Health Industry Alert

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Senate HELP Committee Unveils Draft FDA User Fee Reauthorization Legislation, with Major Reforms to In Vitro Diagnostics, Cosmetics and Dietary Supplements

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On May 17 the Senate Health, Education, Labor and Pensions (HELP) Committee released a bipartisan legislative discussion draft of the Food and Drug Administration (FDA) Safety and Landmark Advancements Act (FDASLA), which includes reauthorization of the four FDA user fee programs that would expire this year, as well as other reforms related to regulation of drugs, devices, in vitro diagnostics, dietary supplements and cosmetics. On May 6, the House Energy and Commerce Committee unveiled its own user fee reauthorization legislation and, on May 18, the full Energy and Commerce Committee voted unanimously to move their bipartisan bill, the Food and Drug Amendments of 2022, forward for full House consideration.

The Senate HELP Committee's release of its much anticipated discussion draft represents another critical development in the reauthorization process. The release of this package suggests that the range of FDA policy reforms in play for this "must pass" bill may be historically significant. The Senate HELP Committee has asked for feedback on their discussion draft by May 22, in anticipation of a Committee markup hearing in the weeks that follow.

User Fee Agreements: Background and Commitment Letters

The current five-year reauthorization of the user fee programs for human prescription drugs and biologics, medical devices, generics and biosimilars is set to expire on September 30, 2022. Congress will seek to pass a final user fee reauthorization package sufficiently ahead of this deadline to avoid disruptions in FDA operations with respect to user fee-funded activities. The foundation of the broader package is the reauthorization of the Prescription Drug User Fee Amendments of 2017 (PDUFA), Generic Drug User Fee Amendments of 2017 (GDUFA), Biosimilar User Fee Amendments of 2017 (BsUFA) and the Medical Device User Fee Amendments of 2017 (MDUFA). A significant portion of the review activities for these products is supported through user fees.

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The HELP Committee's discussion draft would reauthorize FDA's authority to collect fees under PDUFA, MDUFA, GDUFA and BsUFA through September 30, 2027, and use the revenue to support specified activities for the review of brand-name drugs, generic drugs, biosimilars and medical devices, as outlined in the commitment letters agreed to between FDA and applicable industry groups for the Fiscal Year (FY) 2023-2027 period. The draft legislation would reauthorize all four programs and update the corresponding user fee revenue amounts beginning in FY 2023.

As previously outlined in our analysis of the user fee reauthorization process, the submission of commitment letters to Congress for PDUFA VII, GDUFA III, BsUFA III and MDUFA V reflected a multiyear effort consisting of public meetings and opportunities for public comment, extensive negotiations and industry discussions. Each of these commitment letters includes goals and procedures aimed at advancing a modern and efficient pre-market review of medical products so that patients can benefit from approved medical products in as timely a manner as possible consistent with FDA's mission to protect and promote public health:

- PDUFA VII includes performance goals related to enhancing support for the development of cell and gene therapy products and advancing the use of real-world evidence and novel clinical trial designs.
- GDUFA III aims to achieve earlier cycle approvals for generics and support the review of complex generic products.
- Thirty-five biosimilars have been approved to date, and FDA expects additional supplements for these products to be submitted during the third iteration of BsUFA. BsUFA III outlines goals to expedite the review of certain supplements, including the review of safety labeling updates. The agreement also calls on FDA to establish a new meeting type for faster responses from the agency; advance the development of review processes for biosimilar biological-device combination products; and support the development and review of interchangeable biosimilars.
- MDUFA V includes new hiring goals for FDA and proposes additional staff training in artificial intelligence and machine learning. Notably, the fifth iteration of MDUFA also includes a total product life cycle (TPLC) advisory program (TAP) pilot, beginning in FY 2023 with the enrollment of 15 breakthrough devices. The program is intended to spur more rapid development of new devices by facilitating early interactions with participants and includes corresponding performance goals that reflect the TAP pilot's objective to provide meaningful and fluid feedback to sponsors.

The discussion draft also includes several changes intended to improve the transparency of the user fee reauthorization process. Notably, the bill enhances reporting requirements for FDA with respect to PDUFA, MDUFA, GDUFA and BsUFA and requires the agency to provide regular updates to Congress on reauthorization negotiations. The legislation also requires FDA to publish the minutes of all negotiation meetings within 30 days after each meeting.

Related Legislative Provisions

Every previous reauthorization of these user fee programs has been accompanied by FDA policy reforms. This reauthorization cycle appears poised to continue this trend, potentially in a dramatic fashion. In addition to policy riders related to drugs and

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devices, the Senate package includes comprehensive reforms to in vitro diagnostics (including laboratory developed tests) as well as cosmetics and dietary supplements.

