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FDA Legislative Developments: What to Expect in Potential Year-End Packages

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Q1/Q2

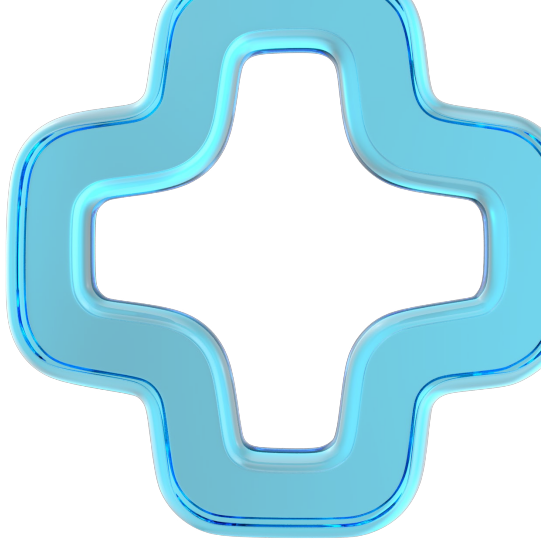
What is Q1 / Q2 Sameness?

> "Generally, a drug product intended for ***parenteral use*** must contain the ***same inactive ingredients and in the same concentration as the reference listed drug*** identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product."

21 CFR 314.94(a)(9)(iii) (emphases added)

There are similar requirements for generic versions of ophthalmic, otic, and topical products. Q1/Q2 sameness may also be important to gain waivers of in vivo clinical or pharmacokinetic bioequivalence studies under applicable Product-Specific Guidances

H.R. 1843/S. 1302, the Increasing Transparency in Generic Drug Applications Act



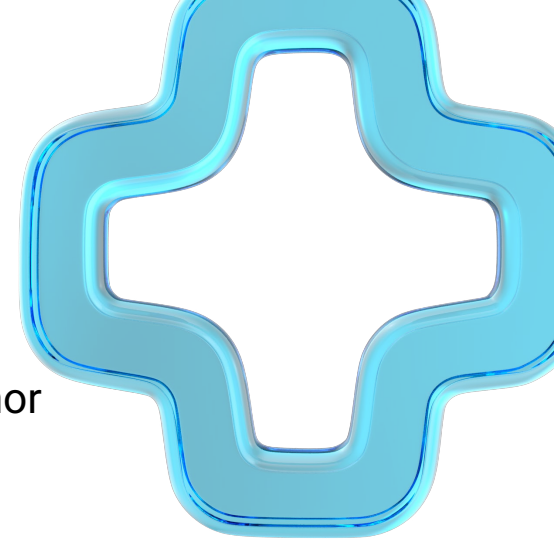
- Requires FDA to disclose to generics (1) the ingredient(s) causing a Q1/Q2 difference, and (2) the amount of any such difference
- Requires FDA to adhere to previous Q1/Q2 guidance unless (1) the formulation of the RLD has changed for reasons of safety or effectiveness, or (2) FDA makes a written determination that the prior determination must be changed because an error has been identified
- On September 17, advanced unanimously out of House Energy & Commerce markup as part of the Give Kids a Chance Act of 2025. Previously included as part of 2024 year-end funding bill, before it was pulled
- Scored to save $1B+ over 10 years

Interchangeability

Interchangeable Biosimilar Biological Products

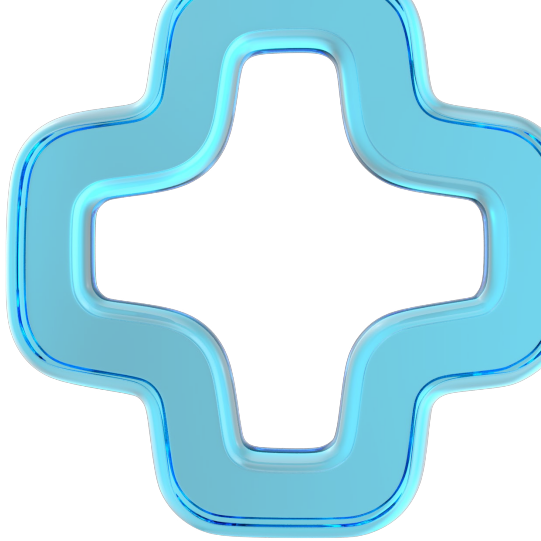
- The BPCIA passed as Title VII, Subtitle A of the Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119, §§ 7001-03. Signed into law on March 23, 2010.
- Key Provisions
  - Approval pathway
  - Biosimilar Data requirements
  - Interchangeability
  - Data/Marketing exclusivity
  - Patent issues
  - Biologic definition expansion
- Amends the PHS Act by adding:
  - § 351(k) – licensure requirements for biologicals as either Biosimilar or Interchangeable
  - § 351(l) – patent infringement disputes

