FDLI MEMBER MAGAZINE | WWW.FDLI.ORG | SUMMER 2023

UPDATE

Food and Drug Law Institute

FDLI

IN THIS ISSUE:

FDLI MEMBERSHIP

CONNECTING THE FOOD AND DRUG LAW COMMUNITY IN A HYBRID WORLD

FDLI members continue to drive the food and drug law community forward with innovative in-person and virtual programs, resources, and networking events. In 2023, we're on pace to connect with more people in more places than ever before.

In 2022 FDLI Members Have Brought Together:

5,885 Attendees

1,008 Speakers

154 Authors

356 Committee Members

ACROSS

580 Cities

76 States/Provinces

24 Countries

BUILD THE COMMUNITY

fdli.org /getinvolved

FDLI
Food and Drug Law Institute

contents

Summer 2023

Features

FDLI News

UPDATE
Food and Drug Law Institute
FDLI

ISSN: 1075-7635 - 2023 Spring

General Information:

Update is published four times per year by the Food and Drug Law Institute (FDLI).

FDLI is a nonprofit membership organization that offers education, training, publications, and professional networking opportunities in the field of food and drug law. As a neutral convener, FDLI provides a venue for stakeholders to inform innovative public policy, law, and regulation.

Articles and any other material published in *Update* represent the opinions of the author(s) and should not be construed to reflect the opinions of FDLI, its staff, or its members. The factual accuracy of all statements in the articles and other materials is the sole responsibility of the authors.

Membership:

Update magazine is an FDLI member benefit. For more information on other member benefits or to join, please visit fdli.org/membership.

Article Contributions:

We invite you to share your expertise and perspective and to comment on articles or ideas covered in recent issues of *Update*. All manuscripts are subject to editing for style, clarity, and length. Manuscripts and inquiries should be directed to Paige Samson, Editor in Chief, at publications@fdli.org, or at 202-222-0891.

FDLI

1032 15th St. NW, Ste. 417
Washington, DC 20005
Ph: 202-371-1420
E-mail: info@fdli.org
Website: fdli.org

Important Recent Updates to DOJ Policy on Voluntary Self-Disclosure and Corporate Compliance Programs

by Donald D. Ashley & Cynthia Schnedar

In February and March of 2023, the U.S. Department of Justice (DOJ) announced significant policy updates affecting a broad range of businesses, including those regulated by the U.S. Food and Drug Administration (FDA). The first concerns the specific circumstances under which DOJ will not seek a guilty plea from a company that voluntary self-discloses misconduct. The second addresses how, when evaluating the adequacy of corporate compliance programs, DOJ assesses executive compensation structures as well as company policies on the use of messaging applications and personal devices to conduct company business.

Both updates implement revisions to DOJ's corporate criminal enforcement policies first announced in a September 2022 memorandum by Deputy Attorney General Lisa Monaco (Monaco Memorandum).[1] In her speech announcing these new policies, Deputy Attorney General Monaco explained:

> With a combination of carrots and sticks—with a mix of incentives and deterrence—we're giving general counsels and chief compliance officers the tools they need to make a business case for responsible corporate behavior. In short, we're empowering companies to do the right thing—and empowering our prosecutors to hold accountable those that don't.[2]

We recommend FDA-regulated entities become familiar with DOJ's newly announced "carrots and sticks," and consider incorporating them into their own policies and procedures.

Voluntary Self-Disclosure Policy

The Monaco Memorandum instructed all DOJ components prosecuting corporate crime to draft and publicly share their specific policies on corporate voluntary self-disclosure to adhere to new core principles on self-disclosure identified in the Monaco

Donald D. Ashley, Executive Vice President of Regulatory Compliance, Greenleaf Health, is an expert in compliance and enforcement matters. Ashley joined Greenleaf following a distinguished 25-year career at the U.S. Food and Drug Administration (FDA) and the U.S. Department of Justice, including six years as Director of the Office of Compliance for FDA's Center for Drug Evaluation and Research.

Cynthia Schnedar, Principal, Greenleaf Health, provides strategic advice to clients in the life sciences industry on compliance issues spanning the product life cycle. Schnedar was formerly Director of the Office of Compliance for the U.S. Food and Drug Administration's Center for Drug Evaluation and Research and previously served as Acting Inspector General for the Department of Justice. Schnedar serves as a member of the FDLI Board.

Memorandum.[3] DOJ's Consumer Protection Branch (CPB) published its Voluntary Self-Disclosure Policy for Business Organizations (Self-Disclosure Policy) in February 2023.[4]

CPB leads DOJ's efforts to enforce laws protecting consumer health and safety and is specifically charged with prosecution and oversight of all criminal matters arising under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, et. seq.[5] To carry out its mission, CPB brings criminal cases throughout the United States, often working with local U.S. Attorneys' Offices to do so.

Pursuant to its policy, CPB encourages companies to voluntarily self-disclose directly to CPB potential violations of federal criminal law involving the manufacture, distribution, sale, and marketing of products regulated by FDA.[6] One of the stated purposes of this new policy is to encourage companies to implement strong compliance programs to prevent and detect such violations.[7]

The Benefits of Voluntary Self-Disclosure

As described in the CPB policy, voluntary disclosure confers two benefits on disclosing firms: 1) CPB will **not** seek a guilty plea from a company for disclosed conduct, absent the presence of aggravating factors discussed further below; and 2) CPB will not require imposition of an independent compliance monitor for a cooperating company that has voluntarily self-disclosed.[8]

Avoiding criminal conviction through voluntary disclosure provides clear benefit, given the serious direct and indirect consequences that can arise from nearly any corporate criminal conviction, especially in a highly regulated industry such as medical products manufacture and distribution. To qualify for this benefit, however, a company must have: 1) voluntarily self-disclosed directly to CPB; 2) fully cooperated;[9] and 3) timely and appropriately remediated the criminal conduct,[10] including providing restitution to victims and improving its compliance program to mitigate the risk of future illegal activity.[11] In addition, to avoid imposition of an independent compliance monitor, which can result in substantial corporate expenditures and significant disruption to corporate operations, CPB's Self-Disclosure Policy requires a company to demonstrate that it has implemented and tested an effective compliance program.[12]

What Constitutes Voluntary Self-Disclosure

Before affording a company any benefits under this policy, CPB advises that it will carefully assess the circumstances of any corporate self-disclosure to ensure several elements are present. First and foremost, the company must disclose the conduct directly to CPB and must do so prior to "an imminent threat of disclosure or government investigation"[13] and "within a reasonably prompt time after becoming aware of the offense."[14] Further, the company must not have a pre-existing obligation to disclose the conduct to DOJ, for example, pursuant to the resolution of a prior criminal or civil matter. The company's disclosure must also be accompanied by the timely preservation, collection, and production of all relevant documents and information. Finally, the company must disclose all relevant facts known to it at the time of the disclosure, including as to any individuals (or other third parties) substantially involved in or responsible for the misconduct at issue.[15]

Disclosure Must Be to CPB, not a Regulatory Agency

While not trying to discourage additional self-disclosure to regulatory agencies, CPB places great emphasis on self-disclosure **directly** to CPB and notes that if a company chooses to self-report only to a regulatory agency, such as FDA, and not also to CPB directly, the company will not qualify for benefits under CPB's Self-Disclosure Policy.[16] CPB further notes that neither the elements described above nor credit for voluntary self-disclosure itself requires the waiver of attorney–client privilege or work product protection.[17]

Potential Aggravating Factors

Even where a firm demonstrates all the elements necessary to establish voluntary self-disclosure, CPB's policy puts companies on notice that aggravating factors, if present to a significant degree, could result in CPB pursuing a more stringent resolution for a company, including requiring a guilty plea from a corporate defendant in a particular case.[18] CPB identified the following non-exhaustive list of potential aggravating factors:

- deeply pervasive misconduct throughout the company;
- intentional or willful conduct placing consumers at significant risk of death or serious bodily injury;
- intentionally or willfully targeting vulnerable victims; and
- knowing involvement of upper management in the criminal conduct.[19]

Deciding When to Voluntarily Self-Disclose

While CPB's new policy provides firms an additional strong incentive to voluntarily disclose criminal conduct to DOJ, the decision to do so nevertheless remains a complicated matter. A company needs time to internally investigate any new allegation to determine whether it has merit. It is also unclear what DOJ will consider to be "within a reasonably

prompt time."[20] However, the clock will be ticking to meet these conditions so that the disclosure is both "reasonably prompt" and "prior to imminent threat of disclosure or government investigation." On the other hand, if the company errs on the side of reporting before ascertaining whether the conduct rises to the level that should be disclosed, the company risks bringing upon itself unwarranted scrutiny from DOJ.

It is particularly interesting that CPB requires companies to disclose potential criminal conduct directly to CPB; disclosure to FDA or another regulatory agency would not be sufficient.[21] Companies often make early disclosures to FDA of potential data integrity issues and then work with FDA on determining the impact on the regulated product. Data integrity issues such as these may or may not rise to the level of a criminal violation, but they are often referred to FDA's Office of Criminal Investigations for evaluation. It is now clear that companies will receive no credit from CPB under its Self-Disclosure Policy for this type of early disclosure to FDA.

This myriad of factors must be considered as a company determines whether a voluntary self-disclosure to CPB is warranted. Voluntary self-disclosure also necessarily requires a company to have knowledge of the potential criminal conduct; companies should therefore have effective policies and procedures in place to detect misconduct, including those that encourage employees to promptly report any allegations of misconduct and those that facilitate adequate and timely investigation and preservation of evidence when allegations arise. Because these matters involve complicated issues with wide-ranging consequences, companies are well advised to quickly seek the advice of experienced legal counsel when considering such a disclosure.

Evaluation of Corporate Compliance Programs

In March 2023, DOJ's Criminal Division issued an updated version of its guidance for prosecutors, Evaluation of Corporate Compliance Programs (ECCP Guidance),[22] which expands on the directives in the September 2022 Monaco Memorandum. Significantly, the latest revision adds two important factors that prosecutors should consider when assessing the adequacy of a corporation's compliance program: 1) corporate compensation schemes; and 2) corporate policies on business use of personal devices and messaging applications and platforms.

Overview of ECCP Guidance

The ECCP Guidance is meant to assist prosecutors in making informed decisions about the adequacy and effectiveness of corporate compliance programs when considering whether to bring criminal charges against a company, as well as when determining what monetary penalties or other obligations (e.g., an independent monitor or required reporting) to seek in any corporate criminal resolution.[23] Although not part of DOJ's Criminal Division, CPB follows the same principles when assessing corporate compliance programs for charging and resolution purposes.[24]

The 2023 revision of the ECCP Guidance, like earlier versions, directs prosecutors to focus on three fundamental questions when assessing a corporation's compliance program: 1) is it well designed; 2) is it applied earnestly and in good faith, or in other words, is it adequately resourced and empowered to function effectively; and 3) does it work in practice?[25] The new version adds two significant factors that prosecutors are advised to take into account when answering these fundamental questions.

Corporate Compensation Schemes

The ECCP Guidance recognizes compensation schemes can play an important role in fostering a culture of compliance. Accordingly, prosecutors are specifically advised to consider whether a company has designed its compensation systems to incentivize compliance, for example, by escrowing certain compensation to ensure conduct tied to that compensation is consistent with company values and policies before final payout or by clawback provisions permitting the company to recoup previously awarded compensation when the recipient is later found to have engaged in corporate wrongdoing. Prosecutors are further instructed to evaluate not only the design of the compensation systems but also whether they are enforced in practice in accordance with company policy and applicable law.[26]

The 2023 ECCP Guidance also directs an assessment of a company's commercial targets and how financial incentives are structured for senior-level executives. The recommended analysis starts by asking whether a company has considered if its commercial targets are achievable when the business operates in a compliant and ethical manner. Among other questions, the guidance also asks what role the compliance function has in designing and awarding financial incentives at senior levels of the company and what percentage of executive compensation is structured to encourage enduring ethical business objectives.[27]

Messaging Applications and Personal Devices

The 2023 ECCP Guidance recognizes that the use of personal devices and messaging applications has become commonplace at home and at work and that these new technologies pose challenges to both DOJ and companies themselves

when investigating suspected misconduct by company employees. Accordingly, the 2023 ECCP Guidance adds new discussion to guide prosecutors when considering whether corporate compliance programs enable companies to effectively conduct timely and thorough investigations of misconduct.[28]

When evaluating a company's mechanisms to identify, investigate, report, and remediate potential misconduct, prosecutors are specifically advised to consider policy and procedure governing the use of personal devices, communication platforms, and messaging applications, including those designed to be ephemeral.[29] The 2023 ECCP Guidance makes clear that corporate policy and procedure should ensure, as appropriate and to the greatest extent possible, that business-related electronic data are both accessible and amenable to preservation by the company, including the data held on private phones for those companies that choose to utilize a "bring your own device" (BYOD) program for its employees.[30] Ultimately, prosecutors are advised to consider whether a company's approach to permitting and managing communication channels, including BYOD programs and the use of messaging applications, are reasonable in the context of the company's business needs and its risk profile.[31]

Assessing Your Corporate Compliance Program Against the New Provisions in the ECCP Guidance

Companies should be assessing their corporate compliance programs to ensure they are consistent with all the provisions of 2023 ECCP Guidance, and in particular with these two new provisions. First, companies should evaluate their financial incentives for executives within both the operational side and the quality side of their business. Financial incentives that focus too much on profit and not enough on ensuring quality and compliance could result in DOJ determining that your corporate compliance system is inadequate. Companies should also implement appropriate clawback provisions as a measure of financial deterrence against misconduct. Second, considering their risk profiles and legitimate business needs, companies should ensure they have both reasonable as well as effective policies and procedures in place governing when, if ever, and how business communications may take place on personal devices and messaging platforms. If such communications are permitted, companies should ensure they have policies and procedures in place to adequately preserve and access those communications.

Conclusion

FDA-regulated companies need to be aware of the new principles announced in the September 2022 Monaco Memorandum as well as the subsequent implementing policies by CPB and DOJ's Criminal Division. Companies should be carefully reviewing all three documents to ensure their policies are consistent with the new guidelines announced for voluntary self-disclosure, compensation structures, and the preservation of business communications on messaging applications and personal devices. To benefit from these new policies, it is important for firms to act in advance of any allegations of misconduct arising to maximize the likelihood that DOJ will positively assess the company when DOJ is making its enforcement decisions. More importantly, adopting an effective corporate compliance program with strong systems to ensure quality, compliance, and integrity makes it more likely that a company may never have to deal with the scrutiny of DOJ in the first place.

1. Memorandum from U.S. Dep't of Justice, Off. of the Deputy Att'y Gen., Further Revisions to Corporate Criminal Enforcement Policies Following Discussions with Corporate Crime Advisory Group, (Sept. 15, 2022), https://www.justice.gov/opa/speech/file/1535301/download [hereinafter Monaco Memorandum].
2. *Deputy Attorney General Lisa O. Monaco Delivers Remarks on Corporate Criminal Enforcement*, U.S. Dep't of Justice (Sept. 15, 2022), https://www.justice.gov/opa/speech/deputy-attorney-general-lisa-o-monaco-delivers-remarks-corporate-criminal-enforcement.
3. Monaco Memorandum, *supra* note 1, at 7–8.
4. U.S. Dep't of Justice, Civil Division, Consumer Protection Branch, Voluntary Self-Disclosure Policy for Business Organizations (Feb. 2023), https://www.justice.gov/file/1571106/download.
5. *Id.* at 1.
6. *Id.*
7. *Id.* at 4.
8. *Id.* at 2.
9. *Id.* (The meaning of "fully cooperated" is described in the Department of Justice, Justice Manual § 9-28.700).
10. *Id.* (The meaning of "timely and appropriate remediated" is described in United States Sentencing Guidelines (U.S.S.G.) § 8B2.1(b)(7)).
11. *Id.*
12. *Id.* (The meaning of an "effective compliance program" is defined by U.S.S.G. § 8B2.1).
13. *Id.* (The meaning of "prior to an imminent threat of disclosure or government investigation" is defined by U.S.S.G. § 8C2.5(g)(1)).
14. *Id.* (The meaning of "within a reasonably prompt time after becoming aware of the offense" is defined by U.S.S.G. § 8C2.5(g)(1)).
15. *Id.* at 3.
16. *Id.* at 1–2, note 2.
17. *Id.* at 3.
18. *Id.*
19. *Id.*
20. While CPB's voluntary disclosure policy cites to U.S.S.G. § 8C2.5(g)(1) when defining "within a reasonably prompt time after becoming aware of

the offense," the U.S.S.G. application note for § 8C2.5(g)(1) only speaks to the timeliness of cooperation following an organization having been officially notified of a criminal investigation, rather than the timeliness of a voluntary disclosure prior to learning of a government investigation. *See* U.S.S.G. § 8C2.5, application note 13 ("To qualify for a reduction under subsection (g)(1) or (g)(2), cooperation must be both timely and thorough. To be timely, the cooperation must begin essentially at the same time as the organization is officially notified of a criminal investigation."). No guidance is provided concerning the timeliness of a "voluntary disclosure" necessary to meet the "reasonably prompt" standard following a company becoming aware of the offense.

21. CPB's Self-Disclosure Policy is silent on whether voluntary self-disclosure to another DOJ component, such as a U.S. Attorney's Office, would qualify under the policy.
22. U.S. Dep't of Justice, Criminal Division, Evaluation of Corporate Compliance Programs (June 2020, updated Mar. 2023), https://www.justice.gov/criminal-fraud/page/file/937501/download [hereinafter DOJ ECCP Guidance].
23. *Id.* at 1.
24. *See* Madeleine Giaquinto & Cynthia Schnedar, *The Impact of DOJ's Evaluation of Corporate Compliance Programs on FDA-Regulated Products*, FDLI Update Mag. (Summer 2020) (quoting then-DOJ Deputy Assistant General David Morrel's explanation from his keynote address at the FDLI Enforcement Conference in December 2019 that CPB "follows the same principles as DOJ's Criminal Division of assessing compliance programs for charging and resolution purposes"), https://www.fdli.org/2020/04/the-impact-of-dojs-evaluation-of-corporate-compliance-programs-on-fda-regulated-products/.
25. DOJ ECCP Guidance, *supra* note 22, at 1–2.
26. *Id.* at 12.
27. *Id.* at 13–14.
28. *Id.* at 16–18.
29. *Id.* at 17.
30. *Id.*
31. *Id.* at 18.

Sheppard Mullin's Life Sciences and Food & Beverage Teams counsel clients whose activities are regulated by the FDA on matters spanning the entire product lifecycle, from concept to commercialization. Our attorneys bring an innovative and business-oriented approach to resolving complex legal and regulatory issues that complements our clients' cutting-edge technologies and novel products.

www.sheppardmullin.com/life-sciences

Contact:

Scott Liebman | 212.634.3030 | sliebman@sheppardmullin.com
Dominick DiSabatino | 202.747.1957 | ddisabatino@sheppardmullin.com

www.sheppardmullin.com/food-and-beverage

Contact:

Sascha Henry | 213.617.5562 | shenry@sheppardmullin.com
Abby Meyer | 714.424.2811 | ameyer@sheppardmullin.com

SheppardMullin

Product Testing, Questionable Science, and the Smallest, Big Developments in Consumer Product Litigation

by John Ewald, Shaila Rahman Diwan & Luke Bosso

In recent years, a growing number of seemingly scientific reports claim that U.S. Food and Drug Administration (FDA)-regulated products contain toxic substances. Many of these claims, however, are not properly vetted by the scientific community before they are blazoned in national headlines and discussed in congressional testimony. These reports also cause panic among the general public and lead to costly litigation, even if the testing is ultimately determined to be nothing more than proverbial "junk science."[1]

By way of background, analytical technology is always advancing. These advancements, coupled with unexpected findings across a variety of products, have increased pressure on regulators to issue new guidance and take novel action related to quality monitoring of products marketed in the United States. For instance, in 2021, the Biden–Harris Administration took significant steps to investigate and address per- and polyfluoroalkyl substances (PFAS) levels in foods and various consumer products, which included intradepartmental coordination by agencies such as FDA and the Environmental Protection Agency.[2] Throughout 2022, FDA took a series of actions to address benzene levels in a variety of drugs and consumer products.[3] In the beginning of 2023, FDA released its "Closer to Zero" action plan to identify mitigation strategies to lower levels of naturally occurring heavy metals in foods eaten by babies and young children.[4]

The issue, however, is that even if companies fully comply with regulatory expectations for quality monitoring, they may still face lawsuits alleging that the manufacturers' products are hazardous because they contain very low levels of allegedly toxic substances. Indeed, courts have experienced an uptick in mass tort and class action litigation involving foods and food packaging, drugs, supplements, and an array of consumer products ranging from underwear to cosmetics—all alleged to contain trace substances, such as benzene, PFAS, and compounds that claimants argue are dangerous.

The increasing popularity of this type of litigation is due, in part, to advancements in analytical technology that allegedly allow researchers to identify trace levels of various substances at concentrations, which were ostensibly not possible in the past. The use of analytical technology, however, is not without fault. Litigants often hire experts who use questionable analytical methods that may lead to false positive detections or—if the substance is present—bias the results toward higher concentrations. The methodological shortcomings are further compounded when experts then extrapolate from the results to infer that a product causes adverse human health outcomes.

This article both identifies potential methodological shortcomings employed by litigation experts during analytical testing and offers strategies to challenge that testing leading up to and throughout the trial. The first part of this article addresses

ways to challenge the use of novel analytical methods. The second part discusses common issues from inferring that a product causes harm by containing a trace substance. Lastly, this article provides practical tips companies can use to defend against litigation-driven testing and questionable science. While many features of this article are geared towards defending against claims that a product contains impurities, the same principles can be used by claimants wishing to challenge a defendant's own litigation testing.

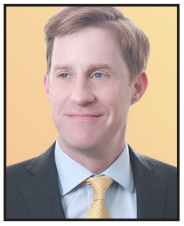
Confirming Reliability of the Analytical Testing

Is the substance really there? And if so, how much is there? These types of questions, while relatively simple, cause significant disputes in litigation because the test methods used to answer these questions may be unreliable. Indeed, questionable scientific reports claiming that products contain trace substances are causing courts to face novel issues in evaluating the reliability, and thus the admissibility, of new analytical methods. Although analytical testing has been used in litigation for decades, limited guidance exists related to how courts can confirm the reliability of the testing. Often, the go-to resource for judges to understand complex science, the Third Edition of the *Reference Manual for Scientific Evidence*, only briefly mentions analytical testing within the chapter, "Exposure Sciences," and focuses on traditional toxic tort issues where validated test methods are already well-established, such as testing for heavy metals in environmental media.[5] Notably, the *Reference Manual* does not describe issues with the development and validation of new analytical methods. Additionally, while regulatory bodies and independent scientific organizations have established guidelines for validating analytical methods, these guidelines may be general and flexible in application. In turn, the lack of concrete guidance can make it difficult to challenge new test methods developed solely for purposes of litigation.

There are a number of issues that arise when considering the reliability of the analytical method. The following is a non-exhaustive list of issues that commonly arise during litigation involving trace substances. This list is not intended to provide a set of criteria that, if fulfilled, would be sufficient to admit test results. Rather, this list identifies independent reasons to potentially exclude test results.

1. **General Acceptance in the Scientific Community.** Courts routinely consider whether methods are generally accepted within the relevant scientific community.[6] In many cases, established methods used during routine quality monitoring may not be sensitive enough to detect trace-level substances. Moreover, even where validated, extremely sensitive methods exist, litigation experts may nonetheless reject these methods, develop their own, and claim—without adequate basis—that their methods are improvements of the prior methods. In many jurisdictions, the development of new methods solely for use in litigation, in combination with a lack of peer-review, can render any results without any indicia of reliability.[7]

2. **Use of Standard Operating Procedures and Protocols.** The *Reference Manual* suggests that courts



John Ewald, partner, King & Spalding LLP, is a nationally recognized trial lawyer focused on product liability and toxic tort cases for clients in the consumer product, petrochemical and pharmaceutical industries, among others. In representing companies in mass tort litigation, Ewald focuses on developing and coordinating the client's national scientific and medical defense.

Shaila Rahman Diwan, trial partner, King & Spalding LLP, represents a range of Fortune 500 consumer product, technology, financial services, and pharmaceutical companies in product liability and complex commercial litigation. Diwan develops precisely crafted litigation strategies to deliver top results for clients facing public scrutiny in difficult jurisdictions.

