FDA UPDATES FOR A MODERN WORLD

2020
EDITION

Keeping up with changing healthcare regulations for advertising, UDI, Industry 4.0 and more.

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FDA Guidance: Providing Regulatory Submissions for Promotional Labeling and Advertising Materials

Final guidance includes seven examples of appropriately submitted promotional materials, including video games, exhibit booth banners, and kit materials.

Keren Sookne, Director of Editorial Content

The FDA released new guidance this week, "Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs."

According to the FDA release, this document is intended to offer guidance to manufacturers, packers and distributors (firms) for submissions of promotional materials for human prescription drugs. Promotional labeling is generally any labeling, other than the FDA-required labeling, that is devised for promotion of the product and can include TV ads, brochures, booklets, websites and more.

As the FDA notes, "Specifically, this guidance pertains to submissions made to the Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) and the Advertising and Promotional Labeling Branch (APLB) in the Center for Biologics Evaluation and Research (CBER). This guidance also explains certain aspects of electronic submission of promotional materials in module 1 of the electronic common technical document (eCTD), using version 3.3 or higher of the us-regional-backbone file."

The 37-page document contains recommendations for submission fulfilling post marketing reporting requirements, pre-submissions for accelerated approval products and voluntary submissions for advisory comments.

The guidance details formatting for paper and e-submissions, and offers considerations for presentation related to appearance, layout, format, and visible impression of promotional materials submitted. "Each promotional material should include a concise description of use. The description may include, but should not be limited to, the purpose of the piece, setting of use for the piece, and/or an explanation of additional materials that will be used in conjunction with the piece," according to the guidance.

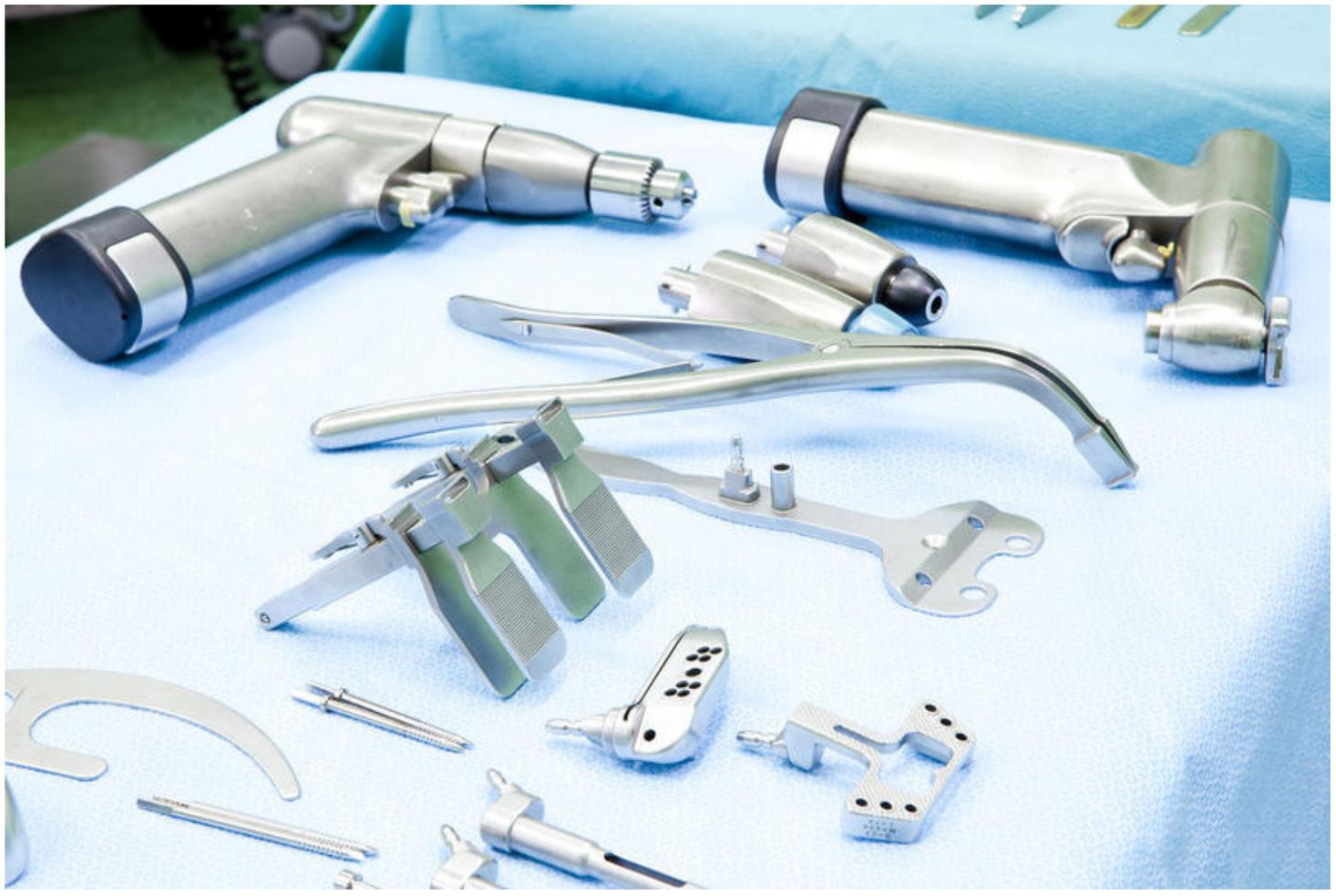
Additionally, the document includes a section of seven examples of appropriately submitted promotional materials, including video games, exhibit booth banners, and kit materials.

