Top 10 Latest FDA & DEA Developments — And A Look Ahead to 2021

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During 2020, the focus of the Food and Drug Administration (FDA) was squarely on dealing with the COVID-19 pandemic, which preoccupied the agency's regulatory and, to a great extent, its enforcement resources. Some plans that the FDA had for the year necessarily were postponed as the agency and much of the federal government reacted to the pandemic, which by year's end had left 20 million Americans infected and nearly 350,000 Americans dead.

Developments during 2020 related to FDA and Drug Enforcement Administration (DEA) regulatory and enforcement activities — including the FDA's activities related to the pandemic — are likely to reverberate throughout 2021. Below is our list of the 10 most important FDA and DEA developments of 2020 — and some predictions of what to expect during 2021.

Top 10 Latest FDA & DEA Developments

1. Pandemic Upends FDA Inspections, Forces Agency To Use Alternative Regulatory Oversight Tools

On Feb. 24, 2020, the FDA suspended its inspections of facilities in China because of the COVID-19 public health emergency. Just over two weeks later, on March 10, the agency suspended most foreign inspections.

In a March 10 statement, Commissioner of Food and Drugs Dr. Stephen M. Hahn said that the agency based its decision on Department of State Level 4 travel advisories restricting U.S. government employee travel, travel recommendations from the Centers for Disease Control and Prevention (CDC), "access restrictions being imposed on foreign visitors by certain countries," U.S. Office of Personnel Management guidance, and the importance of agency employee health and safety.

Hahn expressed confidence in the FDA's ability to maintain regulatory oversight over non-U.S. manufacturers and imported products "using alternative tools and methods," which he said gave the agency confidence that it could continue its regulatory oversight of foreign manufacturers of FDA-regulated products. The tools cited included:

- denial of entry of unsafe products into the United States;
- physical examination and product sampling at U.S. borders;
- agency reviews of facilities' previous compliance histories;
- the use of information shared with the agency by foreign governments under mutual recognition and confidentiality agreements; and
- the agency's authority to request records in advance of or in lieu of onsite drug and biologics inspections under Section 706 of the Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-114 (FDASIA), which created Section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. §374(a)(4)).

Eight days later, on March 18, Hahn announced that, "for the health and well-being of our staff and those who conduct inspections for the agency under contract at the state level, and because of industry concerns about visitors," the FDA had temporarily postponed all domestic routine surveillance facility inspections as well.

About four months later, the agency moved to resume prioritized domestic on-site surveillance inspections. The FDA announced on July 10 that it planned to use a COVID-19 risk rating system to help the agency determine when and where it was safe to inspect the facilities of FDA-regulated companies. The agency restarted in-person inspections during the week of July 20.

Hahn also said that “for the foreseeable future” most prioritized domestic inspections conducted by FDA investigators would be preannounced.

In a guidance document for drug and biological product manufacturers issued Aug. 19, the FDA provided answers to frequently asked questions about agency inspections, pending drug applications, and changes in manufacturing facilities for approved pharmaceutical products during the COVID-19 public health emergency.

The guidance can help drug and biologics companies determine whether their facilities are likely to be inspected as the agency resumes its inspectional program.

As 2021 began, with a full reopening of the economy postponed due to the ongoing pandemic, the FDA was likely to continue to use remote regulatory assessments — remote reviews of records that a company is required to maintain for agency review — in lieu of onsite inspections.

2. COVID-19 Pandemic Changes Clinical Trial Operations

Recognizing that the COVID-19 pandemic could affect the conduct of clinical trials, the FDA on March 18, 2020, issued a final guidance to aid in assuring the safety of trial participants, maintaining compliance with good clinical practice, and minimizing risks to trial integrity during the COVID-19 pandemic.

“With this guidance issued today, the FDA is helping industry and investigators navigate the COVID-19 pandemic and help assess how to move forward with critical clinical trials,” said Anand Shah, the FDA’s deputy commissioner for medical and scientific affairs. “The FDA released this guidance to emphasize that at all times, patients’ safety should continue to be at the forefront of considerations. We want to support the continuance of these clinical trials in compliance with good clinical practice and minimizing risks to trial integrity, while also safeguarding the health and well-being of study participants.”

The FDA addressed several concerns for the conduct of clinical trials in revised guidance released on April 16. In addition, the Department of Health and Human Services (HHS) issued guidance on meeting Common Rule requirements when COVID-19 affects clinical trials.

