KING & SPALDING
Client Alert

FDA and Life Sciences

JUNE 1, 2022

For more information, contact:

Eva Temkin
+1 202 626 5418
etemkin@kslaw.com

Lisa Dwyer
+1 202 626 2393
ldwyer@kslaw.com

Jessica Ringel
+1 202 626 9259
jringel@kslaw.com

Allison Kassir
+1 202 626 5600
akassir@kslaw.com

Jessica Greenbaum
+1 202 626 3731
jgreenbaum@kslaw.com

Jonathan Trinh
+1 202 626 8994
jtrinh@kslaw.com

King & Spalding

Washington, D.C.
1700 Pennsylvania Avenue, NW
Suite 900
Washington, D.C. 20006
Tel: +1 202 737 0500

Act II: The Senate Unveils Its Draft

On May 27, 2022, Senate Health, Education, Labor, and Pensions ("HELP") Committee leaders introduced the Food and Drug Administration Safety and Landmark Advancements Act of 2022 ("FDASLA Act of 2022"), which, if passed, would reauthorize the U.S. Food and Drug Administration ("FDA" or the "Agency") user fee agreements (the "Senate Draft").[1] As described by HELP, the legislation "includes provisions to strengthen oversight of cosmetics and dietary supplements, modernize the regulation of diagnostic tests, bring more competition to the market, and prepare the FDA for the next generation of medical products to benefit Americans."[2] The HELP package follows tightly on the heels of the recently unveiled legislative package from the House Energy and Commerce ("E&C") Committee (the "House Draft"), which is moving full steam ahead.[3] The Senate Draft, which both tweaked provisions from the Senate's discussion draft[4] previously released on May 17 and added new ones, reflects a number of key differences from the House Draft. Ultimately, these differences between the House and Senate drafts will need to be reconciled before the legislation can move forward.

BACKGROUND ON USER FEE PROGRAMS

As described in King & Spalding's House Draft Client Alert,[5] 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 certain applications, which can facilitate timely access to safe and effective drugs and devices. The user fee programs must be reauthorized every five years, with the current authorizations ceasing on October 1, 2022. Prior to reauthorization, FDA and regulated industry negotiate proposed user fees and FDA performance goals, which are then presented as recommendations to the E&C Committee and the HELP Committee and to the public.[6] It has become typical for Congress to bundle additional policy measures to the "must-pass" reauthorizing legislation, which generally reflect congressional, FDA, and other stakeholder priorities. Like the E&C legislative package, this round is no exception, with the Senate Draft containing HELP's priorities.

HIGHLIGHTS FROM THE HELP LEGISLATIVE PACKAGE

Other than the reauthorization of user fees and other programs that would otherwise be set to expire, there are limited areas of alignment between the Senate Draft and the E&C legislative package. Several high-profile topics included in the House Draft are notably absent from the Senate's version—

including clarification of the orphan drug exclusivity provisions and a redrawing of the line between drugs and devices for certain products in the wake of the *Genus* decision.[7] And, several topics have not made the cut in either the House or Senate bills, like the possibility of a new pathway for biologics. Instead, the Senate Draft takes on several big-ticket items, including *in vitro* clinical tests, cosmetics reform, and a boost for dietary supplement regulation, none of which appeared in the House Draft. We will continue to monitor the proposed *in vitro* clinical test and cosmetics reform regulatory regimes, so stay tuned for additional client alerts as those provisions develop. A high-level look at these provisions is below, along with other noteworthy proposals in the Senate Draft.

In Vitro Clinical Tests. Following much discussion among the Senate, FDA, industry, and other stakeholders, Subtitle C of the Senate Draft contains the Senate's proposal for the Verifying Accurate Leading-edge IVCT Development Act of 2022 ("VALID"). VALID would rewrite 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 be 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 give FDA explicit statutory authority over laboratory-developed tests ("LDTs") for the first time. Under the Senate's proposed VALID Act, LDTs would be subject to the same processes and requirements as IVCTs that are developed and marketed by commercial test developers which are currently regulated as medical device manufacturers. To ease the transition from the regulation of IVDs as medical devices to the regulation of clinical tests as IVCTs, VALID also contains provisions that would: (1) deem as approved IVCTs certain tests that are authorized by FDA for marketing under a 510(k), PMA, De Novo, HDE, or BLA prior to the effective date of VALID, which is proposed to be October 1, 2027; (2) grandfather LDTs that are offered for clinical use prior to the enactment of VALID; and (3) provide a transitional period for the continued marketing of LDTs first offered for clinical use between VALID's enactment and effective dates. As noted above, King & Spalding is monitoring these provisions closely and will prepare dedicated client alert(s) as VALID marches on.

