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Food and Drug Omnibus Reform Act of 2022

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EXECUTIVE SUMMARY

On December 29, 2022, the President signed into law the Food and Drug Omnibus Reform Act of 2022 (“FDORA”) as part of the Consolidated Appropriations Act, 2023, Pub. L. No. 117-328 (2022).¹ FDORA primarily amends the Federal Food, Drug, and Cosmetic Act (“FDC Act”) and the Public Health Service Act (“PHS Act”). The law enacts significant changes that will have considerable short- and long- term effects on the regulated industry and the Food and Drug Administration (“FDA”).

FDORA includes six subtitles, Subtitle A- Reauthorizations, Subtitle B- Drugs and Biologics, Subtitle C- Medical Devices, Subtitle D- Infant Formula, Subtitle E--Cosmetics and Subtitle F- Cross-Cutting Provisions.

This memorandum summarizes FDORA—focused on the provisions that likely are of most interest to our clients—and analyzes FDORA’s potential effects on the FDA-regulated industry. It is organized to summarize each subtitle in the order presented in FDORA. In addition to this memorandum, Hyman, Phelps & McNamara, P.C. will periodically report on various FDORA issues on our firm’s blog, the FDA Law Blog (www.thefdalawblog.com). You can register for free e-mail updates on the blog.

SUBTITLE A—REAUTHORIZATIONS

- Sec. 3101. Reauthorization of the critical path public-private partnership.**
- Sec. 3102. Reauthorization of the best pharmaceuticals for children program.**
- Sec. 3103. Reauthorization of the humanitarian device exemption incentive.**
- Sec. 3104. Reauthorization of the pediatric device consortia program.**
- Sec. 3105. Reauthorization of provision pertaining to drugs containing single enantiomers.**
- Sec. 3106. Reauthorization of certain device inspections.**
- Sec. 3107. Reauthorization of orphan drug grants.**
- Sec. 3108. Reauthorization of reporting requirements related to pending generic drug applications and priority review applications.**
- Sec. 3109. Reauthorization of third-party review program.**

¹ A copy of FDORA (H.R. 2617) is available at 1349, <https://www.congress.gov/117/bills/hr2617/BILLS-117hr2617enr.pdf>. In this memorandum, references to the Secretary of the Department of Health and Human Services (“DHHS”) will be translated as FDA, to whom the duties will generally be delegated, unless the context indicates that DHHS will execute the responsibility independent of FDA.

Subtitle A of FDORA (FDORA §§ 3101-09) reauthorizes nine existing FDA programs through fiscal year 2027.

Sec. 3101. Reauthorization of the critical path public-private partnership.

The Critical Path Public-Private Partnership (FDCA § 566), a program through which FDA may enter into collaborative agreements with institutions of higher education or 501(c)(3) organizations to develop innovative projects that foster medical product innovation. *See* FDORA § 3101.

Sec. 3102. Reauthorization of the best pharmaceuticals for children program.

The Best Pharmaceuticals for Children Program (Public Health Service Act § 4091), which provides an incentive of additional marketing exclusivity to sponsors who voluntarily complete pediatric clinical studies outlined in a Written Request issued by FDA. *See* FDORA § 3102.

Sec. 3103. Reauthorization of the humanitarian device exemption incentive.

The Humanitarian Device Exemption (FDCA § 520(m)), which provides an exemption from the effectiveness requirements for premarket clearance or approval of devices if FDA grants a request confirming, among other criteria, that the device is designed to treat or diagnose a disease or condition that affects not more than 8,000 individuals in the U.S. *See* FDORA § 3103.

Sec. 3104. Reauthorization of the pediatric device consortia program.

The Pediatric Device Consortia Program (Section 305(e) of the Food and Drug Administration Amendments Act of 2007), through which FDA awards grants or contracts for projects that promote pediatric device development. *See* FDORA § 3104.

Sec. 3105. Reauthorization of provision pertaining to drugs containing single enantiomers.

The FDCA provisions regarding drugs containing single enantiomers (FDCA § 505(u)), which permit FDA to grant the same five-year exclusivity to chiral switches that is accorded to new chemical entities. *See* FDORA § 3105.

Sec. 3106. Reauthorization of certain device inspections.

Device facility inspections conducted by “Accredited Persons” (FDCA § 704(g)). *See* FDORA § 3106.

Sec. 3107. Reauthorization of orphan drug grants.

Section 5 of the Orphan Drug Act, which permits FDA to issue grants to public and private entities to assist in defraying the costs of developing drugs, devices, and medical foods for rare diseases or conditions. *See* FDORA § 3107.

Sec. 3108. Reauthorization of reporting requirements related to pending generic drug applications and priority review applications.

Reporting requirements related to pending generic drug applications and priority review applications (Section 807 of the FDA Reauthorization Act of 2017). *See* FDORA § 3108.

Sec. 3109. Reauthorization of third-party review program.

The Third-Party Review Program (FDCA § 523), which is a voluntary program through which device sponsors can submit 510(k) premarket notifications to accredited third parties for review. *See* FDORA § 3109.

SUBTITLE B—DRUGS AND BIOLOGICS

CHAPTER 1—RESEARCH, DEVELOPMENT, AND COMPETITION IMPROVEMENTS

Sec. 3201. Prompt reports of marketing status by holders of approved applications for biological products.

Sec. 3202. Improving the treatment of rare diseases and conditions.

Sec. 3203. Emerging technology program.

Sec. 3204. National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing.

Sec. 3205. Public workshop on cell therapies.

Sec. 3206. Clarifications to exclusivity provisions for first interchangeable biosimilar biological products.

Sec. 3207. GAO report on nonprofit pharmaceutical organizations.

Sec. 3208. Rare disease endpoint advancement pilot program.

Sec. 3209. Animal testing alternatives.

Sec. 3210. Modernizing accelerated approval.

Sec. 3211. Antifungal research and development.

Sec. 3212. Advancing qualified infectious disease product innovation.

Sec. 3213. Advanced manufacturing technologies designation program.

Sec. 3201. Prompt reports of marketing status by holders of approved applications for biological products.

Section 3201 requires holders of applications approved under section 351(a) and 351(k) of the PHS Act to notify FDA prior to withdrawing an approved drug for sale or if the drug will not be available for sale within 180 days of approval. *See* FDORA § 3201(a). The law also requires application holders of currently approved biologics listed in the Purple Book to review and submit a report that either confirms or corrects the listing of their products as discontinued or not. FDORA § 3201(b). A failure to meet these requirements may result in FDA moving the application holder's products from the active section to the discontinued section of the Purple Book. FDORA § 3201(c).

Sec. 3202. Improving the treatment of rare diseases and conditions.

Section 3202 requires FDA to publish a report summarizing its activities related to designating and approving or licensing drugs and biologics for rare diseases. *See* FDORA § 3202(a). Additionally, the law requires FDA to publish a final version of the 2019 draft guidance titled "Rare Diseases: Common Issues in Drug Development" and to commission a study reviewing processes for evaluating drugs for rare diseases or conditions in the United States and the European Union. FDORA § 3202(b)-(c).

FDA is also directed to convene at least one public meeting to address increased and improved engagement with rare disease patients, rare disease patient groups, and experts on small population studies – all in order to improve the understanding of patient burden, treatment options, and the side effects of treatments. FDORA § 3202(d).

This section also requires the drafting of a Government Accountability Office ("GAO") report assessing FDA's policies, practices, and programs regarding treatments for rare diseases. *See* FDORA § 3202(f). This report will assess the effectiveness of these policies and practices, as well as their applied consistency across review divisions, and include recommendations to address challenges and deficiencies. FDORA § 3202(f)(2).

Sec. 3203. Emerging technology program.

Section 3203 requires FDA to develop and implement an Emerging Technology Program ("ETP") to "support the adoption of, and improve the development of, innovative approaches to pharmaceutical product design and manufacturing." The ETP effectively expands an existing ETP so that FDA may solicit the public for information, convene meetings, working groups, support education and training for regulatory staff and scientists, advance regulatory science, and award grants or contracts in support of the adoption, or improvement, of innovative approaches to drug product design and manufacturing. Section 3203 requires FDA to "issue or update guidance" on an ETP.