The FDA later expanded its guidance on conducting clinical trials during the COVID-19 pandemic to include information on considerations for using alternate laboratories or imaging centers, holding trial participant visits via video conference, and conducting required postmarket clinical trials. The FDA also released guidance to assist sponsors in the clinical development of drugs and biological products for the treatment or prevention of COVID-19.

Later in the year, the FDA updated its guidance on the conduct of clinical trials during the pandemic with several recommendations for obtaining informed consent and for dealing with the possibility that trial participants with COVID-19 may experience a number of serious and unexpected adverse clinical events, which may increase the volume of safety reports.

The FDA also provided sponsors and investigators with considerations for approaches to measure and analyze common COVID-19-related symptoms in outpatient adult and adolescent subjects of clinical trials conducted to evaluate drugs or biological products intended to prevent or treat COVID-19.

3. DOJ Reaches $8 Billion Global Settlement with Purdue Pharma

On Nov. 17, 2020, a federal bankruptcy court in New York approved an $8 billion global settlement between the opioid manufacturer Purdue Pharma L.P. and the Department of Justice (DOJ) (*In re Purdue Pharma L.P.*, No. 7:19-bk-23649-RDD (Bankr. S.D.N.Y.)).

The action by the U.S. Bankruptcy Court for the Southern District of New York advanced the resolution of criminal and civil investigations into the company and individual shareholders from the Sackler family. The investigations had focused on the company's marketing of its opioid drugs.

The global settlement included criminal penalties totaling more than $5.5 billion, the largest ever levied against a pharmaceutical manufacturer.

As part of the settlement, Purdue Pharma agreed to plead guilty in the U.S. District Court for the District of New Jersey to a criminal information charging the company with one count of dual-object conspiracy to defraud the United States and to violate the FD&C Act, as well as two counts of conspiracy to violate the federal Anti-Kickback Statute.

To resolve the criminal charges, the company agreed to pay a criminal fine of $3.544 billion and to pay $2 billion in criminal forfeiture.

The company also agreed to pay $2.8 billion to resolve civil liability under the False Claims Act. In addition, members of the Sackler family agreed to pay $225 million to resolve civil false claims liability.

The DOJ stressed that the resolutions "do not include the criminal release of any individuals, including members of the Sackler family, nor are any of the company's executives or employees receiving civil releases."

Under the global resolution, Purdue Pharma would emerge from bankruptcy as a public benefit company (PBC) owned by a trust or a similar entity "designed for the benefit of the American public, to function entirely in the public interest," federal enforcement officials said.

The PBC would continue to "endeavor to deliver legitimate prescription drugs," the DOJ said, but it also "will aim to donate, or provide steep discounts for, life-saving overdose rescue drugs and medically assisted treatment medications to communities." Proceeds from the trust "will be directed toward state and local opioid abatement programs," the department added.

Because of the value that state and local governments would realize through the PBC, the DOJ said, the department was "willing to credit up to $1.775 billion against the $2 billion forfeiture amount." The company was to pay the remaining $225 million of the criminal forfeiture on the effective date of the bankruptcy.

4. After Years of Resistance, HHS Finalizes Rule Permitting Importation of Rx Drugs from Canada

On Sept. 24, 2020, HHS finalized regulations allowing programs authorized by the FDA to import certain prescription drugs into the United States from Canada under conditions that HHS said will "ensure the importation poses no additional risk to the public's health and safety while achieving a significant reduction in the cost of covered products to the American consumer." The rule was published in the *Federal Register* on Oct. 1, 2020 (85 Fed. Reg. 62094). A proposed drug importation rule had been issued in December 2019.

The final rule stemmed from a commitment that the FDA and HHS made in July 2019 to pursue two pathways for importing prescription drugs as a means to lower their prices.

The rule implements parts of Section 804 of the FD&C Act to allow importation of some prescription drugs shipped from Canada (21 U.S.C. §384(b)-(h)). Under the rule, Section 804 Importation Programs (SIPs) are to be authorized by the FDA for up to two years initially and managed by a state, the District of Columbia, or an Indian tribe.

In addition to imports from Canada, a second pathway — the importation by drug manufacturers of prescription drug products that are FDA-approved, manufactured abroad, authorized for sale in a foreign country, and originally intended for sale in that foreign country — was addressed in a guidance document that the FDA finalized on Sept. 24, 2020.

The guidance, "Importation of Certain FDA-Approved Human Prescription Drugs, Including Biological Products, and Combination Products under Section 801(d)(1)(B) of the Federal Food, Drug, and Cosmetic Act," addressed the importation of FDA-approved drugs that were also authorized for sale in a foreign country in which the drugs were originally intended to be marketed.