Cosmetics. As we predicted in January, 2022 is the year that the efforts to modernize safety standards in the United States for cosmetics and other personal care products, ongoing since 2013, are coming to fruition.[8] However, while the Personal Care Products Safety Act[9] generated significant buzz with its introduction last June, the requirements tucked into Title VIII of the Senate Draft are not as sweeping as anticipated, softening or omitting numerous provisions from previously the introduced bill. For example, rather than directing FDA to promulgate a rule banning the intentional addition of perfluoroalkyl or polyfluoralkyl substances ("PFAS") in cosmetics, the Senate Draft would obligate the Agency to assess the use of PFAS in cosmetics and the scientific evidence regarding their safety. Additionally, provisions requiring FDA to review the safety of cosmetic ingredients or non-functional constituents annually are notably absent, and the Senate Draft includes appropriations, but no user fees.

Instead, the Modernization of Cosmetics Regulation Act of 2022 in the Senate Draft would (1) require establishments that manufacture, pack, or distribute cosmetics whose name appears on the label of the cosmetic ("responsible persons") to register and list with the Agency and ensure that there is "adequate substantiation of safety" for each cosmetic product, (2) require the labeling for cosmetics to identify each fragrance allergen included in the product (and directs FDA to promulgate regulations identifying such fragrance allergens); (3) require compliance with good manufacturing practices; and (4) require the reporting of serious adverse events to the Agency. The Senate Draft also provides FDA with mandatory recall authority over cosmetics and compels the Agency to promulgate regulations to establish standardized testing methods for detecting and identifying asbestos in talc-containing products. Lastly, although state law requirements differing from, or in addition to, those relating to registration and product listing, good manufacturing practice, recordkeeping, recalls, adverse event reporting, and safety substantiation would be preempted, prohibitions and limitations on the use or amount of an ingredient in a cosmetic product are explicitly carved out from preemption, as are state tort laws and state laws and referendums, like California's Prop 65.

Dietary Supplements. The Dietary Supplement Health and Education Act of 1994 ("DSHEA")[10] amended the Federal Food, Drug, and Cosmetic Act ("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.

Section 811 of the Senate Draft would 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 require such responsible persons to list certain information with FDA. The listing information would be required to be provided to the Agency at the time of introduction into interstate commerce (or, for dietary supplements offered in interstate commerce on or before January 1, 2024, 18 months after enactment) and would include, among other things: (1) the name of the dietary supplement; (2) the business name and mailing address of all locations at which the responsible person manufactures, packages, labels, or holds the dietary supplement; (3) a list of ingredients required to appear on the label; (4) warnings, notice, and safe handling statements; (5) any major food allergens; (6) any health claims or structure or function claims; and (7) the dietary supplement product listing number (which can be reserved in advance of listing, presumably to limit the potential for listing obligations to delay marketing). Additionally, if FDA requested, the responsible person would be required to provide FDA the full business name and physical and mailing address from which such responsible person receives a dietary ingredient (or combination of dietary ingredients) used in the manufacture of the dietary supplement or the dietary supplement.

Section 811 also would require FDA to establish a publicly available electronic database containing the listing information described above[11] and to finalize the Draft Guidance for Industry, *Dietary Supplements: New Dietary Ingredient Notifications and Related Issues* (Aug. 2016), which would be updated to include recommendations on compliance with the listing requirements.[12] The provision also would instruct FDA to direct resources to inspections of facilities, suppliers, and dietary supplement types that present a high risk to public health. Finally, under the Senate Draft, failure to comply with the listing requirement would misbrand the relevant dietary supplement, and it would be a prohibited act to introduce or deliver for introduction into interstate commerce any product marketed as a dietary supplement that does not meet the definition[13] or that has been prepared, packed, or held using the assistance of, or at the direction of, a debarred person.[14] Overall, Section 811 seems designed to provide FDA with sharper tools to identify potentially dangerous products and increase transparency within the DSHEA regulatory framework.