FDORA requires FDA to report to Congress its annual accounting of the new program's allocated funds, use of FDA staff, number of meetings FDA held or participated in, and number of drug products approved or licensed that used an innovative approach to drug product design and manufacturing.

Sec. 3204. National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing.

Within a year of enactment of section 3204, FDA must create a National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing to “support the advancement, development, and implementation of advanced and continuous pharmaceutical manufacturing.” Institutions designated as a National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing, including institutions of higher education, are to collaborate with FDA to publish reports, to share research data with the FDA, and to develop strategic plans for developing advanced and continuous pharmaceutical manufacturing workforce, and to improve existing or develop new partnerships in support of developing advanced and continuous pharmaceutical manufacturing. The National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing is intended to assist FDA in creating a regulatory framework that supports adoption of continuous manufacturing.

Sec. 3205. Public workshop on cell therapies.

Under section 3205, FDA must convene a public workshop within three years of enactment with relevant stakeholders to discuss best practices on generating scientific data necessary to further facilitate the development of stem cell and other cellular therapies.

Sec. 3206. Clarifications to exclusivity provisions for first interchangeable biosimilar biological products.

Section 3206 amends statutory language regarding exclusivity for the first interchangeable biosimilar product, defining the term “first interchangeable biosimilar biological product” to mean any interchangeable biosimilar biological product that is approved on the first day on which such a product is approved as interchangeable with the reference product. As such, multiple products can receive this exclusivity using the same reference product.

Sec. 3207. GAO report on nonprofit pharmaceutical organizations.

Section 3207 mandates instructs the drafting of a GAO report on what is known about nonprofit pharmaceutical manufacturing organizations and their impact on the development, availability, and cost of prescription drugs in the United States, as well as

recommendations to address challenges related to shortages or other manufacturing challenges.

Sec. 3208. Rare disease endpoint advancement pilot program.

Section 3208 directs FDA to establish a pilot program to provide increased interaction with sponsors of rare disease drug development programs for the purposes of advancing the development of efficacy endpoints, including surrogate and intermediate endpoints. FDA must conduct up to three public workshops to discuss topics relevant to the development of endpoints for rare diseases. FDA must also issue guidance describing best practices and strategies for the development of such endpoints. It is worth noting that FDA had already announced the launch of this program following its description in the PDUFA VII Goals Letter.

Sec. 3209. Animal testing alternatives.

Section 3209 attempts to encourage the use of alternatives to animal studies in both the IND and biosimilar context. The law describes other types of tests that could be used to support an IND, such as “a test conducted in vitro, in silico, or in chemico, or a nonhuman in vivo test.” FDORA § 3209(a). As such potential alternatives, this section lists options as including cell-based assays, organ chips and microphysiological systems, computer modeling, and other nonhuman or human biology-based test methods such as bioprinting. Regarding establishing biosimilarity, FDORA revises the statutory language to clarify that while an assessment of toxicity is required, it may rely on or consist of the analytical studies to demonstrate similarity or the clinical studies to demonstrate safety, purity, and potency.

Sec. 3210. Modernizing accelerated approval.

Section 3210 makes significant changes to accelerated approval. If no postapproval study is required, FDA must publish a rationale on its website explaining why no such study is required. If a postapproval study is required, FDA must specify conditions, which may include enrollment targets, study protocol, and milestones, including the target date of study completion. This section explicitly includes a failure to meet these conditions as being part of the determination that the sponsor failed to conduct a required postapproval study with due diligence. This section authorizes FDA to require a postapproval study or studies to be underway prior to approval, or within a specified time period after approval.

Sponsors must report the progress of any required study, including progress toward any conditions specified by FDA, not later than 180 days following approval and

not less frequently than every 180 days thereafter until the study is completed or terminated. Previously, progress reports on these studies were only required annually.

As additional enforcement authority, this section enables FDA to initiate enforcement actions for a failure to conduct a required post approval study with due diligence, including a failure to meet any required conditions specified by FDA or to submit timely reports.

The new law also describes the procedures to be used for the expedited withdrawal of approval of a product approved under accelerated approval, the details of which had previously been delegated to FDA. These include notice and an explanation for the proposed withdrawal, an opportunity for a meeting and written appeal, an opportunity for public comment on the proposal to withdraw with the publication of the Secretary's response to such comments, and the convening of an advisory committee if requested by the sponsor if no such committee had previously advised the Secretary on such issues with respect to the withdrawal of the product prior to this request.

Finally, FDA must publish guidance on the topic of identifying novel surrogate or intermediate clinical endpoints, the use of novel clinical trial designs for post-approval studies, and considerations related to the use of surrogate or intermediate endpoints that may support accelerated approval. FDA must establish an intra-agency Accelerated Approval Council to ensure the consistent and appropriate use of accelerated approval across FDA.

Sec. 3211. Antifungal research and development.

Section 3211 directs FDA to publish guidance to assist entities seeking approval of antifungal therapies designed to treat coccidioidomycosis (commonly known as Valley Fever). FDA must also hold a public workshop to assist entities developing preventive vaccines for fungal infections and Valley Fever.

Sec. 3212. Advancing qualified infectious disease product innovation.

FDORA § 3212 amends the qualified infectious disease product ("QIDP") incentive provisions in the FDC Act. Prior to the amendment, the QIDP provisions applied to drugs but not biologics. The new language clarifies that biologics may be eligible for QIDP designation and the priority review that accompanies such designation, but they are not eligible for the exclusivity extensions, including extensions to orphan drug exclusivity, available to products approved via NDA.

Regarding the priority review incentive available to QIDP-designated drugs and biologics, FDORA adds a requirement that the application be the first application

submitted for approval of such drug or biologic that requires clinical data, other than bioavailability studies, to demonstrate safety or effectiveness. Previously, clinical data were not required for this incentive. As with drugs, QIDP-designated biologics will be eligible for fast track designation upon request. FDORA amends the definition of QIDP to include any drug or biologic that acts on bacteria or fungi or on substances produced by bacteria or fungi rather than only drugs specifically targeting bacteria or fungi.

Sec. 3213. Advanced manufacturing technologies designation program.

Section 3213 directs FDA to initiate an “Advanced Manufacturing Technologies Designation Pilot Program” that would review manufacturing methods that incorporate “a novel technology, or uses an established technique or technology in a novel way, that will substantially improve the manufacturing process for a drug while maintaining equivalent or providing superior, drug quality” Within six months of enactment, FDA shall hold a public meeting to discuss the program procedures and requirements and the ways FDA will support the use of advanced manufacturing technologies and other innovative manufacturing approaches for drugs.

Following the public meeting, FDA shall publish a draft guidance regarding the goals and implementation of the program, the designation criteria, the designation request process, and the process to expedite the development and review of applications. Designation shall be based on information demonstrating that the method of manufacturing is novel and reduces the development time of a drug, increases or maintains the supply of life-supporting, life-sustaining or critically important drugs, and/or addresses drug shortage. The benefits of the designation include expedited development and review of applications using the designated technology. FDA is directed to report to Congress on its evaluation of the program within three years and annually thereafter.

CHAPTER 2—TRANSPARENCY, PROGRAM INTEGRITY, AND REGULATORY IMPROVEMENTS

Sec. 3221. Safer disposal of opioids.

Sec. 3222. Therapeutic equivalence evaluations.

Sec. 3223. Public docket on proposed changes to third-party vendors.

Sec. 3224. Enhancing access to affordable medicines.

Sec. 3221. Safer disposal of opioids.

FDORA modifies the statutory provision on packaging and disposal as an additional potential element of risk evaluation and mitigation strategies (“REMS”). Prior

to FDORA, FDA could require that a drug subject to a REMS be dispensed to certain patients with a “safe disposal packaging or safe disposal system”² for purposes of rendering drugs “non-retrievable” as that term is defined in Drug Enforcement Administration (“DEA”) regulations.³ FDORA strikes the “for purposes of rendering drugs non-retrievable” language and the reference to the DEA definition, meaning FDA will be able to require safe disposal packaging or systems for purposes other than rendering drugs non-retrievable (e.g., abuse deterrence). While this section is titled “safe disposal of opioids,” there is nothing in the statute that would prevent FDA from including packaging and disposal as a REMS element for prescription drugs other than opioids.