Drug Proposals

The package includes a number of reforms related to FDA regulation of prescription drugs, biologics, generics, and biosimilars, including the following.

- **Pre-clinical non-animal testing**. The discussion draft would allow for pre-clinical non-animal testing to be used in the evaluation of safety and efficacy of drugs, as well as in the demonstration of biosimilarity to a reference biologic with respect to toxicity. Current law specifies that "animal" testing is permitted in such evaluations. The proposed change would also allow for "nonclinical test(s)," including in silico or in chemico tests, cell-based assays and microphysiological systems. Importantly, the proposal explicitly allows for the use of computer models in place of human or animal-based testing.
- **Regulatory exclusivity for interchangeable biosimilars**. The Senate proposal also addresses the regulatory exclusivity that applies to interchangeable biosimilar products. Under the current provisions of the Public Health Service Act ("PHS Act"), the first approved interchangeable biosimilar is entitled to "first interchangeable exclusivity," which lasts for 12 months or more depending on the calculation under the PHS Act. During that time, other interchangeable biosimilars (to the same reference drug) cannot be given final approval by FDA. The Senate bill purports to clarify FDA's authority in two ways: First, FDA is explicitly given the authority to issue a tentative approval to an interchangeable biosimilar while the exclusivity period for a first-approved interchangeable biosimilar is still pending. Second, interchangeable exclusivity will be shared where more than one interchangeable biosimilar is "approved" by FDA on the same day.

Of note, this Senate discussion draft does not address several proposals that were included in the bill advanced by the House Energy and Commerce Committee. The House bill includes provisions that limit orphan drug exclusivity to the specific indication or use approved by FDA; require FDA to specify conditions of post-approval studies for drugs that obtain accelerated approval; permit use of real world evidence to support such post-approval studies; and codify an expansion of FDA's prior guidance on manufacturer communications with payors, formulary committees and similar entities.

Diagnostics Reform

The FDASLA discussion draft includes the long awaited update of legislative reform to regulation of in vitro diagnostics (IVDs) and in vitro clinical tests (IVCTs). The Verifying Accurate Leading-edge IVCT Development Act of 2022 (the "VALID Act") was previously introduced in both the House and Senate on March 5, 2020, and again on June 24, 2021, by U.S. Reps. Diana DeGette (D-CO) and Larry Bucshon (R-IN) and U.S. Sens. Michael Bennet (D-CO) and Richard Burr (R-NC). The VALID Act seeks to modernize regulatory oversight of IVDs, including laboratory developed tests (LDTs), by creating a single, diagnostics-specific, regulatory framework under the authority of the FDA aimed at promoting innovation and improving patient and public health. The 2022 version of the VALID Act represents years of collaboration between the sponsors and key stakeholders and has undergone many revisions in the past several months

as committee staff have updated the bill to reflect feedback from a variety of sectors, including IVD manufacturers, clinical laboratories, patient groups and hospital systems.

The new version of the VALID Act has several significant changes.

- **Extension of transition period**. One of these is the extension of the transition period and implementation period from three years to five years: the new framework would take effect on October 1, 2027. This will provide industry and regulators alike with much needed lead time as the rules and guidance contemplated in the VALID Act are drafted and published.
- **Risk categorization and definitions**. This iteration of the VALID Act refines and clarifies many of the definitions and standards, and adopts a three-tiered risk categorization (low, moderate and high), unlike the earlier version.
- **Technology Certification Program**. The new version also broadens eligibility for the Technology Certification Program ("Tech Cert"). As drafted, the Tech Cert provisions extend eligibility under the program to most kinds of tests and allow for the possibility that a Tech Cert Order could cover more than one technology (which had not previously been contemplated). The drafters have also streamlined some of the application requirements, and clarified what types of test modifications would require a new submission.

Finally, it is worth noting that the user fee provisions from the previous version have been replaced with user fee process provisions, such that FDA and industry would negotiate user fees for IVCTs just as they do for other medical products.

The updated version addresses a wide variety of issues raised by stakeholders. However, the text also identifies numerous areas (via brackets) on which the HELP Committee is still deliberating.

Dietary Supplements

The HELP Committee's inclusion of dietary supplement reforms is a significant development for many members of Congress who have called for action in this area. Indeed, the last major congressional reform related to dietary supplements regulation was the passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA). The Committee's dietary supplement provisions aim to improve FDA oversight of dietary supplements by requiring dietary supplement manufacturers to list their products with FDA.

