids, a belly band and compression socks.

The "COVID Care Kit" provides patients and members with facemasks, hand sanitizer, antibacterial wipes, facial tissue, a digital thermometer and a COVID-19 home test kit.

"We take into consideration the demographics of those receiving the kits, which helps us decide how elaborate or simple the packaging design needs to be," says Williams. "We've also learned the importance of providing messaging with the care kits. We take advantage of the real estate on the box itself including under the inside lid to provide clear and concise information about the contents of the kits and any instructions for how to use them. In the medical space, for example, the end user is often over the age of 65; by including written instructions on the packaging itself, we ensure the products in the care kits are easily accessible and their intended use is understood."

It is critical that the layout is simple while attractive, and that the kit and contents arrive safely. They ensure branding fits with the product

families. Explains Williams, “Everything—from the product itself to after the packaging is disposed of—is taken into consideration during this initial phase.”

Materials

Material selection is a collaboration between RRD and the customer. One client might prefer the kit to act as its own shipping container, in which case the material for the kit would be corrugated to withstand shipping. Alternatively, if a client requests a high-end or lower-volume kit, RRD would build a corrugated shipper around a rigid box or folding carton.

Logistics: assembly and distribution

RRD reports that development and execution of these kits involves a high level of supply chain complexity, including secure PHI (Protected Health Information) handling, component and commodity shortages, and logistical planning. Taking a kit from design and procurement to assembly and distribution requires the input of multiple teams early on.

“Our facilities are equipped with the systems to handle PHI and FDA-

regulated items during the assembly and distribution process, which is important in the healthcare space where sensitive information and proper product handling need to be followed in accordance with HIPAA and cGMP guidelines," notes Williams.

With existing supply chain services, Ken Gammon, vice president at RRD Healthcare Solutions, explains that they are able "to address healthcare industry challenges, such as compliance, cost and speed to market, with ease."

Navigating challenges

RRD developed care kits at the end of 2020 that required a very quick process. "Our flexibility and scale allowed us to curate nearly three million care kits on behalf of several clients. In situations where we produced and distributed diagnostic testing kits, we were up against complex elements, such as lab test turnaround. In these situations you have to weigh many factors, ultimately prioritizing timely delivery and turnaround time. We streamlined the process of returning specimens to a lab for testing and ensured we were creating an efficient process for our clients and the end user," says Williams.

Beyond COVID-19

Telehealth has been gaining steam for years as many patients and consumers prefer to treat conditions in the comfort of home, provided they are comfortable with smartphones and other devices. As manufacturers and healthcare providers look to improve patient adherence, comfort, and satisfaction, at-home kits offer convenience to supplement telehealth appointments and home care.

Pharma Supply Chain: Master Data Exchange in 2021

The exchange of data needs to move from today's manual processes to automated operations. Experts recap current progress, challenges, and what a "happy path" looks like.

By Keren Sookne

In order to arrive at the unit-level traceability sought by the Drug Supply Chain Security Act (DSCSA) by its 2023 deadline, the pharmaceutical industry as a whole must tackle the issue of interoperable systems to share data with trading partners.

The overall goal of DSCSA legislation is to verify product legitimacy, make recalls more efficient, and enhance detection of illegitimate products in the supply chain. A major component of this is the requirement of serialization, the practice of assigning a unique serial number linked to product data—product origin, batch number, and expiration date—to each saleable unit of each prescription drug product.

"But the exchange of master data today is a manual process," explained Allison Sheldon, senior manager, Pfizer Digital Serialization, Pfizer Inc. at a recent HDA Traceability Webinar event. Serialization data is manually pulled

from internal systems, and spreadsheets are maintained and emailed back and forth to trading partners.

Part of what manufacturers are trying to sort out now is how their trading partners are managing data on their end. "Are they taking HDA's forms and applying changes that are required in their systems? How do we keep that data up to date? We'll see that when there's any type of mismatch, that creates failures when we're exchanging our serialized data. It's certainly not sustainable—we need to come to an automated approach," said Sheldon.