Sec. 3222. Therapeutic equivalence evaluations.

Under Section 3222, FDA must consider therapeutic equivalence determinations for drugs approved through the 505(b)(2) pathway for which the sole difference from the listed drug relied upon in the application is a difference in inactive ingredients that is not permitted under FDA regulations for drug products intended for parenteral, ophthalmic, or otic use.⁴

For applications submitted after the enactment of FDORA, FDA is required to perform the therapeutic equivalence evaluation either at the time of approval or no later than 180-days after approval, provided that the sponsor requested a therapeutic equivalence evaluation and provided the necessary data. For applications (1) approved prior to or on the date of enactment or (2) submitted prior to the date of enactment but not yet approved, FDA will complete the therapeutic equivalence evaluation no later than 180 days after receipt of the request, which must be submitted as an application supplement.

Sec. 3223. Public docket on proposed changes to third-party vendors.

Within 90 days after the date of enactment, FDA is instructed to open a public docket to solicit comments on factors that should be considered when reviewing requests from sponsors of drugs subject to REMS to change third-party vendors used to aid in the implementation and management of the REMS. The factors to be considered include the potential effects of changes in third-party vendors on patient access and prescribing and administration of the drugs by healthcare providers. The GAO will submit a report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate no later than December 31, 2026.

² 21 U.S.C. § 355-1(e)(4)(B).

³ 21 C.F.R. § 1300.05.

⁴ 21 C.F.R. § 314.94(a)(9)(iii-iv).

While the public docket is not specific for any one REMS program, healthcare professionals and patients have had ongoing difficulties with the Clozapine REMS program which has led FDA to temporarily exercise enforcement discretion with respect to certain program requirements.⁵

Sec. 3224. Enhancing access to affordable medicines.

Generic drugs are generally required to have labeling that is identical to the reference listed drug (“RLD”), meaning that if the RLD labeling changes while the ANDA is under review by FDA, the sponsor would need to update the labeling, likely delaying approval. FDORA will allow for approval of an ANDA whose proposed labeling differs from that of the RLD if the RLD labeling was changed within 90 days of when the ANDA would otherwise be eligible for approval, so long as the RLD’s labeling change was not to the “Warnings” section. If such a labeling change occurs while the ANDA is under review, the ANDA sponsor must agree to submit revised labeling no later than 60 days after approval.

SUBTITLE C—MEDICAL DEVICES

Sec. 3301. Dual submission for certain devices.

Sec. 3302. Medical Devices Advisory Committee meetings.

Sec. 3303. GAO report on third-party review.

Sec. 3304. Certificates to foreign governments.

Sec. 3305. Ensuring cybersecurity of medical devices.

Sec. 3306. Bans of devices for one or more intended uses.

Sec. 3307. Third party data transparency.

Sec. 3308. Predetermined change control plans for devices.

Sec. 3309. Small business fee waiver.

Sec. 3301. Dual submission for certain devices.

This section allows the holder of an emergency use authorization (“EUA”) for an in vitro diagnostic device that FDA has determined meets the criteria for use in CLIA-waived settings (e.g., physician offices) to submit a single application comprising a de novo request for classification and a request for CLIA waiver. This dual-submission approach is ordinarily permitted only for IVD devices eligible for 510(k) clearance. The

⁵ FDA, FDA is temporarily exercising enforcement discretion with respect to certain Clozapine REMS program requirements to ensure continuity of care for patients taking clozapine (Nov. 2, 2022), <https://www.fda.gov/drugs/drug-safety-and-availability/fda-temporarily-exercising-enforcement-discretion-respect-certain-clozapine-rems-program>.

provision foreseeably will streamline the process for getting COVID-19 diagnostics into non-laboratory setting even after the government-declared health emergency ends.

Sec. 3302. Medical Device Advisory Committee meetings.

This section directs FDA to convene a medical device advisory committee panel at least once a year to advise on topics related to medical devices, including IVDs, used in pandemic preparedness and response. At least one panel member must have expertise in population health.

Sec. 3303. GAO report on third-party review.

This section directs the GAO to submit a report to Congress addressing FDA's 510(k) third-party review program by September 30, 2026. The report must include a description of the resources used to carry out the program and the actions taken by FDA related to accreditation of third-party reviewers, and results of an audit of the performance of select accredited entities.

Sec. 3304. Certificates to foreign governments.

This provision directs FDA to grant requests for a Certificate to Foreign Government ("CFG") for foreign-manufactured devices imported or offered for import into the United States, provided the device complies with applicable provisions of the FD&C Act, including registration and listing and premarket authorization if needed. This provision broadens the availability of CFGs for foreign-manufactured devices.

Sec. 3305. Ensuring cybersecurity of medical devices.

This section establishes several new requirements aimed at enhancing medical device cybersecurity. First, it expands the scope of cybersecurity-related information that sponsors must include as part of premarket submissions for devices meeting the definition of a "cyber device." A cyber device includes standalone software or software included in a medical device that is validated, installed, or authorized by the sponsor of the premarket submission, can connect to the internet, and contains characteristics validated, installed, or authorized by the sponsor that could be vulnerable to cybersecurity threats. Sponsors must submit a plan to monitor, identify, and address postmarket cybersecurity vulnerabilities, including through disclosure of such vulnerabilities, must maintain processes and procedures to provide "reasonable assurance" that the device and related systems are cybersecure, and must make postmarket updates and patches available when vulnerabilities are identified. Sponsors also must provide FDA with a software bill of materials that includes commercial, open source, and off the shelf software components. FDA may exempt certain devices from meeting these requirements.

Second, this section makes it a prohibited act under 21 USC 331 to fail to comply

with any requirement relating to ensuring device cybersecurity. These provisions take effect 90 days after the enactment of FDORA. Submissions made prior to that date are not required to meet the new requirements.

Third, this section directs FDA to issue updated guidance for addressing cybersecurity in premarket device submissions within two years and directs FDA to update its website with information on improving device cybersecurity within 180 days.

Finally, this section directs the GAO to publish a report within one year of enactment identifying challenges in cybersecurity for medical devices.

Sec. 3306. Bans of devices for one or more intended uses.

This section overturns a court decision to give FDA authority to ban a device for specific intended uses while allowing it to be marketed for other intended uses, and states that a device that has been banned for a specific intended use is not lawfully marketed when intended for such use.

Sec. 3307. Third party data transparency.

This section requires FDA to request the datasets and other components underlying or comprising third party analyses, conclusions or findings funded by or prepared under contract with FDA. If such findings are used to support regulatory decision making, FDA must provide manufacturers a summary of such information to the extent possible. This section also directs FDA to prepare a report regarding the number of postmarket device signals communications issued by FDA, the source of data for such signals, and how they were reviewed or resolved. The report must be submitted to Congress and published on FDA's website. The first report must be completed by September 30, 2023, and subsequent reports must be prepared every two years.

Sec. 3308. Predetermined change control plans for medical devices.

This section allows postmarket changes to be made to a device marketed pursuant to a 510(k) or PMA without the need for a supplemental application provided that the changes are consistent with a predetermined change control plan, the device would remain safe and effective without any change and, in the case of a 510(k) device, the modified device remains substantially equivalent to the predicate.

The plan must be submitted as part of the original marketing application and approved by FDA. FDA may require the plan to include labeling for safe and effective use as the device changes pursuant to the plan, notification if the device does not function as intended, and performance requirements for changes made under the plan. It states that a 510(k)-cleared device modified pursuant to a change control plan cannot be used as a predicate device; only the version of the device initially authorized by FDA may be

used as a predicate.

Sec. 3309. Small business fee waiver.

Section 3309 authorizes FDA, starting October 1, 2024, to waive establishment registration fees for businesses reporting \$1 million or less of gross receipts or sales in the most recent federal tax returns, including affiliate returns, if FDA determines that paying the fee for that year would represent a financial hardship.

SUBTITLE D—INFANT FORMULA

Sec. 3401. Protecting infants and improving formula supply.

Section 3401 includes several requirements to address the regulatory shortcomings made evident by the national shortage of infant formula that developed last year. Some of those requirements also extend to medical foods.