Specifically, manufacturers, packers or distributors of a dietary supplement whose name appears on the label of the supplement (i.e., the responsible person) would be required to provide FDA with detailed information about their products, including any health, structure or function claims, and a dietary supplement product listing number for the product provided by the Secretary, which would be a part of a publically available electronic database of all dietary supplement product listings. For dietary supplements currently on the market, the bill would require a listing be submitted no later than 18 months after the enactment of the legislation. For new supplements (offered after January 1, 2024), a listing would be required at the time the product is introduced.

The draft legislation would also render misbranded dietary supplements for which a responsible person has failed to comply with the listing requirements, prohibit the marketing of dietary supplements that fail to meet the definition of a "dietary supplement," prohibit the introduction or delivery of dietary supplements by debarred persons, instruct FDA to publish final guidance related to new dietary ingredient notifications no later than 18 months after enactment, and direct resources to inspections of facilities, suppliers, and dietary supplement types that present a high risk to public health as identified by FDA.

Cosmetics Regulation

Existing FDA authorities to regulate cosmetic products and their ingredients have changed little since passage of the Food, Drug, and Cosmetic Act of 1938, and are much more limited than the agency's authorities related to other FDA-regulated products. The HELP Committee's discussion would reduce this disparity through the "Modernization of Cosmetics Regulation Act of 2022" ("Cosmetics Act"), which would significantly broaden and modernize FDA's regulatory oversight of cosmetics. The Cosmetics Act would establish a regulatory framework for cosmetics similar to that of other FDA-regulated products, including requirements related to registration and listing, safety substantiation, good manufacturing practices, and recalls. As part of this framework, the Cosmetics Act would impose numerous obligations on "responsible persons," a term that includes manufacturers, packers or distributors of a cosmetic product whose name appears on the label of cosmetic products with a few limited exemptions (e.g., small businesses). Provisions of the Cosmetics Act include:

- **Registration and listing**. Owners or operators of manufacturing facilities for cosmetic products must register each facility, and responsible persons must submit a product listing for each cosmetic product within specific timeframes.
- **Safety substantiation**. Responsible persons must ensure that there is "adequate substantiation of safety" for cosmetic products. The discussion draft defines "adequate substantiation of safety" as "tests or studies, research, analyses, or other evidence or information that is considered, among experts qualified by scientific training and experience to evaluate the safety of cosmetic products and their ingredients, sufficient to support a reasonable certainty that a cosmetic product is safe." Under the draft, in determining whether a product is "safe," FDA may consider the cumulative or other relevant exposure to the cosmetic product or any ingredient in the product. The proposed legislation defines "safe" to mean a cosmetic product, including any ingredient thereof, that "is not injurious to users under the conditions of use prescribed in the labeling thereof, or under such conditions of use as are customary or usual."
- **Serious adverse events**. The discussion draft requires responsible persons to make reports of serious adverse events and any "new and material medical information" related to the serious adverse event report within certain timeframes. A responsible person must maintain records related to each report of an adverse event for six years and permit access to such records during an inspection.
- **Good manufacturing practices**. FDA must establish good manufacturing practice (GMP) regulations and be allowed to inspect records necessary to demonstrate compliance with such regulations.

- **Preemption**. The discussion draft provides that this Act preempts state law requirements for cosmetics related to registration and product listing, GMPs, recordkeeping, recalls, adverse event reporting or safety substantiation. It also clarifies that the Modernization of Cosmetics Regulation Act of 2022 does not preempt state law, except those that are expressly preempted.
- **Effective date**. The Cosmetics Act would become effective one year after enactment.

The discussion draft also outlines labeling requirements, authorizes FDA to access and copy certain records, allows FDA to suspend a facility's registration, permits the Commissioner of Food and Drugs to order a mandatory recall of a cosmetic product in certain situations and establishes misbranding provisions applicable to cosmetics.

Next Steps

Legislation to reauthorize FDA's user fee programs is expected to continue advancing in Congress in the weeks ahead, including with further action by the Senate HELP Committee as they look to mark up their user fee reauthorization package. There is no shortage of focus on FDA-related topics in Congress. The FDA user fee reauthorization policy riders being considered by the House and Senate are not the only FDA issues Congress is working on—earlier this year the Senate HELP Committee advanced their bipartisan PREVENT Pandemics Act, which included FDA policy reforms, and may be folded into any final user fee reauthorization bill.

While the exact timing in the House and Senate remains fluid, the "UFA clock" is steadily ticking, and any final bill will need to make its way through both the full House and Senate on its way to the President's desk. One thing that is certain is that the stage is set for a summer focused on moving "must pass" legislation and Congress is advancing policy riders as part of their reauthorization process this year. The full contours of these reforms will become even more clear as the legislative process plays out in the months ahead. In the interim, this process will be closely watched given its significance for patients, consumers, the agency, industry and public health.

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