To view the guidance document, click here.

Healthcare Packaging's
UDI Resource Guide

The 2019 UDI Conference is over for this year, so where can device packaging professionals get the information they need to meet the UDI regulations right now? Use Healthcare Packaging's UDI Resource Guide as a launch pad.

Dirk Rodgers, Founder of RxTrace.com



I recently returned from the 2019 UDI Conference in Baltimore. It's one of my favorite conferences because it is co-sponsored and heavily attended by the Unique Device Identification (UDI) team of the U.S. Food and Drug Administration (FDA). You can get your UDI questions answered directly by those responsible for administering the regulations. The FDA UDI team even has a booth in the tradeshow. Compared with the drug side of the FDA, this is unheard of, and device labelers and packaging professionals should take advantage of this annual event.

But the event is over for this year. So how can device packaging professionals get the information they need to meet the UDI regulations right now? Use Healthcare Packaging's UDI Resource Guide as a launching pad to find everything you need to stay in compliance.

We've collected all the links you'll need whether you are using GS1, HIBCC or ICCBBA as your number issuing agency. Plus, all the links are annotated to help you narrow your search before you start clicking.

UDI BACKGROUND

Unique Device Identification was originally proposed in the early 2000s through a global harmonization effort organized by the World Health Organization and attended by a group of national regulators from markets around the world. The goal of that effort was to facilitate "...a convergence in standards and regulatory practices related to the safety, performance

and quality of medical devices." The group published "Medical Device Regulations, Global overview and guiding principles" in 2003, which established a blueprint for harmonized national regulations of medical devices.

In 2011, the regulatory agencies who participated in the WHO effort started the International Medical Device Regulators Forum (IMDRF) to build on the foundational work of the WHO. In August of 2012 the FDA was the first member of IMDRF to publish proposed rules for a unique identifier for medical devices and the associated regulations that included many elements of the original WHO blueprint. The FDA published the UDI Final Rule on September 24, 2013.

Since then the European Union has published a very similar regulation and the regulatory concept appears to be sweeping the world. Countries that are in various stages of work on future UDI regulations that use the WHO blueprint include Turkey, Columbia, China, Saudi Arabia, South Korea, Russia, Japan, Australia and others.

Considering the focus of these efforts, the original goal of global regulatory harmonization for UDI has largely been met, but every UDI regulation is still different, reflecting local regulatory norms and existing laws. Device manufacturers, labelers and packagers need to know the specifics of each regulation in the markets they target.

UDI RESOURCE GUIDE IN THE U.S.

The U.S. regulation contains specific requirements for device identification, labeling and product data registration. This typically involves many departments within the organizations of device manufacturers/labelers, contract manufacturers and contract packagers. We hope these resources help you understand the regulation, the requirements you are facing and the technologies available to meet them.

We've broken our list down by the primary sources: The FDA, the three current FDA accredited number issuing agencies and a few other sources. We've also broken it down by general UDI background resources, device identification resources, labeling resources and product data registration resources.

FDA GENERAL UDI RESOURCES

The U.S. FDA provides a wealth of information and guidance about the regulation and how to meet it.

FDA's main UDI page

The main FDA web page for UDI is a great place to start any search for information about the regulation. Note the helpful quick-links along the margins. You can also sign up for FDA's email list for updates on UDI at the bottom of the page.

UDI Basics
This is a good high-level explanation of the UDI requirements.

Compliance Dates for UDI Requirements
A great page that breaks down all the deadlines for compliance by device type, including devices that are exempted. That's right, there is a deadline, even for devices that are exempt from the UDI rule! Most deadlines are in the past, which means these devices must comply today.