Brad Pine, vice president, brand pharma & regulatory at Smith Drug Company, Div. J M Smith Corporation, agreed. "Everybody gets HDA spreadsheets and adds the GTIN [Global Trade Identification Number]—it's still not very well-adopted. You're constantly sending them back to manufacturers and saying, 'You didn't have the GTIN on here.' Then loading information from a spreadsheet is painstaking and it's prone to errors because of the formatting. If I don't capture lead zeros correctly, there are issues with that."

Panelists offered resources for those starting out. (Credit: HDA)

EPCIS onboarding

The answer, panelists said, lies in pharma manufacturers using a common framework to exchange data: EPCIS (Electronic Product Code Information Services) files.

EPCIS is a global GS1 Standard for creating and sharing visibility event data, both within and across enterprises, to enable users to gain a shared view of physical (or digital) objects. Physical objects include products, logistics units, documents, and more, while digital objects can refer to items such as music downloads, e-books, and e-coupons.

Adoption is off to a rocky start. “Our biggest challenge is finding manufacturers that are willing to send us EPCIS events and get that onboarded,” said Pine. In a best-case scenario, Sheldon offered a chart showing that it takes around six weeks to onboard, covering three main activities:

- Exchanging master data
- Testing
- Moving into production

The six weeks represents a “happy path” where everyone is talking consistently and maintaining momentum. It involves a variety of stakeholders between the trading partner and internal personnel from marketing, IT, logistics, and warehouse operations. “And this could be for just one trade partner. So keep that in mind as we look at the volume of onboarding work that we need to do over the next year and a half or so,” advised Sheldon.

Challenges

Working with wholesale distributor or dispenser partners, pharma manufacturers are running into a number of issues once they are testing or live in production. There are errors in master data files that cause failures, or a trade partner didn't have a particular GTIN—possibly due to scanning an "inner pack."

Following standards is key. There may be timestamp issues in a file, and as Sheldon pointed out, it's one thing to determine the file failed because of a timestamp issue, "but then from the manufacturer side, we need to go back and look at, 'Why was there a timestamp issue?' and then you might uncover other process changes that need to happen to address that going forward. As I'm sure everyone knows, process changes, don't happen overnight."

Pine echoed the need to follow standards and start soon: "You find that there's a lot of syntax errors and aspects that are glitchy. When you talk to the bigger manufacturers, they are certainly in test phases with the big three—a few of them are testing with us—but the big three are definitely pushing the issue. It's really important that we start testing and putting together production as soon as possible, because there's a lot to be done before November 2023," said Pine.

Jeff Falardeau, manager, pharmaceutical information technology at Cardinal Health, Inc., said that in working with their manufacturing partners, another challenge is readiness. "We cite in our onboarding guide things that the company must be proficient at before starting. Communication is

another area where time could be compressed. We might get a test file and we'll respond usually within a business day. But we don't know what happens once we send that response out—it may go into some kind of rework and come back. I'm not sure how closely mailboxes are monitored, but there's an awful lot of time lost just in exchanging messages back and forth," Falardeau said. "Proficiency is all over the place. Some companies are very proficient, some are less so. That leads to situations where we might get chronology errors with the EPCIS event times—probably the largest source of errors that we get. We might be missing master data altogether, missing master data elements, or have extra master data inserted where it doesn't belong. Quite a wide variety of things."

Baseline format

One audience member asked if there a difference in the EPCIS formats being used by various solution providers. The answer is no according to Michael Ventura, vice president, solutions & innovations at LSPediA. EPCIS standards have evolved over time from 1.0 through 1.2 (ratified Sep. 2016). "There is a 1.3 in development... it's fluid on its timeline. There's no guarantee that it would be done and adopted by November 2023. I'll get up on my soapbox here... you need to be able to do version 1.2 to go live. That should be an expectation, because we see this all the time. One of the biggest problems we have right now is there are people running on 1.1 or even 1.0 at the beginning of the supply chain that are failing files and broken files, and they can't figure out why. Everybody needs to be working with their solution providers to be up and running on 1.2 and testing

with their supply chain partner," he said.

