King & Spalding
Client Alert

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Not Quite the Titanic: The Food and Drug Omnibus Reform Act Rescues Some FDA Policy Initiatives

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The Food and Drug Administration ("FDA" or the "Agency") user fee negotiations may have hit an iceberg, but it did not sink all the legislative riders that accompanied this summer's House[1] and Senate[2] bills. Buried within the 4,000-plus page broader spending package in the Consolidated Appropriations Act, 2023 is the Food and Drug Omnibus Reform Act of 2022 ("FDORA").[3]

The Prelude: FDA User Fee Programs and the 2022 Negotiations

As described in King & Spalding's prior Client Alerts on the House and Senate Bills,[4] the Prescription Drug User Fee Act ("PDUFA"), the Medical Device User Fee Act ("MDUFA"), the Generic Drug User Fee Act ("GDUFA"), and the Biosimilar User Fee Act ("BsUFA") (collectively the "user fee programs") authorize FDA to collect user fee payments for the review of applications in order to facilitate timely access to safe and effective drugs and devices. The user fee programs must be reauthorized every five years, and it has been commonplace for Congress to bundle additional policy measures—often at the behest of FDA and regulated industry—to the "must-pass" reauthorizing legislation.

The 2022 House and Senate bills were no exception, each including a laundry list of congressional, agency, and industry priorities. But, although the House passed its bill on June 8, 2022, negotiations to have the bill considered by the full

Senate stalled. Ultimately, after weeks of impasse and with the expiration date of FDA's authority to collect user fees imminent, on September 30, 2022 Congress passed a "clean" bill.[5] The bill reauthorized PDUFA, MDUFA, GDUFA, and BsUFA, and temporarily reauthorized a handful of programs through December 16, 2022;[6] all of the policy riders, however, were thrown overboard to save the user fee programs.

For better or worse, the temporary reauthorization meant that Congress had another try to make a go of it with the enactment of FDORA. The legislation targets mainly low-hanging fruit, jettisoning many of the highly anticipated, although more controversial, riders. Below, we provide a high-level discussion of the provisions that ultimately made the cut, and the implications for the topics that did not.

The Survivors: Highlights of the Legislation

Accelerated Approval. The modernization of the accelerated approval pathway for drugs is not surprising; it represented one of the few overlapping provisions in the House and Senate Bills. FDORA did not directly take on the much-publicized issue of "dangling" accelerated approvals, approvals that are not converted to traditional approval (*i.e.*, the requisite study was not completed or did not confirm the anticipated clinical benefit) but for which FDA has not initiated withdrawal procedures. Instead, in perhaps the most significant of FDA's new drug authorities, post-FDORA, it is a prohibited act for a sponsor of an accelerated approval product to fail to conduct any post-approval study "with due diligence" or to fail to submit "timely reports" with respect to such product. In comparison to existing authorities, and even against the new proposed expedited withdrawal authority, this will give FDA a hammer to wield against "dangling" approvals.

In what FDA likely also considers a big win, FDORA created a new statutory expedited withdrawal process, which enables FDA to withdraw accelerated approvals for drugs arguably without first promulgating implementing regulations. That statutory process requires: (1) due notice; (2) an explanation for the proposed withdrawal; (3) an opportunity for the sponsor to meet with the FDA Commissioner (or their designee); and (4) an opportunity to submit a written appeal to the FDA Commissioner (or an independent designee). FDORA also included a rule of construction that clarifies that the provisions do not affect ongoing withdrawal proceedings, a change likely motivated by FDA's recent initiation, for only the second time, of withdrawal proceedings under the pre-FDORA scheme.[7]

Congress also granted FDA the express authority to require initiation of a confirmatory clinical trial prior to accelerated approval, and to specify the conditions for a sponsor's post-approval studies (which can include enrollment targets, study protocols, milestones, and study completion target date) at the time of an accelerated approval. FDA also is required to publish 180-day progress reports on its website. Additionally, the new provisions require FDA to establish an

intra-agency Accelerated Approval Council to "ensure the consistent and appropriate use of accelerated approval" across FDA. Although industry stakeholders may bristle at enhanced Agency authorities in this space, the Council may assuage some oft-repeated complaints of the uneven use of accelerated approval across Centers and review divisions. Notably, although the earlier House and Senate bills made explicit reference to using real-world evidence ("RWE") to augment or support postapproval studies, the enacted version in FDORA did not. This may be because Congress believes FDA already has the authority to use RWE in this way, or it may be that (as with other FDORA provisions), the RWE provisions could not garner sufficient support.