UDI Exceptions, Alternatives and Time Extensions
An FDA page with information about the various exceptions, alternatives, FDA Decisions and time extensions offered by the FDA after the final rule was published. Make sure you check this page before you implement.

UDI Rule and Guidances, Training, Resources, and Dockets
FDA-compiled page with links to all the existing UDI-related FDA guidance and rules, training Dockets and other resources.

Unique Device Identifier System: Frequently Asked Questions, Vol. 1
This is a "final guidance" document with answers to 33 different questions you might have about UDI in the U.S.

FDA UDI Resources Page
Here's the link to FDA's own UDI Resources page.

FDA UDI Help Desk
Still have a question? Use this page to submit a question to the FDA UDI Team.

DEVICE IDENTIFICATION RESOURCES

Fundamentally, UDI is about standardizing the identification of devices. The requirement is that every type and variation of a device must have a single, standardized way of identification—an identifier that the FDA and companies in the supply chain will use to refer to that specific model and variation.

The UDI rule breaks identifiers into two categories: a "device identifier" (DI) and "production identifiers" (PI). Each type/variation of a device must have one DI. PIs include lot numbers, serial numbers and software version numbers. Every production unit of a device introduced into the supply chain must have at least one PI associated with it. Additional PIs are optional.

Device labelers must choose at least one of three FDA-accredited "number issuing agencies" to obtain the DI that will be used to refer to their device. It is possible, though rare, to

use more than one number issuing agency to define multiple DIs for a single device. The three agencies are GS1, the Health Industry Business Communications Council (HIBCC) and ICCBBA.

Labelers of medical products of human origin should use ICCBBA as their number-issuing agency because their identifiers incorporate special features that enable a linkage to donors. Labelers of other types of devices may choose either GS1 or HIBCC.

FDA DI RESOURCES

Contact an FDA-Accredited Issuing Agency
FDA page with all the contact information for the issuing agencies.

UDI Formats by FDA-Accredited Issuing Agency (January 27, 2017)
FDA page with information about the UDIs—both DIs and PIs—issued by each of the issuing agencies.

GS1 DI RESOURCES

GS1 Standards Resources for U.S. FDA UDI Implementation Support
GS1's main UDI resources page. Start here when you are evaluating or using GS1 standards for FDA UDI compliance.

Healthcare Supplier FDA UDI Quick Start Guide
A high-level overview of the U.S. UDI regulation and the steps to become compliant using GS1 standards.

GS1 Guide on Unique Device Identification (UDI) implementation in the USA and in the EU
Another overview—this one published by GS1 (global)—of UDI concepts with emphasis on meeting the U.S. and EU UDI regulations using GS1 standards.

Implementation Guideline – Applying the GS1 System for U.S. FDA Unique Device Identification (UDI) Requirements
Indispensable information for labelers using GS1 standards for U.S. UDI compliance.

U.S. FDA Unique Device Identification (UDI) Rule Frequently Asked Questions (FAQs)
Despite the title, this is an FAQ document published by GS1 Healthcare US. It contains questions and answers about the FDA UDI rule in general, and how to apply GS1 standards for meeting it.

GS1 US FDA UDI Rule: Education and Implementation Resources
A web page with links to GS1 resources for evaluating and using GS1 standards for FDA UDI compliance.

Standards Guidance for Assigning DIs Using Global Trade Item Numbers (GTINs)
Important technical guidance for creating GS1 GTINs that meet your needs and meet the DI requirements of the U.S. FDA UDI Rule.

GS1 DI Check Digit Rules
A GS1 DI is a GS1 Global Trade Item Number (GTIN). This page provides an online calculator to calculate the necessary check digit.

HIBCC DI RESOURCES

Apply for a Labeler Identification Code (LIC)
To create HIBCC UDI identifiers, you must obtain an HIBCC Labeler Identification Code (LIC). Once you have an LIC, you can create your own HIBCC-based UDI identifiers using the HIBCC Health Industry Bar Code (HIBC) standard.

HIBCC UDI and Labeling Resource Center
A collection of all the links you will need to create and use HIBCC UDI DIs and PIs in product labeling. This is a great place to start evaluating and using HIBCC standards for UDI.

How to Become FDA UDI Compliant: Getting Started: HIBCC's Guide to UDI Compliance
A document with the six steps you need to follow to get started using HIBCC for FDA UDI compliance. Each step includes a link to the resources you need.

HIBC Supplier Labeling Standard (SLS) 2.6
Indispensable document explaining the technical details of using the HIBC standard for creating and using UDI DIs and PIs.

HIBCC DI Check Digit Calculation
The HIBCC DI is an HIBCC Label Item Code (LIC). This document explains how to calculate the necessary check digit.

