

FTC Biosimilars Workshop FTC Questions / Hospira Responses

1. How State Substitution Laws May Affect the Development of FOB Competition:

Question	Hospira Response
<p>1. How would new state substitution laws passed in 2013, or similar proposals pending in other states, affect competition expected to develop between biosimilar or interchangeable biologics and reference biologics? In the context of state substitution laws, what is the likely competitive impact of a biologic product being designated “interchangeable?”</p>	<p>Multiple states still need to pass pharmacy laws that will allow pharmacists to substitute interchangeable biosimilars.</p> <p>The time to pass the state substitution laws is now, and Hospira feels it's necessary for the states to pass these laws to recognize the intent of BPCIA and the authorities granted to the FDA by Congress. It is the FDA's stance that only an interchangeable biosimilar can be substituted by a pharmacy without physician written consent, and Hospira agrees with this stance.</p> <p>It is important for stakeholders, especially consumers, to understand that biosimilars are not the same as small molecule generics. It is misleading to compare the two entities. Due to the complexity of protein-based biologic drugs, the requirements to gain approval of a biosimilar are more robust and complicated than for a small molecule generic. To diminish the significant costs of attaining approval of safe, efficacious biosimilars by comparing them to small molecule generics is a disservice to the regulatory bodies that have advanced and approved biosimilars and are developing the guiding principles of this new industry. Biosimilars are not generics; they are a new, evolutionary science and need to be recognized as one. Those manufacturers with real-life experience gaining approval of biosimilars can attest to the difference.</p> <p>It is also important for stakeholders to understand that there will be two levels of biosimilars in the United States those that are approved as interchangeable and those that are not approved as interchangeable by the FDA.</p> <p>The FDA has stated publicly on its website that only an interchangeable biosimilar is approved to be substituted by a pharmacy without physician consent.</p> <p>Hospira expects, as written in the BPCIA and initial guidelines proposed by the FDA, that to achieve an interchangeable rating approval by the FDA, a higher bar of evidence and data may be necessary than the evidence submitted just to achieve approval of biosimilarity. The timing of how and when a biosimilar would be approved as interchangeable will also not be uniform for each biosimilar, or each applicant. Hospira expects that interchangeability will most likely be approved on a case-by-case basis, based on the level of evidence submitted by the applicant and the complexity of the biologic. Interchangeability should not be a “one size fits all” recipe.</p> <p>At Hospira, we have publicly stated that we plan to have approval of one of our biosimilars by mid-decade, which is around the corner, so we feel strongly that the state substitution bills need to be passed this year, in 2014.</p> <p>Hospira supports physician communication as an important tool for pharmacovigilance, medical record keeping, physician education and building physician confidence in biosimilars. The communication should be advanced by an electronic communication system appropriate to the pharmacy setting in which the substitution occurs; for some this will be an interoperable electronic health record, for some this could be a computerized physician order entry system, for others, the communication may need to be done by fax or phone call. The consensus language proposed for state substitution of biosimilars was drafted with that intent. We encourage stakeholders who do not feel the language is adequate for their pharmacy setting to engage in constructive dialogue to further the consensus. Communication is not a barrier to biosimilar uptake; our experience shows that communication enhances biosimilars uptake.</p> <p>Over the past several years, Hospira has learned from our EU experience that physician education, confidence and communication are essential tools for the success of biosimilars uptake.</p>