Clinical Trial Diversity. Congress granted FDA new authorities that provide critical tools to support increasing enrollment of underrepresented populations in clinical trials. The newly enacted provision requires sponsors to submit diversity action plans ("DAPs") in connection with Phase 3 or other pivotal studies (other than bioequivalence or bioavailability studies). A DAP must include the sponsor's study enrollment goals, rationale(s) for those goals, and a plan for how the sponsor will meet the goals. Balancing out the expanded triggers for submission of a DAP, FDORA also provided FDA with waiver authority. Either in response to a sponsor's request or on its own initiative, FDA may waive any of the DAP requirements if it finds that a DAP is not necessary, conducting a clinical trial in accordance with a DAP would be otherwise impracticable, or waiver is necessary to protect the public health during a public health emergency.

The codified text applies to a large swath of drugs, even those for which an investigational new drug application ("IND") may not be needed, and excluding only a subset of 505(b)(2) New Drug Applications ("NDAs") with only bioequivalence and/or bioavailability data.[8] For devices too, Congress expanded the required diversity action plan, extending it to cover all device clinical trials (except those devices not subject to 21 C.F.R. part 812[9])—regardless of whether an investigational device exemption ("IDE") application is required.

FDORA also imposed obligations on FDA, including: (1) publishing guidance on the form and content of DAPs, and sponsor enrollment goals and rationales; (2) hosting one or more public workshops to solicit input from stakeholders on increasing the study enrollment of historically underrepresented populations; and (3) developing an annual report (with two years' grace after enactment) to Congress that summarizes received DAPs and is to be published on FDA's website.

We noted that the codified text also contains two conspicuous omissions. First, in connection with the required public workshops, Congress omitted an earlier reference to utilization of RWE—one of multiple instances in which FDORA discarded explicit use of RWE. Second, although the House Bill stopped short of granting FDA explicit authority to require sponsors to conduct postapproval studies or postmarket surveillance if they do not meet their DAP enrollment goals, it directed FDA to evaluate whether it believes such authority is needed. It may be that Congress

believes it has already granted FDA this authority under existing study and surveillance requirements.

RWE. FDORA took some wind out of the RWE sails, but it did codify the House Bill's provisions regarding issuing RWE guidance and a role for RWE in the approval of drugs and devices previously authorized for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act ("FD&C Act").[10] Thus, FDORA still opens the door for the use of RWE and real world data ("RWD") to support new drug applications and device clearances, approvals, and De Novo classifications—a not inconsequential step given that, previously, the utility of RWE for drugs generally has been limited to post-approval supplements and similar considerations.

Modernizing and Decentralizing Clinical Studies. FDORA delegated to FDA a fair bit of work related to modernizing and improving clinical trials. FDA must issue guidances on several subjects, including with respect to: (1) use of digital health technologies in clinical trials to help improve recruitment, participation, and data collection; (2) decentralized clinical trials and their use to improve engagement of trial participants, advance the use of novel clinical trial designs, and retain diverse clinical populations (in terms of race, ethnicity, age, sex, and geographic location); and (3) innovative clinical trial designs, including seamless and concurrent designs, to support expedited development and review of drugs and biologics.

Inspections. Congress did not pass on the opportunity to bolster FDA's inspection authorities after the COVID-19 public health emergency shined a spotlight on the current regime's limitations and challenges. Similar to the House Bill, FDORA focused on section 704(a)(4) of the FD&C Act,[11] expanding the use of the Agency's Record Request authorities, and FDA's reliance on such records and other information to satisfy inspection requirements and resolve deficiencies, and also including devices for the first time. The provisions also obligate FDA to issue guidance on its use of these authorities. Additionally, in amending section 809(a)(1) of the FD&C Act,[12] FDORA expands FDA's U.S. and European Union Mutual Recognition Agreement to include pre-approval inspections—a long-planned step by FDA that will now have a statutory underpinning.

