Testimony to the FDA hearing

"The need for an Ethical Pathway"

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Knowledge Ecology International (KEI) would like to submit the following Testimony to the FDA hearing on an Approval Pathway for Biosimilar and Interchangeable Biological Products.

On March 23, 2010, President Obama signed into law the Patient Protection and Affordable Care Act (Affordable Care Act). The Affordable Care Act contains a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) which amends the Public Health Service Act and other statutes to create an abbreviated approval pathway for biological products.

The BCPI Act created 12 years of exclusive rights to rely on test data for biological products. The mechanism for implementing this protection in effect requires second or subsequent applications for FDA approval to unethically and unnecessarily duplicate clinical trials on human beings and animals.

In order to avoid this unethical consequence, last month, U.S. Senator Sanders introduced S. 3921 to the 111th Congress, the Ethical Pathway Act of 2010. Complete Title: A bill to ensure that rules for the approval of pharmaceutical and biological products do not require violations of medical ethics in the testing of products in humans and vertebrate animals.

S. 3921 would ensure that an applicant for regulatory approval of a pharmaceutical or biological product or vaccine is not essentially forced to violate ethical standards prohibiting the unnecessary repetition of testing of products in humans and vertebrate animals. S.3921 establishes that in cases where the repetition of a clinical trial would violate medical ethics, a second or subsequent applicant for FDA approval would be allowed to rely upon the originators's data. If the test data was still under the effective term of protection as mandated by the BCPI Act, the reliance would be subject to a cost sharing agreement.

KEI suggests that the FDA Panel recommend approval of this legislation by Congress.

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.

S.3821 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:

• 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.

• 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.

• 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:

• The actual out-of-pocket costs of the applicable clinical investigations.

• The risks of the investigations, as reflected in the probabilities that similar investigations result in successful applications for marketing.

• Any Federal grants, tax credits, or other subsidies that reduce the net cost of the investigations.

• The expected share of the global market for the product involved, by the party seeking to rely upon the investigations for marketing approval.

• 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 World 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:"]
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> "(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."

KEI draws the attention of the FDA Panel to the following paragraphs of the Helsinki Declaration on Ethical Principles For Medical Research Involving Human Subjects:

> 20. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. 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.
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> 21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.

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KEI is a NGO with international staff and offices in Washington, DC and Geneva. For more than 20 years, KEI staff have provided intellectual and strategic leadership to the access to medicines movement in the US and in developing countries. For more information about KEI work program, contact us or visit our website www.keionline.org