From a solution provider perspective, he added that they have the advantage of viewing partners sending and receiving data: "We're watching the type of errors that are going on that will be experienced by the entire supply chain as they get up to that space. It becomes a matter of knowing that the quality and the viability of your files are meeting the needs of your partners. Do you have some sort of monitoring and alert to know that when you fail a file? Somebody needs to be acting on it. What is the automation or the process you built to resolve that so that product isn't sitting around and you're maintaining that supply chain continuity."

Lower volume manufacturers

EPCIS-formatted messages are usually generated through L4 enterprise systems. But there are options for generating EPCIS messages for low volume or low frequency shipments to avoid the additional costs related to new L4 modules. Falardeau explained that for those who don't have an internal IT group that can extract information and formulate EPCIS files, there are solution providers that will take data in most any form and convert it.

There is a standard template for master data that manufacturers can send to wholesale distributors to avoid sending different Excel files formatted for different wholesalers. Justine Freisleben, vice president, industry relations at

HDA noted, “We have an HDA Standard Rx Product Information Form that manufacturers can fill out. We also have a short form for GTIN updates that manufacturers can utilize.”

Distributors noted they have Excel forms or CSV files that specify the elements they need to load master data.

3PL vs. manufacturer responsibilities

Audience members were curious if manufacturers will need to have all their distributors or wholesalers onboarded to their serialization system to track transaction information directly, or whether their 3PL can send that information if they have it. Pine explained, “If you read the law, the law just says that the manufacturer has to send the information to us [a distributor]. So that’s descriptive in who’s going to be sending it to me. But I’m just as happy to get data from the 3PLs as I am from the manufacturer. I think each manufacturer is thinking that through a little bit differently. Some of them want to have control and others are happy with allowing their 3PL do the work for them.”

Just don’t forget that while a 3PL facilitates many activities on behalf of the manufacturer, when an FDA auditor comes in and asks for information, the manufacturer is ultimately responsible.

Verification router service

When Pine’s company surveyed manufacturers about whether they would be using a verification router service (VRS) system for the DSCSA’s saleable

returns verification requirement, many mentioned they wanted to use EPCIS files instead. “A lot of them were using 3PLs. I think that they’re thinking that they can get around the VRS by using EPCIS, and in a lot of events, that’s probably going to be true. But VRS is the only viable thing that we can think of for really verifying products upon return when we don’t have the EPCIS events,” said Pine.

Ventura said this brings up an important point about VRS and industry preparedness: “Something as philosophically simplistic as ‘I put a number on a product, I put it into the supply chain, it’s on a barcode somebody can scan, and with a network, hit my database and verify its authenticity’ should be clean and simplistic. We received that FDA enforcement discretion [for returns verification] in 2020 for an obvious reason. There was a concern that it wasn’t that simplistic and that it could cause supply chain disruptions. [Master data exchange] is exponentially greater in its magnitude and its detail to get right, so obviously the challenges are real here.”

Future considerations

At present, there are downstream trading partners saying that they haven’t had distributors approach them about data exchange. Panelists said they would be turning their focus to dispenser interactions in 2022.

How will data flow work for drop shipments in the future? This is a topic the panelists have just begun working on with an HDA work group or in their organizations. Pine noted that in the DSCSA, that action is a manufacturer-

to-dispenser issue. They're just beginning to see if there are ways that wholesalers can be a conduit in a meaningful way. The work group is the HDA Traceability Implementation Work Group, which is a member-exclusive group. For more information, contact jfreisleben@hda.org.