In several ways, section 3401 gives Congress more direct visibility into the regulation of infant formula. FDA is required to submit annual reports to Congress that provide information on the agency's receipt of new infant formula notifications and its inspectional activity. In the wake of an infant formula recall, FDA must promptly notify Congress, and must also transmit to Congress the manufacturer's plan to backfill its supply if the recall impacts over 10% of the formula intended for sale in the U.S. More broadly, FDA is required to submit to Congress a national strategy on infant formula to increase supply chain resiliency, protect against potential causes of disruption, and ensure that parents have access to infant formula.

The legislation also includes measures to ease market entry and augment formula availability. It provides immediate relief by allowing importation for personal use from Canada and the EU during the first 90 days after enactment, without the need to notify FDA. Authority is also granted FDA to waive requirements to facilitate importation of specialty infant formula (e.g., formula for infants with inborn errors of metabolism). Further, in cases of shortage, the requirement to submit a new infant formula notification to FDA at least 90 days prior to market is shortened to 30 days.

Finally, the legislation directs FDA to establish an Office of Critical Foods within the Center for Food Safety and Applied Nutrition to coordinate activities related to "critical foods," which are defined to include infant formula and medical foods. Manufacturers of a critical food are required to have a redundancy risk management plan that evaluates risks to the supply of that food, for each manufacturing establishment. Further, the manufacturer of a critical food is required to notify FDA within five business

days of a permanent discontinuance or interruption that is likely to lead to a meaningful disruption in the supply of that food.

Taken together, these and other changes ensure that infant formula will continue to be subject to strict regulatory requirements, while providing some flexibility to ease barriers to market entry. In the long term, this legislation has the potential to significantly alter the competitive landscape for infant formula in the U.S.

SUBTITLE E—COSMETICS

Sec. 3501. Short title.

Sec. 3502. Amendments to cosmetic requirements.

Sec. 3503. Enforcement and conforming amendments.

Sec. 3504. Records inspection.

Sec. 3505. Talc-containing cosmetics.

Sec. 3506. PFAS in cosmetics.

Sec. 3507. Sense of the Congress on animal testing.

Sec. 3508. Funding.

Sec. 3501. The Modernization of Cosmetics Regulation Act of 2022.

For more than a decade, cosmetics stakeholders have been working to modernize FDA’s regulation of cosmetic products, which had not changed significantly since 1938. The Modernization of Cosmetics Regulation Act of 2022 (“MOCRA”) amends Chapter VI of the FDC Act, significantly expanding FDA’s authority over and regulation of cosmetic industry and cosmetic products.

Before the enactment of MOCRA, the FDC Act requirements for cosmetics included some bare bones provisions concerning the definition of an “adulterated” cosmetic which related to “filthy, putrid or decomposed substance[s]” and “prepared, packaged or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.” FDC Act § 601(b)&(c). MOCRA expands this definition to include conditions that do not meet the good manufacturing practice (GMPs) requirements and cosmetic products (and ingredients) for which a company does not possess adequate substantiation for safety. Although MOCRA’s focus is on safety, it adds several new cosmetic misbranding provisions to section 602. In addition, it adds several new prohibited acts to FDC Act § 301.

MOCRA significantly expands FDA’s enforcement authority, with provisions for

mandatory recalls, inspections, and access to records. In addition, it mandates that FDA issue regulations on GMPs, regulations regarding fragrance allergens, evaluates use and safety of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in cosmetics, and develops and publish a test for asbestos in talc. MOCRA also imposes a range of new requirements on the cosmetic industry, including registration and product listing requirements, adverse event reporting, compliance with GMPs, labeling requirements related to fragrance allergens, and requirements for labeling of products to be used by licensed professionals. Below the relevant provisions are discussed in detail.

Sec. 3502. Amendments to cosmetic requirements.

This section adds to the FDC Act, new definitions (§ 604), adverse event reporting requirements (§ 605), a provision requiring that FDA develop GMPs (§ 606), facility registration and product listing (§607), a requirement or safety substantiation for cosmetic products (§ 608); new labeling requirements (§ 609); a provision authorizing FDA access certain records (§ 610); a provision giving FDA mandatory recall authority (§ 611); a definition of small businesses exempt from certain requirements under the FDC Act (§ 612) and a new preemption provision (§ 614).

New Definitions

New section 604 sets out definitions for several terms: (serious) adverse event, facility, cosmetic product, and responsible person. Compared to the definition for serious adverse event in the context of dietary supplements and over-the-counter (OTC) drugs, the term serious adverse event for cosmetics is expanded to include an event that results in an infection or “significant disfigurement (including serious and persistent rashes, second- or third-degree burns, significant hair loss, or permanent or significant alteration of appearance), other than as intended, under conditions of use that are customary or usual.” FDC Act § 604(5)(A)(vi), § 760(a)(3).

Facility is defined as “any establishment . . . that manufactures or processes cosmetic products distributed in the United States.” The definition includes a list of exceptions, such as facilities that prepare products for research, cosmetic retailers, etc. Importantly, the term facility does not include “[a]n establishment that solely performs one or more of the following with respect to cosmetic products: (I) Labeling. (II) Relabeling. (III) Packaging. (IV) Repackaging. (V) Holding. [and] (VI) Distributing.” FDC Act § 604(3)(B)(viii). As a result, these establishments need not register or list products.

Expanded FDA Enforcement Authority

MOCRA grants FDA several enforcement authorities.

Mandatory Recall Authority (FDC Act § 611): FDA may order a recall of a cosmetic product when the Agency determines that:

- There is a “reasonable probability” that a cosmetic is adulterated or misbranded under the FDC Act;
- The use or exposure to the cosmetic will cause serious adverse health consequences or death; and
- The responsible individual or entity has refused to voluntarily recall the product or cease distribution.

Suspension of Facility Registration: FDA may suspend facility registration if the Agency determines that a product manufactured at that facility has a “reasonable probability of causing serious adverse health consequences” and that other products manufactured by the facility may be similarly affected. FDC Act § 607. Suspended facilities will be entitled to notice and an opportunity for a hearing to determine whether the suspension is necessary and, if so, will be required to develop corrective action plans. Cosmetic products from a suspended facility may not be introduced into commerce. The provisions regarding suspension of cosmetics facilities are similar to the current process for food facilities.

Access to Records: MOCRA gives FDA the right to access certain records pertaining to product safety and to request a list of ingredients in a product’s fragrances or flavors if the Agency has reason to believe that a fragrance or flavor contributed to a serious adverse event. FDC Act § 610.

Expanded Agency Rulemaking Authority

MOCRA requires that FDA develop and issue several regulations.

GMPs: FDA must develop GMPs consistent with national and international standards by 2024, with a final rule no later than 2025. FDA last issued revised nonbinding cosmetic GMP guidance in 2013. The GMP regulations may provide FDA with authority to inspect records to demonstrate compliance with GMPs. The regulations are to “take into account the size and scope of the businesses engaged in the manufacture of cosmetics, and the risks to public health posed by such cosmetics.” FDC Act § 606(b). Moreover, FDA must promulgate simplified GMPs for smaller businesses (e.g., include longer compliance times). Small businesses, as that term is defined in FDC Act § 612(a), are exempt from GMP requirements unless they manufacture or process specific cosmetics, which carry a higher safety risk, i.e., cosmetics that come into contact with mucus membrane of the eye, cosmetics that are injected, cosmetics intended for internal use, cosmetics that are intended to alter appearance for more than 24 hours. FDC Act § 612(b). MOCRA mandates that, before FDA issues GMP regulations, it consults with cosmetics manufacturers and consumer organizations.

Labeling of Fragrance Allergens: No later than 18 months after enactment of MOCRA, FDA must issue a notice of proposed rulemaking promulgating a regulation specifying fragrance allergens that must be disclosed on the label of a cosmetic product. FDC Act § 609(b). No later than 180 days after the date on which the public comment period for the proposed rulemaking closes, FDA must issue a final rulemaking. In promulgating the fragrance allergen labeling regulation, FDA must consider international, State, and local requirements for allergen disclosure, including the substance and format of requirements in the European Union, and may establish threshold levels of amounts of substances subject to disclosure pursuant to such regulation. A cosmetic product label that does not include a required fragrance disclosure will be considered misbranded under FDC Act § 602(b).