The document describes procedures through which a manufacturer can demonstrate that a prescription drug or biological product offered for import from any foreign country is an FDA-approved product manufactured in accordance with the agency's requirements. The agency designates these as "multi-market approved products" (MMA products).

The guidance outlines procedures through which a manufacturer may obtain an additional National Drug Code (NDC) for an MMA product that is imported into the United States in compliance with Section 801 of the FD&C Act.

The additional NDC would provide "an additional avenue through which drugs could be sold at a lower cost in the U.S. market," the FDA said. By obtaining additional NDCs for MMA products, manufacturers may be able to offer the products at lower costs by helping them address "certain challenges in the private market" — including being locked into contracts with other parties in the product supply chain that prevent the manufacturers from offering the products at a lower cost.

The guidance describes:

- the process for submitting a supplement to an approved FDA application for an MMA product;
- the recommended labeling for an MMA product (including a recommended statement to help pharmacists accurately identify, dispense and bill for the product);
- the process for registration and listing of an MMA product and for obtaining an additional NDC for the product;
- relevant requirements under the Drug Supply Chain Security Act (21 U.S.C. §360eee-1);
- recommendations for importing MMA products, including the filing of import entries and providing manufacturer authorization information to the FDA; and
- other requirements applicable to MMA products, including requirements under the Controlled Substances Act, FD&C Act provisions regarding adulteration and mislabeling, and requirements related to adverse event reporting, recalls and Risk Evaluation and Mitigation Strategies (REMS).

5. HHS Blocks FDA From Requiring Premarket Review of Laboratory-Developed Tests Without Rulemaking

On Aug. 19, 2020, HHS announced a policy aimed at restricting the FDA's regulation of laboratory-developed tests (LDTs) — in vitro diagnostic (IVD) tests that are designed, manufactured and used within a single laboratory.

Under the policy, the FDA cannot require premarket review of LDTs "absent notice-and-comment rulemaking, as opposed to through guidance documents, compliance manuals, website statements or other informal issuances."

The move upends the agency's controversial policy on the regulation of LDTs, which had evolved over several years with the release of draft guidance, a possible framework for regulating the tests, and other agency proposals and statements.

HHS said that the policy resulted from a request by department leadership that the HHS Office of the General Counsel examine the underlying legal authority for requiring premarket review of LDTs. "The legal review concluded that FDA must issue a requirement for premarket review by notice-and-comment rulemaking, or it can be required by an act of Congress," HHS said.

The department said that the policy was consistent with Executive Order 13771, issued in January 2017, which was intended to decrease the overall level of federal government regulation, as well as Executive Order 13924, a May 2020 order calling for federal government agencies to temper regulatory requirements and enforcement to help spur recovery from the economic damage caused by the COVID-19 public health emergency.

The HHS policy also was expressly presented as being "part of HHS's ongoing department-wide review of regulatory flexibilities enacted since the start of COVID-19."

Despite the new policy's references to the pandemic, HHS said in an accompanying set of frequently asked questions and answers that the policy "is broadly applicable to all LDTs, regardless of what they are testing for."

The FDA had long argued that it had comprehensive regulatory authority over all IVD tests, including LDTs, as part of its statutory authority to regulate medical devices. However, it traditionally had not enforced its purported authority because LDTs had been "relatively simple" and generally available only on a limited basis.

In July 2014, however, the FDA released a draft "framework for regulatory oversight" of LDTs that signaled the agency's intention to increase enforcement of regulatory requirements for the tests. The agency said at the time that it was proposing "a risk-based, phased-in framework for oversight of LDTs in a manner that is consistent with FDA's current regulation of [IVD] devices."

The agency said that the framework was intended to respond to an increase in the complexity and general availability of LDTs that posed risks that were like those posed by IVDs subject to the FDA's premarket review. Under the framework, regulatory requirements would have been phased in over particular periods of time for various types of LDTs, depending on their level of risk.

There was substantial opposition to the proposed framework. In November 2018, a group of stakeholders, including industry trade associations, hospitals, clinical laboratories and physicians, called for the FDA to withdraw the framework and any guidance released in connection with the framework. The stakeholders insisted that any changes in the regulatory treatment of LDTs should be established through a full agency rulemaking procedure.

A legal analysis by former Solicitor General Paul D. Clement and Harvard Law School Professor Laurence H. Tribe released by the American Clinical Laboratory Association in January 2015 concluded that the FDA "lacks legal authority to exercise jurisdiction over laboratory-developed testing services" and that the agency "violate[d] well-settled principles of administrative law in attempting to exercise such jurisdiction through guidance documents."