Luke Bosso, associate, King & Spalding LLP, focuses on litigating scientific defenses in mass tort litigation and routinely works with preeminent experts from the world's leading scientific institutions to analyze issues surrounding exposure, risk, and medical causation. Bosso has experience taking expert depositions and has successfully argued to exclude experts in high-stakes litigation.

consider the use of standard operating procedures when assessing the reliability of laboratory work.[8] This is consistent with the fact that courts have often recognized the importance of using protocols in scientific disciplines that are prone to data dredging or unacceptable levels of manipulation. Within laboratory work, "standard operating procedures" typically refer to universal guidelines that every test within the laboratory should follow. "Protocols" provide similar guidance but are tailored to a specific test method. Therefore, one should consider compliance with both the laboratory's standard operating procedures and the specific protocols used to evaluate the reliability of the testing.

3. **Ability to Measure the Substance at Issue.** Courts should consider whether and how analytical methods are able to measure the substance at issue. Referred to as a test method's "selectivity" (or sometimes "specificity"), this criterion can be critical to understand. For nearly all types of analytical testing, even if a machine does a substantial portion of the work, an expert will ultimately use some level of subjective judgment to interpret whether the results are measuring the substance at issue. For some types of testing, such as scanning electronic microscopy (SEM), the raw data may only produce images that must be interpreted. In these instances, the definition of what qualifies as the substance at issue may be ambiguous and malleable, providing the opportunity for manipulation. For other types of testing, such as chromatography-based methods, a machine may be able to provide numeric results about whether the substance at issue is present, but ultimate interpretation about whether any substances may be interfering with the reading, i.e., confounding the result, is still left to the subjective interpretation of the analyst. Understanding the level of discretion utilized in testing can be important for evaluating an adversary's test data.

4. **Measurement of Surrogate Substances as a Proxy for the Analyte at Issue.** In some cases, litigation experts may choose to measure a proxy substance instead of the true substance—or substances—at issue. For example, PFAS are a class of chemicals with hundreds of distinct chemical identities. In lieu of developing methods suitable for each PFAS, litigation experts may instead look for the presence of organic fluorine as a surrogate indicator that PFAS are present. These methods, however, have significant limitations that may undermine the reliability of an expert's opinion depending on how the expert tries to use the data.

5. **False Comparisons to Regulatory Investigations.** Litigation experts may misapply concepts used in regulatory testing programs in ways that increase the amount of substance measured in the product. Take, for example, the utility of testing expired products. For regulatory purposes, companies may test expired products because if a product contains an acceptable level of impurities upon expiry, there is a reasonable expectation that the levels were also acceptable earlier during the product's shelf-life. In this way, companies test expired products for a limited purpose. Litigation experts may also test expired products but then use the results in inapposite ways, such as estimating patient exposure. When challenged, the experts argue that testing expired products is standard practice but fail to acknowledge that the purposes are materially different.

6. **Reporting Results in Misleading Terms.** Reporting results in the proper context is critical for communicating

with both judges and juries. Analytical measurements are typically reported as concentrations.[9] At trace levels, these concentrations are often parts-per-million (ppm) or parts-per-billion (ppb). For example, 1 ppm means that the substance being measured makes up one-millionth of the total sample by weight or 0.000001%. While this should underscore that the substance is present at an extremely low concentration, litigation experts may translate analytical results into terms that strip the values of their context in ways that can be misleading. For instance, in talc litigation, rather than reporting that asbestos is present at ppm levels, experts may quantify in terms of "asbestos structures per gram," which can cause corresponding numbers to appear more jarring to a lay audience. This is essentially the difference of reporting that a substance is present at a concentration of, for example, 0.000001% versus, for example, 20,000 asbestos structures/gram.

7. **Conflating Worst-Case Scenarios with Reasonable Probability.** Even once analytical testing exists, further statistical extrapolation is necessary to estimate total exposure. There are, however, a host of questionable assumptions that underlie these methods. For instance, litigation experts may infer levels of the substance in historical products that were never tested. Also, experts may opt to extrapolate from worst-case scenarios, even if those values are outliers and unrepresentative of true probability.

8. **Misapplication of Detection Limits.** Scientists are limited in the ability to confirm the absence of substance.[10] This is because there is always the possibility that substance is present at concentrations lower than what can be detected by the analytical technology. Therefore, the absence of a finding is generally reported as "not detected" or "below limit of detection"—as opposed to a true zero—as a matter of scientific convention.[11] Litigation experts may misuse the convention to support speculation that: 1) all samples have the substance, but 2) the technology is only sensitive enough to detect the substance in some of the samples. This reasoning attempts to shift the burden on companies to prove that a substance is not present—a scientific impossibility.

Confirming Reliability of the Causation Analysis

Even if a substance is present, there is not necessarily any realistic risk to human health. This illustrates an important point that analytical testing alone would be insufficient to carry the claimant's burden of proof. As discussed further below, claimants would also need admissible expert testimony establishing that exposure to the product actually caused their injuries. The process of trying to prove causation based on exposure to a product containing trace substances presents further opportunity for litigation experts to engage in questionable scientific reasoning. While not exhaustive, the below list provides some examples of how litigation experts may misconstrue scientific concepts, particularly analytical data, when formulating their causation opinions.

1. **Reliance on Hazards Instead of Risks.** The difference between hazards and risks is critical. As the *Reference Manual* explains, all substances are intrinsically hazardous because at high enough doses, all substances, including water, can be toxic.[12] The concept of risk, however, considers whether an adverse outcome is likely to occur at a certain dose. Information on the hazards of a substance provides no value when the levels are so low that there is no risk. Therefore, epidemiological data evaluating the specific product at issue—and de facto, any trace substances that may be in those products—is needed to evaluate true risk. In the absence of such evidence, essentially all reputable medical and

scientific organizations would consider the evidence insufficient to determine that the product causes the alleged outcome. Nonetheless, litigation experts may resort to lesser forms of evidence, such as high-dose animal studies or in vitro toxicological assays. These lines of evidence, however, can only support a potential hazard and cannot reliably establish risk in humans at low doses.

2. **Assumptions That No Level is Safe.** To avoid evidentiary burdens of establishing that a particular claimant was exposed to sufficient doses to cause an adverse event, some claimants argue that there is no safe level of exposure. These types of theories assume there are no practical thresholds before toxicity may occur.[13] The issue claimants run into, however, is that many substances are ubiquitous, either because they occur naturally in the environment or because of the prevalence of their use across manufacturing industries. Therefore, all people are exposed to some level of the substance at issue, regardless of whether they use the product, which calls into question the viability of no-threshold theories. Faced with tension between real-world exposure and assumptions of no-safe-exposure thresholds, litigation experts may retreat to an alternative position that any additional exposure from use of these products is additive to background exposure and must result in an increased risk. This reasoning, however, generally lacks support by empirical data, such as data that compares how total exposure (also referred to as body burden[14]) modifies risk. Thus, these assumptions are merely speculative.

3. **Use of Analogies to Substitute for Associations.** Analogy may be used as a criterion to infer causation as one of the Bradford Hill criteria. Reasoning by analogy, however, is only ever used *after* establishing a consistent, statistically significant association between the specific product at issue and the specific outcome at issue when the association cannot be explained by chance, bias, or confounding.[15] Litigation experts, however, may use analogy in lieu of finding a reliable association. For instance, as noted earlier, PFAS are a class of compounds with thousands of unique and distinct species. Small differences in molecular structure can result in significant differences in potential toxicity, potency, target organs, and other important differences, such that each PFAS species must be separately evaluated for risk. Nonetheless, litigation experts may improperly import risk information for one PFAS species onto another PFAS species by means of analogy to fill evidentiary gaps. Using analogies as a substitute for a valid association erroneously skips the first step of a causation analysis and would render an expert opinion unreliable.

Strategies to Combat Litigation-Driven Science

Even if methodological shortcomings in litigation testing are apparent, companies still need to develop strategies for how to distill complex science for both judges and juries. Upfront investment in a rigorous scientific defense can yield substantial litigation advantages and prevent prejudicial junk science from reaching the jury's ears.

1. Pre-Litigation Strategies

Some of the most critical steps to combat litigation-driven science occurs before the first lawsuit is ever filed. A company can position itself for potential litigation by pressure-testing a company's quality systems to ensure that they are well-maintained and follow best scientific practices. This can be critical because when an adversary conducts new scientific testing for purposes of litigation, a company will want the full opportunity to hold the litigation-driven testing to rigorous scientific standards. Attacks against litigation-driven science can be bolstered when the company can also point to their own internal testing that

meets higher scientific standards than used in litigation. Additionally, should the case proceed to trial, educating the jury on the operation and safeguards within a company's quality systems can be critical to mounting a persuasive defense.

In a similar vein, any conclusions drawn from a company's investigations, including health risk assessments, should provide appropriate context that details the rationale for the investigation and any inherent limitation to those statements. Including appropriate qualifications to any scientific analysis can curb the ability for litigants to later take the analysis out of context. In litigation, a claimant may attempt to draw false comparisons between their own expert's causation opinions and a company's actions done out of an abundance of caution. Therefore, appropriately documenting and contextualizing a company's investigations can be critical to mount an effective scientific defense.

2. Pre-Trial Strategies

If, and when, a company is faced with litigation-driven testing brought by an adversary, companies should seek full discovery of the underlying documentation. Most jurisdictions have rules that require automatic disclosure—or at minimum allow discovery—of an expert's litigation testing. While the exact documents to request will depend on the type of analytical test utilized and other case-specific factors, at minimum one would need a laboratory's standard operating procedures, all test protocols, all laboratory notebooks, all raw data, and executed chain of custody forms in order to evaluate the reliability of test results. A careful review of this documentation may elucidate critical flaws that undermine the reliability of the testing and thus erode confidence in any expert's opinion that relies on such testing.

Moreover, even if an adversary's analytical measurement is entirely reliable, companies should consider whether to challenge litigation testing because the expert failed to reliably interpret the results and apply them to the facts of the case. As discussed above, litigation experts may utilize a number of questionable assumptions and extrapolations that extend otherwise reliable results beyond their natural interpretation. For instance, litigation experts may test a limited set of products and then generalize those findings to all products. Very few experiments, however, can support such broad generalization. Litigation experts may also test the product under certain conditions and assume that the product would behave similarly under different conditions, even when there is no empirical data to support these assumptions. There are endless ways in which litigation experts may misuse data, and not every logical leap may be readily apparent. However, an investment in a rigorous scientific defense can elucidate the most critical issues underlying a set of experiments.

Beyond the reliability of the testing in and of itself, companies may also challenge the admissibility of testing through traditional motions in limine if the testing is not relevant for a particular trial. For instance, if a litigation expert tested products—but not a claimant's specific product—the testing is likely irrelevant and unduly misleading. While these arguments may appear similar to challenges based on the reliability of an expert's opinion, there may be strategic reasons to move to exclude the results on relevance grounds. Firstly, depending on the jurisdiction, the case law on relevance may be more robust and favorable. Secondly, many judges may feel more confident in excluding an expert based solely on legal grounds, such as relevance,

as opposed to weighing in on scientific methodology.

3. Trial Strategies

Companies facing a prospective jury trial risk that the potential jurors adopt a "zero tolerance" attitude to trace substances in products, especially in absence of evidence that the product is lifesaving or bestows justifiable benefit. This attitude can lead jurors to assume the company may have acted recklessly, despite evidence that a company maintained quality systems. Jurors may also be tempted to disregard scientific evidence beyond analytical testing, even if the evidence overwhelmingly reinforces the product's safety. Therefore, companies facing a prospective jury trial should consider strategies to effectively defend the company's reputation and quality processes.

First, perspective is everything. Depending on the case, people are likely to be exposed to the exact substance at issue on a regular basis. If applicable, comparing background exposure to the doses in a product can provide the jury with much-needed perspective that the product contributes, at most, de minimis additional exposure above background. Working with graphic consultants can prove useful to develop accessible demonstratives that show a product's contribution, if any, is dwarfed by the overall background exposure.

Second, a critical trial strategy dates back to the sixteenth century when the philosopher Paracelsus first articulated a central tenet of toxicology: "the dose makes the poison."[16] This phrase refers to the concept that even hazardous substances are unlikely to cause adverse effects at low doses. Because trace substances are, by definition, present in infinitesimally small levels, comparing the doses that result in appreciable increased risk versus the levels present in a product can elucidate evidentiary failures in proving causation. Companies should consider targeted strategies to develop these accessible, jury-friendly admissions through the opposing expert witnesses. These themes should be incorporated into overall deposition strategy so that the company can establish the necessary admissions for an effective cross examination at trial.

Third, telling the story of a company's due diligence cannot take a backseat and should always be paired with the scientific evidence. In fact, explaining the reality surrounding how scientists identify and control trace substances can be critical for the jury to contextualize the analytical findings. Jurors often begin with the misconception that the presence of a trace substance is an atypical occurrence and that it is evidence of a quality failure. These assumptions, however, fail to acknowledge that no substance is truly "pure." And since no product or material is truly pure, the pertinent question is whether the presence of the newly discovered substance was reasonably foreseeable. Of course, foreseeability always seems easier in hindsight, so a company should develop strategies for how to leverage its manufacturing and quality control practices affirmatively in its defense.

Finally, the burden of proof is key. As described above, an adversary may rely on arguments such as assuming that there is no safe level of exposure to a substance, assuming that a non-detect test result could mean the substance is nevertheless present, or making leaps of logic from high-dose animal studies to lower doses in humans. An adversary's reliance on these opinions

should be to their own detriment if that party carries the burden of proof.

Conclusion

Trace substance litigations are rising in popularity, and all manufacturers should begin to consider how best to position themselves for potential litigation in the event new substances are discovered in their products. While specific strategies vary based on the needs of the litigation, there is a common set of strategies for companies to apply both before and across varying litigations.

1. U.S. Dep't of Justice, Report of the Tort Policy Working Group on the Causes, Extent and Policy Implications of the Current Crisis in Insurance Availability and Affordability (Feb. 1986).
2. The White House, FACT SHEET: Biden-Harris Administration Launches Plan to Combat PFAS Pollution (Oct. 18, 2021), https://www.whitehouse.gov/briefing-room/statements-releases/2021/10/18/fact-sheet-biden-harris-administration-launches-plan-to-combat-pfas-pollution/?utm_source=link.
3. *E.g.*, U.S. Food & Drug Admin., FDA Alerts Drug Manufacturers to the Risk of Benzene Contamination in Certain Drugs (current as of Dec. 23, 2022), https://www.fda.gov/drugs/pharmaceutical-quality-resources/fda-alerts-drug-manufacturers-risk-benzene-contamination-certain-drugs.
4. U.S. Food & Drug Admin., Closer to Zero: Action Plan for Baby Foods (current as of Jan. 12, 2023), https://www.fda.gov/food/environmental-contaminants-food/closer-zero-action-plan-baby-foods.
5. Reference Manual for Scientific Evidence, 3rd Ed. at 528–30.
6. Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 594 (1993).
7. *See id.*
8. Reference Manual for Scientific Evidence, 3rd Ed. at 529–30.
9. *Id.* at 541.
10. *Id.* at 530.
11. *Id.* at 530.
12. *Id.* at 636.
13. *Id.* at 642.
14. *Id.* at 537.
15. *Id.* at 598–99.
16. *Id.* at 603, n. 160.

Juul Labs, Inc. v. FDA: A FOIA Twist on the Challenge to FDA's Marketing Denial Order

by Robert S. Claiborne, Jr., Bryan M. Haynes & Agustin E. Rodriguez

Recent Freedom of Information Act (FOIA) litigation raises an interesting question: When federal agency action requires analyses under a holistic, multi-factor statutory standard, may the agency withhold from disclosure as "deliberative" records related to analyses that purportedly were not factored into the agency's final decision? A federal court will address this question of public disclosure in litigation between Juul Labs, Inc. (JLI) and the U.S. Food and Drug Administration (FDA).

On June 23, 2022, JLI petitioned the U.S. Court of Appeals for the D.C. Circuit to review FDA's marketing denial order (MDO) on its premarket tobacco product applications (PMTAs).[1] The PMTAs presented FDA with the question of whether JLI's tobacco products are appropriate for the protection of the public health (APPH) under the Federal Food, Drug, and Cosmetic Act (FDCA),[2] and JLI's petition presents the court with the question whether the MDO was arbitrary and capricious under the Administrative Procedure Act (APA).[3] On September 20, 2022, JLI filed a separate action against FDA, in the U.S. District Court for the District of Columbia,[4] alleging that FDA unlawfully failed to produce records in response to JLI's FOIA requests for records related to the MDO.[5] FDA withheld certain records that it created in connection with its review of JLI's PMTAs, claiming that those records were exempt from FOIA's disclosure requirement under the deliberative process privilege.

The MDO, FOIA Requests, and Litigation

The facts and timing of events around the issuance of the MDO raise questions regarding FDA's withholding of related records. Although "people familiar with the matter" had informed *The Wall Street Journal* earlier,[6] FDA issued the MDO to JLI on June 23, 2022. According to the MDO, JLI submitted insufficient information regarding toxicological risks to evaluate whether its products are APPH.

Less than an hour before the FDA Center for Tobacco Products' (CTP) Office of Science (OS) issued the MDO, Michele Mital—CTP's Acting Director at the time—signed a memorandum to file[7] (Memo to File) regarding the MDO and two separate OS technical project lead review reports (TPLs) created in

review of JLI's PMTAs. Generally, a TPL is foundational to FDA's grant or denial of a marketing order. A TPL documents whether a product meets the APPH standard and includes OS's description of the multidisciplinary review completed on the PMTA. Of the two TPLs on JLI's PMTAs, one addressed toxicology (Toxicology TPL) and the other addressed all other relevant scientific disciplines (Second TPL). OS issued the Toxicology TPL on June 23, 2022, before OS issued the MDO and before Ms. Mital signed her Memo to File. OS apparently also issued the Second TPL that day, but the specific time is not stated in existing court filings.

Additionally, although it ordinarily stores its TPLs and disciplinary review documents in a designated, internal database, CTP "decided that the [Second TPL] should not be stored in the . . . database, but instead maintained with other working files." According to a declaration of Ms. Mital filed in the FOIA litigation, this was done "[t]o prevent internal confusion regarding whether the [Second TPL] provided any part of the basis of the agency's ultimate decision." Former FDA employees have informed the authors that such segregation of files within the agency is highly irregular.

According to Ms. Mital's Memo to File, her office reviewed the Toxicology TPL and "concur[red] that the toxicological issues are dispositive of the applications," so it was "not necessary . . . to review and resolve (and thus CTP has not resolved) any other aspects of the applications." She added that "the discipline reviews and related conclusions in the [Second TPL] . . . have not been adopted by [her office] and do not reflect complete agency consideration or a final agency decision," but "the MDO letter should indicate that the list of deficiencies supporting the denial is not necessarily exhaustive."

The Memo to File was apparently issued as part of the CTP Director office's "practice" of "review[ing] any conclusions reached by OS for this bundle [of JLI's PMTAs] before those conclusions became a final agency decision." According to the Memo to File, this was a "longstanding practice, during consultations related to the Juul application bundle."

On the same day that JLI received the MDO, it filed its petition for review with the D.C. Circuit and sent FOIA requests to FDA. JLI later requested (and FDA granted) FDA's supervisory review of the MDO, which remains ongoing. Pending the outcome of the supervisory review, FDA has administratively stayed the MDO, and the D.C. Circuit is holding the case in abeyance. JLI's FOIA requests sought the TPLs, the disciplinary review documents, and any other documents related to the review of its PMTAs. In response, FDA produced the Toxicology TPL and related toxicology review documents but asserted the deliberative process privilege to withhold other records, including the Second TPL and non-toxicology disciplinary review documents. The FOIA litigation ensued over these documents, and the parties have filed cross-motions for summary judgment, which are pending before U.S. District Court Judge Randolph D. Moss.

Deliberative Process and Final Action

In view of the APPH standard and several apparent anomalies in FDA's handling of JLI's MDO, FDA's invocation of the deliberative process privilege raises interesting questions.

Under the FDCA, FDA may issue an MDO if "there is a lack of a showing that permitting such tobacco product to be marketed would be" APPH.[8] The APPH finding "shall be determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account . . . the increased or decreased likelihood that existing users of tobacco products will stop using such products; and . . . the increased or decreased likelihood that those who do not use tobacco products will start using such products."[9] Congress intended APPH "to be a flexible standard that focuses on the overall goal of reducing the number of individuals who die or are harmed by tobacco products."[10] It is a holistic, multi-factor standard. Moreover, the APA prohibits FDA from making an APPH finding that is "arbitrary" or "capricious," and agency action may be set aside as such if it "entirely failed to consider an important aspect of the" matter before it.[11]

Under FOIA, a federal agency "upon any request for records . . . shall make the records promptly available to any person."[12] This requirement does not apply to "inter-agency or intra-agency memorandums or letters that would not be available by law"—including under the deliberative process privilege—"to a party other than an agency in litigation with the agency."[13] The deliberative process privilege covers an agency's pre-decisional, deliberative records created in the course of selecting an action but not the records reflecting the final agency action or its rationale.[14] In other words, FOIA does not require an agency "to operate in a fishbowl," but the deliberative process privilege does not require a requestor "to operate in a darkroom."[15]

Members of Congress have expressed concerns that the "deliberative process privilege is the most used privilege and the source of the most concern regarding overuse," with some commentators "calling it the 'withhold it because you want to' exemption."[16] Such concerns have

resulted in legislative reforms, including a limitation on the permissible withholding of exempt records to circumstances where "the agency reasonably foresees that disclosure would harm an interest protected by an exemption."[17] Moreover, courts will not necessarily accept an agency's characterizations in support of the privilege. "[D]etermining whether an agency's position is final for purposes of the deliberative process privilege is a functional rather than formal inquiry."[18] A court will not go along with an agency's "charade" pretending that a record is pre-decisional and deliberative when the evidence shows that it is not.[19] The privilege is not a "get-out-of-FOIA-free card" for the agency.[20]

In view of these legal standards, there are at least three primary issues apparent in FDA's withholding of the Second TPL and non-toxicology disciplinary review documents.

First, it appears odd that FDA issued two TPLs compartmentalizing different aspects of FDA's multidisciplinary APPH analysis. The authors have never seen FDA issue bifurcated TPLs for any other request for tobacco product marketing authorizations. Consistent with an example on FDA's website,[21] as well as other publicly available TPLs referenced in JLI's court filings, every TPL of which the authors are aware—except JLI's—reflects the entire multidisciplinary analysis for the respective product. The irregularity of this approach is also reflected in CTP's decision to keep the Second TPL outside of its ordinary database "[t]o prevent internal confusion[.]" The fact that the Toxicology and Second TPLs were compartmentalized based on OS's "consultations" with the CTP Director's office and subject to that office's "review" leads one to wonder what else was discussed. And FDA's assertion that the Second TPL was pre-decisional is also questionable, given that *The Wall-Street Journal* learned of FDA's decision before OS issued the TPLs or MDO and before Ms. Mital issued her Memo to File.

Second, the regularity of FDA's public disclosure of TPLs undermines claims that its disclosure of the Second TPL and non-toxicology disciplinary review documents would harm interests protected by the deliberative process exemption. Judge Christopher R. Cooper of the U.S. District Court for the District of Columbia recently issued an instructive decision in *Vanda Pharmaceuticals, Inc. v. FDA*.[22] Addressing FDA records relating to its multidisciplinary review of a supplemental new drug application, Judge Cooper held that FDA "failed to show any foreseeable harm that would arise if the requested reviews were released."[23] FDA argued that disclosure would have a chilling effect on internal communications, claiming that its reviewers might be deterred from giving honest assessments if they knew that their review records could be disclosed. Judge Cooper was "not convinced."[24] FDA publicly discloses the review records "in a variety of circumstances,"[25] and FDA did not establish that its reviewers expected their deliberations to remain private. "Disclosure cannot chill deliberations if those deliberating do not reasonably expect their deliberations to remain private."[26] Although Judge Cooper's *Vanda* decision does not bind Judge Moss in *JLI*, *Vanda*'s reasoning could be followed as the factual matters regarding supplemental new drug applications, FDA review records, and the prevalence of those records' disclosure are materially similar to those regarding PMTAs, TPLs, and disciplinary review documents, and those documents' usual disclosure.

Robert S. Claiborne, Jr. is an associate at Troutman Pepper Hamilton Sanders LLP in Richmond, Virginia. Claiborne is engaged by businesses dealing in tobacco products subject to FDA's regulatory authority and assists with matters relating to marketing authorizations, administrative procedure, and public records requests.

Bryan M. Haynes is a partner at Troutman Pepper Hamilton Sanders LLP in Richmond, Virginia. Haynes is engaged by businesses dealing in tobacco products subject to FDA's regulatory authority and assists with matters relating to marketing authorizations, administrative procedure, and public records requests.

Agustin E. Rodriguez is a partner at Troutman Pepper Hamilton Sanders LLP in Richmond, Virginia. Rodriguez is engaged by businesses dealing in tobacco products subject to FDA's regulatory authority and assists with matters relating to marketing authorizations, administrative procedure, and public records requests.