Asbestos in Cosmetics: MOCRA mandates that FDA issue a regulation to establish and require standardized testing methods for detecting and identifying asbestos in talc-containing cosmetic products. The proposed regulation must be issued no later than one year after enactment of MOCRA, and a final rule must be issued no later than 180 days after the close of the public comment period for the proposed rule. FDORA § 3505.

MOCRA further requires that FDA evaluate the use of PFAS in cosmetic products and the safety of such use in cosmetic products, and mandates that the Agency publish a report on its findings no later than three years after enactment of MOCRA. FDORA § 3506.

New Requirements for the Cosmetic Industry

MOCRA imposes several significant new requirements on the cosmetic industry. Requirements that do not depend on FDA action (rulemaking) are effective within one year after enactment of MOCRA, except that the requirement for identification of contact information for adverse event reporting information on the label is effective two years after enactment of MOCRA.

Facility registration for any domestic or foreign facility that manufactures or processes cosmetic products intended for sale in the United States within one year of the MOCRA's enactment for existing facilities, and for new facilities, the later of 60 days after commencement of manufacture or 60 days after the deadline for existing facilities. FDC Act § 607. As noted earlier, the definition of facility excludes establishments that are solely involved in labeling, relabeling, packaging, repackaging, holding and distributing. Foreign facilities must have a U.S. agent. Registrations must be renewed biennially, and FDA must be notified within 60 days of any changes to information registrants are required to submit as part of registration.

Product and ingredient listing, including location of manufacture, effective within one year of the MOCRA's enactment for existing products, and within 120 days of marketing for new products. FDC Act § 607(c). Note that listing does not include a requirement for label submission. In addition, a single listing submission for a cosmetic product may include multiple cosmetic products with identical formulations, or formulations that differ only with respect to colors, fragrances or flavors, or quantity of contents. FDC Act § 607(c)(4)(B). The law does not include requirements for FDA to develop a registration and listing platform and it remains to be seen if the Agency will use the platform currently used for voluntary registration and product listing.

Updated Cosmetic Labeling Requirements: MOCRA includes several labeling related provisions, i.e., a requirement for:

- Identification of contact information for adverse events on cosmetic product labels (effective two years after MOCRA's enactment);
- Identification of fragrance allergens on product labels consistent with the new regulation FDA must develop; and
- Labeling for products intended for professional use. Prior to MOCRA, cosmetic products for use by licensed professions were subject to minimal labeling requirements, i.e., a net content statement and the name and address of the manufacturer, packer or distributor. New section 609(c) requires that the label for a cosmetic product for use by license professionals include:
 - A clear and prominent statement that the product must be administered or used only by licensed professionals; and
 - Must be labeled “in conformity with the requirements of the Secretary for cosmetics labeling under [the FDC] Act and section 4(a) of the Fair Packaging and Labeling Act.”

Safety Substantiation and Records: New FDC Act § 608 requires that the responsible person “ensure, and maintain records supporting [an] adequate substantiation of safety of [each] cosmetic product.” This includes tests, studies, research, analyses or “other evidence or information” that is deemed by experts to be “sufficient to support a reasonable certainty that a cosmetic product is safe” and not injurious to its user under the listed conditions of use. For purposes of determining whether a product is safe, FDA may consider, as appropriate and available, the cumulative or other relevant exposure to the cosmetic product or any ingredient in the product. Coal-tar hair dye products are exempt from the safety substantiation requirements and remain subject to the provisions in section 601 of the FDC Act for such products. Responsible persons for coal-tar hair dyes must maintain records related to the safety of such products.

Adverse Event Reporting Requirements: The new requirements for adverse event reporting for cosmetics, FDC Act § 605, are similar to the requirements for serious

adverse event reporting requirements for dietary supplements and OTC drugs, *see id.* §§ 760 & 761. Responsible parties required to report adverse events include those who manufacture, pack, or distribute the cosmetic product whose name appears on the cosmetic product's label. FDC Act § 605. Responsible parties must keep records on adverse events associated with the use of the cosmetic for three years (for small businesses) to six years (for other businesses). We note that the requirement for contact information for the responsible person for receipt of adverse event reports includes electronic contact information, in addition to the domestic address and the domestic phone number. Electronic contact information is not an option OTC drugs and dietary supplements.

Preemption

FDC Act § 614 preempts state and local requirements differing from the updated federal framework relating to:

- Cosmetic product establishment registration and product listing;
- Good manufacturing practice;
- Recordkeeping;
- Recalls;
- Adverse event reporting; and
- Safety substantiation.

However, MOCRA does not amend the FDC Act to block states from prohibiting or limiting the amount of an ingredient in a cosmetic product or continuing any state requirements regarding ingredient reporting that are in effect at the time of the MOCRA's enactment, such as California's Proposition 65. FDC Act § 614. The preemption provision further clarifies that MOCRA, nor any other requirement shall be construed to modify, preempt, or displace any actions for damages or the liability of any person under the law of any state, whether statutory or based in common law. *See id.*

Cosmetics with Active Pharmaceutical Ingredients or Making "Drug" Claims

FDC Act § 613 clarifies that for products considered both a drug and a cosmetic under the FDC Act, drug requirements of Chapter V of the FDC Act apply instead of the cosmetic requirements of Chapter VI, except with regard to fragrance allergen disclosure and professional use labeling requirements mentioned above.

Small Business Accommodations

New section 612 exempts small businesses, defined as owners and operators whose average gross annual domestic sales for the previous three years is less than \$1 million, from the requirements pertaining to good manufacturing practices and

establishment registration and product listing, with the exception of those that manufacture the following products:

- Injectables;
- Cosmetics intended for internal use;
- Products that alter appearance for more than 24 hours under normal use; or
- Products that regularly come into contact with the mucus membrane of the eye.

Sec. 3503. Enforcement and conforming amendments.

This section describes the specific amendments to the prohibited acts under section 301; the amendment to adulterated cosmetics, misbranded cosmetics and adverse event reporting.

Sec. 3504. Records inspection.

This section amended section 704(a)(1) of the FDC Act by inserting a statement about inspecting the records of cosmetic facilities.

Sec. 3505. Talc-containing cosmetics.

Sec. 3506. PFAS in cosmetics.

These sections concern the mandate that FDA investigate PFAS and develop a test for asbestos in talc mentioned above.

Sec. 3508. Funding.

Unlike previously proposed legislation for modernization of cosmetic law, MOCRA does not impose industry user fees. Instead, Congress appropriated to FDA \$14.2 million for fiscal year 2023, \$25.96 million for fiscal 2024 and \$41.89 million for each of fiscal years 2025 through 2027 for developing regulations and performing the other activities under MOCRA. FDORA § 3508.

What MOCRA Does Not Include

Unlike previous proposals for modernization of cosmetic regulation, MOCRA does not prohibit certain substance and does not require that FDA evaluate safety of cosmetic ingredients, other than PFAS. Also, it does not prohibit or otherwise restrict the use of animal testing for cosmetics. It merely includes a statement that “[a]t the sense of the Congress that animal testing should not be used for the purposes of safety testing on cosmetic products and should be phased out with the exception of appropriate allowances.” FDORA § 3507.

MOCRA does not address labeling (other than the provisions discussed above related to fragrance allergens, products indented for professionals and identification of responsible party for adverse event reporting), such as meaning of terms “clean,” “natural,” “nontoxic” or “cruelty-free,” and so-called greenwashing or environmental impact concerns. Furthermore, it does not alter the legal framework that cosmetics that contain active pharmaceutical ingredients are drugs. Also, it does not change the legal framework that cosmetics making drug claims such as structure function claims will be deemed drugs. In addition, MOCRA does not affect the relationship between the Federal Trade Commission and FDA regarding the regulation of the advertising and promotion of cosmetics.

Conclusion

MOCRA significantly expands FDA’s rulemaking and enforcement authority over cosmetics and several gaps in the existing regulatory framework. New rules and regulations are coming over the next three years and FDA now has authority to recall products and shut down facilities. It establishes a heightened standard for safety substantiation, i.e., reasonable certainty of safety threshold and cosmetic GMP regulations expand FDA’s inspection authority.

SUBTITLE F—CROSS-CUTTING PROVISIONS

CHAPTER 1—CLINICAL TRIAL DIVERSITY AND MODERNIZATION

Sec. 3601. Diversity action plans for clinical studies.