ICCBBA DI RESOURCES

ISBT-128 GRID Checksum Calculator
The ICCBBA DI is encoded using ISBT 128. This page explains the check digit calculation.

What is ISBT 128?
A web page with text and video explanation of the ISBT 128 standard and how it is used.

Frequently Asked Questions
FAQs for ISBT 128.

Unique Device Identifier (UDI) Generator
A downloadable spreadsheet that helps labelers construct the ISBT 128 code suitable for use as a DI.

Device Identifier Checker
A downloadable spreadsheet thatallows you to parse the various elements of an existing ISBT 128 DI.

Multiple Device Identifier Checker
A downloadable spreadsheet that allows you to parse the various elements of a list of existing ISBT 128 DIs.

OTHER DI RESOURCES

IMDRF: Unique Device Identification system (UDI system) Application Guide
Remember, IMDRF does not set requirements for the U.S., but these may be helpful in understanding what might be coming in future updates to the UDI regulation.

RxTrace: FDA Proposed UDI: A Revolution In Number Assignment
A little dated, but still valid explanation of the UDI rule when it was just an FDA proposed rule.

LABELING RESOURCES

Many UDI resources discuss labeling in just a section of a larger document so please check many of the resources listed in other sections. The resources below (many of which are mentioned above) include at least one example of a UDI-conformant device label as an example.

FDA LABELING RESOURCES

UDI Basics
A good high-level explanation of the UDI requirements, including an explanation of a UDI product label.

Unique Device Identifier System: Frequently Asked Questions, Vol. 1
This is a "final guidance" document with answers to 33 different questions you might have about UDI in the U.S.

Unique Device Identification (UDI)
FDA presentation outlining the UDI regulation and requirements, including at least one example label image.

GS1 LABELING RESOURCES

GS1 Guide on Unique Device Identification (UDI) implementation in the USA and in the EU
An overview—this one published by GS1 (global)—of UDI concepts with emphasis on meeting the U.S. and EU UDI regulations using GS1 standards.

Sample UDI Labels
Three example UDI labels emphasizing the use of GS1 standards.

HIBCC LABELING RESOURCES

HIBCC UDI and Labeling Resource Center
A collection of all the links you will need to create and use HIBCC UDI DIs and PIs in product labeling.

HIBCC UDI Compliant Label Examples
A document that shows examples of several UDI-compliant labels that use HIBCC DIs and PIs.

How to Use HIBCC Date Formats for UDI
A document that explains how to use the HIBCC formats under the FDA UDI regulation.

ICCBBA LABELING RESOURCES

ISBT 128 STANDARD: Coding and Labeling of Medical Devices Using ISBT 128
The definitive explanation for how to apply ISBT 128 to meet the U.S. FDA UDI final rule.

Product Description Code Request Form - HCT/P Medical Device
Start here to begin labeling human cells, tissues, and cellular and tissue-based products (HCT/P) that must be registered with the FDA as medical devices.

Medical Devices - Documents
Web page listing documents explaining the use of ISBT 128 to meet the U.S. UDI regulation.

UDI Labelers
Webpage with information and links pertinent for labeling medical devices with ISBT 128 to meet the U.S. UDI rule.

Label Examples - HCT/P Medical Devices
Webpage with examples of medical device labels using ISBT 128 for UDI.

OTHER LABELING RESOURCES

IMDRF: Principles of Labelling for Medical Devices and IVD Medical Devices
Remember, IMDRF does not set requirements for the U.S., but these may be helpful in understanding what might be coming.

2017 UDI Conference, AIM North America: Your Morning Dose of UDI Fundamentals
A presentation covering information about UDI including multiple examples of UDI labeling.

RxTrace: FDA Proposed UDI: AIDC Requirements
A little dated, but still valid explanation of the AIDC requirements of the UDI rule when it was just an FDA proposed rule.

REGISTRATION REOURCES

Registration means submitting your medical device DI and its associated product data to the FDA Global UDI Database (GUDID). GUDID is a database administered by the FDA that serves as a reference catalog for every device with a unique device identifier (UDI). GUDID may be accessed by industry and the public through the AccessGUDID website.

FDA REGISTRATION RESOURCES

Global Unique Device Identification Database (GUDID)
FDA page listing FDA resources for GUDID.

Global Unique Device Identification Database (GUDID) User Manual
Indispensable guide for getting started registering your medical devices on the GUDID database.

GUDID Guidance
FDA downloadable document containing valuable guidance explaining the GUDID database and how to interact with it as an FDA-licensed medical device labeler. Don't miss the section on the Global Medical Device Nomenclature (GMDN) and how it fits into your submissions.