In November 2016, the FDA announced that it was postponing the release of any final guidance on the agency's regulation of LDTs, saying that it would work with the incoming Trump administration and Congress to devise a comprehensive regulatory approach.

Since then, members of Congress have attempted to work with LDT developers to craft legislation that would reform the government's regulation of LDTs. It is likely that the issue will arise again during the 117th Congress, which convened on Jan. 3, 2021.

6. District Court Hands Down Sentences — Including Prison Time — for Seven Insys Executives

A federal district court in Boston sentenced seven top former executives of Insys Therapeutics Inc. for their roles in the company's illegal marketing of Subsys, its highly addictive fentanyl-based pain medication. Each of the sentences included prison terms — ranging from just over a year to five and a half years.

Five of the former executives had been convicted of conspiracy under the Racketeer Influenced and Corrupt Organizations Act (RICO) in May 2019. The other two executives entered into plea agreements and cooperated with the government's investigation into the company.

A grand jury originally returned an indictment outlining various charges against six of the defendants in December 2016, including racketeering conspiracy (18 U.S.C. §1962(d)), conspiracy to commit wire fraud (18 U.S.C. §1349), conspiracy to commit mail fraud (18 U.S.C. §1349) and conspiracy to violate the federal Anti-Kickback Statute (18 U.S.C. §371).

The U.S. District Court for the District of Massachusetts imposed the following sentences on the five former officials convicted last spring.

- John N. Kapoor, 76, the founder and former executive board chairman of Insys, was sentenced Jan. 23, 2020, to serve 66 months in prison, followed by three years of supervised release. The court also ordered Kapoor to pay forfeiture and restitution.

- Richard M. Simon, 48, the company's former national director of sales, was sentenced Jan. 21 to 33 months in prison, followed by three years of supervised release. The court also ordered Simon to pay forfeiture of approximately $2.3 million, as well as restitution.

- Sunrise Lee, 38, a former regional sales director for Insys, was sentenced Jan. 22 to a year and a day in prison, followed by three years of supervised release. She was also ordered to pay restitution and forfeiture.

- Joseph A. Rowan, 45, another former Insys regional sales director, was sentenced Jan. 21 to serve 27 months in prison followed by three years of supervised release. In addition, Rowan was ordered to pay approximately $2 million in forfeiture as well as restitution.

- Michael J. Gurry, 56, the former vice president of managed markets at Insys, was sentenced Jan. 13 to serve 33 months in prison followed by three years of supervised release. The court ordered Gurry to pay forfeiture of approximately $3.6 million as well as restitution.

The two former Insys executives who pleaded guilty and testified at the trial of the other five also received sentences that included prison terms.

- Former Insys President and Chief Executive Officer Michael L. Babich, 43, was sentenced on Jan. 22 to 30 months in prison and three years of supervised release. He was also ordered to pay restitution and forfeiture. In January 2019, Babich pleaded guilty to one count of conspiracy to commit mail fraud and were fraud and one count of mail fraud.

- Former Vice President of Sales Alec Burlakoff, 46, was sentenced Jan. 23 to 26 months in prison followed by three years of supervised release. He was also sentenced to pay restitution and forfeiture. In November 2018, Burlakoff pleaded guilty to one count of racketeering conspiracy.

7. Abrams Retires from OPDP

Tom Abrams, long-time director of the FDA Center for Drug Evaluation and Research (CDER) Office of Prescription Drug Promotion (OPDP), retired in October 2020. OPDP policy director Catherine Gray become the office's acting director.

Abrams became director of the FDA's drug marketing and promotion office in February 2000 when it was the Division of Drug Marketing, Advertising and Communications (DDMAC). Abrams was DDMAC's acting deputy director when he was appointed director, succeeding Norm Drezin.

Abrams joined the FDA in 1993 as a regulatory review officer for DDMAC and became a branch chief in 1995. He was named DDMAC acting deputy director in 1999.

"Tom has done an outstanding job in managing OPDP for so many years," said Wayne Pines, editor-in-chief of Thompson Information Services' *FDA Advertising and Promotion Manual*. "Companies can rely on OPDP for timely and comprehensive advisory opinions and for an ongoing need for guidance."

Before joining the FDA, Abrams worked in pharmaceutical sales and marketing for Merck & Co.

Gray previously served as OPDP's policy director. In that role she supervised policy development, social science research, regulatory counseling and operational support to the office. She has more than 20 years of experience including roles in clinical pharmacy and the pharmaceutical industry. Her prior positions in OPDP include division director, team leader, policy analyst and reviewer.

