Health Industry Alert

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Congress' Year-End Appropriations Package Brings FDA Legislative Changes, Leaves Unresolved Policy Issues

January 10, 2023

In a break with past precedent, last year's Food and Drug Administration (FDA) user fee reauthorization legislation did not contain significant FDA policy changes. Although the Senate Health, Education, Labor and Pensions (HELP) Committee (but not the Senate) and the House of Representatives advanced significant FDA-related legislative changes, the ultimate user fee reauthorization signed into law ended up being a relatively "clean" reauthorization of the applicable user fee programs. Congress nevertheless included many FDA-related legislative changes in the Consolidated Appropriations Act, 2023 ("Omnibus" or "Act"), which President Biden signed into law on December 29, 2022.[1]

This client alert highlights FDA-related provisions in the Omnibus, including but not limited to those in the FDA-specific title, the Food and Drug Omnibus Reform Act (FDORA). This legislation represents the culmination of the user fee reauthorization legislative process for the prescription drug, medical device, generic drug and biosimilar user fee programs. The stage is now set for FDA to implement these provisions, some of which require rulemaking, guidance or other agency actions. Despite the scope of this legislation, numerous significant policy issues were not addressed, and will potentially be considered by Congress in 2023 and beyond.

Key Takeaways

- The Omnibus, including FDORA, makes important changes to several aspects of device and drug premarket review, and drug marketing exclusivity, while also enhancing or clarifying important aspects of agency enforcement authority; many of these provisions will require FDA implementation in 2023.
- Regulation of cosmetics is significantly revamped, and will also require agency implementation beginning in 2023.
- The Omnibus reauthorizes a variety of important FDA programs, such as funding incentives for orphan drugs and rare disease products.
- Numerous policy reforms under consideration in the 117th Congress were not included, notably the VALID Act (reform of in vitro diagnostics regulation), changes

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to the regulation of dietary supplements and revisions to device shortage reporting; the new Congress may continue to consider these and other areas of FDA.

1. *Appropriations*

After months of negotiations between House and Senate Appropriations leadership, the Consolidated Appropriations Act, 2023 (P.L. 117-328) passed the Senate by a vote of 68-29 on December 22. The House passed the Omnibus on December 23 by a 225-201 vote and President Biden signed the bill into law on December 29. The Omnibus provides the FDA a total of $3.5 billion in discretionary funding, a $226 million increase above the fiscal year 2022 funding level. With user fees, total FDA funding for fiscal year 2023 is $6.6 billion. Along with program reauthorizations, the Omnibus directs FDA to use $35.8 million for medical safety, $41 million for food safety activities, $122 million for cross-cutting initiatives and $50 million for accelerating medical development as authorized by the 21st Century Cures Act.

2. *Preparedness*

The Omnibus includes the Prepare for and Respond to Existing Viruses, Emerging New Threats and Pandemics Act (PREVENT Pandemics Act).[2] The enactment of the PREVENT Pandemics Act reflects the culmination of a multiyear, bipartisan legislative process with the goal of strengthening our nation's medical and public health preparedness and response framework. The timing of the enactment of these reforms and the ongoing COVID-19 response efforts raise questions about how Congress may approach reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA), provisions of which are set to expire at the end of the current fiscal year (September 30, 2023). Key themes of the PREVENT Pandemics Act include structural leadership changes, increasing accountability and transparency around preparedness and response activities through more rigorous and frequent reporting requirements, and the importance of partnerships and innovation as part of a nimble, all-hazards preparedness framework. The PREVENT Pandemics Act also includes new funding opportunities. Additional information regarding the PREVENT Pandemics Act and PAHPA Reauthorization is available here.

3. *Drugs and Biologics*

The provisions of FDORA include some, but not all, of the drug policy riders that were initially considered as part of the FDA reauthorizing legislation impacting pharmaceutical products, which we noted in our previous client alerts here and here. The following is an assessment of select provisions of FDORA that may be of the greatest interest to drug and biologic sponsors and other stakeholders:

a. Exclusivity, Orphan and Rare Disease Issues

Several FDORA provisions impact the scope and qualifications for various FDA market exclusivities.