Accelerated Approval. We noted in our earlier House Draft Client Alert that FDA has the authority to withdraw accelerated approval drugs under the current statutory provisions—but that there has been a lot of discussion about the fact that FDA generally has not done so.[15] Some critics have focused on the sponsors' roles in not completing required post-approval studies (or on their inaction when those studies do not confirm expected clinical benefits); other critics have focused on FDA's historical reluctance to initiate withdrawal procedures in those circumstances. More recently, the Agency has demonstrated—in at least some arenas[16]—that it is becoming incrementally more assertive in managing accelerated approval drugs and their post-approval studies.

Section 506 of the Sente Draft, like section 804 of the House Draft, would provide a statutory expedited withdrawal process that would require: (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). FDA would be required to publish guidance on the expedited withdrawal procedures. Also like the House Draft, the Senate version would add or clarify certain programmatic requirements, including:

- clarifying that FDA may require the sponsor to have commenced a post-approval study or studies at the time of accelerated approval;
- making explicit that sponsors can use real world evidence to meet post-approval study requirements;
- requiring that FDA specify the conditions for a sponsor's post-approval studies (which can include enrollment targets, study protocols, milestones, and the study completion target date) at the time of accelerated approval;
- requiring sponsors to report their progress to FDA every 180 days until study completion or termination—a more stringent requirement than that currently required by FDA's regulations;
- requiring FDA to justify on its website any decision not to require a sponsor to conduct a post-approval study; and
- authorizing a rare disease endpoint advancement pilot and requiring FDA to publish guidance regarding the use of novel endpoints and clinical trial designs in accelerated approval.

There are also two notable additions in the Senate's version. First, the Senate version quietly makes it a prohibited act for a sponsor of a product approved under accelerated approval 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 would give FDA a hammer to wield against so-called "dangling" approvals. Second, the Senate Draft would require FDA to establish an intra-agency Accelerated Approval Council to "ensure the consistent and appropriate use of accelerated approval" across FDA. The Council would include the CDER and CBER Center Directors or their designees, as well as Directors or their designees from specified offices across the Agency, and would meet at least three times per year, "directly" engage with review teams, and, at its discretion, work to develop best practices guidance, train review teams, and provide application-specific advice. Perhaps this attempt to cure another oft-heard complaint about accelerated approval—its uneven usage across the Centers and review divisions—will balance out the increase in enforcement authority for the Agency in the eyes of industry stakeholders.

Opioid Disposal Legislation. The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act ("SUPPORT Act"),[17] signed into law on October 24, 2018, provided FDA new authority to use a Risk Evaluation Mitigation Strategy ("REMS") for certain drugs to require safe disposal packaging or safe disposal systems to render such drug "nonretrievable,"[18] *i.e.*, permanently altered the physical or chemical condition or state of the controlled substance through irreversible means and thereby rendered the controlled substance unavailable and unusable for all practical purposes.[19] Specifically, under the SUPPORT Act, FDA can require such a REMS for drugs, including opioids or other drugs that pose a serious risk of abuse or overdose if, among other things, FDA determines that such safe disposal packaging or system may mitigate such risks and is sufficiently available.[20]

FDA recently issued a Federal Register notice seeking public comment on the potential application of this new authority,[21] and whether commercially available in-home disposal products would satisfy the requirements added by the SUPPORT Act.[22] Section 502 of the Senate Draft would resolve any such ambiguity by removing current limitations in the FD&C Act REMS authorities (which require these REMS be for the purposes of rendering the drug nonretrievable) and would broaden the types of disposal packaging and systems that could be required through a REMS. With the docket set to close next month, and nearly 50 comments received thus far, it remains to be seen if FDA will continue to press forward with mail-back envelopes or whether this draft legislative amendment might change FDA's plans.

First Interchangeable Exclusivity. Current section 351(k)(6) of the Public Health Service Act ("PHS Act")[23] provides exclusivity for first interchangeable biological product(s) by precluding FDA from making a "determination" that a "second or subsequent biological product is interchangeable" with the same reference product as the first interchangeable biological product for a period of time calculated based on a complex set of criteria specified in the statute.[24] This language differs in significant ways from other exclusivity provisions in the FD&C Act and PHS Act, which has raised a number of questions with respect to implementation. To facilitate implementation of this provision as FDA continues to gain real world experience with interchangeable products, section 503 of the Senate Draft proposes several technical changes. First, the proposed language would clarify the availability of shared exclusivity in the event that multiple "first" interchangeable biological products (referencing the same reference product) are approved on the same day—though the Senate Draft language does not address how the duration of a period (or periods) of shared exclusivity would be calculated. Second, the Senate Draft would edit the language effectuating the exclusivity bar to more closely align with the statutory text of other exclusivity provisions, which should help to clarify the availability of tentative approval during a period of first interchangeable exclusivity.[25]