8. Proposed Rule Outlines Evidence Relevant to FDA's Determination of Intended Uses of Medical Devices

On Sept. 22, 2020, the FDA proposed to update its regulations dealing with the types of evidence that the agency considers when determining the intended use of a medical device or other medical product.

A new proposed rule would specify that a company's knowledge that a health care provider has prescribed or used an approved or cleared medical product for an unapproved use, standing alone, is not sufficient to establish the product's intended use.

The proposed rule was published in the *Federal Register* Sept. 23 (85 Fed. Reg. 59718).

The action – which would amend 21 C.F.R. §801.4, dealing with the meaning of "intended uses" in the context of device labeling, as well as the drug labeling provision at 21 C.F.R. §201.128 — follows a series of regulatory initiatives through which the FDA has sought to have the regulations reflect its current policies on intended uses, which are crucial to compliance with the agency's requirements for premarket approval or clearance and for device advertising and promotion.

A September 2015 proposed rule — drafted to help determine when a tobacco product was subject to regulation by the agency as a drug, device or combination product — sought to change how the agency determined the intended use of a device. The proposed rule was intended to remove language that required a device manufacturer to provide labeling to cover uses to which the manufacturer knew a marketed device was being put, even if the manufacturer did not intend the product to be used in those ways (80 Fed. Reg. 57756, Sept. 25, 2015).

In January 2017, the FDA published a final rule that reflected comments received concerning the proposed rule (82 Fed. Reg. 2193, Jan. 9, 2017). Under that version of 21 C.F.R. §801.4, the intended uses of devices were to be determined by "the objective intent of the persons legally responsible for the labeling of devices."

That intent, according to the rule, was "determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article," such as labeling claims, advertising matter, or oral or written statements. "It may be shown, for example," the final rule stated, "by circumstances in which the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised."

"If the totality of the evidence establishes that a manufacturer objectively intends that a device introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than ones for which it has been approved, cleared, granted marketing authorization, or is exempt from premarket notification requirements (if any)," according to the January 2017 final rule, "he is required … to provide for such device adequate labeling that accords with such other intended uses."

The final rule was scheduled to go into effect in February 2017. However, in response to criticism of the final rule, the FDA delayed its effective date twice (82 Fed. Reg. 9501, Feb. 7, 2017; 82 Fed. Reg. 14319, March 20, 2017). In March 2018, the agency delayed the effective date indefinitely (83 Fed. Reg. 11639, March 16, 2018). That delay was intended "to allow for additional consideration of the substantive issued raised in the public comments," the agency said.

In a Sept. 22 press release, Commissioner of Food and Drugs Dr. Stephen M. Hahn stated that the FDA was proposing to repeal and replace the intended use portion of the January 2017 final rule "to clarify the regulatory language describing the types of evidence [the agency considers] relevant to determining a product's intended use."

The proposed changes, he said, "do not reflect a change in the FDA's policies and practices," but rather "better reflect the FDA's long-standing approach to intended use and provide greater clarity for regulated parties."

"We believe that this update will provide greater certainty and predictability for regulated parties," Hahn said.

The proposed rule would continue to provide that the objective intent demonstrating a device's intended use may be shown by circumstances in which the product is offered or used — with the knowledge of the device's labeler — for a purpose for which the product is neither labeled nor advertised.

However, the proposed rule would specify that "a firm would not be regarded as intending an unapproved new use for an approved or cleared device based solely on that firm's knowledge that such device was being prescribed or used by health care providers for such use."

The proposed rule would remove language in the January 2017 final rule under which, if "the totality of the evidence" established an objective intent by the manufacturer for the device to be used for unapproved or uncleared uses, the device's labeling would have to reflect those uses.

9. FDA Moves Toward All-Electronic Device Submissions with Pilot Program Testing New 510(k) Template

Taking the next step toward requiring that medical device premarket submissions be provided to the FDA solely in electronic format, the agency invited device manufacturers to participate in a voluntary pilot program to test an improved electronic submission template for premarket notifications (510(k)s).

The FDA's Electronic Submission Template and Resource (eSTAR) Pilot Program, announced in a Feb. 27, 2020, *Federal Register* notice (85 Fed. Reg. 11371), offered a 510(k) template featuring an interface that is more intuitive than a previously available electronic template, will not require the installation of special software, and will provide mobile device and Apple iOS support.

