November 2, 2010

Margaret Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Hamburg:

Thank you for hosting the important Food and Drug Administration hearing on November 2-3, 2010, on the Approval Pathway for Biosimilar and Interchangeable Biological Products.

I write to call your attention and the attention of the hearing's panel members to an important defect in the Biologics Price Competition and Innovation Act of 2009, the first instance of which I am aware of a licensing barrier that, in effect, legislatively mandates that an applicant for marketing approval violate the ethical standards set out in, among other ethical codes to which the United States, its doctors and its researchers adhere, Article 20 of the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.

I refer to the 12-year period of data exclusivity included in the new law, which would prevent an applicant for marketing approval of a biosimilar or bioequivalent product from relying on existing data establishing the safety and efficacy of the product. Setting aside for the moment the relevant fact that such clinical trial data will likely have been paid for in large part by the taxpayer, my concern is with the ethical implications of such a bar to reliance on the data: an applicant for licensing approval of a bioequivalent or biosimilar product is left with only one option (short of abandoning its product): to repeat clinical trials to answer questions that have already been answered.

Article 20 of the Helsinki Declaration states, in pertinent part, "Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results." Yet a 12-year data exclusivity period by design requires exactly that: the conduct of a clinical trial despite the fact that "conclusive proof of positive and beneficial results" already exists.

By establishing such a de facto requirement, the biologics industry has achieved something quite profound: a virtually absolute bar to competitors for a full 12 years from market entry of a new product, regardless of the patent status of the product and despite that the industry itself reports that R&D costs for biologics are roughly equivalent to those of small molecule drugs for which a 12-year data exclusivity period is not in place. While such a stifling of competition is bad for our economy and health outcomes, among other things, its implicit requirement that companies, doctors and researchers must conduct unethical clinical trials in order to bring an affordable equivalent product to the market crosses a new line.

My legislation, S. 3921, the Ethical Pathway Act of 2010, would reform this indefensible requirement and is based on a simple premise: The US government should honor and respect international ethical standards for medical research, including the Declaration of Helsinki, by avoiding unnecessary repetition of clinical trials in human subjects. It is pro-patient, pro-research,

and pro-taxpayer, while providing for a system of cost sharing for drug registration data that will protect the legitimate financial interests of the innovators. S. 3921 would mandate that applicants for drug marketing approval, including generic and biosimilar producers, be allowed to rely on existing test data when applying for marketing approvals, subject to paying an appropriate share of the costs to rely upon the results of such trials.

I urge the Food and Drug Administration to pay close attention to the ethical implications of the new law it has been charged to implement, and to recommend to Congress that this fundamental flaw be addressed legislatively as soon as possible.

Sincerely,

Bernard Sanders
United States Senator

Summary:

Summary of Sanders Legislation
Ethical Pathway Act of 2010 - S. 3921

Background: The US government should honor and respect international ethical standards for medical research, including the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, by avoiding unnecessary repetition of clinical trials in human subjects. Specifically, applicants for drug marketing approval, including generic and biosimilar producers, should be allowed to rely on existing test data when applying for marketing approvals, subject to paying an appropriate share of the costs to rely upon the results of such trials.

Effect of S. 3921: S. 3921 would ensure that an applicant for regulatory approval of a pharmaceutical or biological product or vaccine is not effectively forced to violate ethical standards prohibiting the unnecessary repetition of testing of products in humans and vertebrate animals.

The bill would require an applicant for marketing approval, prior to initiating human or animal clinical trials, to verify that tests and studies necessary to support an application under section 505(j) of the Federal Food, Drug and Cosmetic Act (21 USC 355(j)), under section 351(k) of the Public Health Services Act (42 USC 262), or for a license to sell a drug in the U.S. that has been approved for marketing in a foreign country, have not already been performed or initiated.

It would direct the Secretary of HHS through the FDA Commissioner to establish a cost-sharing mechanism by which an applicant would be able to rely upon existing data. The applicant relying on such data would be required to pay a reasonable and fair fee to the entity that bore the costs of producing the relied-upon data or the rights holder, thus sharing in the cost of the data.

This arrangement could be arrived at in one of the following three ways:

(1) The holder of the rights over the data and the applicant could voluntarily negotiate a reasonable and fair fee and authorize reliance upon the data.

(2) If either party failed to voluntarily negotiate, or such negotiation failed to produce an agreement, the holder and applicant could be referred to binding arbitration by the FDA Commissioner to determine a reasonable and fair fee for reliance upon the data.
(3) If either party refuses to participate in such binding arbitration, the Commissioner would determine a reasonable and fair fee.

Determination of a reasonable and fair fee would take into consideration the following factors:

(1) The actual out-of-pocket costs of the applicable clinical investigations.
(2) The risks of the investigations, as reflected in the probabilities that similar investigations result in successful applications for marketing.
(3) Any Federal grants, tax credits, or other subsidies that reduce the net cost of the investigations.
(4) The expected share of the global market for the product involved, by the party seeking to rely upon the investigations for marketing approval.
(5) The amount of the time the holder or holders of the relevant applications or licenses has benefitted from exclusive rights, and the cumulative revenue earned on the products that relied upon the regulatory test data at issue.

Furthermore, for transparency and to make the system more predictable for rights holders and applicants, rights holders would be required to disclose the costs of generating the test data, and the cost- sharing payments by the applicants would be made public.
Related policies and proposals: The proposal is based in several precedents in both the United States and Europe, and is shaped by norms adopted by the Worlth Health Assembly in 2008, supported by the United States.

* In the United States, there is precedent for this type of cost-sharing arrangement under EPA approvals of certain agricultural test data.
* Switzerland, Norway and other countries have included in several recent trade agreements provisions that provide the possibility that pharmaceutical test data be protected by cost sharing, rather than through exclusive rights.
* More recently, in response to a campaign by animal rights advocates, the European Union has proposed in a new trade agreement with Canada, in the context of plant protection products, that both countries be required to develop "rules to avoid duplicative testing on vertebrate animals." In such cases, rather than protect test data through exclusive rights, an applicant would have a right to rely upon information from tests and studies already performed or initiated and, rather than granting the holder or holders of the relevant authorizations exclusive rights in the information, such holder or holders would have a claim on the prospective applicant for a fair share of the costs incurred in conducting the tests or studies.
* The 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, supported by the United States, addresses this issue in element 6.2., which reads as follows:
["The actions to be taken to improve delivery and access are as follows:"]
"(6.2) establishing and strengthening mechanisms to improve ethical review and regulate the quality, safety and efficacy of health products and medical devices...
... (g) promote ethical principles for clinical trials involving human beings as a requirement of registration of medicines and health-related technologies, with reference to the Declaration of Helsinki, and other appropriate texts, on ethical principles for medical research involving human subjects, including good clinical practice guidelines."