GUDID Data Elements Reference Table
This document lists all the various master data elements—including some very helpful data entry notes—you might need to include in your GUDID submissions.

HL7 SPL Implementation Files
A zip file containing everything you'll need to submit your GUDID data records using Health Level 7 (HL7) Structured Product Labeling (SPL) XML files, including example files and the complete HL7 SPL Implementation Specification.

Prepare for GUDID
A checklist for preparing to submit your medical device product master data for your DIs to the GUDID database.

Request a GUDID Account
Application form for requesting an account that can be used to submit your medical device product master data for your DIs to the GUDID database.

Submit Data to GUDID
FDA information about submitting your medical device prod-

uct master data for your DIs to the GUDID database. This page provides information about manual data entry through the GUDID Web Application and submitting with HL7 SPL files.

GUDID Data Submission Portal
This is where you use your existing GUDID account to submit your product master data to the GUDID database.

GS1 REGISTRATION RESOURCES

Leveraging GDSN for the FDA Global Unique Device Identifier Database (GUDID) Implementation Guideline

Detailed explanation of how to make use of the GS1 Global Data Synchronization Network (GDSN) infrastructure to securely supply data about your medical devices to the FDA Global Unique Device Identification Database (GUDID).

HIBCC REGISTRATION RESOURCES

HIBCC's Guide to GUDID Device Identifiers
Guide explaining how to apply the HIBC UDI codes for compliance with the UDI rule and for uploading data into the FDA GUDID database.

ICCBBA REGISTRATION RESOURCES

Unfortunately, ICCBBA offers no specific information about how to register your ICCBBA-labeled medical devices in the FDA GUDID database.

ISBT 128 STANDARD: Coding and Labeling of Medical Devices Using ISBT 128
The definitive explanation for how to apply ISBT 128 to meet the U.S. FDA UDI final rule.

OTHER REGISTRATION RESOURCES

IMDRF: Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC)
Remember, IMDRF does not set requirements for the U.S., but these may be helpful in understanding what might be coming.

IMDRF: In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC)

GMDN Agency: GMDN Agency
The homepage of the organization that maintains the medical device nomenclature that must be used when describing your devices in the FDA GUDID database. The agency is identified in the UDI Final Rule as the official supplier of the nomenclature used in the database.

RxTrace: FDA Proposed UDI: The GUDID Database
A little dated, but still valid explanation of the GUDID database requirements of the UDI rule when it was just an FDA proposed rule.

Batch 4.0

Food and pharmaceutical industries are adopting Industry 4.0 technologies to modernize manufacturing for both regulatory compliance and continuous improvement.

Stephanie Neil, Senior Editor, *Automation World*

Earlier this year, the U.S. Food and Drug Administration (FDA) issued a draft guidance on quality considerations for pharmaceutical companies as they move to a continuous manufacturing process. The push to continuous processing in active pharmaceutical ingredients (APIs) and biologic drug manufacturing is predicated on the need to modernize the decades-old traditional "batch" manufacturing in which drugs are manufactured in multiple disconnected steps with testing delays and manual operations between them. Continuous manufacturing minimizes operational stops for a steady flow between processes that can ensure consistency, efficiency, scalability and a shortened supply chain that may even minimize drug shortages.

A move in this direction requires new kinds of equipment and technology. Pall, which provides high-tech filtration, separation and purification technologies for a variety of industries, is on the forefront of equipment that plays a key role in the development of life-saving drugs ranging from Ebola vaccines to cancer-curing monoclonal antibodies. Part of the effort of the organization is to help companies move to continuous bioprocessing, which will allow manufacturers to build flexible, multi-drug facilities.

But there are still some technology gaps in the continuous manufacturing process.

"We need new analytics and new automation technology," says Loe Cameron, Pall's Director of Analytics and Controls.

Pall is working on adding analytics into continuous single-use processes for biologic drug manufacturing. Source: Pall

"Because as you tie all of these individual unit operations together to act in an organized manner, you need real-time information for control strategies that balance the flow through the process. You no longer have time to take a sample and run to the analytics lab to make decisions. It all has to be online."

There's a similar need for new technologies to analyze and track data in the food and beverage industry given FDA directives such as the Food Safety Modernization Act (FSMA), which outlines good manufacturing practices, hazard analysis, risk-based preventive controls and more to prevent food-

borne illness.

"If there's ever a pathogen in the food and an [FDA] auditor comes in for the data, if [the company] can't produce the data in 48 hours, they'll get shut down," says Travis Cox, Co-Director of Sales Engineering at Inductive Automation. That could mean losing millions of dollars a day. "All because they didn't have a digital strategy to capture that information automatically."

