BIO Principles on Follow-On Biologics

In order to ensure that new pioneer biotechnology products continue to reach patients and physicians, any statutory pathway for the approval of follow-on biologics must protect patient safety and preserve incentives to innovate.

"Biologics" are complex medicines that are manufactured using living organisms. These drugs are different and far more complex than most small molecule chemical drugs, and include many of the latest breakthrough medical therapies for serious and life-threatening illnesses, such as cancer, multiple sclerosis, diabetes, and HIV/AIDS, as well as many serious rare diseases. Due to their size and complexity, biologics generally cannot be scientifically characterized to the same degree as small molecule chemical drugs.

Follow-on biologics are not generic drugs. A generic drug is a product that is shown to be the same as an innovative drug, and is generally designated as therapeutically interchangeable with the innovator drug. Unlike generic drugs, a follow-on biologic (or "biosimilar") is a product that is similar to, but not the same as, the innovator drug. Because of the complex science involved, the Food and Drug Administration (FDA) and foreign regulators have indicated that the generic drug approval pathway is not appropriate for complex biologics.

As Congress explores the creation of any regulatory pathway for follow-on biologics, it is essential that Congress recognize and adopt the following key principles:

- **Ensure Patient Safety.** Patients should not have to accept greater risks or uncertainties in using a follow-on product than an innovator's product. Thus, Congress should:

    - Ensure that approval of follow-on biologics is based on the same rigorous standards of safety, purity, and potency applied by FDA for the approval of pioneer biotechnology products.
    - Recognize that clinical trial evidence and data are fundamental for evaluating and demonstrating the safety and effectiveness of a follow-on biologic, and must be conducted on a product-by-product basis. In particular, immunogenicity testing is necessary to avoid putting patients at risk of adverse effects from immune reactions.

- Not preclude adequate post-market evaluation of follow-on biologics products. It is critical that follow-on biologics are properly evaluated through post-marketing surveillance and post-marketing clinical studies as needed.
- Avoid specific constraints on the scientific conclusions FDA can reach in evaluating the similarity or comparability of follow-on biologics.
- Ensure that follow-on biologics will be assigned a non-proprietary name readily distinguishable from that of the innovator's version of the product. Assigning the same name to a product that is not the same would be confusing and misleading to patients, physicians, and pharmacists, could result in inadvertent substitution of the products, and would make it difficult to quickly trace and address adverse events that may be attributable to either the innovator or follow-on product.

- **Recognize Scientific Differences Between Drugs and Biologics.** Biologics are much more complex than small molecule chemical drugs. Thus, Congress should:

  - Recognize that the methods used to show that one chemical drug is the same as another are different from and insufficient for biologics. Thus, versions of a biological product made by different manufacturers must be evaluated on a case-by-case basis, because they will differ from each other in certain respects. The methods used by innovators to demonstrate continued safety and effectiveness after a manufacturing process change are insufficient to demonstrate safety and effectiveness of a follow-on biologic made by a different manufacturer using a different process.
  - Recognize that, as innovator companies' experiences with respect to pioneer biotechnology products have shown, and as FDA has long emphasized through its regulation and guidance, small product or manufacturing differences in biologics can result in significant safety and/or effectiveness differences.

- **Maintain the Physician-Patient Relationship.** Small molecule generic drugs can be designated as therapeutically equivalent and may be dispensed interchangeably with innovator products without physician knowledge. In contrast, the current state of science is not sufficient to establish interchangeability for complex follow-on biologics. Indeed, FDA recently stated that it "has not determined how interchangeability can be established for complex proteins." Accordingly, Congress should ensure that patients are not given follow-on biologics unless expressly prescribed by a physician.

- **Preserve Incentives for Innovation.** In order to preserve incentives to research, develop and manufacture new innovative therapies and cures, as well as new indications for such products, any statutory pathway for follow-on biologics must:

  - ***Include substantial non-patent data exclusivity***, during which time follow-on manufacturers could not rely on FDA's prior approval of pioneer biologics to support approval of their own products. Such data exclusivity is necessary

because a follow-on biologic may be similar enough to a pioneer biologic for regulatory approval purposes, but different enough to avoid the innovator's patents. Thus, non-patent exclusivity is necessary to maintain effective market protection. Further, the fledgling nature of the biologics industry, its heavy dependence on access to significant amounts of high-cost public and private investment capital, and the high risks and costs involved in the development of new biologic medicines all warrant a substantial period of exclusivity.

- ***Respect intellectual property and other legal rights.*** Follow-on biologic products should not be approved until after all statutory protections, including data exclusivity and patent protections, are no longer available for the approved pioneer product. Any follow-on biologics pathway should fully respect existing trade secret protections for innovators' data and not permit the use of protected data for the purpose of approving follow on products. It also must not abrogate or limit constitutional or statutory rights of patent holders to protect against infringement.

- ***Provide adequate notice and process rights.*** Any follow-on biologics regulatory pathway should ensure that any patent challenge involving the follow-on biologic product will be litigated prior to marketing approval of the follow-on product, in order to protect the innovator's intellectual property rights and avoid confusion in the medical, patient, and payer communities. Further, any follow-on biologics regulatory pathway should not create special patent litigation rules that favor follow-on biologics manufacturers.

- **Ensure Transparent Statutory and Regulatory Processes.** Manufacturers of innovator products should be provided full and fair opportunities to engage Congress and other stakeholders in a meaningful public process. Establishing a balanced and rigorous statutory pathway for follow-on biologics requires deliberative evaluation of numerous complex scientific, legal, intellectual property and economic issues. Further, any such pathway must require that FDA follow a transparent and public process in determining data requirements for the approval of specific follow-on biologics.

- **Continue to Prioritize FDA Review and Approval of New Therapies and Cures.** Any applications for approval of follow-on biologics will raise novel and complex questions of science and law, requiring substantial time and additional resources to ensure a thorough regulatory review for safety, purity, and potency. In order to avoid slowing down FDA's review and approval of new therapies and cures, many for currently untreatable and serious diseases, Congress must ensure that workload associated with these new applications does not harm FDA's ability to efficiently review new drugs and biologics, and that new treatments continue to have the highest review priority.

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