FTC Biosimilars Workshop FTC Questions / Hospira Responses

<p>2. What are the compliance costs associated with new state law requirements? How are those costs likely to affect competition from biosimilar and interchangeable biologics?</p>	<p>Most hospitals, pharmacies and physician offices are implementing electronic health records and computerized physician order entry as part of the CMS meaningful use requirements, so the number of pharmacies that would not have the ability to communicate electronically is estimated to be relatively low.</p> <p>Hospira understands that this electronic communication is happening now in the majority of cases and is expected to be a part of normal pharmacy operations in the coming years.</p> <p>The consensus language proposed for state substitution of biosimilars was drafted with that intent. We encourage stakeholders who do not feel the language is adequate for their pharmacy setting to engage in constructive dialogue to further the consensus. Communication is not a barrier to biosimilar uptake, our experience shows that communication enhances biosimilars uptake.</p>
<p>3. What are the rationales behind new state proposals and laws for regulating FOB substitution? Which provisions are most important? Are some provisions redundant or otherwise unnecessary?</p>	<p>The state pharmacy substitution laws have to be passed because 30 years ago, when the generic industry was formed under Hatch-Waxman, the concept of biosimilars did not exist. The pharmacy regulations do not allow for the substitution of an interchangeable biosimilar, and we need to pass these laws now.</p> <p>The most important provision is that only an interchangeable biosimilar can be substituted by a pharmacist without physician orders. This is the FDA standard.</p> <p>Physician communication post-substitution of an interchangeable biologic from the pharmacies that do not have means for electronic communication is also a good idea.</p>
<p>4. Could an FDA publication concerning biologics and FOBs, comparable to the Orange Book, provide an authoritative listing of FOBs that are biosimilar to or interchangeable with reference biologics? Would such a publication facilitate substitution? Would such a publication need to be limited to interchangeable FOBs, or should it include both biosimilar and interchangeable FOBs?</p>	<p>Yes, and the FDA publication should list both interchangeable and non-interchangeable biologics. This is very important to physicians, pharmacies and consumers.</p>
<p>5. Does the potential for many different state laws regulating FOBs affect the prospects for the development of FOBs? Does the answer differ between biosimilar versus interchangeable biologic products?</p>	<p>Yes. Multiple state laws on the substitution of biosimilars will confuse pharmacies, physicians and consumers.</p> <p>This is why Hospira, with other key biosimilar leaders, supports moving forward with a consensus on state substitution bills in 2014.</p> <p>The FDA standard is that non-interchangeable biologics cannot be substituted by a pharmacy without the written order of a physician. This is an important distinction from a biosimilar that is not approved as interchangeable. As stated earlier, Hospira expects that a higher bar of evidence will be necessary to demonstrate interchangeability.</p>

FTC Biosimilars Workshop FTC Questions / Hospira Responses

<p>6. Would it be helpful to develop a model state substitution biosimilar law? If so, what provisions should the law include? Should state laws coordinate their guidance with provisions in the BPCIA and guidance from FDA?</p>	<p>Yes, we are pleased to join with other biosimilars leaders to advance a consensus on a model state law for biosimilar substitution.</p> <p>The model law is quite simple and flexible:</p> <ul style="list-style-type: none"> • State pharmacy laws should be updated to enable pharmacy substitution of interchangeable biologics, as approved by the FDA. • <u>After</u> substitution and dispensing, pharmacists shall communicate the information of the interchangeable biologic product dispensed to the prescriber within 10 days. . • Communication is not required where no FDA-approved interchangeable biologic product is on the market or where a refill prescription is not changed from the product originally dispensed. This is because the physician will know what biologic is dispensed, because they have written the prescription. • Electronic communication, such as interoperable health records, will meet the communication requirements. Where EHR's are not available, and another source of electronic communication is available in the pharmacy setting, that source should be considered by the state board of pharmacy as to whether or not it would meet the post-dispensing notification. <p>The consensus language is written to allow for flexibility across pharmacy settings, states, and time. All stakeholders are encouraged to engage in constructive dialogue to advance these state substitution laws now, because biosimilars will be on the market soon in the United States and we want patients to have access to them.</p>
--	--

2. How Naming Conventions May Affect FOB Competition:

Question	Hospira Response
<p>1. What has been learned from the experience under Hatch-Waxman about the incentives necessary to encourage physicians and patients to switch between branded and lower cost, therapeutically substitutable products? Do naming and name changes affect switching? If so, how?</p>	<p>The FDA determines which pharmaceuticals can be safely substituted by a pharmacy without physician consent. In the case of biosimilars, this will require an FDA approval as an interchangeable biosimilar. A pharmacy cannot perform therapeutic substitution without physician consent.</p> <p>Biosimilars need the same INN name as their reference biologic to prevent confusion and medication errors and to advance the uptake of biosimilars in the US.</p>
<p>2. How do the European Medicines Agency ("EMA") and other regulatory authorities comparable to the FDA handle the names of FOBs?</p>	<p>In Europe, biosimilars have the same INN as their reference biologic and a unique brand name. This is the same in other countries as well. In Europe, the physician prescribes the biosimilar. There is no substitution at the pharmacy level in Europe.</p>
<p>3. A prefix or suffix, such as "ado" or "TBO", has been attached to the nonproprietary names of several biological products licensed under a stand-alone biologic license application. How does the use of such prefixes or suffixes affect the inclusion of that product in third-party publications, compendia references, and health information systems, such as electronic health records and prescription processing systems?</p>	<p>Hospira feels that a prefix or a suffix added to the INN will confuse patients and physicians and will lead to medication errors. Hospira does not support a prefix or a suffix that would be attached to the INN.</p>

**FTC Biosimilars Workshop
FTC Questions / Hospira Responses**

<p>4. How does the use of certain identifiers, such as National Drug Codes, brand names, or nonproprietary names, work with existing adverse event reporting, track and trace, or other pharmacovigilance systems?</p>	<p>The current level of unique identifiers; brand names, NDCs, coupled with the same INN, are adequate for robust pharmacovigilance.</p>
<p>5. With respect to prescription drugs, does the use of nonproprietary names globally contribute to or detract from competition and consumer protection? Do any studies exist to show increased or decreased consumer benefits or harms, due to changes in names or naming conventions?</p>	<p>Same INN is a necessary GLOBAL requirement for biosimilars to reduce confusion and medication errors.</p>