Whether it's regulatory pressure or a business requirement to keep up with consumer needs for new medicine or demands for a variety of food products and packaging, the movement to modernize manufacturing has made its way to pharma and food industries. It's actually an Industry 4.0 initiative that has hit these industry segments with the most important element being access to information and real-time analytics.

"Where Industry 4.0 comes into play in these industries is in accessing intelligent devices and coming up with intelligent analytics to help drive value back into the process, whether it is a higher throughput or quality to maintain competitiveness," says Dan UpDyke, Market Development Manager for Consumer Packaged Goods (CPG) and Life Sciences Industries at Rockwell Automation.

Though the basic core principles of Industry 4.0 apply (modularization, data exchange, cloud and cognitive computing), it is how Industry 4.0 technologies and practices are implemented that is important because they need to be compliant with the requirements of the particular industry.

Pharma 4.0

In biotech, there are many monoclonal antibodies that are coming off patent, which means there is more activity around biosimilars coming into the space. Biosimilars—almost identical copies of an original product manufactured by a different company—are influenced by the manufacturing process that takes place.

"There are so many specific things that impact how a biosimilar works in the end," Cameron says. "As things come off patent and biosimilar development increases, we are seeing a lot of people think about the process more deeply."

To that end, analytics need to be directly tied to the process and need to be delivered fast enough to establish control, Cameron says, noting that Pall is working on adding analytics into continuous single-use processes. "We are trying to find new analytical tools that are more online and purpose-built for this kind of paradigm," she says.

Pall's continuous process demo lab uses Inductive Automation's Ignition to connect equipment and analytical tools. "It gets the data where it needs to go and feeds directly into the historian," Cameron says. "Being able to quickly establish communication and prototype workflows saves us a lot of time as we are trying to develop new control strategies for

continuous."

For example, operators used to pull samples to send to an analytical lab, with results delivered within a few weeks. Now, there's a move to put analytics directly into the manufacturing suite and hook these instruments into the centralized historian. "When information is digitized and closer to where the process is happening, there are all types of things you can do with it," Cameron says. "You can do multivariant analysis in real time, which enables advanced process control. And eventually the industry can move toward real-time release."

In another example of how Industry 4.0 technology is shifting the biotech industry, Rockwell Automation and GE Healthcare announced a collaboration that combines Rockwell technology with GE Healthcare's FlexFactory single-use biomanufacturing equipment. The goal of the collaboration is to deliver a flexible and scalable platform that enables pharmaceutical companies to manufacture smaller batches of tailored medicines. Specifically, the two companies will digitize batch files and processes to reduce review times by weeks. It will also enable them to deliver instructions to workers with augmented reality (AR) to improve batch execution, operations, and equipment setup and training.

"Mobile equipment doesn't [always] have an HMI present or great visualization," UpDyke says. "By providing digital work instructions through augmented reality, we can guide operators through connecting systems to make sure everything is correct. And in life sciences, it is important that all of that is captured in an audit trail by making sure connections are in the right place and put in an electronic batch record."

Though this application is specific to biopharma, "the concept of digital work instructions could be carried across all industries," he adds.

Food 4.0

Whether biosimilar or bourbon—digitalization is happening across industry. The technologies vary from AR to analytics to cloud computing, but the goal is the same—plant floor continuous improvement.

In an effort to keep up with demand for its bourbon whiskey, Jim Beam recently upgraded sections of its facility to maximize throughput while taking into account process constraints. Jim Beam was able to optimize control and decrease variability in the product by using Rockwell's Pavilion8 model predictive control (MPC), which adds a layer of intelligence on top of the basic automation systems. By maximizing feeds and manipulating steam and reflux flows, Jim Beam was able to decrease variability by 60 percent.

Rockline Industries, a CPG company specializing in disposable wipes, is also trying to keep up with demand in a germ-conscious world. To add to that, the wet wipes market is hyper-competitive, according to Frank Hacker, Director

of Manufacturing, North American Wipes Division at Rockline Industries. To become more cost-competitive, Rockline started by taking a closer look at its production equipment.

"They were having performance issues on a line that was operating at less than 50 percent," UpDyke says. By applying Rockwell's FactoryTalk Metrics software, Rockline was able to provide accurate, timely, granular and specific information on machine production, performance and activities. An analytic model on the line pointed to problems with the raw materials—specifically, the capper on one of the cells was showing a significant amount of intermittent downtime, triggering stops on the line. By analyzing production data, engineers identified the raw material as the root cause.

"FactoryTalk Metrics allowed us to take advantage of all incremental capacity," Hacker says in a video. "Quality is also up because line operators can react to problems sooner."