Third, and more broadly, the holistic standards of the FDCA and APA are in tension with the decision to base the MDO solely on toxicology concerns reflected in the Toxicology TPL. OS's creation of separate TPLs raises questions about how FDA evaluated all of the relevant evidence consistent with its obligations under the law. Those legal questions remain to be briefed by the parties, and it will be interesting to see how FDA's compartmentalized, toxicology-only review measures up against its respective FDCA and APA obligations to consider overall "risks and benefits to the population as a whole"[27] and each "important aspect"[28] of the PMTAs.[29]

****

While it remains to be seen what exactly happened with JLI's PMTAs, it is not difficult to imagine that an agency could assert pretextual or piecemeal grounds for an action, withhold records that may undermine those asserted grounds, and attempt to more-or-less insulate its action from meaningful review. And it is not farfetched to think that an agency could be overeager to use the deliberative process privilege to shield records that may lead to scrutiny of its actions. That is reflective of the reasons why we have FOIA and the APA. Congress intended these laws, respectively, "to assure the availability of Government information necessary to an informed electorate"[30] and to "require[] adequate, fair, effective, complete, and just determination of the rights of any person in properly invoked proceedings."[31]

1. Juul Labs, Inc. v. Food & Drug Admin., Case No. 22-1123 (D.C. Cir.).
2. 21 U.S.C. § 387j(c).
3. 5 U.S.C. § 706(2)(A); 21 U.S.C. § 387l(b).
4. Juul Labs, Inc. v. Food & Drug Admin., Case No. 1:22-cv-02853 (D.D.C.).
5. *See* 5 U.S.C. § 552(a)(4)(B).
6. Jennifer Maloney, *FDA to Order Juul E-Cigarettes Off U.S. Market*, Wall St. J. (June 22, 2022), https://www.wsj.com/articles/fda-to-order-juul-e-cigarettes-off-u-s-market-11655904689.
7. Generally speaking, a memorandum to file is an internal memorandum, without designation of a specific recipient, that can be used to document contemporaneous observations or impressions for future reference.
8. 21 U.S.C. § 387j(c)(2)(A).
9. *Id.* § 387j(c)(4).
10. H.R. Rep. No. 111-58, at 39 (2009).
11. Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983).
12. 5 U.S.C. § 552(a)(3)(A).
13. *Id.* § 552(b)(5).
14. U.S. Fish & Wildlife Serv. v. Sierra Club, Inc., 141 S. Ct. 777, 785–86 (2021).
15. Am. Mail Line, Ltd. v. Gulick, 411 F.2d 696, 703 (D.C. Cir. 1969).
16. H.R. Rep. No. 114-391, at 10 (2016).
17. FOIA Improvement Act of 2016, Pub. L. No. 114-185, § 2(1)(D), 130 Stat. 538, 539 (codified at 5 U.S.C. § 552(a)(8)(A)(i)(I)). Under this amendment, agencies may alternatively withhold exempt records if "disclosure is prohibited by law." *Id.* (codified at 5 U.S.C. § 552(a)(8)(A)(i)(II)). Congress also singled out the exemption for "the deliberative process privilege," providing that it "shall not apply to records created 25 years or more before the date on which the records were requested." *Id.* § 2(2), 130 Stat. at 539–40 (codified at 5 U.S.C. § 552(b)(5)).
18. *ierra Club, Inc.*, 141 S. Ct. at 788.
19. *Id.*
20. Gellman v. Dep't of Homeland Security, 525 F. Supp. 3d 1, 8 (D.D.C. 2021).
21. *See* U.S. Food & Drug Admin., Technical Project Lead (TPL) Review of PMTAs (Sept. 17, 2021), https://www.fda.gov/media/152504/download.
22. Case No. 1:22-cv-938, 2023 U.S. Dist. LEXIS 51853 (D.D.C. Mar. 27, 2023).
23. *Id.* at *13.
24. *Id.* at *8.
25. *Id.* at *7–12.
26. *Id.* at *11.
27. 21 U.S.C. § 387j(c)(4).
28. *Motor Vehicle Mfrs. Ass'n*, 463 U.S. at 43.
29. Meanwhile, it is notable that an FDA-commissioned study recommended that CTP reform its policy development program "to provide clarity, predictability, and transparency concerning scientific standards for application review." Reagan-Udall Found'n, Operational Evaluation of Certain Components of FDA's Tobacco Program 18 (2022), https://reaganudall.org/sites/default/files/2022-12/Tobacco%20report%20210pm.pdf.
30. H.R. Rep. No. 89-1497, at 33 (1966).
31. H.R. Rep. No. 79-1980, at 41 (1946).

Advancing the field

We proudly support **FDLI** and share its commitment to enhancing understanding of FDA law and regulation.

BakerHostetler

bakerlaw.com

Advancing the Transition to Computer Software Assurance: Responding to the FDA Draft Guidance for Production and Quality System Software

by Jacqueline K. Davidson

Introduction

Life sciences companies increasingly rely on computerized systems within manufacturing and quality, which can include automation, robotics, simulation, and other digital capabilities. These technologies provide significant benefits for enhancing the quality, availability, and safety of medical devices.[1] Over the past decade, most life sciences organizations have transitioned their regulated systems into the cloud. This is reflected by a global market for cloud services in the medical device sector of $2 billion in 2021, forecast to increase by a compound annual growth rate of 17.1% to $4.4 billion by 2024.[2]

Under FDA regulations covering Good Manufacturing Practice and related best practices (known collectively as GxP), it is necessary to validate systems with direct or indirect product and patient impact prior to using them in a production environment. These types of "GxP-facing" systems can include quality management systems, electronic document management systems, batch record systems, laboratory information management systems, clinical systems, product safety and complaint reporting, environmental monitoring, and systems for transferring and analyzing production data.[3] Since these systems form the technological backbone of life sciences companies, computer system validation (CSV) is a highly regulated and required activity for life science companies. The burden placed on organizations to manage CSV has increased with the proliferation of specialized computerized systems and is further amplified by a global staffing shortage. Based on stakeholder feedback, the U.S. Food and Drug Administration (FDA) is now encouraging a transition to computer software assurance (CSA) to support data integrity, product quality, product safety, and patient safety.[4] This transition marks an evolution in validation effort from documenting extensive testing to focusing on critical thinking and risk management up-front.[5] CSA offers a path away from time- and personnel-intensive, burdensome validation to a risk-based, workflow-driven process that preserves data integrity.[6]

On September 13, 2022, the FDA Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) issued a long-awaited document titled, "Computer Software Assurance for Production and Quality System Software: Draft Guidance for Industry and Food and Drug Administration Staff."[7] The draft guidance responds to stakeholder requests for greater clarity on FDA's expectations for software validation for computers and

Jacqueline K. Davidson, Head of Regulatory Intelligence and Innovation at Sware, Inc., brings over 25 years of experience in the life sciences industry. Davidson is a recognized thought leader in IT quality assurance, specializing in software lifecycle management, quality risk management, and software validation for the pharmaceutical and medical device sectors.

automated data processing systems and for a more agile, iterative approach to the validation of software used in these areas.[8] FDA "believes that these recommendations will help foster the adoption and use of innovative technologies that promote patient access to high-quality medical devices and help manufacturers to keep pace with the dynamic, rapidly changing technology landscape, while promoting compliance with laws and regulations implemented by FDA."[9]

Despite the fact that this is draft guidance, FDA and key industry leaders have maintained that risk-based, lean validation approaches are acceptable, and that companies "have the flexibility they need to adjust the extent and stringency of controls based on any factors they choose."[10] CSA falls within this category, meaning that companies can safely adopt CSA approaches. However, to date, adoption has been slow, largely because of concerns about potential inspection risks due to changes in the approach and potential changes in the validation deliverables required, coupled with uncertainty about how to apply critical thinking to validation.

This article provides a regulatory overview and next steps for companies, including key features of the new draft guidance; a comparison between CSV and CSA; suggestions on overcoming reluctance to adopt CSA concepts; a discussion of how to align validation testing with level of risk; ideas on how to move towards inspection readiness with CSA; and potential gaps in the guidance that stand in the way of acceptance and implementation of the CSA guidance by industry.

Regulatory Overview

The September 2022 draft guidance describes CSA as "a risk-based approach to establish confidence in the automation used for production or quality systems," based on a four-step process. This involves identifying the intended use of the software within the production and quality systems, determining a risk-based approach depending on possible outcomes if the software did not perform as intended, determining appropriate assurance activities based on that risk, and establishing an appropriate record with enough evidence to show that the software was assessed and performs as intended (Figure 1).[11]

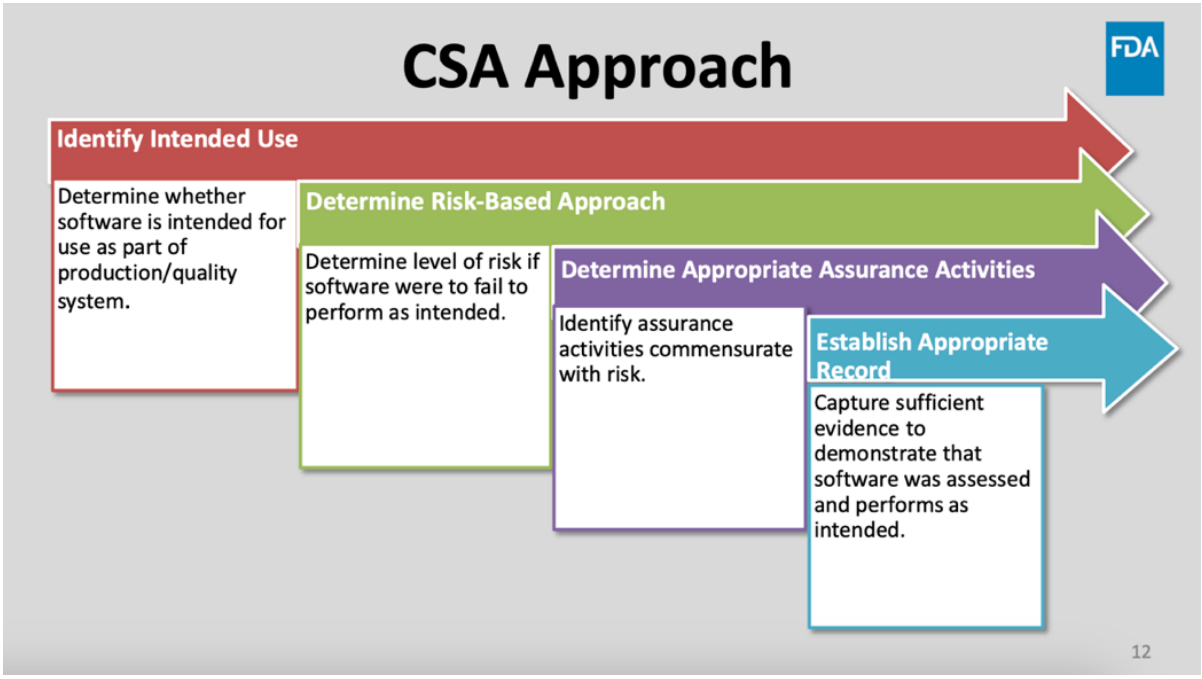


Figure 1: FDA's explanation of the computer software assurance (CSA) approach[12]

FDA Definition: Computer Software Assurance

"Computer software assurance [CSA] is a risk-based approach for establishing and maintaining confidence that software is fit for its intended use. This approach considers the risk of compromised safety and/or quality of the device (should the software fail to perform as intended) to determine the level of assurance effort and activities appropriate to establish confidence in the software. . . . Such an approach supports the efficient use of resources, in turn promoting product quality."

U.S. Food and Drug Administration Draft Guidance on "Computer Software Assurance for Production and Quality System Software;" September 13, 2022[13]

"FDA is issuing this draft guidance to provide recommendations on computer software assurance for computers and automated data processing systems used as part of medical device production or the quality system. FDA believes that these recommendations will help foster the adoption and use of innovative technologies that promote patient access to high-quality medical devices and help manufacturers to keep pace with the dynamic, rapidly changing technology landscape, while promoting compliance with laws and regulations implemented by FDA. This draft guidance is not final nor is it for implementation at this time."

Federal Register Notice on Draft CSA Guidance; September 13, 2022[14]

An FDA Description of CSA

Computer software assurance has the following features:

- Risk-based approach for establishing and maintaining confidence that software is fit for its intended use
- Establishes and maintains that software used in production or quality system is in a state of control throughout its lifecycle ("validated state")
- Effort and records should be "right-sized" to the risk

FDA webinar, "Draft Guidance on Computer Software Assurance for Production and Quality System Software;" October 27, 2022[15]

The draft guidance applies to assurance activities for computer systems and automated data processing systems used as part of medical device production or the quality system, including software for design, development, manufacturing, or the quality system.[16] The document does not apply to software used as a medical device (SaMD) or software in a medical device (SiMD).[17]

Software validation has traditionally involved software testing and verification at every stage of software development, along with exhaustive documentation. According to FDA, software testing alone is often insufficient to establish confidence that the software is fit for its intended use: "FDA believes that applying a risk-based approach to computer software used as part of production or the quality system would better focus manufacturers' assurance activities to help ensure product quality while helping to fulfill the validation requirements of Title 21 of the Code of Federal Regulations or CFR Part 820.70(i)."[18]

The CSA draft guidance builds on the agency's framework for computer system validation issued in 1997 with 21 C.F.R. Part 11.[19] This was later refined in "General Principles of Software Validation: Guidance for Industry and FDA Staff," published in 2002.[20] The draft guidance aligns with multiple recent initiatives, including the FDA Case for Quality program and Advanced Manufacturing efforts,[21] Industry 4.0/Pharma 4.0/Validation 4.0, and the release of the second edition of the International Society for Pharmaceutical Engineering (ISPE) Good Automated Manufacturing Practice 5 (GAMP 5).[22] These publications indicate that regulatory bodies favor a risk-based approach to assure the data integrity and suitability of computer systems to facilitate the speed of innovation, manufacturing, and product delivery.[23]

Computer Systems Validation (CSV) v. Computer Software Assurance (CSA)

Traditional CSV is a burdensome, often paper-based, Stage-and-Gate process that involves a blanket approach to validation testing of systems, features, and changes without regard to risk. Life sciences and medical device manufacturers that are covered by 21 C.F.R. Part 820 (Quality System Regulation) have historically carried out massive validation and verification testing efforts—often recorded as vast numbers of screenshots—in the name of compliance with regulations.[24] Such efforts, however,

may not appropriately test whether a system is fit for the intended use, potentially resulting in risks to product quality and patient safety. Additionally, since traditional validation is time- and resource-intensive, companies often fall behind on validating the scheduled upgrades that come with Software-as-a-Service (SaaS) applications. This can cause them to fall out of compliance and into "technical debt," because they are running on outdated or insufficiently validated systems. If we consider validation activities in the context of the Pareto Principle (or the "80-20" rule), CSV typically comprises 80% effort on documentation and testing and only 20% focus on critical thinking and assurance activities.[25] CSA increases efficiency by reversing these percentages, with an 80% focus on critical thinking and 20% of effort going into documentation and testing (Figure 2).[26] This change in structure of effort can provide significant time and cost savings in the assurance activities (validation) of GxP-facing applications, while promoting a path out of technical debt and into better compliance.

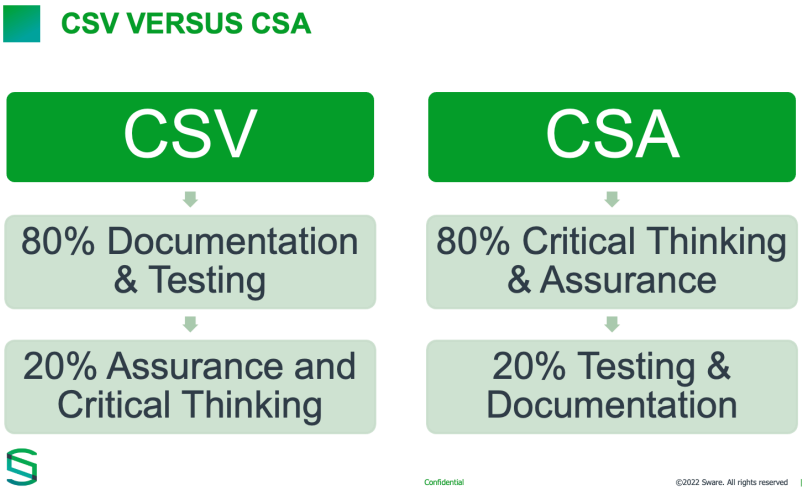


Figure 2: Computer systems validation (CSV) versus computer software assurance (CSA)

Historical factors contribute to making traditional computer systems validation problematic:

- Misunderstanding of the roots of the need to validate**:** The original directive to validate comes from two primary sources, 21 C.F.R. Part 11 (intended to ensure that electronic signatures and records are as robust and reliable as their paper counterparts) and 21 C.F.R. Part 820, the Quality Systems Regulation (in particular, 21 C.F.R. Part 820, Subpart G).[27] Subpart G was initially meant to focus on the underlying processes (such as manufacturing) but was also applied for the purpose of computer systems validation. At the time, the use of computer systems in the life sciences industry was new, and technology was often homegrown due to the lack of off-the-shelf alternatives. IT and QA executives knew they had to test their computer systems, but computer validation could not necessarily be done in the same manner as process validation. This caused confusion around the

Key Features of the September 2022 Draft Guidance

- The draft guidance reflects FDA's current thinking on applying a risk-based strategy, which employs critical thinking to computer systems validation and verification.
- FDA believes that applying critical thinking up front in the assurance (validation) of computer systems used as part of production or the quality system would better focus manufacturers' assurance activities to ensure product quality while helping to fulfill the validation requirements of 21 C.F.R. 820.70(i).
- The CSA framework is designed to help industry meet the requirements of 21 C.F.R. 820, which dictates the need for supplier qualification, validation, and maintenance schedule requirements for medical devices.
- The goal is to make CSA an activity that allows for more comprehensive testing of a system to ensure its fitness for intended use, while decreasing the overall documentation load—saving time, money, labor, and resources.

best ways to test and the extent of testing required to ensure that a computerized system was fit for intended use. The result was a default to a blanket, test-everything approach, laden with screenshots.[28]

- Home-grown, custom-built systems were the norm for life sciences companies in the 1990s, since there were few, if any, commercial options for these specialized systems. Companies often had large software development and CSV departments that built, tested, updated, and retested homegrown systems that resided on local servers—a model that was slow, costly, and difficult to scale. In the 2000s, large-scale development of commercial SaaS systems enabled companies to quickly scale applications and services. Although traditional CSV was a time-consuming barrier that often resulted in technical debt, companies adhered to the CSV approach in the absence of alternatives.

Taking a blanket approach to testing may have been appropriate in the 1990s, when software development was nascent. Since then, there have been major advances in software design and development, as well as in the tools used by software engineers to develop and test systems. The Stage-and-Gate or Waterfall approach commonly used in the late 1990s (Figure 3) aligned well with traditional CSV, but it has not maintained that alignment as technology evolved. The shift to the Agile development methodology, with teams working in sprints and testing iteratively throughout development, meant that systems could be developed and improved with greater speed and efficiency. Traditional CSV cannot keep pace with Agile methodology, posing challenges to regulated companies. ISPE's GAMP 5 was rolled out in 2008 to help bridge this gap and support compliance, and a second edition of GAMP 5 was released in July 2022 to account for advancements in technology.[29] CSA aligns with and expands upon GAMP 5 to provide the life sciences industry with an updated explanation of FDA's thinking around risk-based, iterative, Agile-compatible approach to assuring the quality of computerized systems.

Sidebar: Features of Traditional CSV

The traditional CSV approach:

1) Does not set the level of testing based on risk;

2) Takes a reactive, "audit proofing" approach, as opposed to a proactive, risk-based approach;

3) Generates large, burdensome quantities of paper documents;

4) Is often encumbered by test script errors and large numbers of screenshots; and

5) Involves performing unnecessary activities in an effort to comply with regulations but may not appropriately test the system or its state of validation.

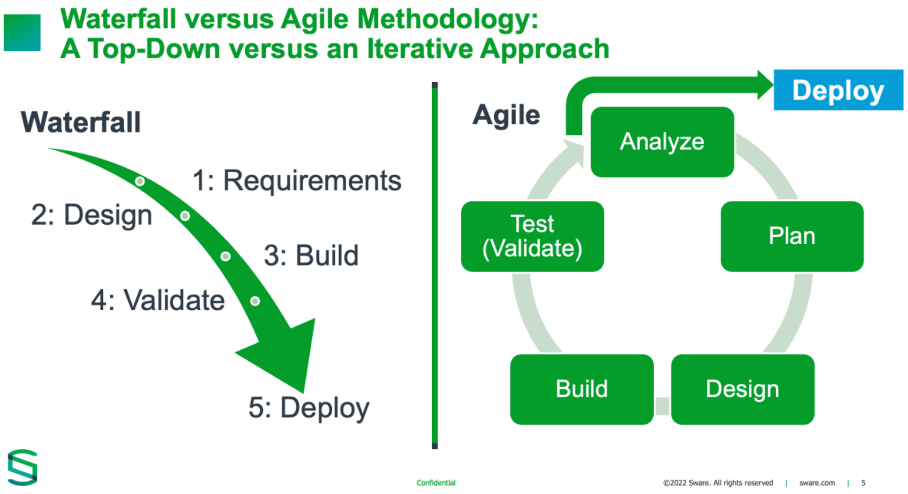


Figure 3: Waterfall versus agile methodology

As technology advanced in the 2000s and cloud computing became the norm, regulations fell behind. While new, cost-effective, scalable applications were available, companies were still using traditional paper-based methods to document and test every feature of every software application being released into production—whether for an initial implementation, upgrade, or change. Compliance with regulations, including 21 C.F.R. Part 820 and 21 C.F.R. Part 11, took priority over the fitness-for-intended use of the software solutions. The reason for this was a perceived concern that if companies departed from the traditional approach, inspectors would find fault with their CSV deliverables, risking poor audit outcomes, Form FDA 483 observations, and/or Warning Letters.[30]

Overcoming Reluctance to Adopt CSA Concepts

The concepts promoted in the CSA draft guidance and similar publications have been slow to gain traction in the medical device industry as well as across other regulated sectors of the life science industry that validate their systems, including pharmaceutical and biotech companies and manufacturers of active pharmaceutical ingredients (APIs). The CSA guidance itself is not a prescriptive document, but rather a reflection of FDA's current thinking on the topic of computer software assurance. As such, the document does not prescribe specific "how-to" approaches for risk assessment, selection, and construction of validation deliverables, nor does it provide a specific measure of how much testing is enough to satisfy an inspection. This has been a stumbling block in gaining acceptance and promoting adoption of the CSA guidance throughout the life sciences industry. Companies may be concerned that using risk-based, less documentation-intensive, more lightweight approaches to validation and verification may result in inspection findings. There is also some confusion around the meaning and applications of critical thinking—not only for the validation testing process itself, but for elements such as vendor qualification (a key to leveraging vendor validation deliverables), assigning appropriate types of testing (especially unscripted and ad hoc testing), and determining the appropriate amount of documentation.

As technology advances and hosted systems (such as SaaS) are increasingly adopted, companies are experiencing challenges in keeping systems in a validated state (also known as "a state of

Demystifying the Application of Critical Thinking to Validation

- The term "critical thinking" has become ubiquitous when discussing CSA, even though the term does not appear in the guidance itself. What is critical thinking, and why is it important? According to Shitamoto and Gurumoorthi (2021), "CSA is the application of critical thinking to validation that adds risk-based documentation to risk-based testing while taking a lifecycle approach, to 'take credit' for activities, and reduce the validation effort."[31] In addition to employing a risk-based approach, critical thinking involves:
- **Identifying appropriate team members early** and involving Quality Assurance early in the project, so the potential impact of the system on patient safety, product quality, and data integrity can be clearly defined.
- **Proactively identifying, assessing, and prioritizing risks early in the project,** and reviewing these risks frequently to ensure proper mitigation.
- **Researching and planning** to fully understand the intended use of the system; determine whether electronic signatures will be used and execute a Part 11 (Electronic Records; Electronic Signatures—Scope and Application) assessment;[32] and ensure that the testing approach is clearly defined based on identified system, design, and regulatory risks. Once created, the validation plan must be documented.
- **Leveraging validation work by the vendor** whenever practicable. If a properly vetted vendor with a high level of maturity has acceptable validation deliverables, then these may be usable to support minimal or no testing of low- and medium-low risk features. For systems with no direct impact on patient safety and product quality, it may be possible to rely entirely on vendor documentation (providing the strategy is explained in the validation plan).
- **Right-sizing validation testing rigor based on identified risk levels** and fully understanding any potential impacts of system failure on patient safety and product quality.

control"). The effort and resources required can be overwhelming—especially considering periodic system upgrades, patches, and interim releases, all of which must be validated prior to being moved into production. Companies that avoid risk-based approaches such as CSA and GAMP 5 run the risk of falling behind and out of compliance.[33]

An approach that considers impact on product safety, product quality, and patient safety will help companies stay abreast of technological change. Knowing which features are most critical, most complex, and highest risk will enable companies to concentrate testing on those features. Software vendors frequently offer customers access to validation documentation, which means that companies can avoid repeating tests already carried out by the vendor. The ability to leverage the validation deliverables of potential software vendors is an important additional factor in determining the risk of a system. Vendors should be vetted to determine the robustness of their quality system, the quality and integrity of their software products, and the strength of their validation documentation. A supplier audit or other form of assessment enables companies to determine whether they will be able to qualify the vendor, and thereby leverage the vendor's systems, services, and/or validation deliverables.