Interchangeable Biosimilar Biological Products



- Under the BPCIA, the term “biosimilar” or “biosimilarity” means:
  - (A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and
  - (B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.
- The term “interchangeable” means:
  - (1) that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product,”
  - (2) can be expected to produce the same clinical result as the reference product in any given patient, and
  - (3) for a biological product that is administered more than once … the risk in terms of safety or diminished efficacy of … switching between use of the [biosimilar] and the reference product is not greater than the risk of using the reference product without such … switch.”

“Switching Studies” – FDA’s Current Position

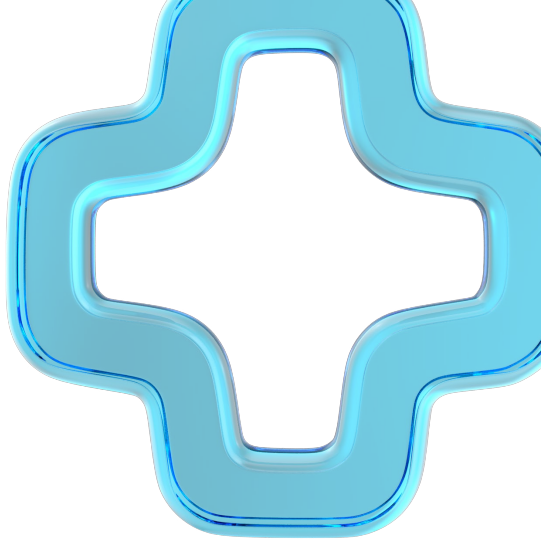


> “Since publication of the interchangeability guidance [in 2019], experience has shown that for the products approved as biosimilars to date, the risk in terms of safety or diminished efficacy is insignificant following single or multiple switches between a reference product and a biosimilar product.”

> “Accordingly, FDA’s scientific approach to when a switching study, or studies, may be needed to support a demonstration of interchangeability has evolved. FDA researchers found no differences in the risk of death, serious adverse events, and treatment discontinuations between participants who switched between biosimilars and reference products and participants who did not switch in a recently conducted systematic review and meta-analysis. Additionally, today’s analytical tools can accurately evaluate the structure and effects biologic products, both in the lab (in vitro) and in living organisms (in vivo) with more precision and sensitivity than switching studies.”

FDA, Guidance for Industry, Considerations in Demonstrating Interchangeability With a Reference Product: Update (June 2024)

“Switching Studies” – FDA’s Current Position

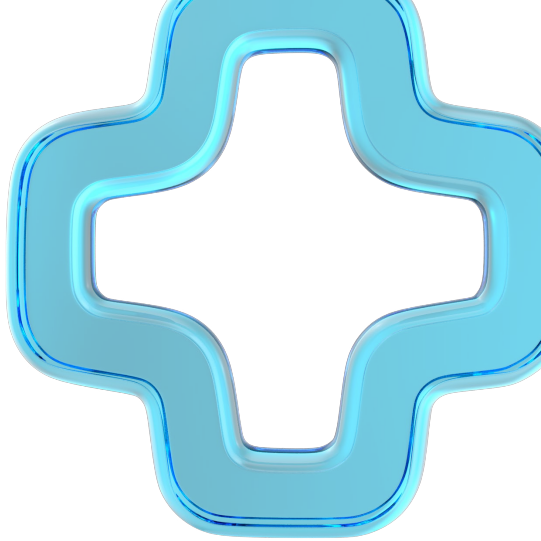


> “FDA has generally recommended switching studies in the past as part of the data package needed to demonstrate interchangeability of a biosimilar; however, of the 13 approved interchangeable biosimilars, 9 were approved without additional clinical (switching study) data. With the publishing of today’s draft guidance, FDA is seeking comment on a revised approach where such studies will generally not be needed.”

> “Applicants may choose to provide an assessment of why the comparative analytical and clinical data provided in the application or supplement support a showing that the switching standard set forth in section 351(k)(4)(B) of the PHS Act has been met.”