Closing advice

The main point panelists hammered home is (1) to ensure you have processes (resources, tools, and SOPs) for exception management and (2) to get help with data exchange as soon as possible if you need it. "Full and timely adoption for exchange with manufacturers and distributors is key. Risk and impacts are very high and extreme if we can't ship product for which we don't have the data. So when files come in, if they fail, we need to react quickly," said Falardeau. "Cardinal Health looks to invest in automation to help with that, to work with manufacturers, and to reduce that turnaround time. But as I alluded to earlier, there's a wide range of proficiency levels right now and manufacturers, if they're not already, really need to start pulling themselves in here to get up to speed more quickly or seek help from solution providers. We also highly recommend conformance testing companies that will help you learn EPCIS or help you be able to test rapidly. For now, we're just really concerned about the runway left and the number of manufacturers that still need to jump in the pool here and start testing with us before 2023."

Questions to ask yourself

Timeliness of exception management: Do you have a process in place that will alert you when there's a failed file? Do you have resources, tools, and SOPs in place to manage this? "The worst thing that can happen here is product piling up on the receiving dock without a good file to receive it against," said Ventura. "Obviously that exception management is going to be critical to not only get everybody onboarded and understand what they're supposed to do, but also what to do when things don't go right."

People: Are you ready for the learning curve in the warehouse to ramp them up? Depending on the size and volume of an operation, you may need additional resources or time. "We talk a lot about the technology and some of the processes, but there's also that big people component in enabling this," noted Sheldon.

Data: Once you have data, are you able to send it to partners? 3PLs are getting onboard and now realizing that they're probably going to have do a lot of the work for the smaller manufacturers. "I was talking to one the other day and they said, "Yeah, we've got all the information and it's going great.' I asked how they're going to get it to me. And it was kind of like, 'Oh, I'm supposed to be sending this down to you, too?' That's where 3PLs I think are really going to help out these smaller manufacturers," said Pine.

Update on the Natural and Organic Market Today

In 2020, the natural and organic products industry grew to $259 billion, an increase of 12.7%, with sales on track to pass $300 billion by 2023.

By Kim Overstreet

This morning, the New Hope Network launched its virtual Spark Brand Success event with an update on the natural and organic products market status.

Of the total natural and organic products market, food and beverage accounted for 70% of industry sales, growing approximately 13% to $186 billion in 2020. Conventional food and beverage grew 8.6% last year, and both markets saw increases brought on by COVID-19 and resulting quarantine trends.

The report acknowledged that consumers continue to seek functionality in the area of food and beverage with the “food as medicine” trend, and sales in this area grew over 9% to $78 billion in 2020. Some of the top growth categories were shelf-stable, frozen, and snacks, while popular ingredients included collagen, mushrooms, adaptogens, nootropics, and healthy fats. Also, plant-based products are reported to be growing twice as fast as their mainstream counterparts.

As consumers seek natural solutions that will boost immunity and reduce stress and anxiety, functional food and beverages are sought out, as well as health and well-being products. Supplement sales increased 14% to $56 billion in 2020 – $3 billion more than anticipated in pre-COVID estimates. (But conversely, it should be noted, consumer trends also saw an uptick in the consumption of junk food and alcohol.)

E-commerce sales growth increased in this market as well as many others in 2020, up 60% in what may be a permanent shift of shopping behavior in some cases. But, the report states, “While total natural and organic e-commerce sales are set to double between 2018 and 2023, retail—especially mass-market retail—will continue to fuel the majority of natural and organic sales.” As consumers shift back to stores as pandemic restrictions lift, an “omni-channel strategy” should be top of mind for a brand’s success.

Retail and E-Comm: 4 Cannabis Considerations in Uncertain Economic Times

How are brands coping with changes in the market, distribution and consumer behavior?

By Keren Sookne

It goes without saying that consumer behavior has changed in the wake of COVID-19. As Blake Patterson, MarketHub CEO, explained at the Hemp Industry Daily Conference, cannabis is no exception. Purchasing behavior, which typically takes years to change, changed in mere months after the onset of the pandemic in March 2020.

"People want to get out of the store as fast as possible. The experience is not what it was before COVID-19," Patterson said. He added that masks can create a bit of tunnel vision as well. Now, the consumer generally has a list and knows what they're going for instead of wandering the aisles looking for what's new.