Animal Testing Alternatives. FDA has long had the goal of reducing the use of animals in accordance with the "3Rs": reduce, refine, and replace animal testing. Now, both the Senate Draft and the House Draft would formally promote alternatives to animal testing by making explicit that nonclinical tests other than animal testing can support an investigational new drug application.[26] The Senate Draft additionally would amend the biosimilars provisions of the PHS Act to strip away the requirement of biosimilar license applications to include data derived from "animal studies (including the assessment of toxicity)." Although the Agency already has the authority to determine that animal studies are unnecessary in any given application, under the Senate's proposed language, a biosimilar application would simply be required to include an assessment of toxicity, which could rely on, or consist of, analytical or clinical studies that the applicant would already be expected to conduct.[27] In addition, the newly framed requirement could be seen as streamlining biosimilar development programs by formally stripping away the animal testing requirement and providing clearer expectations on the necessary studies to support an application.

Therapeutic Equivalence Evaluations. FDA's Orange Book[28] includes the Agency's evaluations of therapeutic equivalents, which facilitate pharmacy-level substitution. FDA considers drug products to be therapeutically equivalent if they are pharmaceutical equivalents[29] for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.[30] This determination is generally automatic for generics, but for New Drug Applications ("NDAs") submitted under section 505(b)(2) of the FD&C Act (referred to as "505(b)(2) NDAs")—which can also be therapeutically equivalent—FDA will make a therapeutic equivalence determination only if the applicant submits a citizen petition requesting that the Agency do so, even if the only difference from the listed drug relied on in the application is a difference in *inactive* ingredients. And, as with all citizen petitions, it can take years before any decision is made. This issue is particularly acute for parenteral, and ophthalmic and otic use drugs; as generics must match both the active and *inactive* ingredients, with limited exceptions,[31] a follow-on applicant that cannot or does not want to pursue the same formulation can only submit a 505(b)(2) NDA.

Under section 505 of the Senate Draft, this subset of 505(b)(2) NDAs would no longer have to use the cumbersome citizen petition process or wait indefinitely for an evaluation of therapeutic equivalence with respect to a pharmaceutically equivalent listed drug relied on in the application. Rather, if the application includes a request for a therapeutic equivalence evaluation and all necessary data and information for such evaluation, FDA would be required to make the determination of therapeutic equivalence "at the time of approval of such application or not later than 180 days after the date of such approval." (Similar provisions govern applications that were submitted prior to the date of enactment, but that were approved on or after the date of enactment.) The provision appears to target the lowest hanging fruit in its bid to balance fostering competition with the Agency's resource constraints, and it represents a significant narrowing of the bill introduced by Senator Cassidy in March 2021, which would have required therapeutic equivalence determinations within 30 days of approval of all 505(b)(2) NDAs, and not just with respect to a pharmaceutically equivalent listed drug relied on in the application.[32]

Improvements to the Purple Book. FDA publishes certain information about listed biological products, including "the licensure status, and, as available, the marketing status,"[33] and biologics license application ("BLA") holders are already subject to certain reporting requirements that can bear on marketing status (*e.g.*, notification of permanent discontinuation or interruption in the manufacture of certain life-saving biological products,[34] submission of distribution reports,[35] and notification of the withdrawal from sale of an approved biological product[36]). However, BLA holders may now have additional reporting obligations.

One of the few areas of overlap between the Senate and House legislative packages, section 504 of the Senate Draft largely mirrors is sister provision, section 801 of the House Draft (but for some minor drafting differences). Section 504 of the Senate Draft would add biologics, including biosimilars, to the requirements in section 506I of the FD&C Act.[37] Accordingly, BLA holders would be required to notify the Agency 180 days prior to withdrawing a biological product from sale or if a biological will not be available for sale within 180 days of approval. BLA holders would also be subject to a one-time reporting requirement, confirming to the Agency whether all of its biological products listed in the Purple Book as not discontinued are available for sale or whether one or more of such products has been withdrawn from sale or has never been available for sale. The Agency would also be required to update the Purple Book to reflect this information. As noted in the House Draft Client Alert,[38] ensuring the Purple Book contains up-to-date and comprehensive information can be critical to biosimilar manufacturers, as the lack of availability of a reference product can add significant risk to a biosimilar development program. This is particularly true because FDA has not addressed whether, or how, an applicant could demonstrate biosimilarity (or interchangeability) to a reference product that is no longer marketed.