Aligning Validation Testing with Level of Risk

Risk—the amount of potential harm to patient safety, product safety, and/or product quality; the likelihood of such harm; and its detectability—is a key element in CSA. In traditional CSV, the customer subsumed all the risk of validating a purchased system, which meant complete retesting of applications to ensure fitness for the intended use. With the CSA approach, the risk is distributed between the customer and the vendor. Enabling the use of vendor-produced deliverables (via supplier qualification activities executed by the customer) avoids the repetition of testing and facilitates compliance with regulatory requirements under 21 C.F.R. Part 820. Risk-related activities should include impact assessments of the potential for the system to malfunction and the extent to which key processes impacting data integrity, data availability, data security, product quality, product safety, and patient safety would be affected.

A thorough risk-impact assessment should be carried out at the beginning of each project to determine potential risks/hazards surrounding the application, and the criticality of the features or requirements to the business process. Risk reviews should be executed periodically throughout the project to ensure that risks are being appropriately mitigated. Risk assessments should be executed consistently and objectively, using standardized, documented risk impact assessment questionnaires with built-in numeric scales. This approach provides a demonstrable assessment of risk, including quantifiable data to support the assessment. Activities can then be planned to ensure that risks are mitigated appropriately.

Rigor and type of testing required are determined based on the overall risk. As a general rule, scripted testing is used for applications that are complex, have features with direct impact on patients and products, and pose the highest levels of risk. Unscripted and ad-hoc testing are used where risk is lower. CSA provides the flexibility to select the testing methodology that suits the size, complexity, and risk of the application. The testing methodologies chosen should be explained in the validation plan and include the results in the validation test summary report.

There are validation automation platforms on the market that include tools to promote the quantifiable and objective assessment of risks, making it straightforward to assess risk initially and to apply the same approach during consequent risk reviews. These platforms also offer the advantage of automating validation protocol workflows, testing, and even reporting and dashboards. As with GAMP 5 (second edition), the CSA draft guidance indicates that it is acceptable to use such tools as systems of record for validation activities.

Moving Towards Inspection Readiness with CSA

FDA recommends that CSA records "retain sufficient details of the assurance activity to serve as a baseline for improvements or as a reference point if issues occur." Documentation of assurance activities "need not include more evidence than necessary to show that the software feature, function, or operation performs as intended for the risk identified."[34]

Based on examples in the draft guidance, the types of deliverables remain the same but may differ slightly from project to project. The size of the documents will likely be smaller than with traditional CSV activities. Cornerstone documents generally remain for most projects, including:

- The validation plan that explains strategy and thinking
- The risk assessment (and results of any risk reviews)
- Test objectives and results of test protocols (depending on the system, these may include installation, operational, performance, and user acceptance testing)

- Records indicating who performed the testing and when
- A summary report of the testing performed and the results, any software issues found and their resolutions, conclusions reached as a result of the testing, and a statement as to the suitability of the system for use in production

Experts responsible for approvals are likely to remain largely the same; however, they may come into the picture in a different order in CSA compared to CSV. In CSA, the Quality function (such as QA-IT) is involved earlier in the project for critical thinking and planning and remains active during risk reviews throughout the project. By contrast, traditional CSV often left QA out until project end, resulting in significant rework and backtracking due to risks and deficits that could have been caught earlier, had Quality experts been made aware.

FDA encourages the use of automated tools for testing, traceability, and electronic capture of test results, as opposed to a paper-based approach. The agency also recommends the use of electronic records, such as system logs, audit trails, and other data generated by the software, as opposed to paper documentation and screenshots, in establishing the record associated with the assurance activities.

The automation focus is consistent with the approach recommended in the second edition of GAMP 5. Automation provides the advantage of ensuring that records of assurance activities are stored in a single location, as a single source of truth, thus preventing errors or discrepancies in transcribing or copying validation collateral packages. Purpose-built validation automation platforms (VAPs) are available to automate these activities. VAPs also provide signature approval capabilities, enabling companies to use them to record validation deliverables, removing the need to cut, copy, and paste this information into static documents. VAPs also enable control of the information that is given to an inspector. Most VAPs include portals that allow inspectors to see the validation deliverables in the same system where they were created, making it easy to prepare for inspections, and provide inspectors with trust through transparency.

Conclusion

Historically, CSV activities resulted in burdensome documentation that may not have adequately tested a system's fitness for its intended use. The updated CSA approach requires companies to assess risks; to think more up-front and test less but more wisely; to bring Quality and IT compliance into the project earlier; to integrate test automation; to leverage work the vendor has already done to assure the quality of the application; and to "right size" evidence to show that the system is performing as per its intended use in a reliable, consistent manner that preserves data integrity. Device companies should consider combining this line of thinking with validation automation technology to streamline testing and the capture of validation data. Growth in the use of VAPs will provide built-in vehicles for validation workflow management that supports these initiatives and provide a valuable source of inspection readiness. The incorporation of VAPs into the assurance process will prove key in implementing CSA successfully and with confidence.

In sum, FDA would like to see the medical device industry advance its focus on device features, automation, and high-quality manufacturing practices that promote data integrity, product quality, and patient safety. The agency has written the CSA guidance to be flexible enough to permit companies to determine the best approach to advance these initiatives while maintaining software quality. FDA recognizes that traditional approaches to CSV have hindered such advancements. Life sciences companies validating their GxP-facing applications should consider the advantages of a move to CSA, even if they remain cautious—keeping in mind that inspectors may be as unwilling to review thousands of pages of test scripts and screen shots as companies are to generate them. Companies can move confidently to modernize validation knowing that FDA supports adoption of CSA (and its advantages, such as fewer screen shots) and that supportive validation technologies are both available and acceptable.

1. Webinar Transcript, *Computer Software Assurance for Production and Quality System Software—Draft Guidance*, U.S. Food & Drug Admin., Ctr. for Devices & Radiological Health, Oct. 27, 2022, https://www.fda.gov/media/163299/download [hereinafter CDRH Webinar Transcript].
2. *Global Data Healthcare, Medical Device Companies Embrace Cloud Services*, Medical Device Network, June 24, 2021, https://www.medical-device-network.com/comment/medical-device-companies-cloud-services/.
3. *Draft Guidance: Computer Software Assurance for Production and Quality System Software: Draft Guidance for Industry and Food and Drug Administration Staff*, U.S. Food & Drug Admin., Sept. 13, 2022, https://www.fda.gov/media/161521/download [hereinafter FDA, *CSA Draft Guidance*].
4. *Final Guidance: Data Integrity and Compliance With Drug CGMP Questions and Answers: Guidance for Industry*, U.S. Food & Drug

Admin., Dec. 2018, https://www.fda.gov/media/119267/download; Federal Register Notice, Computer Software Assurance for Production and Quality System Software; Draft Guidance for Industry and Food and Drug Administration Staff; Availability, 87 Fed. Reg. 56059, Sept. 13, 2022, https://www.federalregister.gov/documents/2022/09/13/2022-19763/computer-software-assurance-for-production-and-quality-system-software-draft-guidance-for-industry [hereinafter CSA Fed. Reg. Notice].

5. White Paper, *Transitioning from CSV to CSA: Taking a More Risked-Based Approach*, ISPE, Feb. 1, 2023, https://ispe.org/pharmaceutical-engineering/transitioning-csv-csa-taking-more-risked-based-approach.
6. Bryan Ennis, *Moving Beyond Paper-Based Validation: An Industry Transformation*, Sware, 2022, https://8383502.fs1.hubspotusercontent-na1.net/hubfs/8383502/SWR-82-Beyond-Paper-based-Whitepaper.pdf?hsCtaTracking=de9e931d-c4ac-4dd0-9955-24193aca708d%7Cb160babe-1dd8-42af-a50a-a3114f943717.
7. FDA, *CSA Draft Guidance*, *supra* note 3; CSA Fed. Reg. Notice, *supra* note 4.
8. CDRH Webinar Transcript, *supra* note 1.
9. *Id.*
10. Ken Shitamoto & Senthil Gurumoorthi, *Understanding FDA's CSA Guidance in the Context of Current Regulations and GAMP*, America Pharmaceutical Review, March 29 2021, https://www.americanpharmaceuticalreview.com/Featured-Articles/574659-Understanding-FDA-s-CSA-Guidance-in-the-Context-of-Current-Regulations-and-GAMP/.
11. *Id.*
12. *Id.*
13. FDA, *CSA Draft Guidance*, *supra* note 3.
14. CSA Fed. Reg. Notice, *supra* note 4.
15. CDRH Webinar Transcript, *supra* note 1.
16. Shitamoto & Gurumoorthi, *supra* note 10.
17. CDRH Webinar Transcript, *supra* note 1.
18. National Archives Code of Federal Regulations Title 21, chapter I, subchapter H, last amended on Apr. 14, 2023, https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-820 [hereinafter 21 C.F.R. Part 820]; *General Principles of Software Validation: Guidance for Industry and FDA Staff*, U.S. Food & Drug Admin., Jan. 2002, https://www.fda.gov/files/medical%20devices/published/General-Principles-of-Software-Validation---Final-Guidance-for-Industry-and-FDA-Staff.pdf.
19. Federal Register notice Food and Drug Administration 21 C.F.R. Part 11 [Docket No. 92N–0251] RIN 0910–AA29 Electronic Records; Electronic Signatures. Mar. 20, 1997, https://www.govinfo.gov/content/pkg/FR-1997-03-20/pdf/97-6833.pdf.
20. *Worried About Computer Software Assurance? Relax, You're Probably Already Doing It*, FiercePharma sponsored content by ValGenesis, Mar. 7, 2022, https://www.fiercepharma.com/sponsored/worried-about-computer-software-assurance-relax-youre-probably-already-doing-it.
21. *Advanced Manufacturing: FDA News, Events, and Funding Opportunities Related to Advanced Manufacturing*, U.S. Food & Drug Admin., current as of Mar. 31, 2023, https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing.
22. *Case for Quality*, U.S. Food & Drug Admin., 2020, https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/case-quality; Chip Bennett, Hans Heesakkers, Stefan Horneborg, Gilad Langer, Line Lundsberg-Nielsen, Anthony J. Margetts & Fritz Röder, *Industry Perspective: Validation 4.0 - Shifting Paradigms, ISPE Pharmaceutical Engineering*, Nov.–Dec. 2020, https://ispe.org/pharmaceutical-engineering/november-december-2020/industry-perspective-validation-40-shifting; ISPE, GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems (2d Ed., July 2022), https://ispe.org/publications/guidance-documents/gamp-5-guide-2nd-edition; Sion Wyn, Christopher J. Reid, Chris Clark, Michael L . Rutherford, Heather D. Watson, Lorrie L. Vuolo-Schuessler & Anthony D. Perez, *Why ISPE GAMP® Supports the FDA CDRH: Case for Quality Program, ISPE Pharmaceutical Engineering*, Pharmaceutical Engineering, Nov./Dec. 2019, https://ispe.org/pharmaceutical-engineering/why-ispe-gamp-supports-fda-cdrh-case-quality-program.
23. Stephen M. Hahn & Colin Rom, *Accelerating the Adoption of Advanced Manufacturing Technologies to Strengthen Our Public Health Infrastructure*, U.S. Food & Drug Admin., Jan. 15, 2021, https://www.fda.gov/news-events/fda-voices/accelerating-adoption-advanced-manufacturing-technologies-strengthen-our-public-health#:~:text=The%20FDA%20and%20industry%20have,memorandum%20of%20understanding%20(MOU.
24. *Worried About Computer Software Assurance?*, *supra* note 20.
25. Mark Best & Duncan Neuhauser, *Joseph Juran: Overcoming Resistance to Organisational Change*, Quality & Safety Health Care, Nov. 2006 Oct;15(5):380–82. Doi: 10.1136/qshc.2006.020016. PMID: 17074878; PMCID: PMC2565827, https://www.researchgate.net/publication/6721371_Joseph_Juran_Overcoming_resistance_to_organisational_change.
26. Mary Beth Walsh, *Computer Software Assurance (CSA): The FDA's New Approach to CSV*, Kalleid Inc., July 15, 2021, https://kalleid.com/computer-software-assurance-csa-the-fdas-new-approach-to-csv/.
27. *Worried About Computer Software Assurance?*, *supra* note 20.
28. *Computer Systems Assurance: Making the Transition from Computer Systems Validation*, AssurX blog, (undated), https://www.assurx.com/computer-systems-assurance-making-the-transition-from-computer-systems-validation/.
29. Hahn & Rom, *supra* note 23.
30. *FDA Form 483 Frequently Asked Questions*, U.S. Food & Drug Admin., current as of Jan. 9, 2020, https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions; *Warning Letters*, U.S. Food & Drug Admin., current as of Apr. 18, 2023, https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters.
31. 21 C.F.R. Part 820, *supra* note 18.
32. *Advanced Manufacturing*, *supra* note 21.
33. Hahn & Rom, *supra* note 23.
34. FDA, *CSA Draft Guidance*, *supra* note 3.

EAS Consulting Group
A Certified Group Company

The Experts in FDA and USDA Regulatory Matters

✓ Consulting ✓ Auditing ✓ Training ✓ Labeling ✓ Submissions ✓ Registrations
✓ Expert Witness ✓ Product Development ✓ Due Diligences






FOODS • DIETARY SUPPLEMENTS • PHARMACEUTICALS • MEDICAL DEVICES • TOBACCO • COSMETICS

easconsultinggroup.com

Regulating Contrast Agents as Drugs: What's Next for FDA?

*by Yifan Wang**

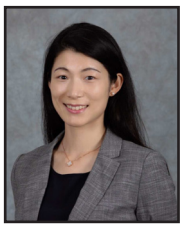
Contrast agents play a crucial role in medical imaging procedures, such as computed tomography (CT) and magnetic resonance imaging (MRI). Contrast agents also include radiopharmaceuticals for disease treatment, especially cancer therapy. The market for contrast media and contrast agents is expected to reach $5.9 billion by 2026.[1] FDA regulation of these products recently attracted congressional attention, spurring a new law passed in December 2022 that requires FDA to regulate all contrast agents as drugs.[2]

The new law ensures regulatory consistency for contrast agents and is Congress's response to the 2021 case *Genus Medical Technologies, LLC v. FDA*. In this case, the U.S. Court of Appeals for the DC Circuit found that the Federal Food, Drug, and Cosmetic Act (FDCA) did not grant FDA discretion to regulate a product as a drug when the product meets the statutory definition of a device under the FDCA.[3] The DC Circuit affirmed the district court's decision vacating FDA's classification of a Genus product as a drug. The agency then announced that it intended to reexamine whether imaging agents used in CT and MRI procedures meet the FDCA's definition of a device.[4]

Under the FDCA, products are classified based on their respective statutory definitions. The FDCA defines "drugs" to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man . . . ."[5] The FDCA defines "devices" to include:

> an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man ... and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.[6]

The DC Circuit noted that the definitions of drugs and devices share a common intended-use clause. However, the FDCA distinguishes devices from drugs by adding both an instrument clause ("an instrument, apparatus, implement,



Yifan Wang earned her JD from University of Maryland Francis King Carey School of Law, and PhD in Chemical and Biochemical Engineering from Rutgers University, New Brunswick. Wang's goal is to embrace the challenges at the intersection between life sciences, law, and policy.

machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory") and a mode-of-action clause ("and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes") to the definition of a device.

Suppose a product is intended for diagnosis, cure, mitigation, treatment, or prevention of disease, yet it does not achieve its primary intended purposes via chemical action on or within the body or via metabolization. In such a case, it should be regulated as a device. However, under the new law, a contrast agent is categorically regulated as a drug, regardless of how the contrast agent achieves the primary intended purpose.

The new law resolves the uncertainty surrounding the regulatory status of contrast agents post-*Genus* decision. FDA has designated the Center for Drug Evaluation and Research to regulate drugs and the Center for Devices and Radiological Health to regulate devices. By classifying all contrast agents as drugs, FDA can achieve administrative efficiency and regulatory consistency. For instance, if some contrast agents were regulated as devices and others as drugs, it could lead to a situation where similar agents are subject to varying safety, efficacy, manufacturing, and post-approval reporting standards. This inconsistent regulation could cause confusion in the industry as manufacturers would need to navigate different regulatory schemes for their products.

Critics of the new law argue that it disregards the scientific fact that contrast agents work through different mechanisms. For instance, some agents merely coat the inside of the esophagus, stomach lining, or intestines and are eliminated from the body intact.[7] Such products are physiologically inert, according to critics, and should be classified as devices. On the other hand, other contrast agents work by detecting body structures or lesions of interest through metabolization.[8] These agents require chemical action in the body to achieve their intended purpose, and therefore, should be classified as drugs. Critics contend that only such contrast agents that require metabolization should be regulated as drugs, while the others should be regulated as devices.

Despite their arguments, critics have failed to consider the risks associated with how contrast agents are delivered into the body as a finished product. For instance, some agents are delivered intravenously via sterile injectables, and any quality defects in these products can lead to serious, life-threatening injuries. Alternatively, when agents are ingested orally as a suspension, microbiological-, potency-, and stability-related manufacturing problems may arise.[9] Moreover, since pediatric and immunocompromised patients often use contrast agents, any quality defects can pose a greater risk to these vulnerable populations. For these reasons, contrast agents should be subject to the same requirements as drugs to maximize patient safety.

Many companies fight jurisdictional battles for their products, since drugs and devices are subject to drastically different regulatory schemes. As a result of these different regulatory schemes, it is more expensive for a sponsor to develop and market a drug than a device. The mean development cost for a novel therapeutic complex medical device is $54 million,[10] while the average development cost of a new prescription drug is almost $2.6 billion.[11] Additionally, the user fee for a new drug application with clinical data is about $3,242,026, while the fee for a device premarket approval is about $441,547.[12]

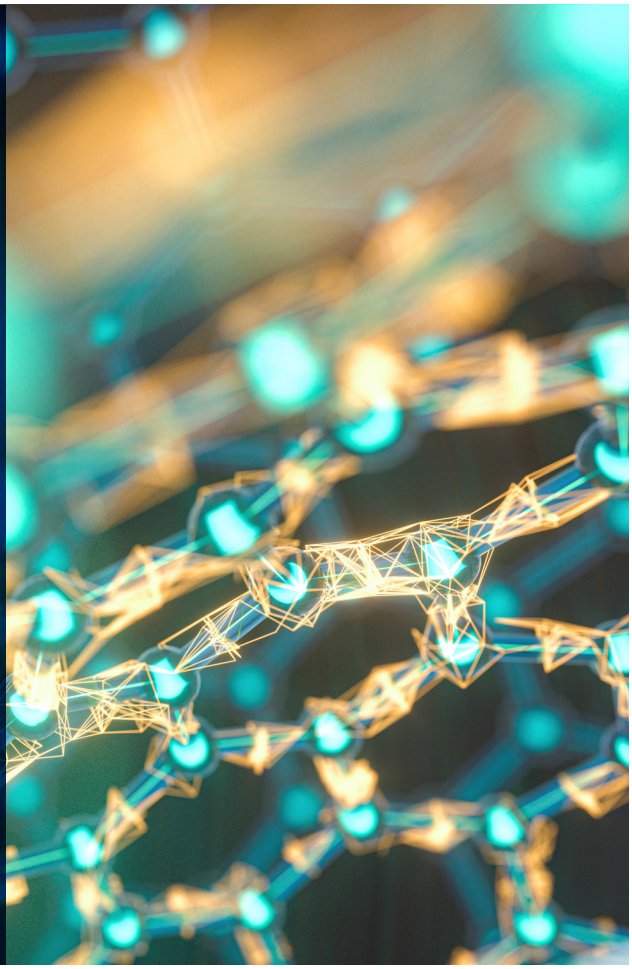
Congress recognizes that the new law will inevitably add a financial burden to companies whose contrast agents were previously regulated as devices but must now be classified as drugs. To ease this burden, the law waives the application fee for such products. FDA should promptly implement the fee waiver policies, especially to support small businesses that currently market contrast agents regulated as devices but now must submit new drug applications due to the law. These fee waiver policies will ensure that small pharmaceutical companies can stay afloat and continue to use their resources for research, development, and innovation to benefit patients.

*The author would like to thank Professor Rena Steinzor for her insightful comments and suggestions.

1. *Contrast Media/Contrast Agent Market*, Imaging Technology News, https://www.itnonline.com/article/contrast-mediacontrast-agent-market (last accessed Mar. 20, 2023).
2. Pub. L. No. 117-328, Consolidated Appropriations Act, 2023, Division FF, § 3621.
3. Genus Med. Techs. LLC v. U.S. Food & Drug Admin., 994 F.3d 631, 639 (D.C. Cir. 2021).
4. Genus Medical Technologies LLC Versus Food and Drug Administration; Request for Information and Comments, 86 Fed. Reg. 43,553 (Aug. 9, 2021).
5. 21 U.S.C. § 321(g)(1)(B).
6. 21 U.S.C. § 321(h)(1).
7. *Barium Sulfate Contrast Medium*, Radiopaedia, https://radiopaedia.org/articles/barium-sulfate-contrast-medium?lang=us (last accessed Mar. 20, 2023).
8. *FDA Approves Iobenguane I 131 for Rare Adrenal Gland Tumors*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/resources-information-approved-drugs/

FDA-APPROVES-IOBENGUANE-I-131-RARE-ADRENAL-GLAND-TUMORS (last accessed Mar. 20, 2023).

9. *Oral Solutions and Suspensions: Guide to Inspections Oral Solutions and Suspensions*, U.S. FOOD & DRUG ADMIN. (Nov. 17, 2014), HTTPS://WWW.FDA.GOV/INSPECTIONS-COMPLIANCE-ENFORCEMENT-AND-CRIMINAL-INVESTIGATIONS/INSPECTION-GUIDES/ORAL-SOLUTIONS-AND-SUSPENSIONS-894 (last accessed Mar. 20, 2023).
10. Aylin Sertkaya, Rebecca DeVries, Amber Jessup & Trinidad Beleche, *Estimated Cost of Developing a Therapeutic Complex Medical Device in the US*, JAMA NETWORK, https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796179 (last accessed Nov. 7 2022).
11. Thomas Sullivan, *A Tough Road: Cost to Develop One New Drug is $2.6 Billion; Approval Rate for Drugs Entering Clinical Development is Less than 12%*, POLICY & MEDICINE, https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html.
12. The fees are for Fiscal Year 2023. *See Medical Device User Fee Amendments (MDUFA)*, U.S. FOOD & DRUG ADMIN., HTTPS://WWW.FDA.GOV/INDUSTRY/FDA-USER-FEE-PROGRAMS/MEDICAL-DEVICE-USER-FEE-AMENDMENTS-MDUFA (last accessed Nov. 7, 2022); *Generic Drug User Fee Amendments,* U.S. FOOD & DRUG ADMIN., https://www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments (last accessed Nov. 7, 2022).



Alternative Proteins: Navigating the Maze of U.S. Federal and State Meat Labeling Requirements

by Xin Tao & Genevieve Razick

The demand for alternative proteins is on the rise in the United States and is estimated to grow from USD 14.2 billion in 2021 to USD 33.75 billion by 2030.[1] Plant-based proteins and cultivated cells are two promising alternatives that are quickly gaining popularity among consumers seeking healthier, sustainable, and ethically conscious food choices.[2] Plant-based proteins are derived from sources such as soy, pea, and rice and are often used as a substitute for animal-based proteins in a variety of foods. Cultivated cells, on the other hand, are cultured from animal cells in bioreactors and provide the same taste and texture of meat without the negative environmental and ethical implications of traditional animal agriculture.

As often is the case with new food technology, the commercialization of these alternative proteins in the United States also raises interesting legal questions. Understanding the legal requirements for labeling alternative proteins is essential for companies to comply with the applicable laws and for consumers to make informed decisions about the products they purchase and consume. Unfortunately, the laws and regulations governing labeling for alternative proteins can be complex and vary across different jurisdictions. In this article, we will explore the labeling requirements that may apply to the two alternative protein sources in more detail, as well as the potential implications for the industry.