Device Classification. Notwithstanding some Congressional hemming and hawing, FDORA continued the tradition of legislating over (at least some) judicial decisions adverse to FDA.[13] The court in *Genus Med. Techs. LLC v. U.S. Food & Drug Admin.*, 994 F.3d 631 (D.C. Cir. 2021), concluded that, "[e]xcepting combination products … devices must be regulated as devices and drugs—if they do not also satisfy the device definition—must be regulated as drugs." FDORA did not restore FDA's discretion in this arena, but rather clarified that contrast imaging agents, radioactive drugs, and over-the-counter ("OTC") monograph drugs are drugs, not devices. Although the provision resolved a procedural question left open by the House Bill, clarifying that certain user fees will be waived for drugs that were legally marketed as devices as of the date of enactment of the Prescription Drug User Fee Amendments of 2022,[14] but are now deemed to be drugs, neither FDORA nor the House Bill addressed the broader questions about the impact of

Genus on other classification decisions beyond the three enumerated categories. Meanwhile, it remains to be seen how FDA plans to reconcile its recently issued guidance regarding the applicability of 21 C.F.R. part 4 to ophthalmic drugs packaged with eye cups, eye droppers, and other dispensers, premised on the obsolescence of 21 C.F.R. § 200.50(c),[15] with the legislation's unambiguous classification of OTC monograph drugs—ostensibly including OTC ophthalmic drugs—as drugs.

Cosmetics. Although the Senate Bill's provisions revamping FDA authority over *in vitro* clinical tests and dietary supplements failed to make the cut (see below), FDORA codified the Modernization of Cosmetics Regulation Act of 2022 ("MOCRA").[16] MOCRA, the first significant expansion of FDA authority over cosmetics since 1938, brings the cosmetics regulatory framework closer to medical products in significant ways, but falls short of imposing a premarket review and approval process. King & Spalding has been monitoring these efforts, ongoing since 2013, to modernize safety standards in the U.S. for cosmetics and other personal cares, and issued a concurrent Client Alert discussing MOCRA and its implications for industry here.

Biosimilars. Biosimilar applicants benefited from a series of small wins in FDORA. *First*, the legislation included important clarifications to the scope of first interchangeable exclusivity, both in terms of shared exclusivity in the event of multiple "first" interchangeable biological products and the availability of tentative approval during a period of first interchangeable exclusivity. *Second*, FDORA also amended the biosimilar provisions of the Public Health Service Act ("PHS Act") to no longer require animal studies as a default in biosimilar applications, clarifying expectations on the necessary studies to support licensure. *Third*, the extension of the marketing status reporting obligations under section 506I of the FD&C Act[17] to biologics will ensure that the Purple Book contains up-to-date marketing status information, which can prove critical to biosimilar development.

Therapeutic Equivalence Evaluations. This provision obligates FDA to make therapeutic equivalence determinations for a relatively narrow subset of NDAs submitted under section 505(b)(2) of the FD&C Act[18]—those for which a follow-on applicant could not submit an ANDA because it cannot or does not want to pursue the same formulation of a parenteral, or ophthalmic or otic use drug. While FDORA provided much needed relief to these applications, the remainder of 505(b)(2) NDA applicants seeking a therapeutic equivalence determination will remain confined to the long and cumbersome citizen petition process.

Misbranding. FDORA amended the misbranding provisions to extend the safe harbor for health care economic information to investigational drugs and devices (and investigational uses), allowing payors, formulary committees, and other similar entities to engage in advance planning of coverage and reimbursements decisions.

Safer Disposal of Opioids. FDORA's amendment of section 505-1 of the FD&C Act[19] broadened the scope of disposal packaging and systems that could be required under a Risk Evaluation Mitigation Strategy ("REMS"), resolving the ambiguity with respect to in-home disposal products.