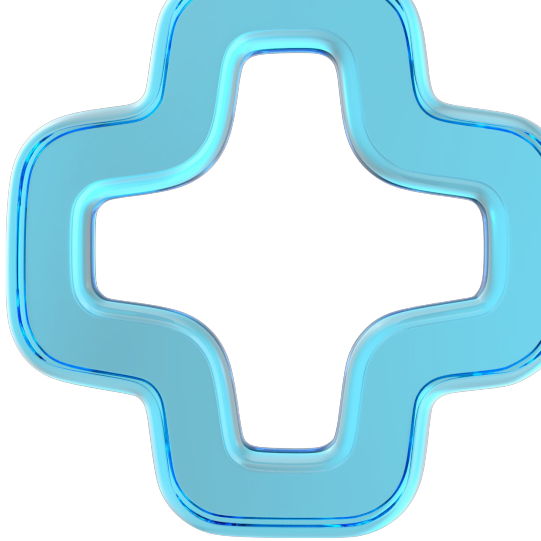
> “Applicants with a pending 351(k) BLA for a proposed biosimilar product may choose to submit an amendment to their pending BLA with the above-described assessment along with any additional data and/or information that they consider relevant to address the requirements in section 351(k)(4) of the PHS Act and request that their BLA be reviewed as a proposed interchangeable biosimilar.”

S.1954/H.R. 5526, The Biosimilar Red Tape Elimination Act - Generally



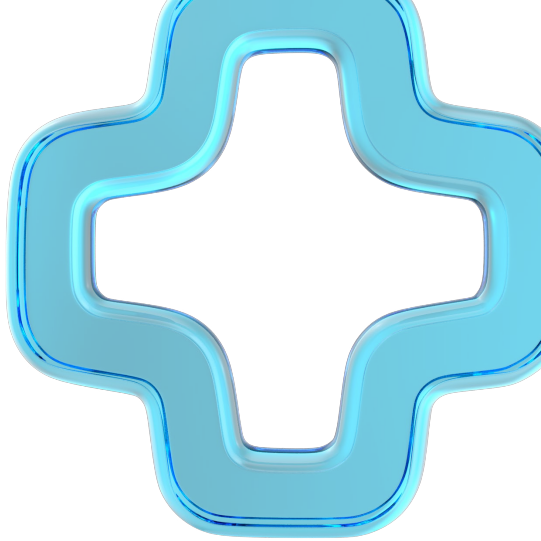
- Would amend the PHS Act to state that all biosimilars, upon licensure, shall be deemed interchangeable with their respective reference product.
    - The bill still uses the term “interchangeable” because states have crafted their own laws around interchangeability. Retaining that word would provide for minimal disruption to current biosimilar distribution.
- Strikes the current PHS Act requirement that has been used to justify switching studies.
- Creates a “cooldown” period for certain biologics that were already granted exclusive interchangeable status.
- Instructs HHS and FDA to issue or retract relevant guidance.

PREA Requirements



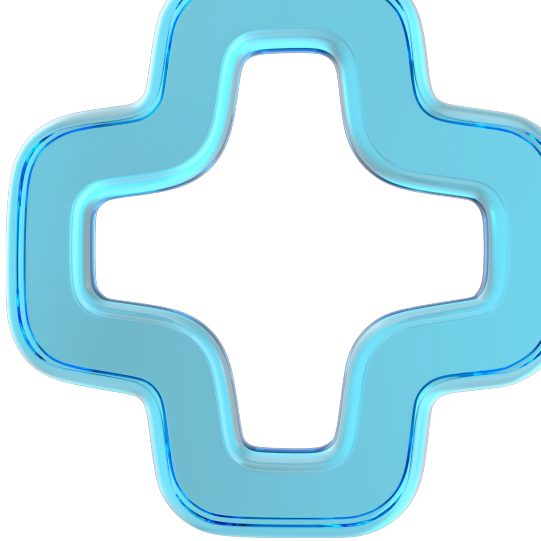
- Under PREA (FDC Act 505B), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain a pediatric assessment to support dosing and administration, safety, and effectiveness of the product for the claimed indication unless this requirement is waived, deferred, or inapplicable.
- Under FDC Act 505B(l), a biosimilar product that has not been determined to be interchangeable with the reference product is considered to have a “new active ingredient” for PREA purposes, and a pediatric assessment is generally required unless waived or deferred or inapplicable.
- An interchangeable product is not considered to have a “new active ingredient” for PREA purposes; however, if an applicant first seeks licensure of its proposed product as a biosimilar product, the applicant must address applicable PREA requirements for its noninterchangeable biosimilar product even if it ultimately intends to seek licensure of the product as an interchangeable product.