Sec. 3602. Guidance on diversity action plans for clinical studies.

Sec. 3603. Public workshops to enhance clinical study diversity.

Sec. 3604. Annual summary report on progress to increase diversity in clinical studies.

Sec. 3605. Public meeting on clinical study flexibilities initiated in response to COVID–19 pandemic.

Sec. 3606. Decentralized clinical studies.

Sec. 3607. Modernizing clinical trials.

FDORA enacts several provisions that aim to modernize clinical trials of both drugs and medical devices, make them more resilient in situations like the COVID-19 shutdowns, and make them more clinically relevant to the U.S. patient population.

Sec. 3601. Diversity action plans for clinical studies.

In 2012, under the Food and Drug Administration Safety and Innovation Act (“FDASIA”), Congress directed FDA to investigate racial and ethnic diversity in clinical trials research participants. FDA took numerous efforts in that regards since then to increase diversity in clinical trials, most recently by publishing draft guidance on increasing enrollment from underrepresented subgroups of the population.⁶ Now, FDORA Section 3601 requires sponsors to consider diversity in nearly every pivotal clinical study for the approval, licensing, or clearance of most drugs and devices by requiring them to submit diversity action plan when they submit key trial documents to the FDA. This requirement will apply to all clinical trials that commence enrollment after 180 days following FDA’s publication of final guidance on the topic. Under Section 3602, Congress directs FDA to develop guidance on the format and content of diversity action plans.

FDORA adds Section 505(z) and 520(g)(9) to the FDC Act to enact this new requirement for drugs and devices, respectively. Once the new provisions go into effect, drug sponsors conducting a phase three study or another pivotal study (but not bioavailability or bioequivalence studies) must submit a diversity action plan to FDA by the time they submit their study protocol. For devices that require an Investigational Device Exemption (“IDE”) application, the sponsor must submit a diversity action plan for clinical studies for their investigational device. Finally, devices that do not require an IDE—except for devices that are being studied under the exemption from the IDE regulations in 21 C.F.R. § 812.2(c)—must also develop a diversity action plan and submit it with any premarket notification under 510(k), request for de novo classification under 513(f)(2), or PMA. The Act specifically exempts diversity action plan requirements for submissions made through the FDC Act expanded access provisions under Section 561.

FDA may waive the requirement to submit a diversity action plan if a waiver is necessary due to the prevalence or incidence of the disease or condition that is the subject of the trial or the patient population that may use the drug or device, or if implementing a diversity action plan would be impracticable, or against the public health interest during a public health emergency. FDA may apply a waiver on its own initiative or at the request of a sponsor. If a sponsor requests a waiver, FDA must grant or deny a waiver within 60 days of receiving such a request.

Sec. 3602. Guidance on diversity action plans for clinical studies.

Section 3602 of FDORA requires FDA to issue or update guidance on the format

⁶ FDA, Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry; Availability (Apr. 2022), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations>.

and content of racial and ethnic diversity action plans within twelve months of its enactment. The Act requires each diversity action plans to describe (1) the sponsor's goals for clinical study enrollment, disaggregated by age group, sex, and racial and ethnic demographic characteristics of clinically relevant study populations, which may include characteristics such as geographic location and socioeconomic status; (2) the rationale for these enrollment goals, including information about (a) the disease or condition and its prevalence or incidence; (b) its pharmacokinetics or pharmacogenetics; (c) its patient population, including demographic (e.g., age group, sex, race, geographic location, socioeconomic status, ethnicity) and non-demographic data (e.g., comorbidities); (d) potential barriers for enrolling diverse participants (e.g., patient population size; geographic location; socioeconomic status); and (e) any other information relevant to selecting their enrollment goals disaggregated by demographic subgroups (e.g., inclusion of pregnant or lactating women); and (3) how the sponsor intends to meet such goals, including demographic-specific outreach and enrollment strategies, study-site selection, clinical study inclusion and exclusion practices, and any diversity training for study personnel.

FDORA also requires the guidance to cover issues around the public posting of key information from the diversity plan on the sponsor's website; criteria that the Agency will consider in assessing sponsor waiver requests; periodic reporting requirements of the sponsor's progress towards its recruitment goals, and whether updates are needed to the plan to reach those goals; and the process to submit modifications to the diversity action plans or notifications that a sponsor does not expect to reach the goals, and why. FDORA requires FDA to finalize such guidance within nine months of the closing of the comment period of the draft guidance.

Sec. 3603. Public workshops to enhance clinical study diversity.

FDORA Section 3603 requires FDA to convene public workshops on increasing the enrollment of historically underrepresented populations in clinical studies and encouraging clinical study participation that reflects the prevalence of the disease or condition among demographic subgroups, open a public docket to receive written comments on the topics discussed therein, and publish a report within 180 days following each such workshop on the recommendations raised in the workshop.

Sec. 3604. Annual summary report on progress to increase diversity in clinical studies.

FDORA Section 3604 requires FDA to report an annual report summarizing the Agency's aggregated experience with sponsors' diversity action plans beginning not later than two years after FDORA is enacted.

Sec. 3605. Public meeting on clinical study flexibilities initiated in response to COVID-19 pandemic.

Within 180 days of the lifting of the COVID-19 public health emergency, FDORA requires FDA to convene a public meeting to discuss with industry and patient stakeholders their experience with FDA’s strategies to mitigate clinical trials disruption during the emergency and publish a report on that discussion. FDA published these strategies in a guidance that was last revised in August 2021.⁷

Congress directs FDA to discuss —how and how often industry used FDA recommendations; characteristics of the studies, patients, and sponsors impacted by the recommendations; how the recommendations intended to mitigate disruption of clinical studies may have affected access to clinical studies for certain patient populations, especially unrepresented or underrepresented racial and ethnic minorities; and additional study disruption mitigation strategies that can improve enrollment by diverse patient populations.

Sec. 3606. Decentralized clinical studies.

Sec. 3607. Modernizing clinical trials.

Sections 3606 and 3607 of FDORA require FDA to issue or revise draft guidance to address the changing nature of clinical trials in the modern world including the use of decentralized studies, digital health technologies, and complex and novel trial designs.

Section 3606 requires FDA to publish guidance to advance the use of decentralized clinical trials, defined as clinical studies in which some or all of the study-related activities occur at a location separate from the investigator’s location.⁸ The guidance would include recommendations on using flexible and novel clinical trial designs and to improve trial participant enrollment by diverse populations, when appropriate. Congress directs FDA to address several topics in this guidance: recommendations on selecting and validating technological platforms for data collection; the use of electronic informed consent; strategies to communicate with remote participants; shipping investigational drugs and devices directly to participants; establishing clinical endpoints in such trials; remote data collection and assessment tools, including using local providers to collect data, and; evaluating data collected in a decentralized clinical trial setting. The guidance should discuss strategies to reduce the burden for clinical trial participants using digital technologies, to facilitate meaningful

⁷ FDA, FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID–19 Public Health Emergency (Aug. 2021), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency>.

⁸ See Division FF, Title III, Subtitle F, Chapter 1, Section 3606(c).

inclusion by underrepresented populations, and protect the privacy and security of participant data.

Finally, the guidance should address designing and evaluating decentralized clinical trial protocols, hybrid centralized and decentralized approaches, and institutional review board (IRB) and sponsor oversight of decentralized clinical trial. FDORA requires FDA to issue a draft guidance within one year of its enactment and finalize it within one year of the close of the draft guidance comment period.

The last section of Subtitle F, Chapter 1 requires FDA to issue or revise two guidance documents within a year of its enactment and finalize them by 18 months after the public comment period to the draft guidance closes. The first guidance would outline FDA's position on the use of digital health technologies in clinical trials to help improve recruitment and data collection. FDA has not provided much guidance on the use of digital health technologies for clinical trials, even though industry has been using them for some time, especially during the COVID-19 public health emergency.⁹

Congress lists several topics for FDA to address in such a guidance document. For example, this guidance should include recommendations on using digital health technologies to acquire electronic informed consent and collect data remotely, while complying with various data privacy and human subjects protection laws and regulations; how FDA and sponsors would communicate to develop such data collection methods; how FDA would assess or evaluate data collected through digital health technologies, and; how the sponsor would validate digital health technology for use in a particular clinical trial. The guidance should also describe how novel data collection methods can facilitate clinical trial participant recruitment, particularly by diverse and underrepresented populations while optimizing data quality and data submission formats.