The Victims: Provisions That Didn't Make It

Orphan Drug Exclusivity. The Eleventh Circuit's rejection of FDA's long-standing interpretation of the Orphan Drug Act ("ODA") in *Catalyst Pharms., Inc. v. Becerra,* 14 F.4th 1299 (11th Cir. 2021), has continued to reverberate across the Agency, with FDA in a state of effective paralysis, deferring decisions on orphan exclusivity determinations and actions on pending applications. Although the Agency had pinned its hopes on a legislative fix, Congress declined to once again swoop in to amend the ODA to align with FDA's interpretation.[20] With FDA having lost its game of chicken with Congress, it can no longer delay grappling with the *Catalyst* decision.

Inactive Ingredient Disclosure. Identity not only of the active ingredient, but also of the inactive ingredients, can be critical for an ANDA. The requirement for qualitative and quantitative (or "Q1/Q2") sameness is not only mandated for certain routes of administration but also can inform bioequivalence study recommendations. At the same time, given labeling requirements and confidentiality considerations, FDA has generally not informed ANDA applicants which ingredients do not match the originator drug, and in what quantities. Included in the House Bill, and adopted by amendment during the Senate HELP Committee mark-up, was a provision requiring FDA to disclose the identity and amount of deviation of any inactive ingredient mismatches upon request from an ANDA applicant. Concerns over the disclosure obligation's impact on confidentiality and the balance between competition and innovation apparently proved persuasive to Congress, and the provision was stripped from FDORA.

VALID. Proposed in the Senate Bill, the Verifying Accurate Leading-edge IVCT Development Act of 2022 ("VALID") would have rewritten FDA's regulation of *in vitro* diagnostics ("IVDs") by separating them from other medical devices and redefining them as *in vitro* clinical tests ("IVCTs"). This new category of products would have been subject to a new and parallel set of regulatory processes specific to IVCTs, including premarket review and approval, registration and listing, adverse event reporting, corrections and removals, and related processes for FDA oversight. Importantly, VALID would have given FDA explicit statutory authority over laboratory-developed tests ("LDTs") for the first time. Notwithstanding the significant discussions among the Senate, FDA, and other stakeholders in developing VALID, it received the axe under FDORA. In advance of the passage of the Consolidated Appropriations Act, 2023, FDA officials signaled that the Agency may use the rulemaking process to regulate LDTs in the absence of legislation.[21]

Dietary Supplements. The Dietary Supplement Health and Education Act of 1994 ("DSHEA")[22] amended the FD&C Act to separate dietary supplements from drugs for unique regulatory treatment as a special category under the general umbrella of foods. Generally, dietary

supplement manufacturers must follow current good manufacturing practices, but, unlike drugs, FDA does not approve dietary supplements before they are marketed. The Senate Bill sought to gently revisit the relatively hands-off treatment by DSHEA of dietary supplement manufacturers (as well as other "responsible persons," *i.e.*, packers and distributors) and would have required such responsible persons to list certain information with FDA. Although these requirements could have afforded FDA with sharper tools to identify potentially dangerous products and increase transparency within the DSHEA regulatory framework, they nevertheless met the FDORA chopping block.

505(b)(2)-like Pathway for Biologics. Absent from either the House or Senate Bills, inclusion in FDORA of the long-awaited, but ever-elusive, 505(b)(2)-like pathway for biologics would have been too much to hope for. However, with the death knell of any scientific rationale for precluding reliance on approval of one biological product to support another sounded by the passage of the Biologics Price Competition and Innovation Act, pressure will only continue to mount for an additional, abbreviated pathway. It will be worth keeping an eye out to see if and how FDA exercises additional flexibility in this arena in the continued absence of any statutory changes.

CONCLUSION

This round of user fee negotiations proved unique. Although FDA ultimately received some important new authorities and stakeholders secured some much-needed clarity, a number of proposals unfairly met an untimely demise or could have been significantly strengthened. In short, the first two Acts, with the House and Senate releasing and debating their bills, entranced the crowd, but the passage of a "clean" bill followed by enactment of the least controversial riders culminated in an anticlimactic conclusion.

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King & Spalding LLP regularly counsels drug and device manufacturers and other life sciences companies on product development and the submission of drug, biological product, and device applications to FDA. Please let us know if you have any questions regarding FDORA.

