DETAILED OUTLINE OF THE ACCESS TO LIFE-SAVING MEDICINE ACT

I. Summary of Bill

- Amends section 351 of the Public Health Service (PHS) Act to authorize the Secretary of HHS to approve abbreviated applications for biological products that are "comparable" to previously approved ("reference") biological products.
- A comparable biological product application must demonstrate that there are no clinically meaningful differences between the two products. The application must also show that the new product shares the "principal molecular structural features" of the reference product and the same mechanism(s) of action, if known.
- The Secretary has discretion on a case-by-case basis to determine what studies are necessary to establish comparability, and may require a clinical study or studies, but only if necessary.
- A comparable biological product application will be subject to user fees.
- An applicant for a comparable biological product may elect, but is not required, to establish interchangeability. The bill establishes tax credits for the cost of studies demonstrating interchangeability and grants the first applicant to obtain approval of an interchangeable version of a biological product a period of exclusive marketing during which no other interchangeable version of the product may be approved.
- Applicants for comparable biological products may elect to ask the holder of the reference product for a list of patents on the product and may elect to notify the reference product holder and owner of one or more of the patents identified that the applicant has filed a comparable biological product application. If the applicant sends such a notice, it must contain a detailed statement explaining why the identified patent(s) is invalid, unenforceable, or not infringed. If the reference product holder fails to disclose a relevant patent, it may not enforce that patent against that applicant. If no patent infringement action is brought within 45 days of notice of a challenge, the remedy in any later action to enforce that patent against that applicant is limited to a reasonable royalty.

II. Section 1: Definitions

A. A biological product is defined as "comparable" to a previously approved ("reference") biological product if 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, based on non-clinical studies and clinical studies, as necessary.

B. An "interchangeable product" is defined as a product that can be expected to produce the same clinical result(s) as the reference product in any given patient.

III. Section 2: Regulation of Certain Biological Products

A. Submission of Comparable Biological Product Applications.

1. The bill requires an abbreviated application for a comparable biological product to contain information showing that, among other things,
    - the product is comparable to the reference product,
    - the two products have comparable principal structural features,
    - the two products have the same mechanism of action, if known,
    - the proposed product label carries one or more of the approved indications for the reference product, and
    - the route of administration, dosage form, and strength, are the same as the reference product.

2. The bill (like comparable provisions of Hatch-Waxman) permits submission of an application for a product that differs from, or incorporates a change to, the reference product, if the application contains sufficient information to show that the new product is safe, pure, and potent.

B. FDA Review of Comparable Biological Product Applications

The bill contains provisions that track the requirements of Hatch-Waxman for abbreviated application review procedures, and requires the Secretary, among other things, to meet with sponsors of comparable biological products and reach written agreements with them on the design and size of studies.

C. Approval of Comparable Biological Applications

1. The bill requires the Secretary to approve a comparable biological application unless the Secretary finds, for example, that:
    - There is insufficient information to show that the product is "comparable" to the reference product, as defined in the bill, for the condition(s) of use in the proposed labeling. If the mechanism of action of the reference product is known, the applicant must demonstrate comparability for at least one proposed condition of use. If the mechanism of action is unknown, the applicant must demonstrate comparability for each proposed condition of use.
    - There is insufficient information to show that product and reference product have comparable principal molecular structural features;
    - There is insufficient information to show that the two products have the same mechanism(s) of action, if known;
    - The new product differs from the reference product in route of administration, dosage form, or strength;

- The inactive ingredients used in, or the composition of, the new product are unsafe;
- The controls used in manufacturing the product are inadequate to assure identity, strength, quality, and purity;
- The reference product has been, or is being, withdrawn for safety or effectiveness reasons; or
- The application contains an untrue statement of fact.

2. The Secretary may also approve an enhanced version of a reference product if the application contains sufficient information to establish safety and efficacy.

D. Interchangeability Determinations, Labeling, and Exclusivity

Interchangeable biological products (those that could be substituted for the brand name product at the pharmacy) would generate the greatest cost savings, but because there currently is no equivalent of a simple "bioequivalence" study for biologics as there is for traditional drugs, would be significantly more costly and difficult to produce than comparable products. The bill therefore provides incentives for the development of interchangeable products, but does not require that each comparable biologic be interchangeable.

1. The bill allows a comparable biological product applicant to request an interchangeability determination. If a determination is made before approval, the Secretary must publish a therapeutic comparability evaluation code for the product at the time of approval.

2. Tax credits are made available for studies conducted to establish that a comparable biological product is interchangeable with the reference product.

3. If the Secretary determines that a comparable biological product is interchangeable with the reference product, the bill permits the label of the product to state that the product is interchangeable with the reference product for the approved conditions of use.

4. If an applicant is the first to establish that its product is interchangeable with the reference product, the bill prevents the Secretary from approving a subsequent application for an interchangeable version of the reference drug, until the earlier of (a) 180 days from first commercial marketing; (b) 1 year after a final court decision or dismissal with prejudice of all patent infringement cases instituted under this subsection; (c) 36 months after approval if such patent litigation is ongoing; or (d) 1 year after approval, if no such patent litigation was instituted. The bill also prohibits the marketing of a "rebranded interchangeable product" distributed with the authorization of the reference product holder during the exclusive marketing period.

E. Final Action on Applications

1. The Secretary must approve or disapprove an application for a comparable biological product eight months after submission, or 180 days after the application is accepted for

filing by the Secretary, whichever is earlier, unless the final action date is extended by joint agreement of the applicant and the Secretary.

2. The bill contains provisions to prevent frivolous petitions from delaying the approval of comparable biologics. The Secretary must not fail or refuse to take action by the final action date on the ground that a third party has made such a request, nor may a court enjoin the Secretary from taking final action or staying an approval except by permanent injunction. A permanent injunction may not be issued unless the person seeking the injunction demonstrates an injury of more than irrecoverable economic loss. The bill also requires a company who files a citizen petition to delay approval of a comparable biologic to do so at least 110 days before the effective approval date. A company may not file a lawsuit concerning a late-filed petition until 180 days after it was filed.

3. The Secretary must report to Congress any extension of the final action date and any failure to meet the final action date.

F. <u>Patents</u>

Early resolution of patent disputes is essential to ensuring that irrelevant or invalid patents do not delay competition in the marketplace. Provisions in Hatch-Waxman to ensure early resolution have not always worked as intended. This bill adds new disincentives for late patent suits, by limiting patent infringement actions and remedies in appropriate cases.

1. **Patent Requests.** Applicants for comparable biological products may elect to ask the holder of the reference product for a list of patents related to the product. The holder must respond within 60 days with a list of all related patents, including process patents, owned by or licensed to the holder, and may demand payment up to $1,000. For a period of two years, the holder must update the list within 30 days of the issuance a new related patent or license.

2. **Patent Notifications**. The comparable biological product applicant may elect to notify the reference product holder and patent owner that it intends to challenge one or more patents from the list provided. Any notice must contain a detailed statement of the factual and legal bases for the claim of invalidity or non-infringement and identify a judicial district in which the applicant consents to be sued.

3. **Patent Remedies.** The patent laws are amended by providing that if a patent is not disclosed in response to a request, that patent may not be enforced against that applicant. If a patent is disclosed and is the subject of a notice, but no patent infringement action is brought within 45 days of notice in the judicial district identified in the notice, or is not maintained through a final decision or dismissal with prejudice, the remedies in any later action to enforce that patent against the submitter of the notice are limited to reasonable royalties. The federal law governing declaratory judgments is amended to prohibit reference product holders from bringing actions for a declaration of patent infringement, validity, or enforceability with respect to patents that were not subject to a notice.