- Interchangeable Biosimilar Exclusivity: Under section 351(k)(6) of the Public Health Service Act, 42 U.S.C. 262(k)(6), the first FDA-approved interchangeable biosimilar to a reference product receives exclusivity blocking the approval of any other interchangeability designations for the earlier of 12 months after the interchangeable product is marketed (or 18 months after its approval even if it is not marketed), 18 months after the conclusion of litigation by final court decision or

settlement or 42 months after approval of the interchangeable if litigation is ongoing. Section 3206 of FDORA now allows for multiple "first" interchangeable biosimilars to qualify for those periods of exclusivity, if they are approved on the same day. This change will significantly alter the competitive landscape for interchangeable biosimilars, providing a considerable incentive for companies to have an approvable product on the first possible day permitted under the Act (which is 12 years from the date of approval of the reference product).[3] Presumably, this would tend to significantly drive down market prices for interchangeable biosimilars (and further drive up rebates for the reference drug) where multiple sponsors have approved products in the market simultaneously. In addition to this weakening of the value of a first interchangeability designation, the industry will be closely watching for other legislative proposals that would weaken the interchangeability designation altogether.

- Enantiomer Exclusivity: Section 3105 of FDORA amends section 505(u) of the Food, Drug and Cosmetic Act ("FD&C Act") to clarify that sponsors of section 505(b)(2) applications for an enantiomer may rely on bioavailability studies of an already approved racemic drug, and still be entitled to the five years of market exclusivity available under section 505(j) of the Act. Prior to this change, the statute was more broadly worded to disallow the five-year exclusivity if the application relied on "any clinical investigations" of the already approved drug.
- Therapeutic Equivalence Determinations: FDA is required to make "therapeutic equivalence" (i.e., "A" rated) determinations based on sponsors' data submissions, including for filings under section 505(b)(2) of the FD&C Act. Section 3222 now requires FDA to make those determinations, if requested by the sponsor in the application, either at the time of approval or not later than 180 days afterward. FDA must make the determination for already approved applications 180 days after receipt of a request by the sponsor, or for applications submitted but not approved as of the effective date of the Omnibus bill, 180 days after the approval.
- Orphan Drugs: FDORA did not include a provision included in the Senate HELP Committee mark up of FDA user fee legislation last year, which would have applied orphan drug exclusivity only to the same approved use or indication within a rare disease or condition by allowing FDA to approve the same drug from different manufacturers if the products are intended to treat different patient populations. It remains to be seen whether the orphan drug exclusivity issues will be revisited in the new Congress, and how and whether FDA will address pending orphan drug exclusivity applications. However, FDORA includes a reauthorization of FDA's Orphan Products Grants Program,[4] increasing the scope of the program and its budget and requires FDA to create a Rare Disease Endpoint Advancement Pilot Program (RDEA) to facilitate work between the agency and sponsors to develop new rare disease endpoints "including surrogate and intermediate endpoints."[5]

b. Accelerated Approvals

Section 3210 contains several detailed reforms to the current FDA approach to accelerated approvals under FD&C Act section 506(c). Although FDA has taken the position that it has authority to revoke a drug's approval based on new safety or efficacy data (or certain other reasons), and has requested that sponsors voluntarily remove their accelerated approval drugs from the market in several cases, section 3210 clarifies FDA's authority to do so with new specific procedures and processes

that must be followed in such cases. These include notice to the sponsor, meetings with the agency, an opportunity for the sponsor and public to formally comment and for FDA to respond, as well as holding an advisory committee at the request of the sponsor.

Post-approval studies for accelerated approval drugs now must be specified by FDA (which may include enrollment targets, a study protocol and milestones including a target date for study completion). FDA also may require that certain of those studies already be underway at the time of accelerated approval. Section 3210 further amends section 506(c) to specifically indicate that in certain cases only one post approval study could be required by FDA (vs. the current statute's requirement for "studies"). Under the new provisions of section 3210, if FDA does not require post-approval studies as part of an accelerated approval, it must give the public notice of why they are not being required. Sponsors now must update FDA on the progress of such studies every 180 days, starting with 180 days after the initial accelerated approval is granted. The law also now explicitly makes failure to conduct the required studies a violation of the FD&C Act, by amending section 331 with new section "(ggg)," which requires sponsors to conduct such post-accelerated approval studies "with due diligence" and to "submit timely reports." As such, the law leaves open the question of whether a violation can occur where the sponsor is in fact conducting the study.

c. Animal Testing

Section 3209 amends section 505 of the FD&C Act to enable sponsors to support their drug approval packages with pre-clinical testing that is in vitro, in silico or in chemico, or a nonhuman in vivo test. Thus, for the first time, sponsors may deploy non-animal testing such as computer modeling to fully support the FD&C Act's required demonstrations of efficacy and/or safety. This section also specifically amends the Public Health Service Act to allow for non-animal biosimilar toxicity testing.