THE (CONTINUED) ROAD TO PASSAGE OF THE UFAS

Now that the Senate has introduced the bill, the next step will be for the Senate HELP Committee to mark-up the legislation. The House Draft, introduced on May 6, 2022 as the "Food and Drug Amendments of 2022" (H.R. 7667), has been moving on its parallel track at a swift pace, passing the Health Subcommittee via unanimous vote with no amendments on May 11, 2022. Even after mark-up by the full E&C Committee on May 18, 2022, the bill remained relatively unchanged. Only two provisions, in addition to a handful of minor tweaks to the existing language, were added: extending hiring authorities previously limited to medical products to all FDA-regulated products (a particularly salient concern given the ongoing infant formula shortage),[39] and providing additional authorities relating to pediatric studies of new combinations of cancer drugs (including biological products).[40] The bill was reported favorably to the House, as amended, by a unanimous vote.

Differences will need to be ironed out and the identical legislative package must pass the House and Senate before it can be enacted. Although the significant divergence in riders between the two bills could, on first blush, suggest trouble down the road, ultimately, it may simply reflect how the Chambers divided up the priorities. Regardless of how the dueling proposals are resolved, we expect additional motion to be fast and furious, with current user fee reauthorizations set to expire on September 30, 2022.

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 the user fee reauthorization process or specific provisions.

[1] *See* Food and Drug Administration Safety and Landmark Advancements Act of 2022, S. __, 117th Cong. (2022).
[2] U.S. Senate Committee on Health, Education, Labor, and Pensions, Press Release, *Senators Murray, Burr Release Legislation to Support FDA Programs to Lower Costs and Spur Innovation* (May 27, 2022), *available at* https://www.help.senate.gov/chair/newsroom/press/senators-murray-burr-introduce-bill-to-support-fda-programs-to-lower-costs-and-spur-innovation-
[3] *See* Food and Drug Amendments of 2022 ("House Draft"), H.R. 7667, 117th Cong. (2022); 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 Draft Client Alert"), *available at* https://www.kslaw.com/news-and-insights/and-so-it-begins-house-energy-and-commerce-leaders-unveil-fda-user-fees-legislative-package.
[4] *See* Food and Drug Administration Safety and Landmark Advancements Act of 2022 Discussion Draft ("Senate Discussion Draft") (2022).
[5] *See id*.
[6] *See generally* section 736B(f)(4) of the FD&C Act (21 U.S.C. § 379h-2(f)(4)) (PDUFA); section 738A(b)(4) of the FD&C Act (21 U.S.C. § 379j-1(b)(4)) (MDUFA); section 744C(f)(4) of the FD&C Act (21 U.S.C. § 379j-43(f)(4)) (GDUFA); and section 744*I*(f)(2) of the FD&C Act (21 U.S.C. § 379j-53(f)(2)) (BsUFA).
[7] *See Genus Med. Techs. LLC v. U.S. Food & Drug Admin.*, 994 F.3d 631 (D.C. Cir. 2021); *see also* House Draft Client Alert.
[8] *See* Lisa Dwyer et al., Client Alert, *Spotlight on PFAS and Other Substances in Cosmetics Likely to Grow in 2022* (Jan. 26, 2022), *available at* https://www.kslaw.com/news-and-insights/spotlight-on-pfas-and-other-substances-in-cosmetics-likely-to-grow-in-2022.
[9] *See* Personal Care Products Safety Act, S. 2100, 117th Cong. (2021) (introduced June 17, 2021 by Senator Dianne Feinstein).
[10] Dietary Supplement Health and Education Act of 1994, Pub. L. 103-417, 108 Stat. 4325 (1994).
[11] Certain information, such as the business name and mailing address of all locations at which the responsible person(s) manufacture(s), package(s), label(s), or hold(s) the dietary supplementary and the amount per serving of dietary supplements in a proprietary blend, would be withheld from public disclosure.
[12] *See generally* U.S. Food & Drug Admin., *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues* (Aug. 2016). This draft guidance pertains to implementation of the premarket safety notifications required under current section 413 of the FD&C Act (21 U.S.C. § 350b).