1. Reaching customers

This sudden behavioral change also represents an opportunity for brand owners to talk with retailers and find different ways to engage.

Franny Tacy is Chief Creative Officer and Farmer at Franny's Farmacy and Franny's Farm in North Carolina. She noted that curbside delivery, text campaigns, local ads, and more have become valuable resources.

Customers are calling in to dispensaries and connecting with budtenders. Tacy said there are many more people with anxiety and stress due to COVID-19, all customers in need. "It extends beyond curbside delivery to using Facebook messenger, chatboxes... everything we're doing now is designed to connect/engage with customers," she explained.

And will these strategies remain even after COVID-19 for reaching customers? "Absolutely. We're a national brand but still an owner-operated business. We've got a lot of different marketing and sales strategies," she said. "There are definitely things we're going to keep in the long-term."

Patterson agreed. The pandemic has caused businesses to set new best practices, with consumer behavior changes likely to hold for the foreseeable future or next five years. He said the onus is on the brand owner to implement these best

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practices—even if consumers go back to a browsing mentality— and provide value that the retailer just can't on their own.

2. Packaging and traceability hurdles

Franny's Farmacy is vertically integrated, so they take their plant all the way from grow through distribution. Even with this control over their supply chain, they experienced problems with packaging and had to make some modifications, "which people don't understand means new labels, it's an entire process that could cost thousands upon thousands of dollars, just because you run into one little packaging issue," Tacy said.

Distribution for some brands was also disrupted when many small retailers went out of business in 2020.

Tacy noted that they set their own standards so that everything is very transparent, from the website to the branding to the Certificates of Analysis (COAs). "You can trace that product everywhere it goes," she said.

But not every brand is so conscious of traceability and quality, so another issue that's surfaced is retailers are scrambling to find reliable brands because customers are aware and will ask for COAs, product origins, etc.

3. Scaling patiently

While the year was daunting for many small businesses, it's also important to remember the flipside. When business is good, don't scale too quickly.

Patterson noted that while his company distributes products (but doesn't manufacture them), "Our advice to our clients is to make sure that they don't grow too fast."

He said what inevitably happens is a brand is so thrilled to get the question "Can you fill my 200, 800, or 8,000 stores?" There may be temptation to say, "Of course I can," but collectively the answer is no. "Maintaining stock is extremely important. You have to plan for your brand to be successful but also have the ability and not fool yourself into thinking that you can fulfill that. It's okay to say 'no' to a retailer to make sure that you're not going to disappoint them down the road because there's no second chance. As far as the manufacturing strategy is concerned, generally we like you to have at least 50% of your on-shelf inventory in back stocks for at least six months."

Tacy agreed that saying "no" has been an important key to their success.

If you put out a great marketing campaign, be prepared for the orders that follow. She added, "You could be back-ordered for two months, and a back order… that is the kiss of death in business. We have got to make sure that the growth is strategic.

"We find that happens all the time… this amazing deal when the timing is not right. It really has been what has put a lot of small businesses out of business. So it's better to hang tight and be patient and just grow your business like a plant," and focus on your roots.

4. Look at pricing parity

Why is it important to create pricing parity between e-commerce and brick and mortar channels?

Tacy said her customers are guaranteed to get the same price across the board everywhere, and that the only place they can get a better deal is in a brick-and-mortar location. “We have franchises, corporate stores, and e-commerce, so this pricing parity is something that is really integrated in every level of our business. And it is so important for the customer to know that no matter what, you will never find our product online less expensive, the only place you could get an additional benefit is going into a brick-and-mortar. It’s just a basic business strategy that has got to be implemented.”

Changes in customer behavior have highlighted pricing parity. “This has certainly garnered more attention lately, I think because retailers are clamoring for customers. More people are shopping online than ever before,” said Patterson. “There’s so many different points for CBD or any product to be sold online that as a brand, you have to make sure that you have good solid contracts in place to protect yourself, to protect your retailers, and to protect your word when you give that word to the retailers.”