4. *Cross-Cutting Issues*

a. Clinical Trials

The Omnibus requires sponsors to submit diversity action plans for certain studies for drugs and devices, and requires FDA to issue or update its guidance regarding these plans.[6] FDA is also required to take steps to modernize clinical trials through issuing a variety of guidance documents and convening workshops, including relating to historically underrepresented populations in clinical studies;[7] flexibilities afforded during the COVID-19 pandemic;[8] digital health technologies in clinical trials; decentralized clinical trials; and use of seamless, concurrent and other innovative clinical trial designs to support expedited development and review applications for drugs.[9] FDA is also instructed to work with foreign regulators to facilitate international harmonization of regulation of decentralized clinical trials, digital health technologies in clinical trials and use of innovative clinical trial designs.[10]

b. Exchange of Product Information Prior to Approval

Section 3630 is a legislative adoption of the main themes already contained in FDA's existing 2018 final guidance on Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities (the "Payor Guidance"). Under that guidance, FDA invoked its enforcement discretion as to certain off-label and pre-approval communications about drugs or devices to "entities with knowledge and

expertise in the areas of health care economic analysis." Technically, section 3630 amends section 502 of the FD&C Act's "adequate directions for use" exception to misbranding violations by adding to the exception the "provision of truthful and not misleading product information to a payor, formulary committee or other similar entity with knowledge and expertise in the areas of health care economic analysis" as to both investigational drugs and devices (meaning off-label uses), and pre-approval and pre-clearance products. The exception is, as was the case in the Payor Guidance, limited to circumstances where the entity is "carrying out its responsibilities for the selection of drugs or devices…," which may mean that communication of the same information in a different context is not protected by the exception. The statute also similarly requires affirmative disclosure that the safety and efficacy of the product or use being discussed has not yet been established, as well as other important data disclosures. In addition, section 3630 requires the Government Accountability Office (GAO) to do a study of the kinds of information provided by sponsors to payors under these new provisions, although it does not specify how GAO will collect such information since these payor materials are not necessarily required to be filed with FDA on a Form 2253.

5. *Medical Devices*

The Omnibus legislation adopts a number of substantive changes to medical device law that had been contemplated during deliberations on the user fee reauthorization, and made a number of clarifications to FDA's authority:

- Predetermined Change Control Plans: Sponsors of devices may now include with their section 510(k) and premarket approval (PMA) submissions proposed change control plans pursuant to which the sponsor could make certain changes to the approved or cleared device without requiring a new marketing submission.[11]
- Cybersecurity: Devices that could be vulnerable to cybersecurity threats are required to include in their marketing submissions information relating to device security, identification of cybersecurity vulnerabilities and a software bill of materials.[12]
- *De Novo*/CLIA Waiver Dual Submissions: Sponsors of in vitro diagnostics authorized under emergency use authorizations (EUAs) may submit a single submission for *de novo* classification and Clinical Laboratory Improvement Amendments (CLIA) waiver designation.[13]
- Data Transparency: The agency shall seek access to data funded by FDA that may be used in regulatory decision-making for devices, provide it to the implicated manufacturers to the extent possible, and report to Congress every two years on device emerging signal communications and their resolution.[14]
- Real World Evidence: FDA shall issue guidance addressing the use of real world data and real world evidence to support device submissions, including the use of evidence obtained as a result of the use of devices under EUAs.[15]
- CFGs: Congress clarified that Certificates to Foreign Governments (CFGs) are available for device establishments located outside the United States for cleared or approved devices that are offered for import into the United States.[16]
- Enforcement Authorities: The Omnibus made numerous changes or clarifications to FDA enforcement and oversight tools, including authorizing FDA to ban a device for

a particular intended use (rather than necessarily banning the device for all uses);[17] strengthening enforcement tools relating to counterfeit devices;[18] and clarifying FDA's inspectional authority relating to non-restricted devices[19] and registration requirements for foreign device (and drug) establishments.[20]

There were other device-related provisions that Congress did not include in the Omnibus. Notably, the VALID Act, which would have significantly reformed the regulation of in vitro diagnostic tests including those offered by laboratories, was not included. Nor were proposed revisions to device shortage reporting or other potential changes to device regulatory pathways.

