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CLIENT ADVISORY

"Comparable" Biologics Bill Introduced

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On September 29, Representatives Waxman (D-CA) and Brown (D-OH) and Senators Schumer (D-NY), Clinton (D-NY), Leahy (D-VT), and Stabenow (D-MI) introduced legislation to provide an abbreviated approval route for "comparable" (generic or follow-on) biologics. The bills, H.R, 6257 and S. 4016[1], which would amend the Public Health Service Act, are essentially a generic manufacturer's wish list. While this legislation has no realistic chance of enactment in its present form, it details the position of the generic industry on the contours of a follow-on biologics statutory framework, and signals the start of what will be a highly polarized legislative debate.

The following summarizes the bills, which are entitled the "Access to Life-Saving Medicine Act":

"Comparable" biologics. To qualify for an abbreviated application, the bill says that the follow-on product must:

- Have comparable principal molecular structural features to the innovator (the bill provides examples of comparable principal molecular structures);
- Have the same mechanism of action as the innovator, if the mechanism of action of the innovator is known;
- Have one or more of the approved indications of the innovator;
- Have the same route of administration, dosage form, and strength as the innovator;
- Not have unsafe inactive ingredients.

However, FDA would be given discretion to approve a comparable biologic even if it does not meet these criteria.

Basis for approval. The bill gives FDA wide discretion as to the type of data that will be required to approve a comparable product. The application can rely

1 The House bill is available at: http://www.house.gov/waxman/issues/health/generic_biologics.htm

The Senate bill is available at: http://www.arnoldporter.com/docs/resources/S4016_ClientAdvisory_ComparableBiologicsBillUpdate_100406.pdf.

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on "publicly available" information regarding the FDA approval of the innovator. It is not clear whether this is the same as the "finding" of safety and effectiveness that FDA says supports approvals of 505(b)(2) applications, but this provision would potentially allow the agency to cite its publicly articulated findings with respect to the innovator biologic to greatly reduce the product-specific data required for approval of a "generic" biologic. FDA could require post-marketing studies only if it has required such studies from the innovator.

505(b)(2)-like[2] follow ons. Follow ons can be approved that rely on innovator data but that differ from the innovator if adequate data to support the difference are submitted.

Therapeutic Substitution. Applicants need not show that their products are interchangeable with the innovator in order to obtain approval. They may, however, seek an FDA finding of "interchangeability" either before or after approval. Incentives are provided to applicants seeking such a finding.

- Whenever FDA makes such a finding, whether or not the finding is made at the time of approval, FDA must publish a therapeutic equivalence code.
- The House bill, but not the Senate bill, provides tax credits for studies conducted to establish interchangeability.
- The applicant can claim interchangeability on the product's label (and thus in advertising).
- The first applicant to get an interchangeability finding is given a potential period of exclusivity. The exclusivity ends at the earlier of:
  - 180-days from first commercial marketing;
  - one year after a court decision resolving all patent litigation brought under the amendments affecting the product;
  - 36 months after approval if such patent litigation is ongoing;
  - one year after approval if there is no such patent litigation.
- Authorized generics are prohibited during any exclusivity period.

FDA review period. FDA must approve or disapprove the application within 8 months of submission or, if earlier, 180 days after FDA accepts the application for "filing." The period can be extended by agreement with the applicant, but FDA must report to Congress any extension or failure to meet the final action date.

Citizen petitions. Several provisions affect citizen petitions or other requests to FDA that it not approve or delay approval of an application for a comparable product:

- FDA cannot miss an action date because of such a request.
- A citizen petition must be filed 180 days before the effective approval date in the absence of a showing of good cause for missing that deadline. (It is not clear how the petitioner is supposed to know in all cases when the application was filed and thus when the approval date might be.)
- Petitions must include a special certification, including disclosure of anyone who paid to have the petition filed.
- FDA must take final action on a citizen petition within 180 days, with no extensions permitted. No suit can be filed until final action on the petition.
- A court cannot enjoin FDA from taking final action on an application for a comparable product except by a permanent injunction. Such an injunction can not be issued, even when the plaintiff has prevailed on the

2 FDA has interpreted Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act to allow it to approve a second applicant's version of an innovator's product, when that second version differs from the innovator and thus would not qualify for approval of an ANDA, by relying on a combination of a "finding" by FDA that the innovator is safe and effective and data submitted by the second applicant that justifies the difference. This FDA policy is arguably not supported by the terms of the statute and remains controversial.

merits, unless failure to issue the injunction will threaten imminent destruction of the plaintiff's business (a standard that would be difficult for most innovator manufacturers to meet).

Requiring patent litigation on the "comparable" biologic applicant's timetable. Several provisions provide comparable biologics applicants with significant advantages in dealing with patents.

- Applicants or prospective applicants can at any time ask the innovator company for a list of all relevant patents. The innovator must provide a list, which must include process patents, within 60 days and update that list with any new patents within 30 days of issuance or of the innovator obtaining a license to the patent. Any patent not disclosed cannot be enforced against the applicant.
- Any applicant can decide to challenge any patent on the list provided by sending the innovator and patent holder a statement of the basis for the challenge.
- The applicant gets to choose the judicial district where it will be sued.
- Patent holders cannot seek declaratory judgment with respect to patents not subject to the notice sent by the applicant.
- If the patent holder does not sue within 45 days of receipt of the notice in the judicial district of the applicant's choice and pursue the case to completion, no remedies other than reasonable royalties can be obtained in any later suit.
- Unlike Hatch-Waxman, the bill would not provide a 30−month or any other delay in approval based on patents that are challenged, or delay approval of the "comparable" product until expiration of unchallenged patents.

The "Access to Life-Saving Medicine Act" is clearly the opening negotiating position of supporters of the generic industry. However, the legislation suffers from very significant gaps that undermine its credibility as a basis for negotiation. In particular:

- The proposed framework lacks an exclusivity period to protect the enormous investment in the data required to develop and achieve approval of an innovator biologic product. Assuming that scientific obstacles to creating a "generic" form of a given biologic can be addressed, the innovator would be subject to immediate patent challenges — on terms favorable to the "generic" applicant — and potential competition from "interchangeable" or even second generation products seeking to rely on the innovator's data.
- The bill, if enacted, would arguably put the United States in violation of its obligations under the TRIPS agreement by failing to provide data protection. It would also, by effectively allowing applicants to rely on the trade secret data of innovators, arguably constitute an unconstitutional taking of the innovator's property.
- The limitations on citizen petitions, while clearly intended to restrict anticompetitive filings, would also hamper legitimate oversight of FDA's scientific judgments regarding extremely complex comparability and interchangeability determinations.
- The bill fails to address the widely-held belief that biologics present unique safety issues, and that follow-on versions of approved products should be subject to additional post-licensure studies and surveillance to ensure that judgments regarding comparability — and certainly interchangeability — vis-à-vis innovators are borne out in actual use settings.

Despite these serious flaws, the follow-on biologics fight has now been engaged in Congress, and an alternative bill will reportedly be introduced by Senator Hatch (R-UT) in the near future. We can expect the

coming year to bring serious attempts to educate Members of Congress and move legislation in this area.

If you have questions about this issue or would like to discuss it, please contact:

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