Federal Legal Framework for Alternative Proteins Labeling

At the federal level, the U.S. Food and Drug Administration (FDA) has primary jurisdiction over the labeling of most food products, including plant-based protein products, while the U.S. Department of Agriculture (USDA) has jurisdiction over the labeling of meat and poultry products, which include most cultivated meat products. However, there may be some overlap in jurisdiction, particularly when it comes to products that

Xin Tao is the head of Baker McKenzie's U.S. Food and Drug Law Practice. A former research biochemist, Tao's practice focuses on empowering global scientific innovation through legal compliance, including providing regulatory counsel to companies with novel foods and emerging and established companies on launching and promoting innovative products such as plant-based proteins and cell-cultured meat.

Genevieve Razick is an associate in Baker McKenzie's U.S. Food and Drug Law Practice. Razick's practice focuses on advising life sciences companies on a broad range of healthcare and FDA regulatory matters and conducting regulatory due diligence as it relates to the sale, acquisition, and restructuring of FDA-regulated entities.

contain both meat and non-meat ingredients. As such, companies producing alternative proteins must be familiar with the specific labeling requirements set forth by both agencies to ensure compliance with applicable regulations.

The Federal Food, Drug, and Cosmetic Act (FDCA) provides FDA with the legal authority to regulate the labeling of foods. Under section 403(g)(1) of the FDCA, a food is deemed misbranded if "it purports to be or is represented as" a food for which FDA has established a standard of identity but fails to comply with that standard.[3]

If no standard of identity applies, as is the case with the alternative protein products, section 403(i)(1) of the FDCA requires that a food's label bear "the common or usual name" of the food.[4] The common or usual name may be a coined term, but it must "accurately identify or describe, in as simple and direct terms as possible, the basic nature of the food or its characterizing properties or ingredients."[5] A common or usual name "shall be uniform among all identical or similar products and may not be confusingly similar to the name of any other food that is not reasonably encompassed within the same name."[6] Each "class or subclass of food shall be given its own common or usual name that states, in clear terms, what it is in a way that distinguishes it from different foods."[7] Finally, if a common or usual name does not exist for the food, the label may bear "[a]n appropriately descriptive term, or when the nature of the food is obvious, a fanciful name commonly used by the public for such food."[8]

As such, when new foods such as alternative proteins are developed, there is some flexibility for determining the name, which needs to be appropriately descriptive and must be uniform for all identical or similar products, while also different than the names of existing foods.

Under the Federal Meat Inspection Act of 1906[9] and the Poultry Products Inspection Act of 1957 (PPIA),[10] USDA's Food Safety and Inspection Service (FSIS) regulates the labeling of all meat and poultry products under its jurisdiction, including cattle, sheep, swine, goats, horses, mules, siluriformes (catfish), equines, domesticated chickens, turkeys, ducks, geese, ratites, and squabs to ensure such products are not misbranded.[11] Under these laws, a meat or poultry product is misbranded under the following circumstances: 1) its labeling is false or misleading in any particular;[12] 2) it is offered for sale under the name of another food;[13] 3) it is an imitation of another food, but not labeled as such;[14] or 4) it purports to be or is represented as a food for which a standard of identity (i.e., specific names, terms, and information to be used on a product label) has been prescribed, but it fails to conform to the standard.[15] FSIS reviews and approves meat and poultry product labels and labels that display special statements or claims, such as those not defined by regulation, before they are used in commercial distribution.[16] Cultivated meat products that fall under FSIS jurisdiction will be subject to premarket review and approval under the same process as other special statements or claims, meaning that establishments must provide documentation and data to support the special statements and claims for the label to be approved.[17]

Although both FDA and USDA agreed to develop joint principles for product labeling to ensure cultivated cell products are labeled consistently, neither FDA nor USDA has published rules or guidance specifically related to labeling cell-cultured meat products.[18] Both agencies have, however, sought public comment on the topic.[19] For example, FSIS published an advance notice of proposed rulemaking (ANPR) on September 3, 2021 to solicit public feedback on how meat and poultry products produced using animal cell culture technology should be identified and described. The proposed rulemaking references a petition filed by the United States Cattlemen's Association on February 9, 2018 requesting that FSIS limit the definition of "meat" to tissue or flesh of animals that have been harvested in the traditional manner, thereby prohibiting foods comprised of or containing cultured animal cells from being labeled "meat."[20] FSIS has not yet issued a proposed rule on this issue.

State Legal Framework for Alternative Proteins Labeling

A number of states have enacted legislation related to alternative proteins.[21] Generally, these laws prohibit the uses of certain terms associated with the traditional meat products (e.g., "meat") on alternative protein product packaging or labeling.[22] For example, Missouri, the first state to pass a law restricting the labeling of plant-based products as meat in 2018, prohibits the representation of a product as "meat" when the product is not derived from harvested production livestock or poultry.[23] The Missouri Department of Agriculture also issued guidelines to provide standards for the inclusion of certain qualifying language on food packaging (e.g., qualifying language such as "plant-based" to make clear the alternative source of the product).[24] In accordance with the guidelines, products must include a prominent statement on the front of the package, immediately before or immediately after the product name, to indicate that

the product is "plant-based," "veggie," "lab-grown," "lab-created," or to include a comparable qualifier.[25] There must also be a prominent statement on the package that the product is "made from plants," "grown in a lab," or a comparable disclosure.[26] If products contain these statements, they are generally not considered to be misrepresented as meat products in violation of Missouri law.[27]

In addition to Missouri, to our knowledge, there are another 13 states that have adopted similar laws that are currently effective. We have provided below a summary of these state labeling laws with the applicable definitions of "meat" and "meat product" when available.

State	Statutes	Effective Date	Definition of Meat / Meat Product
Alabama	Code of Ala. §§ 2-17-10; 2-17-1	August 1, 2019	"Meat food product" means any product capable of use as human food which is made wholly or in part from any meat or other portion of the carcass of any cattle, sheep, swine, goats or poultry, excepting products which contain meat or other portions of such carcasses only in a relatively small proportion or historically have not been considered by consumers as products of the meat food industry and which are exempted from definition as a meat food product by the commissioner under such conditions as he may prescribe to assure that the meat or other portions of such carcasses contained in such product are not adulterated and that such products are not represented as meat food products. Such term as applied to food products of equines shall have a meaning comparable to that provided in this subdivision with respect to cattle, sheep, swine, goats and poultry.
Arkansas	Ark. Code Ann. § 2-1-301 et. seq.	July 24, 2019	"Meat" means a portion of a livestock, poultry, or cervid carcass that is edible by humans. "Meat" does not include a: (i) synthetic product derived from a plant, insect, or other source; or (ii) product grown in a laboratory from animal cells. "Meat product" means an agricultural product that is edible by humans and made wholly or in part from meat or another portion of a livestock, poultry, or cervid carcass.
Georgia	O.C.G.A. § 26-2-152	December 31, 2020	It shall be unlawful for any person, partnership, firm, company, or corporation to label, advertise, or otherwise represent any food produced or sold in this state as meat or any product from an animal unless each product is clearly labeled by displaying the following terms prominently and conspicuously on the front of the package, labeling cell cultured products with "lab-grown," "Lab-created," or "grown in a lab" and plant based products as "vegetarian," "veggie," "vegan," "plant based," or other similar term indicating that the product is plant based and does not include the flesh, offal, or other by-product of any part of the carcass of a live animal that has been slaughtered.
Kansas	Kan. Stat. Ann. §§ 65-656, 65-665	July 1, 2022	"Meat" means the same as provided in 9 C.F.R. § 301.2, as in effect on January 1, 2022. "Meat food product" means the same as provided in 9 C.F.R. § 301.2, as in effect on January 1, 2022.
Kentucky	Ky. Rev. Stat. § 217.035	June 27, 2019	A food shall be deemed to be misbranded: … If it purports to be or is represented as meat or a meat product and it contains any cultured animal tissue produced from in vitro animal cell cultures outside of the organism from which it is derived.
Louisiana	1. La. Rev. Stat. tit. 3, § 4743	October 1, 2020	"Meat" means a portion of a beef, pork, poultry, alligator, farm-raised deer, turtle, domestic rabbit, crawfish, or shrimp carcass that is edible by humans but does not include a: (a) synthetic product derived from a plant, insect, or other source. (b) cell cultured food product grown in a laboratory from animal cells. "Meat product" means a type of agricultural product that is edible by humans and made wholly or in part from meat or another portion of a beef, pork, poultry, alligator, farm-raised deer, turtle, domestic rabbit, crawfish, or shrimp carcass.
Mississippi	Miss. Code Ann. § 75-35-15	July 1, 2019	A food product that contains cultured animal tissue produced from animal cell cultures outside of the organism from which it is derived shall not be labeled as meat or a meat food product. A plant-based or insect-based food product shall not be labeled as meat or a meat food product.

State	Statutes	Effective Date	Definition of Meat / Meat Product
Missouri	Mo. Rev. Stat. § 265.494	August 28, 2018	"Meat" means any edible portion of livestock, poultry, or captive cervid carcass or part thereof.
Montana	Mont. Code Ann. §§ 50-31-103; 50-31-203; 50-31-208; 81-9-217	October 1, 2019	"Meat" means the edible flesh of livestock or poultry and includes livestock and poultry products. This term does not include cell-cultured edible products as defined in this section.
North Dakota	N.D. Cent. Code §§ 4.1-31-01; 4.1-31-05.1; 19-02.1	August 1, 2019	"Meat" means the edible flesh of an animal born and harvested for the purpose of human consumption. "Meat food product" means a product usable as human food which contains any part of a carcass from an animal born and harvested for the purpose of human consumption. The term does not include any product that contains any part of an animal carcass in a relatively small proportion or which historically has not been considered by consumers as a product of the meat food industry, and which is not represented as a meat food product.
Oklahoma	Okla. Stat. tit. 2, § 5-107	November 1, 2020	"Meat" means any edible portion of livestock or part thereof.
South Carolina	2. S.C. Code Ann. § 47-17-510 3.	May 16, 2019	Article 1 of the same title provides the following definitions: The term "meat" means the edible part of the muscle of cattle, sheep, swine or goats which is skeletal or which is found in the tongue, in the diaphragm, in the heart, or in the esophagus, with or without the accompanying and overlying fat, and the portions of bone, skin, sinew, nerve, and blood vessels which normally accompany the muscle tissue and which are not separated from it in the process of dressing. It does not include the muscle found in the lips, snout and ears. The term "meat food product" means any article of food, or any article intended for or capable of use as human food, which is derived or prepared, in whole or in part, from any portion of any livestock, unless exempted by the Director upon his determination that the article (1) contains only a minimal amount of meat and is not represented as a meat food product or (2) is for medicinal purposes and is advertised only to the medical profession.
South Dakota	S.D. Codified Laws §§ 39-4-26; 39-5-6	July 1, 2019	"Meat," the edible part of the muscle of cattle, bison, sheep, swine, goats, equine, ratites, captive cervidae, and other species as requested by the owner and authorized by the secretary, which is skeletal or which is found in the tongue, in the diaphragm, in the heart, or in the esophagus, with or without the accompanying and overlying fat, and the portions of bone, skin, sinew, nerve, and blood vessels which normally accompany the muscle tissue and which are not separated from it in the process of dressing. It does not include the muscle found in the lips, snout or ears. "Meat by-product," any edible part other than meat which has been derived from one or more cattle, bison, sheep, swine, goats, equine, ratites, captive cervidae, and other species as requested by the owner and authorized by the secretary.
Wyoming	Wyo. Stat. §§ 35-7-111; 35-7-119	July 1, 2020	"Meat" means the edible part of the muscle of animals, which is skeletal or which is found in the tongue, in the diaphragm, in the heart or in the esophagus, with or without the accompanying or overlying fat, and the portions of bone, skin, sinew, nerve and blood vessels which normally accompany the muscle tissue and which are not separated from it in the process of dressing, but shall not include the muscle found in the lips, snout or ears, nor any edible part of the muscle which has been manufactured, cured, smoked, cooked or processed.

State Labeling Law First Amendment Challenges

These state laws generally prohibit the use of the term "meat" unless the meat products are harvested from an animal carcass during the traditional meat processing. While avoiding consumer confusion is often listed as the intent of these state laws, the labeling restrictions on the alternative protein products have been subject to multiple legal challenges in the federal court system as violations of the First Amendment under the U.S. Constitution.[28] The First Amendment restricts federal and state governments from depriving citizens of their freedom of speech, and several challengers have alleged that these state laws and their "censorship" requirements restrict the freedom of speech. Many of these legal challenges are still pending and could significantly impact and potentially clarify the requirements for accurately labeling a cell-cultured or plant-based meat product.

For example, in *Turtle Island Foods, SCP et al. v. Richardson*, Turtle Island Foods dba Torfurky Company and the Good Food Institute brought a case in the U.S. District Court for the Western District of Missouri challenging the constitutionality of the Missouri labeling law.[29] The plaintiffs argued that because the Missouri law restricted them from using references to meat products, the law deprived them of their First Amendment right to free speech.[30] The relief sought by the plaintiffs was a preliminary injunction to prevent the state of Missouri from enforcing the Missouri labeling law and its labeling restrictions.[31] The district court denied preliminary injunction, finding that the plaintiffs had not met the required legal threshold to prove a substantial likelihood of success on the merits related to the First Amendment challenge.[32] The district court determined that the law only prohibited misleading speech (i.e., misleading consumers into believing that a product is meat from livestock when it is in fact plant-based or lab-grown), and was not so broad as to prohibit the commercial speech that the plaintiffs used on the products at issue.[33] Plaintiffs appealed denial of the preliminary injunction to the Eighth Circuit Court of Appeals. On March 29, 2021, the Eighth Circuit Court of Appeals affirmed the decision, finding that the district court acted within its discretion in reading the statute as not prohibiting the commercial speech at issue, and that there was no reason to "disturb the district court's ruling as to Plaintiffs' likelihood of success on the merits."[34]

In another case, *Turtle Island Foods SPC v. Soman*, the same company, Tofurky Company (joined by the Good Food Institute, the Animal Legal Defense Fund, and the American Civil Liberties Union) challenged the Arkansas "Truth in Labeling of Agricultural Products that are Edible by Humans Act,"[35] prohibiting purveyors of plant- or cell-based meats from using the word "meat" and related terms (e.g., "sausage") to describe a product that is a plant-based meat alternative in the District Court for the Eastern District of Arkansas.[36] The plaintiffs sought to temporarily enjoin the State of Arkansas from enforcing the law on First Amendment and commercial speech challenges.[37] The U.S. District Court entered a judgment in favor of the plaintiffs and enjoined the defendant from enforcing certain provisions of the law regarding misbranding or misrepresenting an agricultural product as applied to Tofurky.

Implications for Alternative Protein Industry

As plant-based protein products continue to gain momentum in the marketplace, and we approach commercialization of cultivated cells, the U.S. legal framework for their labeling continues to evolve at both the federal and state levels. In light of the lack of clarity from FDA and USDA on the labeling of the cultivated cells, as well as state laws restricting the use of terms such as "meat" for alternative protein products, the alternative protein industry must actively seek to understand and comply with the applicable federal and state requirements.

For cultivated meat products, in particular, we recommend the industry seek guidance from USDA to obtain clarity on the following, when USDA eventually issues its proposed rule on labeling: 1) If new terms should be created to distinguish from traditional meat products, should the industry use "cell cultured," "cell cultivated," "cell-based," or some other terms? 2) If a cultivated meat product is used as an ingredient in other food applications, how should it be declared on the label?

Monitoring state labeling law First Amendment challenges is also crucial for the alternative protein industry. While federal regulations provide a baseline for food labeling requirements, states can also enact their own regulations that go beyond the federal standards. These state labeling laws can create a patchwork of requirements that are difficult for companies to navigate and can increase costs for compliance. Notably, state regulations can face legal challenges, particularly under the First Amendment's protection of commercial speech. In recent years, several states have faced legal challenges to their labeling regulations by the

alternative protein industry. As such, it is important for companies in the industry to stay informed about these challenges and to work with industry organizations, legal experts, and of course federal and state regulatory agencies to ensure that their labeling practices are in compliance with applicable requirements.

1. *See* The Brainy Insights, *Alternative Protein Market to Garner $33.75 Billion By 2030, at 10.1% CAGR, Says The Brainy Insights*, PR Newswire (Aug. 29, 2022, 12:10 PM), https://www.prnewswire.com/news-releases/alternative-protein-market-to-garner-33-75-billion-by-2030--at-10-1-cagr-says-the-brainy-insights-301613783.html.
2. While as of today, there are no commercial cultivated cells in the United States, two cultivated meat companies have received FDA's letter of no-objection and are waiting for USDA to review the process.
3. 21 U.S.C. § 343(g)(1).
4. 21 U.S.C. § 343(i)(1).
5. 21 C.F.R. § 102.5(a).
6. *Id.*
7. *Id.*
8. 21 C.F.R. § 101.3(b)(3).
9. 21 U.S.C. § 601 *et seq.*
10. 21 U.S.C. § 451 *et seq.*
11. 21 U.S.C. § 607(d); 21 U.S.C. § 457(c).
12. 21 U.S.C. § 601(n)(1); 21 U.S.C. § 453(h)(1).
13. 21 U.S.C. § 601(n)(2); 21 U.S.C. § 453(h)(2).
14. 21 U.S.C. § 601(n)(3); 21 U.S.C. § 453 (h)(3).
15. 21 U.S.C. § 601(n)(7); 21 U.S.C. § 453(h)(7).
16. 21 U.S.C. § 607(d); 21 U.S.C. § 457(c).
17. FSIS, Labeling of Meat or Poultry Products Comprised of or Containing Cultured Animal Cells, 86 Fed. Reg. 49491, 49493 (proposed Sept. 3, 2021).
18. *Id.* at 49494.
19. Labeling of Foods Comprised of or Containing Cultured Seafood Cells; Request for Information, 85 Fed. Reg. 63277 (Oct. 7, 2020); FSIS, Labeling of Meat or Poultry Products Comprised of or Containing Cultured Animal Cells, 86 Fed. Reg. 49491 (proposed Sept. 3, 2021).
20. FSIS, Labeling of Meat or Poultry Products Comprised of or Containing Cultured Animal Cells, 86 Fed. Reg. 49491, 49494 (proposed Sep. 3, 2021).
21. *See e.g.*, Ky. Rev. Stat. § 217.035; Miss. Code Ann. § 75-35-15.
22. *See e.g.*, Okla. Stat. tit. 2, § 5-107(C)(1).
23. Mo. Rev. Stat. **§ 265.494(7).**
24. Department of Agriculture State of Missouri, *Missouri's Meat Advertising Law*, Aug. 30, 2018.
25. *Id.* at 2.
26. *Id.*
27. *Id.*
28. *See, e.g.*, Turtle Island Foods, SCP v. Richardson, 425 F. Supp. 3d 1131 (W.D. Mo. 2019), *aff'd*, 992 F.3d. 694 (8th Cir. 2021).
29. *Id.* at 1134–35.
30. *Id.*
31. *Id.*
32. *Id.* at 1140.
33. *Id.*
34. Turtle Island Foods, SCP v. Richardson, 992 F.3d. 694, 704 (8th Cir. 2021).
35. Ark. Code. Ann. § 2-1-305.
36. Turtle Island Foods, SPC v. Soman, 424 F. Supp. 3d 552, 561 (E.D. Ark. 2022).

VALIDANT

Unrivaled **experience**

Skilled **execution**

Demonstrated **results**

As the leading Quality, Compliance and Regulatory consulting firm, we partner with healthcare companies to ensure safe and reliable access to the world's life-saving healthcare products. Our track record of success has earned us the trust of 20 of the top 30 Global Pharmaceutical firms, 25 of the top 30 Medical Device firms, and 7 of the top 10 Biotechnology firms in the world.

Contact us

1.844.VALIDANT

info@validant.com

www.validant.com

Food and Beverage Container Labeling and Allergen Management: Protecting Consumer Health

by George Nelson

The food and drinks that people consume can have a huge effect on their health, which is why it's so important for people to be informed and aware of the contents of their favorite foods and beverages.

That's where labeling comes in. Food and beverage container labels provide essential information for consumers to read and learn, and in this guide, we'll take a look at why beverage container labels, in particular, are so significant.

Importance of Beverage Container Labeling for Consumer Health

When it comes to beverages, people have more choice than ever before—from sodas and fruit juices to bottled mineral water and alcoholic drinks. The nutritional value and health benefits or risks of these drinks can vary wildly, and labels give us the information we need to make the right choices.

Without beverage container labels, consumers wouldn't be able to quickly pick up a beverage and find out exactly how much sugar, sodium, carbohydrates, and other ingredients it contains. This lack of information could lead to people consuming drinks that may be bad for their health, without even being aware of it.

George Nelson is a sustainability consultant at Polyfuze and is passionate about life-changing innovation, and industrial and manufacturing technologies. Nelson loves discovering and sharing new technologies that shape the sustainability agenda.

Beverage Container Labeling

Beverage container labeling can take many forms, from simple sticky or adhesive labels applied to the outside of bottles to more **permanent labels** that are fused directly onto cans and other containers.

These labels must follow certain strict guidelines, as established by the **Food and Drug Administration (FDA)** in the United States and other authorities in different countries. It's important for beverage container labels to be informative, clear, easy-to-read, and properly placed on each container for maximum visibility.

Nutritional Labeling Requirements

As part of FDA's labeling requirements, all beverage container labels **need to provide** clear information about the nutritional contents of each drink. This is done in order to provide consumers with a clear and complete picture of how much nutritional value they can expect to gain from every bottle, can, or other container.

Required Nutrients

The label of any drink should always **list** the following:

- Total fat
- Saturated fat
- Trans fat

- Cholesterol
- Sodium
- Total carbohydrates
- Dietary fiber
- Sugars
- Added sugars
- Protein
- Vitamins
- Minerals

Even if the beverage contains none of these elements, they still need to be marked on the label and listed as "0 grams" if not present.

Daily Values

On their own, individual amounts for fat, sugar, and sodium may be hard for the average consumer to fully understand, which is why Daily Values are also included on beverage labels. **Daily Values** show what percentage of each nutritional element is contained in each serving or bottle as a proportion of the total recommended intake for an average person.

For example, on the label of a bottle of Coca-Cola, we can see that each serving contains 65g of added sugars, which is 130% of a person's daily recommended allowance. This information can be very useful for consumers who might be following a dietary plan or simply want to know exactly what level of sodium, sugar, or other elements they're consuming in each drink.

Ingredient Labeling Requirements

As well as providing information about fat content, carbohydrates, and so on, beverage labels also need to list the ingredients used to make each beverage.

Listing of All Ingredients

The **ingredients list should contain** every single ingredient that can be found in the beverage. For some beverages, like bottled water, the list will be very short, but for certain sodas and other processed drinks, there can be quite a long list of additives, acids, flavorings, and so on.

Allergen Labeling Requirements

Mayo Clinic reports that around 8% of young children and up to 4% of adults suffer from food and drink allergies, and there are many different ingredients that can trigger allergic reactions in people. For this reason, companies are also instructed to list all potential allergens on labels.

This can be life-saving information, and it's useful in many situations. In bars or restaurants, for example, staff can consult allergen labels when preparing their menus and managing **bar equipment** to ensure that their customers can be made aware of any possible allergy risks.

Regulatory Compliance

Any business that is involved with the preparation, sale, or manufacture of drinks needs to ensure that they adhere to all relevant regulations regarding the labeling of these products.

FDA Requirements for Beverage Labeling

In the United States, it's FDA that is responsible for outlining the required beverage label guidelines. FDA rules state that all labels should be clear, easy-to-read, properly placed, and contain all necessary pieces of information, such as allergens, ingredient lists, and Daily Values.

Food Safety Modernization Act (FSMA) and Beverage Labeling

Along with clear nutritional labels to inform people about the contents of the food and drinks they consume, the **Food Safety Modernization Act (FSMA)** was also enacted to increase food and drink standards across the United States and minimize the risk of foodborne diseases spreading among the population.

The FSMA was introduced by President Barack Obama in early 2011 and provides FDA with additional powers to control the way in which foods are grown and processed. Through the Act, FDA has the power to issue mandatory recalls of certain foods or drinks, if necessary, as well as having stricter checks for food and drinks from foreign suppliers and more sanitary transportation of food and drinks.

Along with all the various new FDA powers associated with the FMSA, this Act also imposes stricter requirements for food and drink packaging and labels. For example, the FSMA means that all labels need to be completely thorough when listing ingredients and possible allergens, and any mislabeling could lead to recalls.