The second guidance Congress requires under Section 3607 would address the use of seamless, concurrent, and other innovative clinical trial designs to support the expedited development and review of applications for drugs. This section does not specifically reference medical devices. FDA has previously issued final guidance on the biostatistical considerations when using seamless trials and other adaptive clinical trial designs.¹⁰ More recently, FDA committed to enhancing its capacity to review complex adaptive, Bayesian, and other novel clinical trial designs.¹¹ In the new guidance,

⁹ See, e.g., Caroline Marra, William J Gordon & Ariel Dora Stern, Use of connected digital products in clinical research following the COVID-19 pandemic: a comprehensive analysis of clinical trials, *BMJ Open* (May 2021), <https://bmjopen.bmj.com/content/11/6/e047341>.

¹⁰ FDA, Adaptive Design Clinical Trials for Drugs and Biologics Guidance for Industry (Dec. 2019), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/adaptive-design-clinical-trials-drugs-and-biologics-guidance-industry>.

¹¹ See PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027, VII Performance Goals at 41-42, <https://www.fda.gov/media/151712/download>.

Congress directs FDA to address recommendations related to the use of expansion cohorts and other seamless clinical trial designs to assess different aspect of product candidates in one continuous trial and how these designs can meet the FDC Act’s “substantial evidence standard” for drug approval.¹²

The guidance should include recommendations on concurrently conducting preclinical testing with multiple clinical trial phases to expedite the development of new drugs and facilitate the timely collection of data, recommendations on streamlining trial logistics, data collection and analysis, and data review to facilitate product development. The guidance should assist sponsors in complying with regulations regarding good clinical practice (“GCP”), clinical trial data integrity and reliability, and the rights and welfare of clinical trial participants. The guidance should outline FDA’s plans to communicate with sponsors on developing seamless, concurrent, or other adaptive clinical trial designs, including the review and feedback on protocols, and FDA’s approach to assessing data collected through such trials.

Finally, FDORA encourages FDA to work with foreign regulators to facilitate international harmonization of the regulation and use of decentralized clinical trials, digital technology in clinical trials, and seamless, concurrent, and other adaptive or innovative clinical trial designs.

CHAPTER 2—INSPECTIONS

Sec. 3611. Device inspections.

Sec. 3612. Bioresearch monitoring inspections.

Sec. 3613. Improving Food and Drug Administration inspections.

Sec. 3614. GAO report on inspections of foreign establishments manufacturing drugs.

Sec. 3615. Unannounced foreign facility inspections pilot program.

Sec. 3616. Enhancing coordination and transparency on inspections.

Sec. 3617. Enhancing transparency of drug facility inspection timelines.

Sec. 3611. Device inspections.

Section 3611 on device inspections revises §§ 704(a)(1) and 704(a)(4)(A) of the Act related to factory inspection. The revision replaces “restricted devices” with “devices” in § 704(a)(1) to more broadly authorize inspection of all things, including records, files, papers, processes, controls, and facilities, that may be used to determine whether devices are in violation of the act. Importantly, the revision to § 704(a)(4)(A)

¹² FDC Act 505(d).

allows for a request for any records or other information that may be inspected to be requested in advance or in lieu of an inspection, formally opening the door for remote inspections. This language previously applied only to drug inspections.

In addition, for both drug and device inspections, the request for records or information in advance or in lieu of an inspection must include a rationale for the request. FDA must issue guidance to describe: the circumstances in which a request for records or other information may be issued in advance of, or in lieu of, an inspection; processes for responding to such requests electronically or in physical form; and factors that will be considered in evaluating whether such records and other information are provided within a reasonable timeframe, within reasonable limits, and in a reasonable manner, accounting for resource and other limitations that may exist, including for small businesses. Draft guidance is expected in one year with final guidance one year after the draft.

Sec. 3612. Bioresearch monitoring inspections.

Section 704(a)(5) was added to clarify the authority for inspections related to clinical and nonclinical studies used for marketing authorization, postmarket safety activities, or any other clinical investigation of a drug or device. Section 704(a)(5)(F) further clarifies that the authority and conduct of inspections described “shall not be construed as a basis for inferring that, prior to the date of enactment of this paragraph, the Secretary lacked the authority to conduct such inspections.”

Applicable sites and facilities related to studies that may be inspected are those involved with developing an application or submission for marketing authorization; preparing, conducting, or analyzing the results of a study; or holding records or other information and that are owned or operated by the sponsor, an organization contracted on behalf of the sponsor, an institutional review board, or organization engaged with a non-sponsor in preparing, collecting, or analyzing records or other information related to a study. Inspectors shall be permitted to access, record, and copy information from records and other information related to studies, including access to any electronic information system. FDA must issue guidance to describe processes and practices for inspections of sites and facilities, including “types of records and information required to be provided, best practices for communication between the Food and Drug Administration and industry in advance of or during an inspection or request for records or other information, and other inspections-related conduct.” § 3612(b)(2)(A). Draft guidance shall be issued no later than 18 months after date of enactment of FDORA with final guidance one year after the draft.

Sec. 3613. Improving Food and Drug Administration inspections.

Section 510(h)(4) of the Act relates to risk factors used in establishing a risk-based inspection schedule. It is amended to include compliance history of establishments in a

country or region and history of violations of products exported from a country or region to the list of risk factors considered when scheduling device and drug inspections.

Section 704(a)(4) of the Act relates to request of records in advance of or in lieu of an inspection, discussed above in § 3611 related to inclusion of devices. It is amended to include a new subparagraph (C) to indicate that any records or other information obtained in advance of, or in lieu of, inspection may be relied upon to “satisfy requirements related to preapproval or risk-based surveillance inspections, or to resolve deficiencies identified during such inspections, if applicable and appropriate.” § 3613(b)(1).

Section 809(a)(1) relates to recognition of a foreign government inspection is amended to include preapproval inspections in addition to risk-based inspections. This section is revised to include requirements for periodic review and reports to Congress.

Sec. 3614. GAO report on inspections of foreign establishments manufacturing drugs.

This section of FDORA requires the Comptroller General of the United States to submit a report to Congress related to inspections of foreign establishments manufacturing drugs performed by FDA or by a foreign government or agency. The report will cover topics related to conduct of inspections of foreign establishments by other countries, inspections that make use of agreements with other countries, use of tools used in domestic inspections for foreign inspections, steps taken to identify and evaluate tools, strategies to allow continued oversight when in-person inspections are disrupted, incorporation of alternative tools into inspection activities, and how use of alternative tools may be used to address workforce shortages.

Sec. 3615. Unannounced foreign facility inspections pilot program.

This section of FDORA requires FDA to establish a pilot program for unannounced routine surveillance inspections of foreign human drug establishments and to evaluate differences between unannounced and announced foreign inspections. The pilot program will be initiated within 180 days of enactment of FDORA. At the end of the pilot, a report will be made available including findings and recommendations related to unannounced inspections of foreign human drug establishments and how FDA may achieve parity between domestic and foreign human drug inspections.

Sec. 3616. Enhancing coordination and transparency on inspections.

This section of FDORA amends Section 506D of the Act related to the implementation of a task force and strategic plan related to drug shortages, Section 506C-1(a) of the Act related to the annual report to Congress on drug shortages, and Section 510(h) of the Act related to inspections.

FDA will ensure “timely and effective internal coordination and alignment between field investigators and CDER’s Office of Compliance and Drug Shortage Program” regarding review of inspection reports and “any feedback or corrective or preventive action in response to such reports.” § 3616(a). The sunset clause of Section 506D of the Act is also revised to a temporary sunset. The task force and strategic plan clause is still sunset five years after the enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA), while clauses related to communication, action, review and construction that had previously sunset five years after the enactment of FDASIA will be in effect under FDORA.

The annual report to Congress on drug shortages required by Section 506C-1 of the Act will include additional information on coordination and alignment of activities related to inspections of establishments associated with drug shortages. This will apply beginning with the report submitted on or after March 31, 2024.