FDA Center for Devices and Radiological Health (CDRH) Director Dr. Jeffrey E. Shuren said that the new template would allow pilot participants "to submit applications to the FDA using a more dynamic electronic format capable of organizing the complex information necessary for a robust scientific review."

"Without changing our statutory or data requirements," Shuren added, "this highly interactive submission template is intended to allow manufacturers to provide information to the FDA that's complementary to CDRH internal review templates currently used to review 510(k)s, allowing us to receive information and evaluate the submission more efficiently and consistently."

The boost in productivity that the eSTAR template should provide will let the FDA's 510(k) review staff devote more time and resources to evaluating applications for devices "that pose the highest potential risks to patients," he said.

As part of the negotiations between the agency and device industry stakeholders that led to enactment of the Medical Device User Fee Amendments of 2017 (MDUFA IV), the FDA committed to developing "electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review process."

MDUFA IV was enacted as part of the FDA Reauthorization Act of 2017, which requires device pre-submissions and submissions, including 510(k)s, to be provided in electronic format as specified in final guidance to be released by the agency (21 U.S.C. §379k-1(b)).

The move toward electronic device submissions dates back to commitments that the FDA made in 2012. Since then, an electronic copy (eCopy) — provided to the agency on a CD, DVD or flash drive — has been required for some premarket submissions, including 510(k)s. The agency in 2013 first issued guidance on submitting eCopies, and the guidance was updated in December 2019.

Also that month, the FDA published a final rule on the requirement of a single submission in electronic format, including the eCopy requirement (84 Fed. Reg. 68334).

The FDA also has allowed electronic 510(k) submission packages (eSubmissions) produced through use of the eSubmitter submission template, which contains "all the structured and unstructured data of a complete submission," the agency said in the Feb. 27 notice. The template "is a collection of questions, text, logic, and prompts that guides a user through preparation of a 510(k) submission." The eSubmitter platform and submission process were being piloted for traditional and abbreviated 510(k)s for select product codes through CDRH's Quality in 510(k) Review Program Pilot.

10. Groups, Retailers Ask Court To Force AMS To Rework GMO Labeling Rulemaking

The Center for Food Safety (CFS) spearheaded a lawsuit filed July 27, 2020, by a collection of retailers and food labeling nonprofits challenging the USDA's rules on bioengineered (BE) food disclosures. The suit asked the U.S. District Court for the Northern District of California to declare parts of the regulations unlawful and to order the USDA to rewrite the regulations (*Natural Grocers v. Perdue*, No. 3:20-cv-05151 (N.D. Cal.)).

On Dec. 21, 2018, the USDA's Agricultural Marketing Service (AMS) issued a final rule calling for food manufacturers and other entities that label foods for retail sale to disclose information about BE food and food ingredients (83 Fed. Reg. 65814). The rule established a uniform national standard for disclosure of information to consumers about the BE status of foods — the National Bioengineered Food Disclosure Standard (NBFDS).

The final regulations were effective as of Feb. 19, 2019. The implementation date of the NBFDS was Jan. 1, 2020, except for small food manufacturers, which were given an additional year. The final rule established a mandatory compliance date of Jan. 1, 2022.

According to CFS, the final BE disclosure regulations "include provisions which will leave the majority of GMO-derived foods unlabeled; discriminate against tens of millions of Americans; prohibit the use of the widely known terms 'GMO' [genetically modified organism] and 'GE' [genetically engineered]; and prohibit retailers from providing more information to consumers."

"The American public successfully won GE food labeling after more than a two-decade fight, but the Trump rules fall far short of what consumers reasonably expect and the law requires," said George Kimbrell, CFS legal director and counsel to the lawsuit.

The lawsuit raised four main objections to the rulemaking:

- *USDA's allowance of electronic or digital disclosure on packaging, referred to as "QR code" or "smartphone" labeling, without requiring additional on-package labeling.* "Requiring a smartphone discriminates against at least 20% of the American adult population — primarily poor, elderly, rural and minority populations — who have lower percentages of smartphone ownership or live in areas in which grocery stores do not have internet bandwidth," said Rural Vermont's Caroline Gordon.

- *The use of "bioengineered" on package labeling.* "For 25 years, every aspect of the issue — science, policy and marketplace — have instead used the terms genetically engineered (GE) or genetically modified organism (GMO)," CFS said. "Retailers and shoppers have relied on the term GMO for more than a decade to identify and avoid GMO foods," said Mark Squire, co-founder of Good Earth Natural Foods. "Banning the use of this term and replacing it with a term nobody has ever heard of is misleading and will create massive confusion in the marketplace."