S.1954/H.R. 5526, The Biosimilar Red Tape Elimination Act – PREA Requirements



- In eliminating the distinction between highly similar biosimilars and interchangeable biosimilar biological products, the Biosimilar Red Tape Elimination Act also eliminates the need for companies to conduct expensive and time-consuming PREA studies.
- Exception – biosimilar seeks licensure for:
  - Claimed indication for which RP has been approved in pediatric population + RP assessment deferred
  - Assessment would not involve the development a strength, dosage form, route of administration, or condition of use that could not be licensed under section 351(k)

S.1954/H.R. 5526, The Biosimilar Red Tape Elimination Act – The Rule of Construction

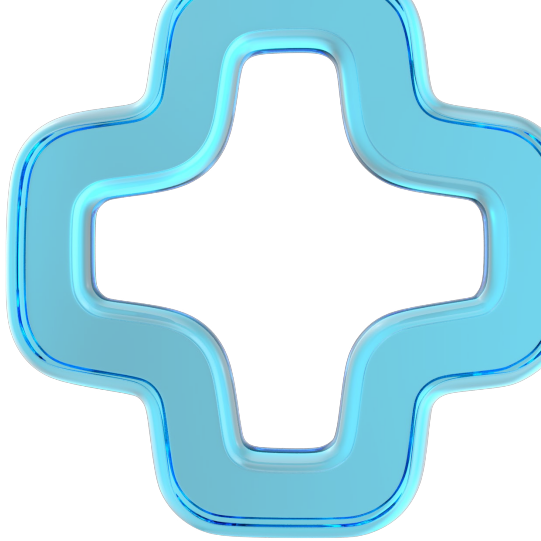


(d) RULES OF CONSTRUCTION.—
The amendments made by this section shall not be construed

> (1) to alter the standard or the information required for licensure of a biological product as biosimilar to a reference product pursuant to section 351(k) of the Public Health Service Act (42 U.S.C. 262(k)); or

> (2) to limit the information that may be required by the Secretary of Health and Human Services to support the licensure of a biological product as biosimilar to a reference product pursuant to such section.

S.1954/H.R. 5526, The Biosimilar Red Tape Elimination Act – The Rule of Construction

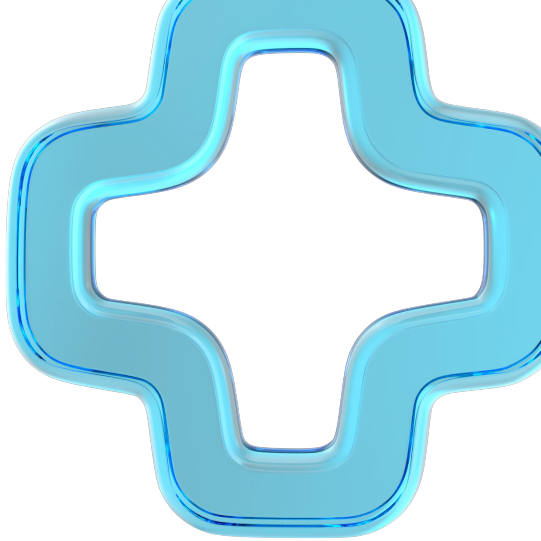


- Rules of construction are frequently used by courts to interpret legislation if, for example, there are disputes that are raised in Citizen Petitions or Administrative Procedure Act litigation.

- A bilateral rule of construction helps ensure balance between brands and biosimilars