Finally, Section 510(h) of the Act is amended to include additional information in the annual report on inspections of establishments. New information will cover the numbers of domestic and foreign inspections, establishments in each region, drug preapproval inspections, surveillance inspections, for-cause inspections, and inspections recognized via a mutual recognition agreement.

Sec. 3617. Enhancing transparency of drug facility inspection timelines.

This section of FDORA amends Section 902 of the FDA Reauthorization Act of 2017 (FDARA) related to the annual report on drug preapproval inspections to report the median time following a request until the beginning of an inspection separately for drugs, devices, and drugs on the shortage list.

CHAPTER 3—MISCELLANEOUS

Sec. 3621. Regulation of certain products as drugs.

Sec. 3622. Women’s Health Research Roadmap.

Sec. 3623. Strategic workforce plan and report.

Sec. 3624. Enhancing Food and Drug Administration hiring authority for scientific, technical, and professional personnel.

Sec. 3625. Facilities management.

Sec. 3626. User fee program transparency and accountability.

Sec. 3627. Improving information technology systems of the Food and Drug Administration.

Sec. 3628. Reporting on mailroom and Office of the Executive Secretariat of the Food and Drug Administration.

Sec. 3629. Facilitating the use of real world evidence.

Sec. 3630. Facilitating exchange of product information prior to approval.

Sec. 3631. Streamlining blood donor input.

Sec. 3621. Regulation of certain products as drugs.

Contrast agents, radioactive drugs, and OTC monograph drugs are deemed to be drugs rather than devices. This amendment addresses, in part, the *Genus* decision in which the court held that FDA did not have discretion to regulate products that meet the device definition as drugs.¹³ The application fees are waived for products legally marketed as devices as of the date of enactment that are now deemed drugs.

Sec. 3622. Women’s Health Research Roadmap.

Within two years from the date of enactment, FDA’s Office of Women’s Health (“OWH”) is instructed to review and update the Women’s Health Research Roadmap (“Roadmap”) issued in December 2015 and brief the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate on the review and any resulting updates. In the Roadmap, the OWH had identified seven broad research priority areas: advance safety and efficacy, improved clinical study design and analyses, novel modeling and simulation approaches, advances in biomarker science, expand data sources and analysis, improve health communications, and emerging technologies.¹⁴

Sec. 3623. Strategic workforce plan and report.

No later than September 30, 2023, and at least every four years thereafter, FDA is required to develop and implement a Strategic Workforce Plan to provide direction for the activities and programs of the FDA to recruit, hire, train, develop, and retain the workforce needed to fulfill the public health mission of the FDA. The strategic workforce plan issued in fiscal year 2023 will address the effect of the COVID-19 pandemic on hiring, retention, and other workforce challenges at FDA, including protecting the workforce during public health emergencies.

Sec. 3624. Enhancing Food and Drug Administration hiring authority for scientific, technical, and professional personnel.

FDA hiring authority is expanded to include “cross-cutting operational positions” in addition to scientific, technical, and professional personnel. The hiring authority will also include positions that support the development, review, and regulation of food and

¹³ *Genus Medical Technologies, LLC v. FDA*, 994 F. 3d 631 (D.C. Cir. 2021).

¹⁴ FDA, Office of Women’s Health, Women’s Health Research Roadmap (Dec. 2015), <https://www.fda.gov/science-research/womens-health-research/womens-health-research-roadmap>.

cosmetics, not solely medical products. FDA is also required to analyze how it has used the increased hiring authority that was granted by the 21st Century Cures Act in December 2016 and how it will use the authority now granted by FDORA.

Sec. 3625. Facilities management.

FDORA clarifies how user fees collected under PDUFA, GDUFA, MDUFA and BsUFA can be used to defray FDA's internal costs of resources allocated to these programs, including costs for any additional full-time equivalent positions.

Sec. 3626. User fee program transparency and accountability.

FDA will report additional data in connection with reauthorization of various user fee programs. For PDUFA, FDA will have to report the number of IND applications submitted per fiscal year for each review division, and the number of face-to-face meetings requested and granted. For MDUFA, FDA will have to report the number of IVD exemption applications submitted and the number of expedited development and priority review requests and designations per fiscal year for each review division. FDA will also solicit public input prior to BsUFA reauthorization and during negotiations and must also hold monthly discussions with representatives of patient and consumer advocacy groups.

Sec. 3627. Improving information technology systems of the Food and Drug Administration.

FDA is required to develop and submit a Data and Technology Modernization Strategy no later than September 30, 2023, and at least every four years thereafter. The Strategic Plan will include agency-wide strategic goals and priorities for modernizing the IT systems to maximize the efficiency and effectiveness of such systems.

Sec. 3628. Reporting on mailroom and Office of the Executive Secretariat of the Food and Drug Administration.

FDA is required to prepare a report to Congress detailing the operations of the FDA mailroom within 90 days from enactment. The report must include the policies and procedures related to taking receipt, tracking, managing, and prioritizing confidential informant complaints; the average number of days for response, number of whistleblower correspondence received, and information on any backlogs in the mailroom, including a rationale for the failure to respond to correspondence in any backlog. FDA must also develop and implement policies and procedures to monitor and ensure the effective receipt, tracking, managing, and prioritization of whistleblower complaints. FDA will also have to submit an annual report on the mailroom operations by the end of fiscal years 2023 and 2024.

Sec. 3629. Facilitating the use of real world evidence.

FDA is directed to issue or revise existing guidance on considerations for the use of real world data (“RWD”) and real world evidence (“RWE”) to support regulatory decision-making. RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, such as product and disease registries, electronic health records, patient-generated data. RWE is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.¹⁵ The guidances should address the use of RWD and RWE to support clearance or approval, including considerations for the inclusion of RWD and RWE obtained as a result of the use of drugs and devices authorized under an EUA during the COVID-19 pandemic. FDA is required to report on the number of applications submitted for clearance, approval, or authorization for which an EUA was previously granted within two years after the end of the public health emergency. Of those applications, FDA will provide the number of applications for which RWE was submitted and used. If RWE was submitted and determined to be insufficient to support a regulatory decision, FDA will provide a summary explanation.

Sec. 3630. Facilitating exchange of product information prior to approval.

The PIE (pre-approval information exchange) Act provides explicit protection for conveying certain information about products or product uses in development to payors and other similar entities, to help expedite patient access upon approval. The PIE Act essentially codifies the concept of pre-approval information exchange that was introduced in the payor communications guidance which was finalized in June 2018.¹⁶ Under the guidance, sponsors could provide payors with unbiased and non-misleading information about unapproved products and unapproved uses of approved products including information about indications sought, descriptions of clinical studies, anticipated timeline for possible FDA approval/clearance, product pricing, patient utilization projections, and product related programs or services.

The PIE Act clarifies that providing such truthful and not misleading information about an investigational drug or device would not render the product misbranded. When sharing pre-approval product information, sponsors must also include a clear statement that the investigational drug or device or investigational use has not been approved or cleared by FDA and that the safety and effectiveness has not been established. Sponsors must also provide complete and accurate information related to the state of development and timeline for possible approval/clearance, including the status of any studies.

¹⁵ FDA, Real-World Evidence (current as of Dec. 12, 2022), <https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence>.

¹⁶ FDA, Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities Questions and Answers, Guidance for Industry and Review Staff (June 2018), <https://www.fda.gov/media/133620/download>.

Sec. 3631. Streamlining blood donor input.

The Paperwork Reduction Act (44 USC 3501 et seq.) does not apply to FDA's collection of voluntary information from blood donors or potential blood donors to support the development of FDA's blood donation recommendations, which should allow FDA to collect this type of information more efficiently. For example, if FDA wishes to publish a notice in the Federal Register soliciting voluntary public comment from donors/potential donors on the creation of new donor eligibility requirements, it is no longer required to first consider and account for the impact on the public when soliciting information or to obtain Paperwork Reduction Act clearance.

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The information in this memorandum is not intended as legal advice. Readers should seek specific legal advice before acting with regard to the subjects mentioned herein. For more information about this memorandum or about FDORA, please contact Kurt R. Karst (kkarst@hpm.com) for issues concerning drug or biological products, or Jeffrey K. Shapiro (jshapiro@hpm.com) for issues concerning medical devices.