- *USDA's restrictions on which foods are covered and require disclosure.* "The vast majority of GE foods (by some estimates over 70%) are not whole foods, but highly processed foods with GE ingredients, like sodas and oils. Yet in the final rule, USDA excluded these 'highly refined' products, unless the GE material was 'detectable,'" CFS said. "A disclosure law that exempts 70% of the foods it is supposed to disclose is not a meaningful disclosure law: it is a fraud and allows producers to keep their GMO ingredients secret," said Tara Cook Littman of Citizens for GMO Labeling.

- *The rule restricts retailers and producers from voluntarily providing more information to consumers.* The only voluntary labeling allowed is "derived from bioengineering" and only in certain circumstances, CFS said. Aimee Simpson, director of Advocacy & Product Sustainability for PCC Community Markets, said, "PCC believes that our members and shoppers have a right to transparency about the food they eat, and that retailers and manufacturers have a fundamental First Amendment right to provide truthful information to customers. The USDA rules unlawfully restrict that protected speech and do not provide the transparency on GMO foods that consumers deserve."

Predictions for 2021

Biden Administration May Step Up FDA, DOJ Enforcement Activity

In recent years, enforcement activity by the FDA and the DOJ has increasingly focused on responding to alleged violations of the FD&C Act that involve real or potential patient harm. For example, federal enforcement officials have become more likely to pursue off-label marketing cases when they involve dangerous products or widespread patient risk. While this focus is likely to continue during the Biden administration, the pace of enforcement activity may nevertheless rise, as it did at the beginning of the Obama administration. A new FDA commissioner appointed by President Biden may increase the agency's enforcement activity, relying on the use of the range of inspection and regulatory oversight tools on which the FDA has come to rely during the course of the COVID-19 public health emergency.

Drive Toward Diversity in Clinical Trials Will Continue

Increasing diversity among clinical trial subjects and investigators will be a key trend in 2021. One of the hard lessons learned in conducting COVID-19-related trials was the difficulty of recruiting minority participants. Although the issue of a lack of diversity in clinical trials has long been discussed, several concrete steps were taken in 2020 that likely will be built upon in 2021.

For instance, in March 2020, the FDA issued draft guidance on the inclusion of older adults in trials. Final guidance may be coming in 2021. In May 2020, Demand Diversity, a campaign looking to raise awareness of the lack of diversity in clinical trials, was launched in the United Kingdom. Look for more from this group during 2021.

In addition, in July 2020, the FDA issued four final guidance documents on cancer clinical trial eligibility. In announcing the guidances, the agency said that it wanted "to encourage a broadening of eligibility criteria" to allow more people to participate in clinical trials of drugs and biological products for the treatment of cancer. Including patients with the conditions covered by the guidances will allow for trial results that "better represent the patient population that will use the drug or biological product," the FDA said.

In August 2020, the American Society of Clinical Oncology and Association of Community Cancer Centers issued a request for ideas for novel strategies and practical solutions to increase participation of underrepresented racial and ethnic populations in cancer treatment trials. The fruits of this effort may appear during 2021.

Also in August 2020, the Multi-Regional Clinical Trials Center released guidance on achieving diversity, inclusion and equity in clinical research. The 341-page guidance aims to clarify the importance of and provide recommendations for improving diverse subject representation in clinical research. The group also released a 129-page toolkit with tools, checklists and case studies.

In November 2020, the Bristol Myers Squibb Foundation and National Medical Fellowships launched a $100 million program to help increase diversity and inclusion in clinical trials by training 250 new clinical investigators and working within communities to build capacity to serve underrepresented patient populations. Also, the National Institutes of Health launched a program to increase outreach and engagement efforts with ethnic and racial minority communities.

Late in 2020, the FDA released final guidance on trial diversity and inclusive trial practices, noting that "there are many approaches a sponsor should take to broaden eligibility criteria in clinical trials to ensure that the study population better reflects the patient population likely to use the drug in clinical practice." The guidance considers not only demographic characteristics, such as sex, race, ethnicity, age, and location of residency, but also non-demographic characteristics, such as including patients with organ dysfunction, comorbid conditions, disabilities, those at the extremes of the weight range, and populations with diseases or conditions with low prevalence. "Enrolling participants with a wide range of baseline characteristics may create a study population that more accurately reflects the patients likely to take the drug if it is approved and allow assessment of the impact of those characteristics on the safety and effectiveness of the study drug," the FDA said.

Sponsors and investigators will need to create trial diversity initiatives in 2021 that reflect the recommendations of the guidance.