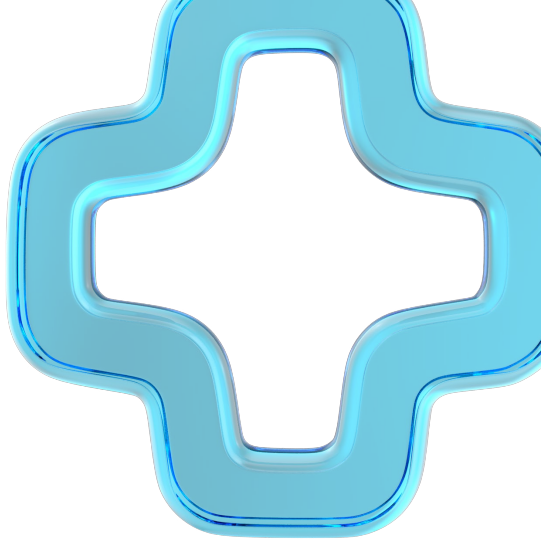
Clinical Trials

Biosimilar Approval Process



- To be approved as a biosimilar by FDA, applicants must demonstrate that the product is highly similar to and has no clinically meaningful differences in terms of safety, purity, and potency from an FDA-approved reference product.
- Biosimilar applications under 351(k) of PHS Act must include information demonstrating that the product:
  - utilizes the **same mechanism(s) of action** for the proposed conditions of use, but only to the extent the mechanism(s) are known for the reference product;
  - the **conditions of use** proposed in labeling have **previously been approved** for the reference product;
  - has the **same route of administration, dosage form, and strength** as the reference product; and
  - is manufactured, processed, packed, or held in a facility that meets standards designed to assure the product continues to be safe, pure, and potent.

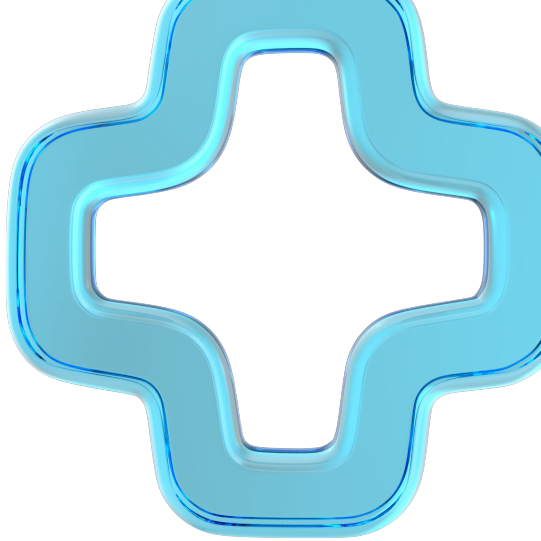
Data Required for Biosimilar Approval



- Under 351(k) of the PHS Act, biosimilar and interchangeable biosimilar products applications must provide data and information demonstrating biosimilarity, including:
  - **Analytical studies** of the structural and functional similarity and any minor differences;
  - **Assessment of toxicity;**
  - **Clinical studies** comparing pharmacokinetics, pharmacodynamics, and immunogenicity;
  - **Comparative clinical studies**, as needed, to address any residual uncertainty and ensure no clinically meaningful differences between biosimilar and reference product.

- FDA has discretion to determine that certain studies are unnecessary.

S.1414, Expedited Access to Biosimilars Act



- Introduced by Sen. Rand Paul (R-KY), the legislation aims to streamline the biosimilar approval process by “eliminating costly and redundant clinical study requirements.”

- S. 1414 amends the clinical study requirements under 351(k) of the PHS Act for biosimilar applications to:

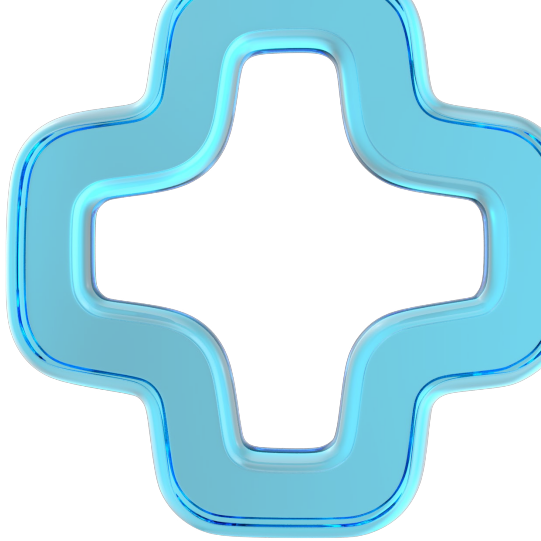
    1) Maintain the requirement for pharmacokinetic studies; and

    2) Require FDA to provide a written justification for immunogenicity, pharmacodynamics, or comparative clinical efficacy studies “not later than the earliest date on which the applicant may file the application”.

- If enacted, this change would mirror similar actions by international regulators to streamline biosimilar data requirements.