Now, think about the ability to see performance data on not just one line, but across multiple lines or even multiple plants. That's what Procter & Gamble (P&G) is testing out as one of the first adopters of the GE Digital Predix Manufacturing Data Cloud (MDC).

It is a cloud-based platform designed to consolidate manufacturing data across plants for analysis. Used in concert with a traditional manufacturing execution system (MES), Predix MDC provides operational analysis in the cloud and greater flexibility of deployment, helping reduce the size of

Using Rockwell Automation's FactoryTalk Metrics software, Rockline line operators are able to react to problems sooner. Source: Rockline

on-premise systems to make them run more efficiently. Predix MDC enables the consolidation of three data sets required for process optimization and analytical applications, including asset data, enterprise resource planning (ERP) data and manufacturing data.

P&G, which has been a long-time user of GE Digital's Plant Applications MES, recently conducted a pilot test of Predix MDC on three of its manufacturing sites.

"P&G is one of the first [companies] we've had using our brand new MDC product," says Steve Martin, acting CEO and Chief Commercial Officer for GE Digital. "We are really bull-

ish on this product line, being cloud-based and addressing a bunch of needs in manufacturing. But it is particularly effective for organizations with multiple plants to get line of site on the performance of one location vs. another, and finding what the best practices are that are driving productivity in one area over another."

P&G, which has since expanded its initial pilot phase to include more manufacturing sites, is getting a detailed, data-supported view into its overall manufacturing processes. Plus, Predix MDC is helping the CPG company meet data compliance regulations.

There is so much data coming off of sensors, like vibration and heat, that helps analyze what needs to be done from an equipment predictive maintenance standpoint, according to Martin. "And the cloud aspect is not one to be overlooked," he adds. "To get that information into a web-based portal to do real-time location-by-location comparisons helps the customer monitor the systems and [gives] the data scientists real-time views into how to further optimize. We are getting closer to converging optimization and operations into a single layer, and the recommendations made to further optimize things can be immediately put into action. That's what we call closed-loop optimization."

Transforming batch

Digitizing data and applying analytics are perhaps the most important elements for moving batch processes into the era of Industry 4.0. But that means more people need to be able to access and understand the information.

"We need a way to leverage the expertise of data scientists," says Lisa Graham, Vice President of Analytics Engineering at Seeq, which provides industrial process analytics software. "Many of us are using Excel to wrangle data, but insight is lost. We need data analytics for the rest of us."

Seeq's software captures time series data from a variety of historians and other storage platforms and leverages machine learning and Big Data to add context around the information and deliver it up in an easy-to-understand dashboard report.

"It's a more holistic approach done in an IT-friendly way," Graham says. This allows engineers to interact with data to make better decisions. "The value of capturing the right information in a way that can accelerate drug development, for example, is the fastest way to get to market and at the same time improve quality."

Pall's Cameron agrees that easy analytics could be the biggest benefit for anything related to Batch 4.0.

"We are trying to find ways to add value to our equipment and bioprocesses without increasing complexity and possibly even simplifying things," Cameron says. "We are trying to make it all easier."

E-Cig Companies Have 10 Months to Submit Applications to FDA

The FDA reduced the deadline for e-cigarette companies to defend why they should be able to keep selling their products.