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[1] Food and Drug Amendments of 2022, H.R. 7667, 117th Cong. (2022) ("House Bill").
[2] Food and Drug Administration Safety and Landmark Advancements Act of 2022, S. 434, 117th Cong. (2022) ("Senate Bill").
[3] Consolidated Appropriations Act, 2023, Pub. L. 117-328, 117th Cong., §§ 3001–3631 (2022) ("Food and Drug Omnibus Reform Act of 2022").
[4] Eva Temkin et al., Client Alert, *And So It Begins: House Energy and Commerce Leaders Unveil FDA User Fees Legislative Package* (May 10, 2022) ("House Bill Client Alert"), KING & SPALDING, https://www.kslaw.com/news-and-insights/and-so-it-begins-house-energy-and-commerce-leaders-unveil-fda-user-fees-legislative-package; Eva Temkin et al., *Client Alert, Act II: The Senate Unveils Its Draft* (June 1, 2022) ("Senate Bill Client Alert"), KING & SPALDING, https://www.kslaw.com/news-and-insights/act-ii-the-senate-unveils-its-draft.
[5] Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023, Pub. L. 117-180, 117th Cong., §§ 1001-5008 (2022) (FDA User Fee Reauthorization Act of 2022).
[6] Although initially reauthorized only until December 16, 2022, a Continuing Resolution extended the time to December 23, 2022. Further Continuing Appropriations and Extensions Act, Pub. L. 117-229, 117th Cong. (2022). The temporary reauthorizations included the best pharmaceuticals for children program, the humanitarian device exemption incentive, the pediatric device consortia program, the provision pertaining to drugs containing single enantiomers, orphan drug grants, certain device inspections, and reporting requirements related to pending generic drug applications and priority review applications. *See* FDA User Fee Reauthorization Act of 2022, §§ 5001-5008.
[7] *See* Notice of Hearing, *Proposal to Withdraw Approval of MAKENA*, 87 Fed. Reg. 50626 (Aug. 17, 2022).
[8] Abbreviated New Drug Applications ("ANDAs") would also be excluded, but, given that such studies rarely require an IND, ANDAs would generally be expected to be excluded under both FDORA and the House Bill.
[9] Devices described in 21 C.F.R. § 812.2(c), including many diagnostic devices, however, are exempted.
[10] 21 U.S.C. § 360bbb–3.
[11] *Id.* § 374(a)(4).
[12] *Id.* § 384e(a)(1).
[13] FDORA also includes a provision clarifying that FDA has the authority to ban a medical device for one or more intended uses—a direct response to the court's decision in *Judge Rothenberg Educational Center, Inc. v. U.S. Food & Drug Admin.*, 3 F.4th 390 (D.C. Cir. 2021).
[14] FDA User Fee Reauthorization Act of 2022, §§ 1001-1007.
[15] *See* U.S. Food & Drug Admin., *Guidance for Industry, Certain Ophthalmic Products: Policy Regarding Compliance With 21 CFR Part 4* (Mar. 2022), https://www.fda.gov/media/157067/download.
[16] Consolidated Appropriations Act, 2023, § 3501 *et seq*. (Modernization of Cosmetics Regulation Act of 2022).
[17] 21 U.S.C. § 356i.
[18] *Id.* § 355(b)(2).
[19] *Id.* § 355-1.
[20] During the previous user fee cycle, Congress amended the ODA in the wake of an adverse court opinion, *Depomed, Inc. v. U.S. Dep't of Health & Human Servs.*, 66 F. Supp. 3d 217 (D.D.C. 2014). *See* FDA Reauthorization Act of 2017, Pub. L. 115-52, 131 Stat. 1005, § 607 (2017).
[21] *See* Ferdous Al-Faruque, *Califf: FDA may use rulemaking for diagnostics reform if VALID isn't passed*, REGULATORY FOCUS (Oct. 25, 2022), https://www.raps.org/news-and-articles/news-articles/2022/10/califf-fda-may-use-rulemaking-for-diagnostics-refo.
[22] Dietary Supplement Health and Education Act of 1994, Pub. L. 103-417, 108 Stat. 4325 (1994).