Industries Affected by Beverage Container Labeling Requirements

As we can see, the rules regarding beverage labels have only grown stricter over the years and are still subject to more potential changes in the future, which is why it's crucial for those operating in relevant industries to find a reliable and trusted labeling partner to ensure compliance with all labeling regulations.

Many different industries and businesses can be affected by these labeling requirements, from bottled water and fruit juice businesses to those in the world of alcohol.

Bars and hospitality workers also need to be aware of the changes and ready to respond if labels are not sufficiently clear or lack certain key pieces of information.

2022 Year in Review—Top 10 Food and Agribusiness Regulatory and Legal Issues in Canada

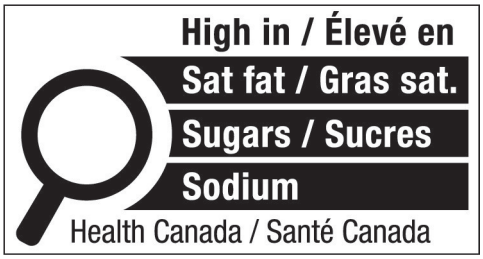
by Eileen McMahon, Yolande Dufresne, Melanie Sharman Rowand & Jacquelyn Smalley

2022 brought many changes to Canada's food and agribusiness regulatory space, and 2023 is shaping up to be another eventful year. Below is our list of the top 10 food and agribusiness regulatory and legal issues in Canada from 2022 and the first quarter of 2023.

Labeling Changes Ahead for Prepackaged Foods High in Saturated Fat, Sugars, and Sodium

After years of consultations and research activities by Health Canada, the Canadian government amended the *Food and Drug Regulations* (FDR) in July 2022 to introduce new front-of-package (FOP) nutrition labeling requirements to help Canadians identify products that are high in certain nutrients of public health concern, namely saturated fat, sugars, and sodium (FOP Labeling Changes).[1] As a result, Canada has become one of only a small group of countries with a mandatory FOP labeling regime for foods high in nutrients of concern. Notably, there is currently no equivalent requirement in the United States at the time of writing.[2]

The FOP Labeling Changes require that an FOP nutrition symbol (an example of which is shown below) be displayed on prepackaged foods, including beverage products, that contain saturated fat, sugars, and/or sodium at levels that meet or exceed a specific threshold. For most prepackaged foods, this threshold is 15% of the designated daily value for the nutrient; however, certain categories of foods have a higher or lower prescribed threshold. The FDR amendments outline specific requirements regarding where an FOP nutrition symbol must appear on packaging, as well as the format, size, visibility, language, and orientation of the symbol.



Certain categories of prepackaged foods have been exempted from the requirement to display the FOP nutrition symbol for technical, nutritional/health-related, or practical reasons (e.g., sugar, honey, maple syrup, salt, and butter are exempted because displaying an FOP nutrition symbol would be redundant on such products). Other products, including those meant to fulfill the nutritional needs of vulnerable groups (e.g., infants or persons requiring oral or tube feeding due to an injury or medical condition), are prohibited from displaying an FOP nutrition symbol. The FOP Labeling Changes also introduce restrictions on the use of certain nutrient-content and health-related claims when the label of a prepackaged food product contains an FOP nutrition symbol because such claims could be misleading.

In accordance with the joint food labeling coordination policy from Health Canada and the Canadian Food Inspection Agency (CFIA),[3] all prepackaged food products are expected to be compliant with the new requirements as of January 1, 2026. However, products imported into or manufactured in Canada or packaged at retail before January 1, 2026 that are not compliant with the new requirements can continue to be sold after this date.[4]

Companies in the food and beverage industry should review the new FOP labeling requirements closely and plan to make packaging, product, and operational changes. For example, some companies may consider reformulating products to reduce the amount of saturated fat, sugars, or sodium below the designated FOP thresholds when relabeling for FOP nutrition symbols may not be feasible.

Gene-edited Plants Get Lighter Regulatory Touch in New Health Canada Guidance for Novel Foods

Health Canada has signaled a favorable regulatory environment for foods derived from gene-edited plants in new guidance on novel foods.[5] Pursuant to Canadian law, foods that meet the definition of a "novel food" require pre-market notification and assessment by Health Canada. New guidance was developed by Health Canada to clarify the interpretation of the definition of a "novel food" under Canada's *Novel Food Regulations*[6] and to address gaps in the guidelines regarding newer technologies, such as gene editing. Although the new guidance does not have the force of law, it does indicate how Health Canada interprets and applies the definition of "novel food" under the *Novel Food Regulations*.

According to the new guidance, foods derived from genetically modified plants (including gene-edited plants)[7] do not meet the definition of a "novel food" and will not require a pre-market notification and assessment unless the genetic modification results in the presence of foreign DNA in the final plant product or alters specified characteristics in the final plant product—such as the introduction of a known allergen or toxin, changes to key nutritional composition, or changes in the food use of the plant. Of specific importance for gene-edited plants, DNA encoding machinery (e.g., CRISPR Cas protein and associated guide RNAs) is considered to be foreign DNA but will only trigger the *Novel Food Regulations* if such DNA is not bred out of the final product. As a result, it is expected that many foods derived from gene-edited plants will not require pre-market notification and assessment under the novel food regime. Since the introduction of the new guidance in July 2022, at least two gene-edited plants have been identified as "non-novel products of plant breeding for food use,"[8] which means that they do not meet the definition of a "novel food" and do not require pre-market notification and assessment. According to the new guidance, an expedited review process is available for pre-market assessment of novel foods derived from genetically modified plants that have been transformed with the same DNA sequence as a previously assessed genetically modified plant (referred to as "retransformants").

While the new guidance is limited to foods derived from plants, Health Canada has signaled an intent to develop similar guidance for novel foods derived from genetically modified animals and microorganisms.[9]

Health Canada has also published a notice of intent to propose amendments to the *Novel Food Regulations* that are consistent with the interpretation of a "novel food" provided in the new guidance.[10] There is currently no projected timing for the proposed amendments; however, there will be an opportunity for stakeholders to comment once the proposed amendments are published. In the meantime, the new guidance signals that Health Canada is taking a lighter regulatory approach to foods derived from gene-edited plants.[11]

End of Transition Period for Amended *Fertilizers Regulations*

Fertilizers and supplements that are manufactured, imported, and/or sold in Canada are regulated under the *Fertilizers Act* and *Fertilizers Regulations* by the CFIA. The *Fertilizers Regulations* were significantly amended in the fall of 2020 as part of an effort to modernize the regulation of fertilizers.[12] Among the amendments were changes made to the exemptions from registration of certain fertilizer products to better align pre-market regulatory oversight with the risk profile of the products. More specifically, pursuant to the amendments, certain low-risk fertilizers and supplements are subject to reduced regulatory scrutiny under the revised regulations, while products with higher or unknown risks are subject to registration under the revised regulations (even if previously exempted under the former regulations).

To provide regulated parties with time to exhaust their existing inventory and seek registration where necessary, the amendments contain transitional provisions to allow regulated parties to comply with either the revised regulations or the former regulations for a period of three years—i.e., until October 26, 2023.

During this transitional period, manufacturers can choose to comply with the revised regulations or the former regulations but cannot combine provisions from the revised and former regulations.[13]

With the deadline to comply with the amended *Fertilizers Regulations* fast approaching, regulated parties should now be completing their transition steps.

Competition Bureau Tackles "Greenwashing"

In early 2022, Canada's Competition Bureau published a news release advising Canadian consumers that a growing demand for "green" products and services has led to an increase in false, misleading, or unsupported environmental claims, also known as "greenwashing."[14] This is a topic of interest for food and agribusiness companies, where environmental concerns are at the forefront of many consumers' minds and where marketing campaigns increasingly seek to make environmental claims. This news release came on the heels of a large settlement between the Competition Bureau and a manufacturer of single-use coffee pods after the Competition Bureau concluded the company's claims regarding the recyclability of, and the steps involved to recycle, its single-use coffee pods were false and misleading.[15] As part of the settlement, the manufacturer agreed to, among other things, pay a $3 million penalty, change its product packaging, and broadly publish corrective notices.

While greenwashing has been on the Competition Bureau's radar for several years, 2022's coffee pod settlement provides an important reminder of the hefty consequences of greenwashing for businesses using, or intending to use, ads, slogans, logos, and packaging that highlight, in a misleading manner, the environmental attributes or benefits of products sold in Canada. The Competition Bureau advises that vague claims, such as "eco-friendly" and "safe for the environment," should be avoided as they can have multiple interpretations and lead to misunderstanding and deception. Rather, claims must be specific and precise about the environmental benefits of a product and must be substantiated and verifiable, among other requirements.

Health Canada Formalizes Approach to "Treated Articles" under the *Pest Control Products Act (PCPA)*

Amendments to Canada's *Pest Control Products Regulations* (PCPR) were published on December 7, 2022,[16] which codify the regulation of "treated articles" by Health Canada's Pest Management Regulatory Agency (PMRA). These specific amendments will come into effect on June 7, 2023, and while food products are exempt, many agribusiness products could be affected.

Specifically, the amended regulations define "treated articles" as a class of regulated products that comprise 1) any non-food inanimate product or substance, 2) treated with a pest control product during manufacturing by (a) incorporating the pest control product into the article, or (b) applying the pest control product to the article, and whereby 3) the product's primary purpose before the treatment was not pest control (i.e., the product alone was not a pest control product).

Eileen McMahon is partner at Torys LLP and Chair of the firm's Food and Drug Regulatory and Intellectual Property Practices. McMahon represents companies on regulatory clearance and intellectual property protection of products across sectors, including the food, agribusiness, life sciences (pharmaceuticals, medical devices, natural health products), and consumer products sectors.

Yolande Dufresne is counsel at Torys LLP. Dufresne's practice focuses on the areas of intellectual property and food and drug regulatory law and advises clients in the food, agribusiness, pharmaceutical, biotechnology, and medical device industries.

Melanie Sharman Rowand is a senior lawyer in the Food and Drug Regulatory and IP Practice Groups at Torys LLP and a scientist with deep food regulatory expertise. Sharman Rowand's practice focuses on food and drug regulatory and intellectual property law, with a special focus on the food and agribusiness, pharmaceutical, and biotechnology sectors.

Jacquelyn Smalley is an associate at Torys LLP with experience advising clients in the food, agribusiness, pharmaceutical, and medical device industries on regulatory, trademark, marketing, and advertising matters.

Once these amendments become law, non-food products that are treated with a pest control product will be subject to regulation and registration under the PCPR as a "treated article," unless otherwise exempted. Manufacturers and importers should therefore review product lines in light of these pending changes, because "treated articles" extend beyond the types of products typically thought of as pest control products such as pesticides for farming or insect repellents. Rather, "treated articles" may include non-food products that have had antimicrobial agents applied to them during the manufacturing process.

There are a number of exemptions under the legislation that exempt products entirely from the PCPA framework or that exempt products from registration with the PMRA. For example, if the treated article is treated with an antimicrobial preservative and is a drug, cosmetic, or class II–V medical device regulated under the *Food and Drugs Act*, feed regulated under the *Feeds Act*, or fertilizer or supplement regulated under the *Fertilizers Act*, the product will be exempt from compliance with the PCPA/PCPR.[17]

Further, a treated article will not need to be registered with the PMRA if: 1) it has only been treated with an antimicrobial preservative (and no other pest control product), 2) the sole purpose of the treatment is to preserve or protect the article, and 3) the preservative used is registered or otherwise authorized or recognized by the PMRA.[18]

As the PCPA and PCPR already include several exemptions and caveats, with new exemptions being added as part of these amendments, the analysis will be very fact specific.

New Framework for Supplemented Foods

A new regulatory framework for prepackaged foods with added vitamins, minerals, amino acids, or other ingredients, such as caffeinated energy drinks and granola bars with added vitamins (Supplemented Foods), came into force on July 21, 2022.[19]

Previously, Supplemented Foods required a temporary marketing authorization (TMA) from Health Canada before they could be sold in Canada. However, under the new framework, a Supplemented Food can now be sold in Canada without the need to seek pre-market authorization from Health Canada if, subject to certain exceptions, the product falls within a permitted food category[20] and contains permitted supplemental ingredients[21] according to the conditions of use prescribed by Health Canada (such as the maximum amount of supplemental ingredient per serving, the specific categories of food to which the supplemental ingredient may be added, required cautionary statements, etc.).

Notably, certain prepackaged foods with added nutrients are not considered Supplemented Foods and are exempted from this new framework, such as foods already permitted to contain added nutrients under the FDR for fortification purposes and foods for special dietary use, subject to certain exceptions.

While the FDR's existing labeling and advertising requirements for prepackaged foods generally continue to apply to Supplemented Foods, new heightened labeling and advertising requirements now also apply to Supplemented Foods to help consumers identify associated risks and make informed decisions.[22] For example, subject to certain exceptions, a Supplemented Food is required to carry a supplemented foods fact table that provides additional information about supplemental ingredients in the product. Additionally, Supplemented Foods containing certain supplemental ingredients, or amounts of supplemental ingredients that meet or exceed specified thresholds, must display cautionary statements, as well as a "Supplemented Food Caution Identifier" (i.e., a prescribed symbol) on the principal display panel.

Supplemented Foods sold in Canada as a result of a TMA that was either approved or applied for before July 21, 2022 have until January 1, 2026 to comply with the new framework, subject to certain conditions.

Going forward, manufacturers can submit a request to Health Canada to add, or revise the conditions of use of, a permitted supplemental ingredient or supplemented food category.

Formal Review of Canada's *Cannabis Act* Underway

Nearly four years after Canada's federal *Cannabis Act* first came into force, the Minister of Health announced a legislative review of the statute on September 22, 2022. This review is intended to assess whether the current legislative framework is meeting its objectives, including deterring criminal activity, displacing the illicit cannabis market, and providing adults access to legal cannabis products.

The federal *Cannabis Act* came into force on October 17, 2018, legalizing the production, sale, and use of recreational cannabis across Canada. At the time it came into force, the Act included a built-in review process requiring Canada's Minister of Health to initiate a review of the Act within three years. The legislation requires the review to consider the impact of the legislation on public health, consumption habits of young persons with respect to cannabis use, the impact of cannabis on Indigenous persons and

communities, and the impact of the cultivation of cannabis plants in personal homes.[23]

Likely due to the COVID-19 pandemic, the review was delayed. As part of the review announced in 2022, Health Canada solicited input from industry and the public in the fall of 2022, to be considered in the review report ultimately provided to Parliament. Pursuant to the *Cannabis Act*, the independent panel's report must be brought before Parliament no later than 18 months after the review commences.

Alternative Proteins on the Front Burner

With exploding interest in alternative proteins, plant-based foods are seeing rapid development. In 2023, the CFIA intends to publish final guidelines for "simulated" meat and poultry products, following extensive consultation with various stakeholders.[24] The FDR provides strict labeling, composition, and fortification requirements for "simulated" meat and poultry products (defined as products that do not contain meat, poultry, or fish but that have the "appearance" of a meat or poultry product).[25] While the regulatory requirements for "simulated" meat and poultry products will not change, the final guidelines are intended to provide direction for determining whether a plant-based food product is a "simulated" meat or poultry product (and thus subject to heightened requirements for simulated meat and poultry products), or whether it is unstandardized food (and thus subject to the general regulatory requirements for unstandardized foods).

In particular, the final guidelines are expected to interpret the word "appearance" in the FDR definition of "simulated" meat and poultry products based on the overall impression of the product, including the sensory characteristics of the food (e.g., visual appearance, texture, flavor, and odor) and how the food is advertised and represented (e.g., if the food is labeled, advertised, or marketed as a food comparable to a meat product or poultry product). For example, a plant-based food that is manufactured to have the appearance of a beef burger (with simulated bleeding or marbling) would be classified as a "simulated" meat product, whereas a tofu patty that does not resemble a meat or poultry product and is not advertised or represented as being comparable to a meat or poultry product would not. The final guidelines are expected to provide examples of representations that are acceptable for plant-based food products without triggering the "simulated" meat and poultry regulations (e.g., "veggie burger" and "soy patty"), provided that the products are not otherwise represented or marketed as having the appearance of a meat or poultry product. Parties selling plant-based foods in Canada may wish to review the guidelines to understand how their products will be classified and to assess what, if any, labeling changes are needed to avoid unintentionally triggering the "simulated" meat and poultry regulations.

Feeds Regulations to Get Major Overhaul

The CFIA is expected to publish amendments to the *Feeds Regulations* in the fall of 2023. These will be the first major updates to the *Feeds Regulations* since 1983. These regulations govern the nutritional requirements, manufacture, sale, and import of substances for use in consumption by livestock, including cattle, sheep, swine, and poultry. Proposed amendments were published in 2021 for public consultation, with follow-up consultations in early 2023.

The proposed amendments are intended to modernize the regulatory framework to improve feed safety, reflect international standards, and keep pace with industry innovation.[26] In particular, the proposed amendments are less prescriptive and more focused on safety outcomes through hazard identification and analysis, preventative control plans (PCPs), traceability, record-keeping, and licensing requirements.[27] The proposed regulations include more flexible labeling requirements and incorporate by reference a table of permissible claims and a table of optional nutrient guarantees that can be used on feed labels without product registration when certain conditions are met. Some provisions are expected to come into force as soon as the final amendments are published, while others (such as PCPs, traceability requirements, and licensing requirements) will have a 12 to 18-month transitional period.[28] At the time of writing, the proposed amendments are still in draft form and subject to change.

Québec Raises the Stakes with New French Language Requirements[29]

In May 2022, the province of Québec adopted Bill 96,[30] resulting in the most significant amendments to Québec's *Charter of the French Language* (*French Charter*)[31] since the *French Charter* was adopted in 1977. While Bill 96 introduced new French language requirements in all areas of Québec's society, food and agribusiness manufacturers operating in Québec should be particularly mindful of the new requirements regarding the use of French language and trademarks on products, signage, advertising, and related materials.

In particular, as of June 1, 2022, product packaging and labeling, catalogues, brochures, order forms, invoices, receipts, and other similar documents provided in Québec in other languages cannot be provided on more favorable terms than the version provided in French.

Further, Bill 96 requires that, as of June 1, 2025, in the province of Québec:

- Only registered trademarks can appear in a language other than French on products and signage and only as long as no corresponding French version of the trademark appears on Canada's trademark register (which may include applied-for marks, in addition to registered marks). In contrast, before the adoption of Bill 96, trademarks "recognized" under the *Trademarks Act* (i.e., common law, applied-for trademarks, and registered trademarks) could appear exclusively in a language other than French if a French version of the trademark had not been registered.
- Trademark owners will no longer be able to rely on the inclusion of generic or descriptive English text in a registered trademark in order to avoid translating text into French on a product sold in Québec. If a registered trademark appearing on a product includes a generic term or description of the product in a language other than French, the generic/descriptive phrase must also appear in French on the product or on a medium that is permanently attached to the product.
- For signage visible from outside premises, French must be "markedly predominant" (i.e., the space allotted to, and characters used in, the text in French must be at least twice as large) as compared to a registered trademark in another language. Before the adoption of Bill 96, trademarks could appear in another language, provided no French version of the trademark was registered, while accompanied by only a "sufficient presence of French."

Stakeholders have requested new regulations and guidance clarifying the interpretation and scope of these amendments, which at the time of writing have yet to be published.

In the meantime, companies doing business in Québec should start assessing their trademark portfolio and existing packaging, signage, marketing, and advertising materials for compliance with Bill 96.

As illustrated by the examples above, 2022 and the first quarter of 2023 have been replete with regulatory and legal developments for the food and agribusiness industry. Many of these issues will continue to evolve over the next year, and our team will continue to monitor any developments closely.

1. Regulations Amending the Food and Drug Regulations (Nutrition Symbols, Other Labelling Provisions, Vitamin D and Hydrogenated Fats or Oils), SOR/2022-168 (20 July 2022) C Gaz II, vol 156, no 15, online: https://canadagazette.gc.ca/rp-pr/p2/2022/2022-07-20/html/sor-dors168-eng.html.
2. *Ibid*, Regulatory Impact Analysis Statement.
3. Canada, Health Canada, *Food labelling coordination: Joint policy statement* (5 August 2021), online: https://www.canada.ca/en/health-canada/services/food-nutrition/legislation-guidelines/policies/food-labelling-coordination/joint-policy-statement.html.
4. Canada, Canadian Food Inspection Agency, *Implementation plan for amendments to the Food and Drug Regulations (Nutrition Symbols, Other Labelling Provisions, Vitamin D and Hydrogenated Fats or Oils)* (20 July 2022), online: https://inspection.canada.ca/food-labels/labelling/implementation-plan/eng/1655824790574/1655824791481; Canada, Health Canada, *Front-of-package nutrition symbol labelling guide for industry* (July 2022, version 1), online: https://www.canada.ca/en/health-canada/services/food-nutrition/legislation-guidelines/guidance-documents/front-package-nutrition-symbol-labelling-industry.html.
5. The new guidance has been attached as two appendices to Health Canada's 2006 Guidelines for the Safety Assessment of Novel Foods. See Appendix 1: Health Canada Guidance on the Novelty Interpretation of Products of Plant Breeding and Appendix 2: Health Canada Guidance on the Pre-Market Assessment of Foods Derived from Retransformants (together, "new guidance").
6. *Food and Drug Regulations*, CRC, c 870, Division 28, part B [FDR].
7. As defined in Section B.28.001 of the FDR, "genetically modify" means to change the heritable traits of a plant, animal, or microorganism by means of intentional manipulation. "Gene editing" is a newer tool of genetic modification "that can be used to generate specific modifications to the genome of living organisms by adding, removing, or altering genetic sequences at precise locations", and refers primarily to CRISPR-Cas, as well as Oligonucleotide Directed Mutagenesis (ODM), Transcription Activator-like Effector Nucleases (TALENs), Zinc-Finger Nucleases (ZFNs) and meganucleases: see Health Canada's "Scientific opinion on the regulation of gene-edited plant products within the context of Division 28 of the Food and Drug Regulations (Novel Foods)".
8. Canada, Health Canada, *List of Non-Novel Products of Plant Breeding for Food Use* (27 March 2023), online: https://www.canada.ca/en/health-canada/services/food-nutrition/genetically-modified-foods-other-novel-foods/transparency-initiative/list-non-novel-products-plant-breeding-food-use.html.
9. Canada, Health Canada, *Notice of Intent to Propose Amendments to Division 28 of the Food and Drug Regulations (Novel Foods)* (20 May 2022), online: https://www.canada.ca/en/health-canada/services/food-nutrition/public-involvement-partnerships/

notice-intent-propose-amendments-division-28-food-drug-regulations-novel-foods.html.