Tim Hayes, Contributing Editor, *Healthcare Packaging*

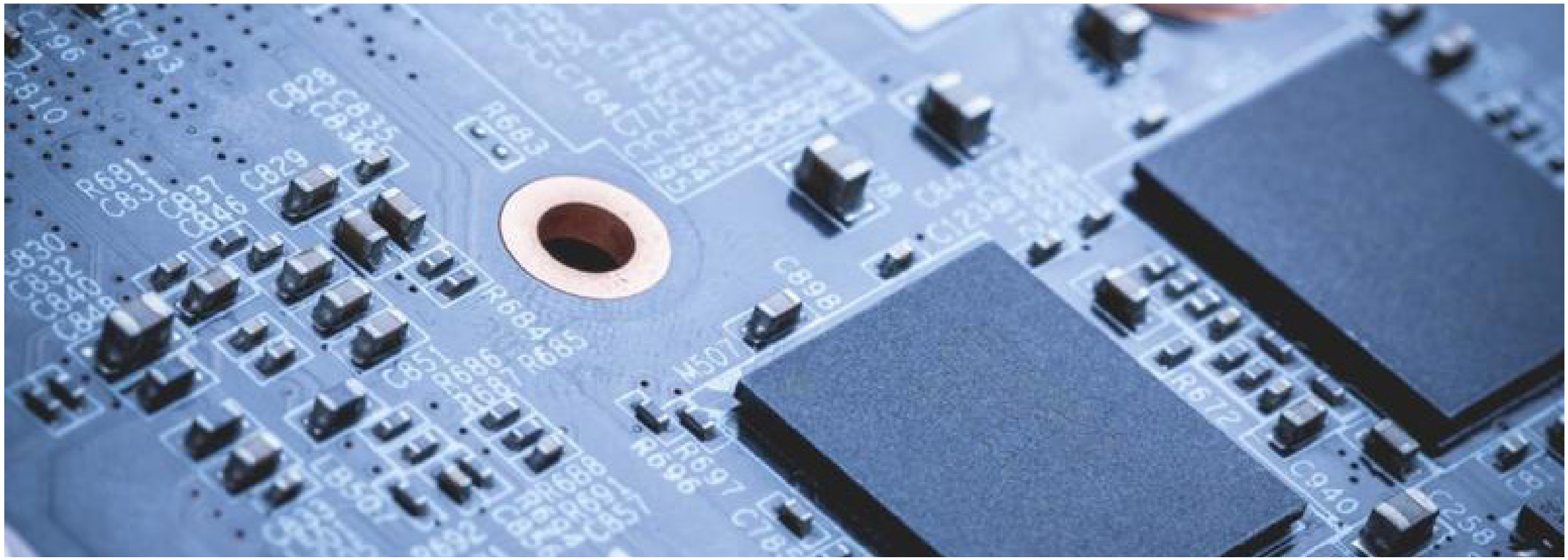
According to a recent Forbes article, the battle between the FDA and the electronic cigarette industry is heating up. The FDA had previously defined a 2022 deadline for e-cig companies to submit applications explaining why they should be allowed to sell their products, but due to a sharp rise in youth vaping, that deadline was reduced by a year.

The FDA still faces scrutiny from anti-tobacco groups that have filed a lawsuit against the agency for allowing companies to sell unapproved e-cigarettes. Ned Sharpless, Acting Commissioner of the FDA, said the agency is prepared to employ “all available regulatory tools at our disposal” to prevent youth vaping.

The FDA is Making Rules for AI in Medicine

The Agency announced that it is developing a regulation system for artificial intelligence products used in medicine.

Tim Hayes, Contributing Editor, *Healthcare Packaging*



No one really knows how artificial intelligence will affect culture and society, but there's no shortage of theories. From increased productivity to doomsday scenarios, every outcome has been explored in sci-fi movies. A recent Stat News article said the FDA wants to take some guesswork out of the equation by creating greater oversight over the quickly evolving segment of AI products in medicine that constantly change based on exposure to new patients and data.

Scott Gottlieb, the current (but not for long) commissioner of the FDA, released a white paper that outlined the agency's approach. The main thesis of the paper is to establish when AI-driven medical products will need FDA review before they're commercialized. A review may look at the underlying performance of a product's algorithms, a manufacturer's plan for modifications, and the manufacturer's ability to manage the risks that come with them.

"Artificial intelligence has helped transform industries like finance and manufacturing, and I'm confident that these technologies will have a profound and positive impact on health care," Gottlieb wrote. "I can envision a world where, one day, artificial intelligence can help detect and treat challenging health problems, for example by recognizing the signs of disease well in advance of what we can do today."

FDA Intends to Deactivate Outdated Drug Listing Records as Supply Chain Security Step

“The agency has found that tens of thousands of drug listing records have not been updated or certified in the past year, and are therefore not in compliance with federal regulations…”

The FDA maintains a catalog of drug products commercially distributed in the U.S. Regardless of country of origin, entities that manufacture, repack or re-label drugs in the U.S. are required to register with the FDA, and are required to list drug products manufactured for commercial distribution in the U.S.

The agency has found tens of thousands of drug listings that haven't been updated (they may no longer be marketed or they are marketed andtheir listings haven't been updated). In order keep up-to-date records and make "accurate and timely decisions to protect public health," they intend to deactivate out-of-date listings, according to a news release.

"It is vital that the FDA database accurately describes drugs currently available to patients in the U.S. so the FDA can more quickly respond to and assess drug quality issues, adverse event reports, inspections, recalls, shortages and other supply chain security issues," said FDA Acting Commissioner Ned Sharpless, M.D.in the release.

Action item

The agency says inactive listings as of Sep. 12, 2019 will be removed from the database.They are urging companies to update inaccurate active drug listing submissions as soon as possible.

For more, see the news release and the federal register notice with updating requirements and deadlines.

FDA Intends to Deactivate Outdated Drug Listing Records as Supply Chain Security Step