[13] 21 U.S.C. § 321(ff).
[14] *Id*. § 335a.
[15] *See* House Draft Client Alert.
[16] *See* U.S. Food & Drug Admin., *FDA In Brief: FDA Oncologic Drugs Advisory Committee to Review Status of Six Indications Granted Accelerated Approval* (Mar. 11, 2021), *available at* https://www.fda.gov/news-events/fda-brief/fda-brief-fda-oncologic-drugs-advisory-committee-review-status-six-indications-granted-accelerated.
[17] *See* Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act, Pub. L. 115-271, § 3032, 132 Stat. 3894, 3940–42 (2018).
[18] Section 505-1(e)(4) of the FD&C Act (21 U.S.C. § 355-1(e)(4)).
[19] 21 C.F.R. § 1300.05.
[20] Section 505-1(e)(4) of the FD&C Act (21 U.S.C. § 355-1(e)(4)).
[21] 87 Fed. Reg. 23869, 23871 (Apr. 21, 2022).
[22] 21 U.S.C. § 355-1(e)(4).
[23] 42 U.S.C. § 262(k)(6).
[24] The time period is determined by multiple factors, including the date of first commercial marketing as well as certain dates related to litigation initiated under section 351(*l*)(6) of the PHS Act (21 U.S.C. § 262(*l*)(6)), and can span 12 months to multiple years. *See* section 351(k)(6)(A)–(C) of the PHS Act (42 U.S.C. § 262(k)(6)(A)–(C)).
[25] For additional information, see Derrick Gingery, *Shared First Interchangeable Biosimilar Exclusivity May Be Allowed Under US FDA User Fee Bill*, PINK SHEET (May 25, 2021), *available at* https://pink.pharmaintelligence.informa.com/PS146098/Shared-First-Interchangeable-Biosimilar-Exclusivity-May-Be-Allowed-Under-US-FDA-User-Fee-Bill?vid=Pharma&processId=31e0f4ed-a13c-4ea6-b671-e492246eabc2.
[26] Senate Discussion Draft § 501; House Draft § 701. The House Draft also proposed to amend section 505(b)(5)(B)(i)(II) of the FD&C Act (21 U.S.C. § 505(b)(5)(B)(i)(II)) to replace the reference to animal studies with nonclinical tests.
[27] *See* section 351(k)(2)(A)(i)(I)(aa) and (cc) of the PHS Act (42 U.S.C. § 262(k)(2)(A)(i)(I)(aa) and (cc)) (requiring biosimilar applications to contain data derived from analytical and clinical studies).
[28] U.S. Food & Drug Admin., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (42d ed. 2022) (commonly known as the Orange Book).
[29] The phrase "pharmaceutical equivalents" is defined in 21 C.F.R. § 314.3(b).
[30] *Id*.; *see also* U.S. Food & Drug Admin., *Orange Book Preface*, *available at* https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface (explaining that FDA classifies as therapeutically equivalent those drug products that meet the following general criteria: (1) they are approved as safe and effective; (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the identical active drug ingredient in the identical dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent in that (a) they do not present a known or potential bioequivalence problem, and they meet an acceptable in vitro standard, or (b) if they do present such a known or potential problem, they are shown to meet an appropriate bioequivalence standard; (4) they are adequately labeled; and (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations).
[31] 21 C.F.R. § 314.94(a)(9)(iii)–(iv).
[32] *See* Modernizing Therapeutic Equivalence Rating Determination Act, S. 1463, 117th Cong. § 2 (2021).
[33] *See* section 351(k)(9)(A)(i)(III) of the PHS Act (42 U.S.C. § 262(k)(9)(A)(i)(III), as amended by Subtitle C, Section 325, the Biological Product Patent Transparency Act, of the Consolidated Appropriations Act, 2021. For additional information on the Biological Product Patent Transparency Act, *see* Eva Temkin et al., Client Alert, *"Purple Book" Patent Listing Under Biological Product Patent Transparency Act: What is Required, and What to Expect?* (Apr. 7, 2021), *available at* https://www.kslaw.com/news-and-insights/purple-book-patent-listing-under-biological-product-patent-transparency-act-what-is-required-and-what-to-expect.
[34] Section 506C of the FD&C Act (21 U.S.C. § 356c); 21 C.F.R. § 600.82.
[35] 21 C.F.R. § 600.81.
[36] *Id*. § 601.2(f).
[37] 21 U.S.C. § 356i.
[38] *See* House Draft Client Alert.
[39] Section 815, as added by an amendment offered by Rep. Brett Guthrie, agreed to by voice vote. The Senate Draft includes a similar provision. *See* Senate Draft § 701.
[40] Amendment offered by Rep. G. K. Butterfield, agreed to by voice vote.