10. *Ibid.*
11. For further discussion of the new guidance, see FDLI publication: Gene-Edited Plants Get Lighter Regulatory Touch in New Health Canada Guidance for Foods, https://www.fdli.org/2022/09/gene-edited-plants-get-lighter-regulatory-touch-in-new-health-canada-guidance-for-foods/.
12. Regulations Amending the Fertilizers Regulations, SOR/2020-232 (11 November 2022) C Gaz II, vol 154, no 23, online: https://gazette.gc.ca/rp-pr/p2/2020/2020-11-11/html/sor-dors232-eng.html.
13. Canada, *Canadian Food Inspection Agency, Notice to Industry – Transitional Provisions* (13 November 2020), online: https://inspection.canada.ca/plant-health/fertilizers/notices-to-industry/transitional-provisions/eng/1604675250185/1604675493951.
14. Canada, *Competition Bureau, Be on the Lookout for Greenwashing* (26 January 2022), online: https://www.canada.ca/en/competition-bureau/news/2022/01/be-on-the-lookout-for-greenwashing.html.
15. Canada, *Competition Bureau, Keurig Canada to Pay $3 million Penalty to Settle Competition Bureau's Concerns over Coffee Pod Recycling Claims* (6 January 2022), online: https://www.canada.ca/en/competition-bureau/news/2022/01/keurig-canada-to-pay-3-million-penalty-to-settle-competition-bureaus-concerns-over-coffee-pod-recycling-claims.html; *The Commissioner of Competition v Keurig Canada Inc.*, CT-2022-0001, online: https://decisions.ct-tc.gc.ca/ct-tc/cdo/en/item/518827/index.do.
16. Regulations Amending the Pest Control Products Regulations (Applications and Imports), SOR/2022-241 (17 November 2022) C Gaz II, vol 156, no 25, online: https://canadagazette.gc.ca/rp-pr/p2/2022/2022-12-07/html/sor-dors241-eng.html.
17. *Pest Control Products Regulations*, SOR/2006-124, s 3(1).
18. *Ibid*, s 4(1).
19. *Regulations Amending the Food and Drug Regulations and the Cannabis Regulations (Supplemented Foods)*, SOR/2022-169 (20 July 2022) C Gaz II, vol 156, no 15, online: https://canadagazette.gc.ca/rp-pr/p2/2022/2022-07-20/html/sor-dors169-eng.html.
20. Canada, Health Canada, *List of Permitted Supplemented Food Categories* (20 July 2022), online: https://www.canada.ca/en/health-canada/services/food-nutrition/supplemented-foods/technical-documents/list-permitted-food-categories.html.
21. Canada, Health Canada, *List of Permitted Supplemental Ingredients* (03 October 2022), online: https://www.canada.ca/en/health-canada/services/food-nutrition/supplemented-foods/technical-documents/list-permitted-food-ingredients.html.
22. Regulations Amending the Food and Drug Regulations and the Cannabis Regulations (Supplemented Foods), SOR/2022-169 (20 July 2022) C Gaz II, vol 156, no 15, Regulatory Impact Analysis Statement, online: https://canadagazette.gc.ca/rp-pr/p2/2022/2022-07-20/html/sor-dors169-eng.html.
23. *Cannabis Act*, SC 2018, c 16, s 151.1.
24. Canada, Canadian Food Inspection Agency, *What We Heard Report - Consultation on Canada's proposed Guidelines for Simulated Meat and Poultry* (09 July 2021), online: https://inspection.canada.ca/about-cfia/transparency/consultations-and-engagement/proposed-changes/what-we-heard-report/eng/1625073587806/1625073588369.
25. *Food and Drug Regulations, supra*, ss B.01.001(1), B.14.085 to B.14.090, online: https://laws-lois.justice.gc.ca/PDF/C.R.C.,_c._870.pdf.
26. Canada, Canadian Food Inspection Agency, *Feed Regulatory Modernization* (06 December 2022), online: https://inspection.canada.ca/animal-health/livestock-feeds/regulatory-modernization/eng/1612969567098/1612971995765.
27. Canada, Canadian Food Inspection Agency, *CFIA Forward Regulatory Plan: 2022 to 2024* (09 November 2022), online: https://inspection.canada.ca/about-cfia/acts-and-regulations/forward-regulatory-plan/2022-to-2024/eng/1505738163122/1505738211563#a1_3_1.
28. Canada, Canadian Food Inspection Agency, *Guide to Timelines for Complying with the Proposed Feeds Regulations, 2022* (15 October 2021), online: https://inspection.canada.ca/animal-health/livestock-feeds/regulatory-modernization/feeds-regulations-2022/eng/1616728050480/1616728692691.
29. Prepared with the kind assistance of Marie-Ève Gingras of the Montréal office of Torys Law Firm.
30. *An Act Respecting French, the Official and Common Language of Québec*, SQ 2022 c 14, online: https://canlii.ca/t/55fcr.
31. *Charter of the French Language*, CQLR c C-11, online: https://canlii.ca/t/55h16.

FDA Center Directors Share Insights and Priorities at the 2023 FDLI Annual Conference

May 17–18, 2023

The FDLI Annual Conference serves as the premiere conference for the food and drug law community, addressing complex legal, regulatory, compliance, and policy issues in all facets of FDA-regulated industry. A highlight for the year's event is the FDA Center Directors' Updates, which address top issues as well as objectives for the coming year for CFSAN, CDRH, CBER, CDER, CVM, and CTP. This article provides an overview of the recent FDA Center Directors' Updates and outlines key takeaways pertaining to food and drug law.

CFSAN Director Dr. Susan Mayne Bids Farewell

By Ricardo Carvajal

During the Center for Food Safety and Applied Nutrition (CFSAN) Director's update, Dr. Susan Mayne took the opportunity to look back over some of the Center's major accomplishments during her eight-and-a-half-year tenure, in anticipation of her departure from FDA at the end of May 2023. Dr. Mayne's remarks highlighted food safety, protection of infants and young children, attention to diet-related chronic diseases, and the initiation of the food program's restructuring.

Food safety has taken priority, given that implementation of the Food Safety Modernization Act required the issuance of nine rules and more than seventy guidance documents. The shift from response to prevention was helped along by enhanced surveillance and microbiological sampling, and improved coordination of outbreak investigations through the Coordinated Outbreak and Response (CORE) Network. Dr. Mayne also noted the dramatic expansion of whole genome sequencing (WGS), with over one million sequences uploaded the GenomeTrakr database to date.

With respect to protection of infants and young children, CFSAN developed and began implementing a national strategy to increase the resilience of the infant formula market. Dr. Mayne noted that in-stock rates are now higher than before the infant formula recall that gave rise to a shortage last year. CFSAN has also implemented its Closer to Zero action plan to further reduce children's exposure to heavy metals in food.

Additional reductions will require an iterative approach, given the presence of heavy metals in the environment and the need to set levels that are achievable.

Dr. Mayne stated that the ongoing epidemic of diet-related chronic diseases can be addressed in part by making foods more nutritious. Notable achievements in that respect included the agency's removal of partially hydrogenated oils from the food supply and implementation of an initiative to reduce levels of sodium in processed foods. CFSAN has also taken steps to facilitate better choices by consumers, such as implementing menu labeling, updating the Nutrition Facts to require declaration of added sugars, and updating the definition of "healthy" to be consistent with the Dietary Guidelines for Americans. Looking forward, a front-of-pack labeling system is in the works that draws on lessons learned from similar initiatives in other countries.

Finally, Dr. Mayne voiced full support for Commissioner Robert Califf's reorganization of the human foods program in the wake of recommendations made by the Reagan-Udall Foundation. The scope of FDA's food-related activities is vast and expanding, and the agency is expected to stay on top of innovations such as cultured meat and precision fermentation, the increasing globalization of commerce, and the need to keep watch over more than 200,000 registered food facilities. The planned reorganization is also expected to help sharpen the agency's focus on nutrition-related diseases and will result in movement of the cosmetics program out of CFSAN and into the Office of the Chief Scientist. That office will be charged with implementation of the Modernization of Cosmetics Regulation Act (MoCRA)—the most significant change in regulation of cosmetics since 1938. However, Dr. Mayne made clear that restructuring alone is no panacea; the Center is going to need additional funding from Congress to keep pace with its increasing responsibilities.

Dr. Mayne finished her prepared remarks with an assurance that new challenges to our food system can be overcome by collaboration between industry, academia, regulators, and consumer advocates—and by affirming that serving as CFSAN Director has been the highlight of her career. What followed was an active question-and-answer session that touched on CFSAN's activities with respect to per- and polyfluoroalkyl substances (PFAS), examples of how increases in funding can help to support innovation, and discussion of potential additional approaches to reduce consumption of added sugars. Dr. Mayne closed out the session by offering some words of advice to her successor: keep the focus on doing good science, treat everyone with respect, and be as transparent as possible. Here's wishing Dr. Mayne much success in her next endeavor.

CDRH Director's Update: Technology is the Future and Flexibility is Key

By Natalie Oehlers

On Wednesday, May 17, 2023, Dr. Jeffrey Shuren, Director of FDA's Center for Devices and Radiological Health (CDRH), sat down with attendees at the 2023 FDLI Annual Conference to address the top issues CDRH is facing and discuss priorities and goals for the coming year.

Throughout this discussion, Dr. Shuren continuously emphasized the importance of staying at the forefront of technological advancements. In doing so, he laid out three major goals related to novel technologies: 1) more than 90% of manufacturers intend to bring their devices to the United States first or in parallel with other major markets; 2) more than 50% of manufacturers would have brought their devices to the United States first or in parallel with other major markets; and 3) FDA identifies and acts on significant safety signals related to medical devices marketed in the United States and other major markets first or in coordination with regulatory agencies of other major markets more than 50% of the time.

Another priority of CDRH addressed by Dr. Shuren is the advancement of health equity through reducing barriers, supporting innovation, facilitating availability and access to existing and novel home-use medical technologies, and empowering people to make informed decisions regarding their care. In doing so, Dr. Shuren recognized the need to enable and create a seamless and integrated approach to technology that expands care outside of the four walls of a hospital. Examples provided include gathering real-world evidence on performance, incorporating technologies ranging from consumer-friendly wearables to traditional medical technologies, and even moving data and processes from local silos to an integrated national network. He also stressed that real change in the healthcare system will require artificial intelligence, although significant issues with datasets that lead to bad outcomes and bias, and the monetization of data itself, has slowed this process.

To further stress the importance of health equity, Dr. Shuren also emphasized that early, frequent, and coordinated stakeholder interaction is key to ensuring timely access to

high-quality, safe, and effective medical devices. More specifically, considering the fact that science and technology are constantly changing, Dr. Shuren expressed his belief that the agency needs to be more nimble and time sensitive, while manufacturers need to better understand the voices of patients and needs of providers during product development and testing.

To achieve these two CDRH and industry objectives, Dr. Shuren described several CDRH policy initiatives, including digital health transformation, international harmonization, work on real-world evidence, quality management, patient and provider engagement, payer engagement, and the Total Produce Life Cycle Advisory Program (TAP) pilot. He also provided another goal for CDRH related to enhanced organizational agility and resilience: by December 31, 2025, CDRH will reduce the average amount of time spent on at least 10 core business programs without reducing performance or adversely impacting outcomes.

Dr. Shuren also spoke to the potential for a voluntary alternative pathway that he believes would give CDRH the authority to take a more customized approach to regulating new technologies in a manner that addresses safety and effectiveness without slowing down innovation or patient access. However, until this authority is granted by Congress, CDRH will continue to use its pilot programs and assist manufacturers in connecting with patient, payer, and provider groups in the planning, testing, and clinical stages of product development.

Moreover, due to recent concerns with respect to the Environmental Protection Agency's (EPA's) proposed rules on ethylene oxide medical device sterilizers, Dr. Shuren agreed that device shortages are a deep concern. However, he stressed that industry can support FDA by being able to share perspectives and data with EPA to make it aware a product itself, along with other dynamics, may be at risk due to these proposed rules.

Finally, in the typical "you heard it here first" fashion that FDLI Annual Conference attendees have come to expect, Dr. Shuren expressed hope that the final harmonization of FDA's Quality System Regulation & ISO 13485 would occur by the end of 2023.

Overall, Dr. Shuren provided conference attendees with a clear snapshot of the state of CDRH and its future direction.

CBER Director Dr. Peter Marks Has a Plan for the Gene Therapy Revolution

by Dan Kracov

Lauded for his efforts in Operation Warp Speed for COVID-19 vaccines, Center for Biologics Evaluation and Research (CBER) Director Dr. Peter Marks is now on another urgent mission. As FDA grapples with a huge wave of gene therapy products, he has embarked on an expedited effort to ensure that such therapies will be safe, effective, efficient to produce, and accessible to patients—including individuals who may be the only ones suffering from their genetic disease. Citing the powerful potential of gene therapy to address both rare and common diseases around the globe, his prescription for this new era of CBER involves rethinking virtually every aspect of the traditional biologic development and approval process, including:

- The recent reorganization of the Office of Tissues and Advanced Therapies (OTAT) into a "super" Office of Therapeutic Products (OTP) designed to increase the timeliness and consistency of interactions with stakeholders.
- Addressing the complexity and cost of manufacture of gene and cell therapies through use of advanced manufacturing technologies, guidance, and collaboration. A particular focus is the optimal scenario of use of small batch gene therapy manufacturing devices.
- Leaning in on the use of accelerated approval in gene therapy, including making reasonable compromises on issues of biomarker validation. He envisions measurement and correlation of enzyme activity and structural protein levels with clinical endpoints in model systems or in humans.
- Fostering regulatory convergence among "high income" countries in this area to make the populations available for treatment commercially viable, as well as a potential framework (with efforts ongoing at the World Health Organization) for low- and middle-income countries. He also noted the possibility of concurrent collaborative review across jurisdictions, along the lines of the Project Orbis model in oncology.
- An Operation Warp Speed for Rare Diseases pilot, under which applicants for products for rare genetic diseases showing promising efficacy would be provided additional informal agency interaction opportunities to advance

product development, similar to the approach used in the review of Emergency Use Authorization products during the pandemic.
- Reconsidering use of certain clinical holds, which can be a very binary and disruptive step—and at times devastating to nascent biotech companies—to ensure that the measures taken to address an investigational new drug issue are commensurate with the concern driving the hold.

Other concepts in development include creating a "cookbook" for the development and manufacturing of bespoke therapeutics for individual patients, and fostering the ability of applicants to leverage nonclinical and manufacturing data from one application to another, thereby focusing efforts on the "distinguishing attributes of offshoot products."

Despite the massive challenges associated with new technologies, Dr. Marks did not neglect the more traditional areas of CBER jurisdiction. He noted the recent decision to move from the highly controversial and indefinite class deferral of blood donors with HIV risk to a more nuanced individual risk assessment algorithm, similar to the approach taken in the UK and Canada. Dr. Marks also provided an update on the progress toward updating COVID-19 vaccine composition and schedules, noting the intention to move toward regular updated vaccination plans for most individuals aged 6–65, with specified regimens for those under six, the elderly, and the immune-compromised.

Summary of the Director's Update for FDA's Center for Drug Evaluation and Research

By Coleen Hill

On May 18, 2023, Dr. Patrizia Cavazzoni, Acting Director of the Center for Drug Evaluation and Research (CDER) addressed the top issues CDER has faced since Dr. Cavazzoni began her role in the summer of 2021. Dr. Cavazzoni also detailed CDER's priorities and goals for the upcoming year.

CDER's past work primarily focused on tackling three issues: the availability of medicines, safety with respect to substance use and misuse and supply chain integrity, and process enhancement and modernization.

On the issue of drug shortages and availability, Dr. Cavazzoni stated that CDER acted to further availability while minimizing risk to patients through several critical programs. By way of example, CDER piloted a new research program for biosimilars to study how biosimilars can be developed and approved more efficiently to get more biosimilars to market. To make drugs more accessible to more patients, CDER made updates for prescription to non-prescription switches, including the approval of non-prescription Narcan. To balance risk, CDER implemented a new requirement for accelerated approvals designed to ensure that post-market confirmatory trials are completed in a timely manner through the Consolidated Appropriations Act, 2023 Section 3120 Modernizing AA.

Ultimately, while CDER's authority is limited with respect to its ability to affect the supply chain in the face of drug shortages, CDER has worked with companies and sponsors on a voluntary basis to prevent and mitigate drug shortages. Dr. Cavazzoni praised the willingness of these entities to cooperate with CDER on such important issues.

Regarding drug safety, including the issues of substance use and misuse and supply chain integrity, CDER developed and implemented the FDA Overdose Prevention Framework. Additionally, CDER's "Opioid Policy Refresh" resulted in a new guidance, safety label changes for stimulants, and advances in safe disposal methods for unused opioids, including mail-back envelope and in-home disposal. CDER also acted to restrict the unlawful import of Xylazine, which is a veterinary drug used to treat large animals that, when combined with opioids, can cause infections serious enough to require amputation. Finally, with respect to nitrosamine impurities, CDER published a Federal Register Notice requesting comments from the public to advance collaborative efforts with industry. CDER hopes its collaborative efforts can help avoid duplicative testing for nitrosamine formation in similar drugs on the market.

Finally, with respect to process enhancement and modernization, CDER achieved reauthorization of the Prescription Drug User Fee Act (PDUFA VI) for fiscal years 2023–2027. With PDUFA VI, CDER implemented multiple pilot programs, including split real-time application review, rare disease endpoint advancement, and advancing real-world evidence. According to Dr. Cavazzoni, PDUFA VI also brings multiple important changes on review of post-marketing requirements, including new processes, timelines, and performance goals to ensure timely availability of public safety and efficacy information. CDER's recently issued decentralized clinical trial guidance clarifies roles and responsibilities of sponsor and investigators and provides recommendations on design, digital technology use, and obtaining informed consent. CDER is hopeful that its new guidance will advance its goal of achieving greater diversity in clinical trial populations. CDER also

modernized its advisory committee processes to ensure access to world-class experts' advice on scientific, technical, and policy matters.

Looking forward, CDER will continue to focus on advancing these goals and others. Specifically, CDER will continue to study Real World Data/Evidence (RWD/RWE), particularly with an eye toward accelerating RWD/RWE for use in post-market requirements. CDER will also work on quantitative medicine under the Accelerating Rare disease Cures (ARC) program and expand the use of modeling in drug development through a multidisciplinary approach. CDER is focused on encouraging clinical trial innovation, and Dr. Cavazzoni expressed a desire for CDER to "turbo charge" that space. On the issue of drug supply chain disruption, CDER plans to spend time analyzing what role CDER should play and how it can involve others to alleviate the issue. Finally, CDER is focused on workforce retention, hiring, and fostering a hybrid work environment in the fiercely competitive labor market to ensure that it can attract the highest quality candidates to continue their important work.

CVM Needs Updated Technology and Expanded Authorities to Regulate in 2023 and Beyond

By Elizabeth Butterworth Stutts

The Center for Veterinary Medicine (CVM) is the smallest Center at FDA. Nonetheless, CVM has a vast portfolio and equities in every other division of FDA. There is "no shortage of things to keep us occupied," joked CVM's new Director, Ms. Tracey H. Forfa, whose good humor and enthusiasm were evident throughout her presentation. Ms. Forfa has worked with CVM since 2002. She is the first attorney Director.

No surprise, as an attorney, Ms. Forfa is a strong advocate for revisions to CVM's regulatory authorities, which are "based back in the 1930s." Smart regulation of new and innovative technologies requires updated authorities.

There are diverse species under the CVM umbrella. Drugs safe and effective for one animal species may not be so for others. *Equally important is human safety.* Drugs must be safe for veterinarians, pet owners, and farm workers. There can be no harmful residue in animal products consumed by humans. Every day, CVM bridges the knowledge gap between veterinary and human medicine. And this is why CVM's update is relevant to your FDA practice, even if you never cross over to animal health.

Ms. Forfa described CVM's Key Initiatives as follows:

- One Health
- Antimicrobial Resistance
- Food Safety Oversight
- Pre-Market Animal Drug Review
- User Fee Reauthorization
- Post-Market Surveillance
- Shortages and Supply Chain
- Emerging Technologies and Innovation
- Data Modernization
- International Affairs
- Stakeholder Engagement and Outreach

Ms. Forfa first discussed One Health and how it relates to CVM's work including antimicrobial resistance (AMR). One Health is an international initiative to improve overall living conditions and fight against antimicrobial resistance, zoonoses, and other threats to our environment by understanding how all living things interrelate. As CVM must consider human health within the context of animal drug regulation on a daily basis, this priority makes sense. Ms. Forfa wants FDA to gain recognition as a One Health Center for Excellence, on par with the Centers for Disease Control and Prevention (CDC) and the United States Department of Agriculture (USDA).

Ms. Forfa continues to advocate for updates to CVM's information technology. Updates improve the ease of exchanging information between CVM and FDA's other Centers. In the "new era for smarter food safety," this is important. Ms. Forfa credits Dr. Solomon for obtaining the requisite budget increases for improvements. "He knows how to tell 'Our Story'," she says, "and it is compelling."

Ms. Forfa believes in dialogue between CVM and its stakeholders. Unlike human medicine, there is no reporting requirement for animal drug supply chain issues, but stakeholders voluntarily reported shortages to CVM during COVID-19. Likewise, there is no formal Risk Evaluation and Mitigation Strategies (REMS) process in veterinary medicine, so CVM relies on its comprehensive database of adverse drug reactions, most of which is voluntarily reported, to help spot trouble signals. Proactivity is key because CVM's post-market authorities are limited.

Ms. Forfa is streamlining facility inspections using technology to coordinate with other agencies. She supports international standards and coordination with FDA's counterparts abroad. She points to the newly expanded conditional approval process for new animal drugs that are proved safe with a reasonable expectation of proof of efficacy over time. This has allowed CVM to make conditionally approved new drugs available for serious conditions in major species.

Another challenge for Ms. Forfa is the old conundrum of unapproved animal drugs. There are more unapproved animal drugs on the market (in excess of 1,500) than approved animal drugs. Some of these drugs have been in regular use for years and are now essential tools in veterinary practice. Others have simply circumvented the approval process and their safety and effectiveness is unknown. CVM must address the body of unapproved drugs and, for those products that fill a critical need, find alternative approval pathways. To do so, CVM's authorities need expansion.

When asked about controversial drugs, Ms. Forfa said she is following FDA's lead on CBD. A recent uptick in human use of animal drugs has put CVM on heightened alert. An example is the illicit use of Xylazine, which has been sold on the internet, not from veterinarians for whom this drug is an important sedative for large animals. Once again, CVM must balance veterinary use with protecting human health.

Finally, generally speaking, FDA's approach to plant and animal biotechnology—including intentional genomic alterations (IGAs) in animals, veterinary regenerative medicine (animal cell, tissue, and cell- and tissue-based products (ACTPs)), and novel food ingredients—is flexible, based on risk to ensure safety, quality, and consumer confidence.

Ms. Forfa described "novel food ingredients" as a prime example of how outdated authorities can hinder overall progress. Novel food ingredients are non-nutritive but claim to act upon the animal's biome after ingestion—in this case, reducing ammonia, methane, and other cattle excretions. In the absence of a new, more appropriate category, novel food ingredients are classified as animal drugs requiring approval. CVM has requested expanded authority.

In contrast, the Veterinary Innovation Program (VIP), which was developed to assist sponsors IGAs and ACTPs through the review process, is a relative success. Thus, when the Center's technologies are up to date and its authorities are kept abreast of the times, CVM can operate at the Center's full potential.

Under the leadership of Ms. Forfa, the Center seems poised to do just that.

CTP Programmatic Update

By Elizabeth Oestreich

Dr. Brian King, Director of the Center for Tobacco Products (CTP), delivered an energized presentation to attendees of the 2023 FDLI Annual Conference on May 18, 2023.

Dr. King opened with the four overarching priorities driving work at the Center:

- sound science,
- stakeholder engagement,
- communication, and
- health equity.

With these overarching priorities in mind, Dr. King described ongoing programmatic activities in four categories:

Rules and Regulations

Product standards are currently the highest priority at CTP. These rules include product standards to prohibit menthol as a characterizing flavor in cigarettes and prohibiting all characterizing flavors, except tobacco, in cigars. Both are in President Biden's Unified Agenda and a priority to finalize by the end of the calendar year. FDA also plans to develop a nicotine product standard, which would establish a maximum nicotine level for combusted tobacco products. The development of this rule remains a priority, but Dr. King did not offer a timeline within which this rule will be developed and proposed.

Dr. King also noted a recently finalized guidance on clinical development of nicotine reduction therapies by the Center for Drug Evaluation and Research (CDER) and CTP's proposed rule on Tobacco Product Manufacturing Practices. The comment period for the TPMP rule is open until September 6, 2023.

Application Review

CTP has reviewed 99% of the over 26 million premarket applications. Thus far, 31 marketing granted orders have been granted, 23 of which are e-cigarette products or devices. Dr. King noted progress on substantial equivalence, exemption requests, and MRTP applications, noting a recent authorization of a modified risk claim for Copenhagen snus.

Enforcement and Compliance

"Nothing is off the table when it comes to enforcement." Dr. King clearly communicated the intent to utilize all tools in the FDA enforcement toolbox to ensure retailers, distributors,

importers, and manufacturers are in compliance. CTP will expand training-, education-, and compliance-related outreach to ensure all stakeholders have the information they need to understand the requirements and comply. To date, FDA has issued over 800 warning letters to manufacturers, over 450 of which were for electronic nicotine delivery system (ENDS) products. FDA has also issued over 123,000 warning letters to retailers (over 19,000 for ENDS products), over 28,000 civil money penalties (over 2,900 for ENDS products), and 221 "No Tobacco Sale Orders."

The agency, in conjunction with the Department of Justice (DOJ), can also utilize recalls, civil money penalties, injunctions, seizures, and criminal prosecution where appropriate. In October 2022, the first injunctions were issued to six ENDS manufacturers, and in February 2023, FDA issued its first civil money penalties to companies selling e-liquids without marketing authorization.

While this high volume of warning letters and enforcement actions far outpace the activity in other product centers, Dr. King hinted at limitations on resources and the need to better target priority areas that will have the greatest impact on public health in this "unprecedented marketplace."

On May 17, the day before Dr. King's remarks, FDA issued an import alert aimed to curtail the amount of unauthorized disposable vapor products on the market.[1] On May 18, the agency issued marketing denial orders to 250 flavored and tobacco-flavored e-liquids. Dr. King responded to a question on these recent actions and disposable product enforcement by saying "we certainly have far more up our sleeves than that" and reiterated the agency's prioritized enforcement against products that appeal to youth.

Consumer Education

Prevention and cessation campaigns continue to roll out of CTP. Specifically, CTP released two new campaigns focused on youth prevention of combustible product use. These new campaigns focus on behavioral health for the first time. In an effort to reach adult smokers, FDA has also initiated formative research on the continuum of risk to identify specific messaging and vehicles for communication. Dr. King reminded the audience of the amount of work that goes into these campaigns and the need for all communications to be data-driven.