6. *Cosmetics*

The Omnibus includes the Modernization of Cosmetics Regulation Act of 2022 (MoCRA), which constitutes the most significant expansion of FDA's authority to regulate cosmetics since passage of the FD&C Act of 1938. Of note, MoCRA establishes a regulatory framework for cosmetics more similar to that of other FDA-regulated products, including requirements with respect to:

- Adverse event reporting;
- Maintenance and inspection of adverse event records;
- Good manufacturing practices;
- Registration and product listing;
- Safety substantiation;
- Product labeling, including identifying fragrance allergens in such product labeling;
- Mandatory recall authority; and
- Records access and inspections.

MoCRA expressly preempts certain requirements under the FD&C Act, but also provides express limitations with respect to such preemption under certain circumstances.

MoCRA also directs FDA, not later than one year after enactment, to propose regulations to establish and require standardized testing methods for detecting and identifying asbestos in talc-containing cosmetic products, and issue final regulations not later than 180 days after the date on which the public comment period on the proposed regulations closes. MoCRA also directs FDA to assess and issue a report regarding use of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in cosmetics and the scientific evidence regarding the safety of such use in cosmetics products, including any risks associated with such use.

7. *Infant Formula*

The Omnibus includes provisions related to the safety and availability of infant formula. Most notably, the Omnibus requires the establishment of an Office of Critical Foods within FDA's Center for Food Safety and Applied Nutrition. This new office is charged with responsibility for oversight, coordination and facilitation of activities related to critical foods, which are defined as infant formula or a medical food (as defined in section 5(b)(3) of the Orphan Drug Act). The Omnibus directs FDA to apply a 30-day premarket submission requirement—as opposed to a 90-day requirement—in the

instance of a shortage of infant formula. The Omnibus also seeks to harmonize international infant formula requirements by allowing the agency to enter into agreements with other countries regarding the inspection of foreign-manufactured infant formula. Further, it requires specific actions by FDA with respect to inspections of infant formula manufacturing facilities, such as annual inspections, including unannounced inspections. The Omnibus calls for a national strategy to increase the resiliency of the infant formula supply chain.

A new section 424 of the FD&C Act sets forth requirements for manufacturers of critical foods, including:

- Notification to FDA in the event of a permanent discontinuance in the manufacture or an interruption of the manufacture of such food that is likely to lead to a meaningful disruption in the United States within five business days after such discontinuance or such interruption.
- Developing, maintaining and implementing, as appropriate, risk management plans that identify and evaluate risks to the supply of the food, as applicable, for each establishment in which such food is manufactured.

8. *FDA Program Reauthorizations*

A number of FDA-administered programs requiring reauthorization were only reauthorized until mid-December 2022 in the user fee reauthorization signed into law on September 30, 2022. The Omnibus reauthorized a number of these for longer periods of time, including orphan drug grants, the Best Pharmaceuticals for Children Act incentive, the Critical Path Public-Private Partnership, third-party device review and third-party device establishment inspections, the humanitarian device exemption incentive program, the Pediatric Device Consortia Grants program, reporting requirements relating to generic drug applications and priority review applications, and a provision relating to drugs containing single enantiomers.[21]

1 Consolidated Appropriations Act, 2023, H.R. 2617, 117th Cong. (2022).

2 *Id*. Title II.

3 *See* 41 U.S.C. § 262(k)(7)(A).

4 Omnibus § 3107.

5 *Id*. § 3208.

6 *Id*. §§ 3601-2.

7 *Id*. §§ 3603-4.

8 *Id*. § 3605.

9 *Id*. §§ 3606-7.

10 *Id*. § 3607.

11 *Id*. § 3308.

12 *Id*. § 3305. This requirement takes effect for submissions made beginning 90 days after enactment.

13 *Id*. § 3301.

14 *Id*. § 3307.

15 *Id*. § 3629.

16 *Id*. § 3304.

17 *Id*. § 3306.

18 *Id*. § 2513.

19 *Id*. § 3611.

20 *Id*. § 2511.

21 *Id*. § 3101-9.

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