Catalyst and Pediatric Issues

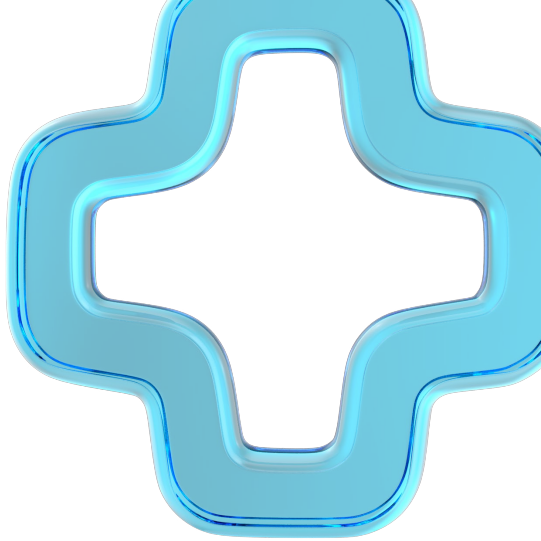
The *Catalyst* and *Neurelis* Orphan Drug Exclusivity Decisions



- In 2019, the U.S Court of Appeals for the Eleventh Circuit, and more recently, the U.S District Court for the District of Columbia, concluded that the Orphan Drug Act unambiguously defines the scope of Orphan Drug Exclusivity (ODE) by reference to the broader "'disease or condition' for which the drug was 'designated under [21 U.S.C.] § 360bb,'" not the particular "use" or "indication" for which FDA initially approved the drug product containing the orphan-designated active moiety.
  - *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021)
  - *Neurelis, Inc. v. Brenner*, No. 1:24-cv-1576-APM (D.D.C. Feb. 14, 2025) (on appeal to the DC Circuit)
- As the *Catalyst* Court explained:

> "The ordinary and plain meaning of [the Orphan Drug Act's ODE provision] yields only one result—the term unambiguously refers to the 'rare disease or condition' designated under § 360bb. Thus, the scope of exclusivity under [21 U.S.C.] § 360cc(a) is determined by what has been designated under § 360bb."

S. 932/H.R. 1262, The Give Kids a Chance Act of 2025



- Sec. 6. Limitations on exclusive approval or licensure of orphan drugs.
  - Strikes “same disease or condition” and inserts “same approved use or indication within such rare disease or condition”
  - Adds “(f) Approved use or indication defined.—In this section, the term ‘approved use or indication’ means the use or indication approved under section 505 of this Act or licensed under section 351 of the Public Health Service Act for a drug designated under section 526 for a rare disease or condition.”
- Retroactive
  - “Application of amendments.—The amendments made by subsection (a) shall apply with respect to any drug designated under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb), regardless of the date on which the drug was so designated, and regardless of the date on which the drug was approved under section 505 of such Act (21 U.S.C. 355) or licensed under section 351 of the Public Health Service Act (42 U.S.C. 262).”

Outlook

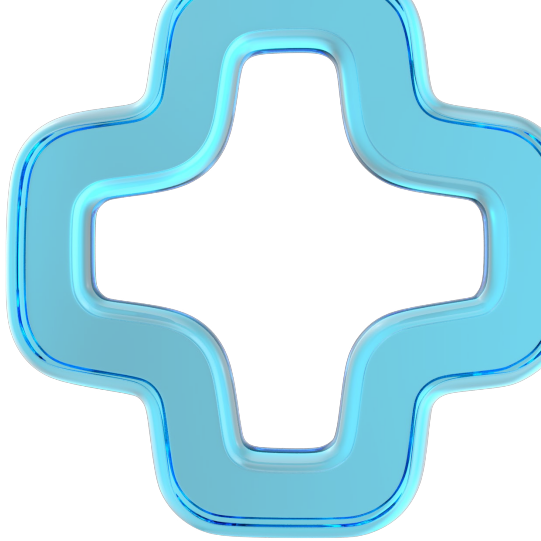
Congressional Outlook

In recent years, FDA and public health legislative packages have moved as a part of omnibus appropriations bills (FDORA, CARES).

To be considered for a larger package, Congressional leadership have maintained bills must have gone through regular order (i.e. hearing, markup).

Legislation that increases generic competition has generally been found by CBO reduce federal spending – which increases potential for Congressional consideration.

Likely legislative targets include upcoming deadline for appropriations, health extenders, or long-term budget deal.



Questions?