Reagan-Udall Foundation Evaluation and CTP Commitments

Dr. King concluded his prepared remarks with an overview of the 15 recommendations articulated in the December 2022 Reagan-Udall Foundation (RUF) Report and CTP's commitment to implement them accordingly.

CTP will complete a five-year strategic plan by the end of this year. An internal comment period for FDA employees is ongoing, and there will be a public comment period this summer for all stakeholders. Dr. King stressed that these comments will be integral in crafting the strategic plan. CTP will convene a forum with DOJ to discuss compliance and enforcement strategies and they plan to craft a parallel plan focused specifically on enforcement.

Other commitments include expanded Tobacco Products Scientific Advisory Committee (TPSAC) utilization, specifically for product applications, enhanced communication with the public, and the opportunity to expand resources by implementing user fees for ENDS products.

After his remarks, Dr. King took audience questions. Two questions stood out as particularly interesting. First, Dr. King was asked about enforcement priorities, specifically the attention given to disposable products and how they plan to work with other federal agencies to address the issue. Dr. King responded that they are engaging internally and with other agencies like DOJ to focus enforcement efforts. Given limited resources, FDA has prioritized products that attract youth. The second question asked about the agency's efforts to combat misinformation. Dr. King stated that he has acknowledged misperceptions and messaging related to the continuum of risk and nicotine and that those misperceptions are on their radar. Going back to the announced campaign on the continuum of risk, he noted they are researching a solution that is scientifically accurate and appropriately targeted.

1. FDA Import Alert 98-06, available at https://www.accessdata.fda.gov/cms_ia/importalert_1163.html.

Ricardo Caravajal is a director at Hyman, Phelps & McNamara, PC. Carvajal's practice focuses on regulatory requirements that apply to the formulation, manufacture, labeling, and advertising of foods.

Natalie Oehlers is an associate attorney at Buchanan Ingersoll & Rooney PC, Washington, D.C. Oehlers focuses her practice on federal and state regulation, legislation, and public policies affecting the pharmaceutical, medical device, biotech, and other life sciences industries.

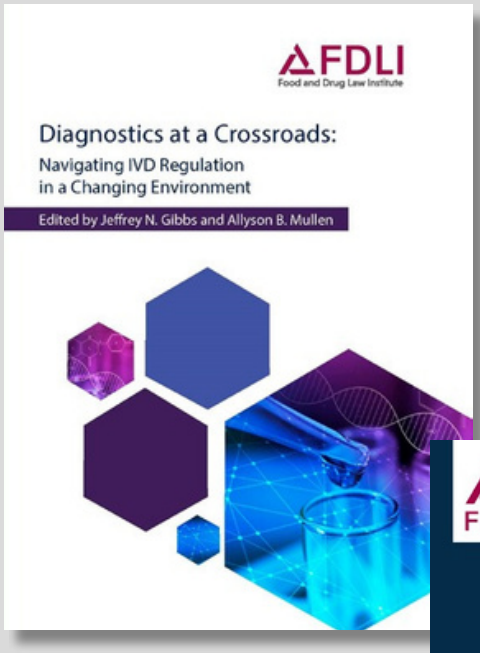
Daniel A. Kracov is co-chair of Arnold & Porter LLP's global Life Sciences and Healthcare Regulatory practice. A particular focus of his practice is assisting pharmaceutical, biotechnology, medical device, and diagnostic companies; including emerging companies, trade associations, and large manufacturers, negotiate challenges relating to the development, manufacturing, approval, and promotion of FDA-regulated products.

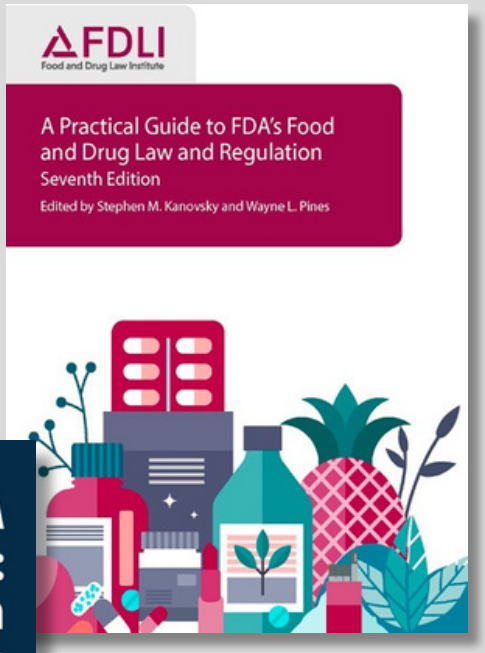
Colleen W. Hill is a trial attorney with Duane Morris LLP, whose practice focuses on representing clients in the Life Sciences industry in complex commercial, regulatory, and products liability disputes. Hill has extensive experience litigating matters involving medical products regulated by the Food and Drug Administration and the Federal Trade Commission, as well as issues arising under the Federal Food, Drug, and Cosmetic Act.

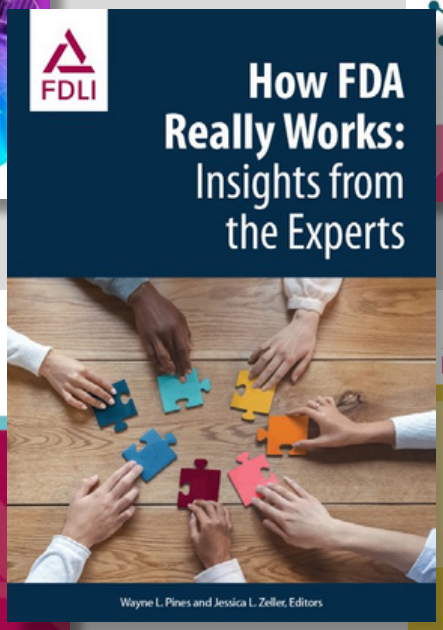
Elizabeth Butterworth Stutts is Principal of Elizabeth Butterworth Stutts, Esq, PLLC, in Richmond (Maidens), VA. Stutts advises clients in human and veterinary healthcare and the animal industry on FDA matters, licensure, contracts, and telehealth.

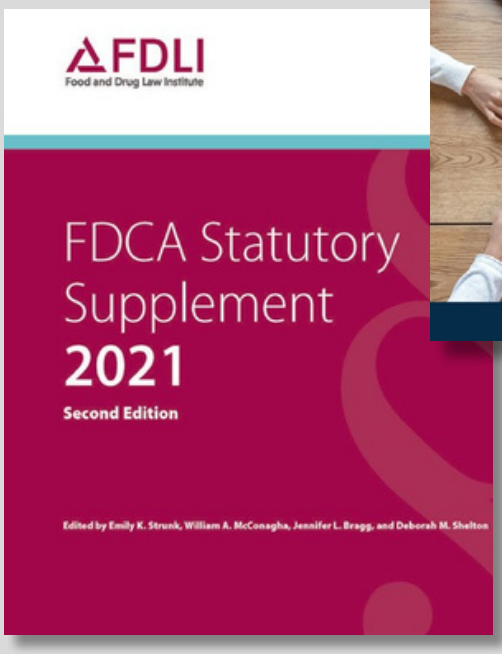
Elizabeth Oestreich is Senior Vice President, Regulatory Compliance at Greenleaf Health Inc. In this role, Oestreich uses her in-depth knowledge of the FDA regulatory process to provide strategic and technical guidance to her clients in all regulated product categories.

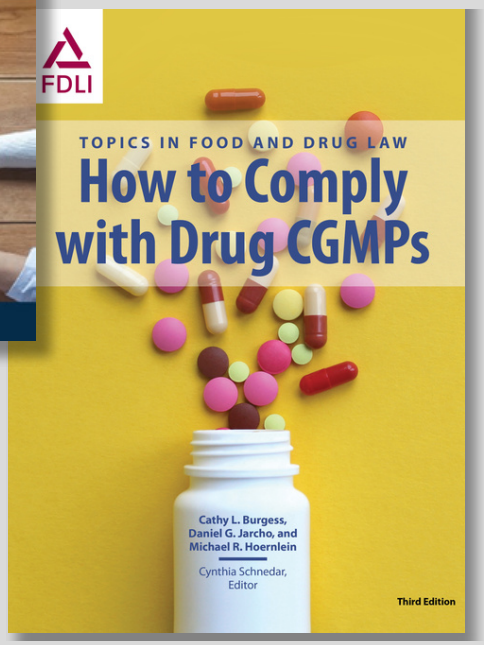
FDLI RESOURCES











FDLI
Food and Drug Law Institute

fdli.org/books

Dr. Harvey Wiley Lecture

FDLI Annual Conference I May 18, 2023

A lectureship in honor of Dr. Harvey W. Wiley, featuring the recipient of the namesake award bestowed by the FDA Alumni Association.

By Steven M. Solomon, Former Director, Center for Veterinary Medicine

I am honored to be the recipient of this year's Wiley award, and thanks to the alumni association for the recognition. Deb, thank you for the kind introduction.

It is hard to believe that it has been 33 years since I left private veterinary practice and first came to FDA. It was a wonderful ride, mostly spent in CVM and ORA with a few other stops along the way. What has made it a most gratifying career is the dedication and commitment of everyone I have worked with over the years. Being surrounded by people with the drive to accomplish our FDA mission, and specifically our CVM mission of protecting human and animal health, has been the motivation for me to always persevere and take the appropriate actions to protect and promote public health.

I need to thank my family, my wife, Lisa, and my three daughters, Laura, Jennifer, and Caroline, who supported me throughout the many trials and tribulations of work life. Too often, there were long days and missed events, such as the "cow that stole Christmas." Without their assistance, I never would have been able to succeed. I am deeply indebted to them, in particular, Lisa, who provided me with great insight and counsel at times of high angst.

When I got the notice about this award, and since it has been a few months since my retirement, it has given me time to reflect on what I have seen over these decades and what I have learned along the way. I never had the time to go to executive leadership training at places like the Federal Executive Institute in Charlottesville, although I have encouraged and supported many of my staff to attend. Rather, I learned by what my father would call the "school of hard knocks." Today, if you will indulge me, I would like to share with you some of my experiences and what I learned from them. My hope is that there may be some value for others to hear of my continuous learning experiences and help those outside the agency gain some additional perspective on the agency.

Dr. Solomon's Remarks at the 2023 FDLI Annual Conference

I have served under 10 Commissioners and 10 Acting Commissioners during my tenure. The FDA budget in

1990 was $568 million, and the agency had approximately 7,700 employees. This was before user fees started under PDUFA in 1992, with subsequent user fees coming into place over the next two decades. This compares to FY 2023 budget of $6.7 billion with $3.2 billion in user fees and approximately 20,000 employees. Back in 1990, we still had the Federal Tea Tester Act and the Board of Tea Testers to evaluate imported tea. The Office of Criminal Investigation had not been established yet, and in fact in my first couple years, I worked directly with DOJ attorneys on multiple criminal prosecutions. We won some cases, lost some, and had some hung juries. It was my introduction to the legal framework we worked under and gave me an up-close perspective of the challenges in our judicial system.

I started working at the infamous Parklawn building, maybe the ugliest government building ever, and have moved to so many different locations, I cannot remember them all. I will spare you by not trying to recount all that I have been involved in—too many different positions and details, outbreaks, initiatives, reports, oversight hearings, etc. But I will share a few events in which I learned lessons that have served me well during the past 33 years. Some of these lessons have become imbodied in my guiding principles, which I will share shortly. I do not suggest that my guiding principles are the ones for everyone but will share them because they have been my guideposts as I have navigated through many demanding issues.

When I started at CVM in 1990, I was conducting post-marketing review work for unapproved animal drugs and devices. We had to handwrite our reviews on legal pads and give them to the division Secretary to type on a word processing machine. Ester was the elderly secretary that did all the typing, and if she did not like you, your reviews went to the end of the queue. So, my first lesson was that there may be a Commissioner and what I called at the time "mucky mucks," at least until I became one, who supposedly are in charge of the agency. However, I quickly understood that the real work of FDA gets done by the civil servants at all grade level and to treat everyone with the respect and dignity they deserve, no matter what their position or title.

We had no personal computers when I started; the agency had large main frames with tapes for storage. We had "dumb" terminals on our desk that used a very primitive email system called "Banyan" mail. When we got the first IBM PC, with five-and-a-half inch floppy disks, Ester got one and I inherited her Lanier work processing machine; it was as big as a refrigerator and barely fit into my office. I could now type my own reviews, and it taught me the lesson of seeking to find efficiency in the work we do. This was also my start of understanding the challenges of information technology in FDA, that, as many of you know, continue to this day. When I started, you either needed to use your own information resources or the FDA library. An important lesson was the need for enhanced information technology available to all staff to have access to the data we need to help make decisions and accomplish our public health mission. This is an area that FDA continues to build that needs continued investment as noted in the infant formula assessment.

After a number of years in CVM, I moved to the Office of Enforcement in ORA. This was at a time when Commissioner Kessler recognized that the agency was a "paper tiger" and developed the warning letter system we know today. I have observed the pendulum swing of greater or fewer enforcement actions many times throughout my time in FDA. I started at a time when we conducted hundreds of seizures a year of adulterated products, and I learned the importance of enforcement as a deterrent impact on those in regulated industry that did not follow the regulations.

My initial assignment was to review the thousands of agency warning letters and to develop a reference guide to help ensure consistency across the agency. Besides, gaining great insight into the agency's priorities for enforcement from each center, I also started learning and advocated for FDA to develop quality management systems to institute appropriate controls and documentation. This experience drove my guiding principle of continuous improvement.

The foundation of FDA is built on the pillars of science, law, and policy. I understood the science from my veterinary training; I learned the law by taking FDA law training and my work with DOJ, along with learning from more experienced staff and Office of Chief Counsel. I started taking classes during nights and weekends in public health policy to strengthen my understanding of how policy is developed and eventually received my MPH. I learned not only from my professors, but since I was in class with other working public health professionals, we shared our learning in the classroom, and I learned the value of recognizing everyone's contributions.

With this foundation, I took on different management and leadership roles. I learned incident management when I was the agency's first incident commander for the December 23, 2003, finding of mad cow disease in the U.S. This was the infamous "cow that stole Christmas." I was lead for or worked on many more outbreaks, including E. coli in spinach in 2006, melamine in pet food in 2007, heparin contamination in 2008, as well as Salmonella in peanut butter that same year. I also served as incident commander for monkeypox in 2013. I was called into the ACRA's office, it was John Taylor at the time, and told that the Secretary of HHS had declared a public health emergency for findings of children with monkeypox, a foreign animal zoonotic disease. I was told that I was in charge and should stop it from spreading. I said, "yes sir," and ran back to my office to look up what the heck monkeypox was. We traced it back to shipments of hundreds of African rodents imported into the U.S., housed at a wholesale facility where there were also prairie dog pups housed. The prairie dogs were purchased at pet stores and taken to school for "show and tell," which resulted in children becoming infected with monkeypox. As a side note, the job in FDA is never dull—you're always learning, such as, who knew that people used giant vacuum cleaners to suck baby prairie dogs out of their holes, or that the endangered black-footed ferret eats prairie dogs and therefore we had environmental concerns with our control measures. I learned the value of collaboration, since to control this outbreak needed FDA, CDC, USDA, Fish and Wildlife, multiple states, and localities. We needed to combine each agency's authorities and jurisdictions to stop this foreign animal disease from becoming established in the U.S. I also learned that some people resist government actions such as quarantine of animals, measures placed to protect public health, and would prefer to let their animals loose rather than quarantine them. Release of African rodents could have established it in our domestic rodent population. We have seen similar resistance to public health measures during the pandemic.

These provided valuable lessons that have stayed with me. Generally, the agency and government work well during an emergency to respond to the issue. Unfortunately, I realized that this level of cooperation is difficult to maintain post the immediate emergency response. I gained a deep appreciation of our working relationships with other international, federal, state, and local public health and regulatory agencies. I became a strong advocate for an integrated national food safety system after observing the opportunity it provides to enhance protection of the public health.

I learned, after testifying before Congress multiple times, something we all understand, that their attention span is short. We too often fail to put systems in place to prevent these public health emergencies from reoccurring. We continue to relearn this lesson and have just revisited it again with the recent COVID

pandemic public health emergency. Our nation's public health infrastructure has eroded. We are not able to adequately respond to the next pandemic, which will occur, or other significant public health incidents.

Over the years, my major management angst did not come from public health emergencies, changes in statutes and regulatory authorities, nor the evolving legal landscape. My biggest concerns were budgeting and government funding. Congress has passed a full appropriation budget, on time, only time three times during my 33 years. As a manager, it is difficult to do fiscal planning not knowing what your budget is going to be from year to year. We frequently did not get our final budget until mid-year, with only a short time to spend it before the need to close out the fiscal year. But this has become the standard and is not unique to FDA.

What is even more challenging is the lapse in appropriations. During my tenure, I underwent nine lapses in appropriations. While some only lasted for hours or a couple days, three went for longer periods of time. However, the time to prepare for and recover from even the short ones are resource-intensive even when they end up only being a threat with last-minute passage becoming the norm. The worst period during my career was the 35-day government shutdown in January 2018. Many in CVM were furloughed, and there were limited exceptions to when we could work, even if not paid. The Antideficiency Act only allows government employees to work if covering the safety of human life or protection of property, not a strict animal health issue. One thing I have learned that the American public cares deeply about, is babies and animals. As evidenced by melamine in pet food and the more recent infant formula recalls resulted in shortages and high levels of concern about what to feed their pets or babies. The impact on CVM families that lived paycheck to paycheck was damaging, but that folks could not volunteer their time to deal with ongoing animal health issues was the antithesis of our mission.

Finally, I will share the guiding principles that I developed during my career and shared frequently with internal and external audiences:

Public Health—I look at every issue through the public health lens first. It may not be the only lens, and I recognize there are many other considerations, but it is the most important first lens to focus on. What is the right thing to do for public health.

Decision-making—Should be based off the best science and evidence you have. However, when dealing with rapidly evolving public health issues, we will never have all the science nor all the data we would like to make a decision on what action to take. However, failure to take an action is also an action that has implications for public health. Mistakes will be made, and that is understandable. When new science or evidence becomes available, you need to be prepared to change your position, or if new data becomes available, it is critical to revise your actions as appropriate to the new information.

Continuous Improvement—We need to learn from every action we take. We should learn from what went right or what we could do better. It is key to develop systems to analyze, assess, and continuously improve our public health actions.

Transparency—Try and be as transparent as possible within the legal restraints we have on protecting certain information. This is a critical issue for enhancing the credibility of the organization.

Engage Stakeholders—There are multiple stakeholders that are interested in the work we do. It is guaranteed that they will be parties on opposing sides of any and all issues. We will make the best decisions when we hear all viewpoints. This does not mean we need to agree with everyone's position, but they all have a right to be heard.

Collaboration—Recognize that we are a public health–regulatory agency, with public health being the goal and regulation one of the ways to accomplish it. We should always lead with the objective of trying to address the public health issue, usually with the need to engage others in the solution. We will never have all the resources, authorities, jurisdiction, or expertise to do it all ourselves. We cannot accomplish our mission by ourselves, but we need others to assist. Sometimes our regulatory tools are appropriate to address the issues, sometimes we need other's tools or need novel approaches. Particularly, we need to recognize, appreciate, and collaborate with our domestic and international regulatory and public health partners.

Communication—Tell your story and explain why. We are not very good at communicating the work we do, the importance of the work, or explaining why we came to the decision we did. Telling your story in layman's terms helps create credibility and trust with the public.

Create and embody your organization's core values to focus on the internal culture of the organization. For example, for CVM the core values created by the staff are:

We Serve:
We are a mission-driven, public health, regulatory Center. Safeguarding human and animal health is what we do. We serve our stakeholders and hold their trust in the highest regard. Collaboration and communication, across all disciplines, are the tools we use to provide the greatest level of service.

We Lead:
Everyone makes a difference. Each of us contributes our ideas and skills to influence CVM's direction regardless of their title or position. New leaders emerge every day.

We Learn:
We continuously learn, stretch, and grow. We provide opportunities for people to develop their skills and cultivate diverse talents. Our individual expertise is the expertise of the organization.

We Honor:
CVM appreciates the exceptional people who work here. We encourage and support everyone to dream, inspire each other, and live our best lives, personally and professionally. We celebrate all life experiences, cultures, and backgrounds for the wealth of perspectives they bring to CVM.

The last lesson I have learned is that we will continue to see evolving public health issues that we never anticipated or we are not prepared for. I strongly support a "One Health" approach that recognizes the interconnection of human health, animal health, plant health, and the health of our environment. We can only solve these substantial public health problems by looking from the larger perspective of One Health and by bringing all parties to the table. To be clear, One Health is not just about zoonotic or infectious disease but also includes areas such as antimicrobial resistance, translational medicine, food and water safety, nutrition and environmental health, to name a few areas. It offers not only the opportunity for enhanced collaboration across FDA Centers but also between government, academia, and the public and private sector. One Health incorporates many of the core principles I have outlined, including focusing on public health, collaboration, engaging stakeholders, transparency, and science-based decision-making.

I know it is a time of profound change in the FDA and government as a whole. I understand that this has been a major focus during this conference. While I have observed a lot of change over my time in FDA, the pace of change has certainly intensified. The 24-hour news cycle and the amount of misinformation and disinformation on the internet and other sources compounds our challenges. In our society, there is

significant skepticism and a lack of understanding of science, there is profound mistrust of government officials and scientists, there is high degree of societal unrest which divides us on political and social issues. Financial concerns about the debt ceiling, inflation, government budget cuts, and the end of a three-year pandemic all create additional uncertainty. Long-standing policies are being challenged in courts. The legal landscape is changing, and we are seeing new interpretations of Food and Drug Law.

All of this creates uncertainty in FDA staff. I have found that using guiding principles is one of the best ways to help provide clarity about how to navigate in a rapidly changing world. This talk is not intended to be about me, but rather to share what I believe are pragmatic approaches to address the ongoing challenges the agency faces.

I will end where I started. With all the changes I have observed during the past 33 years, one thing that has not changed is the dedication and commitment of FDA employees to the FDA mission. It has been an honor and privilege to be part of the FDA. I leave knowing that FDA and CVM are there to continue to protect human and animal health.

Thanks again for the honor of the Wiley award and to FDLI for allowing me some time to speak to you. I hope you enjoy the rest of the conference.

UPCOMING PROGRAMS

fdli.org/programs

FDLI Webinars:
Visit fdli.org/webinars for upcoming webinars

Introduction to Cannabis Law and Regulation
June 5, 2023 | Washington, DC

Legal and Practical Issues in Cannabis Regulation
June 7–8, 2023 | Washington, DC & Virtual

Introduction to Food Law and Regulation
September 2023 | Virtual Course

Food Advertising, Labeling, and Litigation Conference
September 27–28, 2023 | Washington, DC & Virtual

Introduction to Biologics
October 2023 | Virtual Course

Introduction to Advertising & Promotion
October 2023 | Washington, DC

Advertising & Promotion for Medical Products Conference
October 2023 | Washington, DC & Virtual

Introduction to Tobacco Law and Regulation
October 2023 | Virtual Course

Tobacco and Nicotine Products Regulatory Science Symposium
October 2023 | Washington, DC

Tobacco and Nicotine Products Regulation and Policy Conference
October 2023 | Washington, DC & Virtual

Introduction to Medical Device Law and Regulation
November 2023 | Virtual Course

Introduction to Drug Law and Regulation
November 2023 | Virtual Course

Food and Drug Law Journal Symposium
November 2–3, 2023 | Virtual Event

Fundamentals of Digital Health Regulation
Fall 2023 | Virtual Course

Current Developments in Digital Health Technology and Regulation Conference
Fall 2023 | Virtual Event

Enforcement, Litigation, and Compliance Conference
December 2023 | Washington, DC & Virtual

SHARE YOUR IDEAS WITH FDLI!

Submit a Law Over Lunch Topic

Member-Only Opportunity

What timely, interesting topics would you like to discuss with other FDLI members? **Submit a proposal** to facilitate a discussion about a timely topic at an upcoming virtual Law Over Lunch program!

Author Articles

What legal and regulatory issues interest you?

Share your expertise by submitting articles to FDLI publications, including *Update* magazine and *Food and Drug Law Journal*.

For questions, please contact **publications@fdli.org**.

Suggest Webinar Ideas

Have a subject you'd like to learn more about?

The FDLI Webinar Programs Committee invites food and drug law community stakeholders to **submit a proposal** recommending a topic using our webinar portal!

FDLI
Food and Drug Law Institute

fdli.org/ideas