Biden Administration Will Increase FDA Scrutiny of Medical Product Advertising and Promotion

The Biden Administration and the new FDA leadership very likely will seek to escalate the agency's regulatory oversight of the advertising and promotion of medical products, and likely will seek to address issues that exist with current policies and enforcement.

During the past four years, there has been very little movement in the area of ad promo policy. A new commissioner may have more interest in the topic, leading to policy changes during the new administration.

The singular policy that the FDA adopted under President Trump was to apply a public health standard to enforcement actions. It is likely that this standard will undergo review under the Biden administration, which may want to increase the number of enforcement actions taken by the medical products centers through new enforcement initiatives.

One of the major influencers on the FDA in the new administration will be Dr. David A. Kessler, who served as commissioner of the agency from 1990 to 1997 and who created DDMAC, OPDP's predecessor. He increased the CDER staff overseeing ad promo from about half a dozen to 40 in a single year, basically creating the present system of oversight and enforcement. Kessler has been a close adviser to Biden, knows him personally, and is deeply respected by the incoming Biden team. Kessler is likely to have a strong influence over the FDA's pharmaceutical policies. He has retained a keen interest in drug advertising, particularly direct-to-consumer (DTC) TV advertising, and it is likely that we will see his influence on future policies.

Nutrition Facts Compliance Flexibility, Extended to Small Food Companies, May End for Larger Companies

The FDA has provided additional flexibility to small food product manufacturers that needed to comply with updated Nutrition and Supplement Facts label requirements by Jan. 1, 2021 — the compliance date applied to manufacturers with less than $10 million in annual food sales. Although the compliance date would remain in place, the agency said in a constituent update, the FDA would not focus on enforcement actions during 2021 for smaller food manufacturers but instead would "work cooperatively with manufacturers." This additional flexibility included manufacturers of packages and containers of single-ingredient sugars, regardless of the size of the manufacturer.

During 2020, the FDA provided the same enforcement discretion for manufacturers with $10 million or more in annual sales, which were required to comply with the Nutrition and Supplement Facts label requirements by Jan. 1, 2020. However, those larger companies may be subject to increased enforcement scrutiny during 2021.

Proposed Revisions to Quality System Regulation May Emerge During 2021

The FDA planned to issue during 2020 a proposed rule revising the current good manufacturing practice (cGMP) requirements of the quality system (QS) regulation for medical devices, 21 C.F.R. Part 820, to supplant existing cGMP mandates with the specifications of ISO 13485:2016, the international consensus standard for device quality management systems. The need to focus the agency's resources on the response to the COVID-19 public health emergency — including reviewing emergency use authorizations (EUA) applications for testing, personal protective equipment and other COVID-19-related devices — likely caused a postponement in the release of the proposed rule. However, if those resources are sufficiently freed up during 2021, the proposed QS regulation revisions will appear. The FDA has stated that the revisions will "reduce compliance and recordkeeping burdens on device manufacturers by harmonizing domestic and international requirements" and should allow manufacturers to have more globally harmonized systems for quality management.

DEA Enforcement Will Focus on Pharmacies' Response to Red Flags Indicating Drug Diversion

Recent DEA enforcement activity has continued to focus on the ongoing effects of the nation's opioid addiction crisis. Enforcement actions by the DOJ on behalf of the DEA as well as the agency's administrative registration revocation proceedings reflect the vigor of the government's enforcement work and reveal its continuing focus on investigating alleged wrongdoing by both business organizations and individuals dealing with controlled substances.

In particular, a number of recent DEA enforcement and revocation actions have cited red flags signaling the diversion of controlled substances that allegedly were ignored by pharmacies and other companies handling the products. These red flags include requests for refills of drugs before earlier prescriptions have run out, patients traveling long distances to have prescriptions filled, multiple customers filling prescriptions from the same prescriber for the same drugs, unusual increases in drug quantities, and patients who pay for prescriptions with cash.

When the DEA finalizes a November 2020 proposed rule intended to clarify the procedures that a registrant must follow when controlled substance orders are received under such suspicious circumstances, the agency is likely to focus its enforcement activities on companies that do not comply with the clarified procedures. In addition, the incoming Biden administration may expand the government's enforcement of the Controlled Substances Act to pursue actions against smaller companies that manufacture, distribute or dispense controlled substances unlawfully, as well as against individual executives within those companies.

Not only are the mandates governing FDA-regulated products complex and constantly changing, but the consequences of a misstep can be costly. Inspections, Warning Letters, consent decrees, criminal investigations ... All can disrupt your business, taking a huge toll on the bottom line and damaging your company's reputation.

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