CONTINUE TO NEXT PAGE

**FTC Biosimilars Workshop
FTC Questions / Hospira Responses**

3. How FOB Competition Evolved in Other Countries With Comparable Prescription Drug Regulation Regimes, and How FOB Competition Is Evolving in the United States:

Question	Hospira Response
<p>1. What, if any, predictions made in the FTC’s 2009 FOB Report should be revised in light of more recent data available on approved biological products or biosimilar development programs?</p>	<p>Based on Hospira’s experience in Europe since 2007, none of the FTC’s predictions from 2009 need to be revised at this time</p> <ul style="list-style-type: none"> -Competition Between a Biologic Drug and an FOB is Much More Likely to Resemble Brand-to-Brand Competition than the Dynamics of Brand-Generic Competition under Hatch-Waxman. -The substantial costs to obtain FDA approval, plus the substantial fixed costs to develop manufacturing capacity, will likely limit the number of competitors that undertake entry with FOB products. -Given these high entry costs, FOB entrants are likely to be large companies with substantial resources, and it is likely that only two to three FOB entrants will seek approval to compete with a particular pioneer biologic drug. -An FOB drug also may have difficulty gaining market share due to concerns about safety and efficacy differences between a pioneer biologic drug and the competing FOB. -The specialty pharmaceutical characteristics of FOBs also are likely to constrain the ability of an FOB entrant to obtain market share. -Existing Incentives that support Brand-to-Brand Competition Among Biologic Drugs – Patent Protection and Market-Based Pricing – Are Likely to be Sufficient to Support FOB Competition and Biologic Innovation. -A Twelve- to Fourteen-Year Exclusivity Period is Unnecessary to Promote Innovation by Pioneer Biologic Drug Manufacturers. -Special Procedures to Resolve Patent Issues Between Pioneer and FOB Drug Manufacturers Prior to FDA Approval Are Unnecessary and They Could undermine Patent Incentives and Harm Consumers. -FOB Drug Manufacturers Are Unlikely to Need Additional Incentives to develop Interchangeable FOB Products. -Hospira’s experience in global biosimilars demonstrates that the FTC 2009 report is still accurate.

FTC Biosimilars Workshop FTC Questions / Hospira Responses

<p>2. What has been the competitive effect of the market entry of biosimilar competitors in countries with drug regulatory approval standards comparable to those of the U.S. FDA, such as the EU, Australia, or New Zealand? After such entry, have reference biologic manufacturers lowered their prices, offered discounts, engaged in enhanced marketing activities, or increased innovation or next-generation developments?</p>	<p>Hospira’s EU biosimilars experience demonstrates that competitors are doing all of these things. Prices are being lowered, discounts are being offered and significant physician education is an entry-level requirement to advance the uptake of biosimilars.</p> <p>Hospira encourages the FTC and other government agencies to advance consumer education on biosimilars in the US. As we prepare to launch one of the first biosimilars in the US, we ask the U.S. government to advance education on biosimilars. Biosimilars are new innovations, requiring new science and new education. We would appreciate any support in educating consumers and physicians on the unique parameters of biosimilars and their safety and efficacy. This will be important for the success of this new industry.</p>
<p>3. Are there empirical models that could predict the nature of U.S. biosimilar or interchangeable biologics competition based on existing biologic product competition in Europe, Australia, New Zealand, or other countries? Are there empirical models that could predict the nature of U.S. biosimilar or interchangeable biologics competition based on existing competition in specialty drug markets? What factors increase or detract from robust competition between reference biologic and biosimilars or interchangeable biologics in other countries?</p>	<p>The largest factor detracting from robust uptake of biosimilars in Europe is the lack of unbiased consumer, patient and physician education that biosimilars are as safe and effective as their reference products.</p> <p>To achieve the greatest savings and increased patient access to biosimilars once the market forms in the United States, the U.S. government must proactively start educating consumers NOW.</p> <p>It is also important for the United States to understand that interchangeability and pharmacy-level substitution do not exist in Europe; they are U.S.-centric policies. For example, in Europe the definitions are quite different:</p> <p>Interchangeability: The medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with the agreement of the prescriber. In U.S. biosimilars, this will be approved by the FDA.</p> <p>Substitution: Practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber.</p> <p>Switching: Decision by the treating physician to exchange one medicine for another medicine with the same therapeutic intent in patients who are undergoing treatment. Pharmacists cannot switch in Europe without the written consent of a physician. In the United States, pharmacists will only be able to switch if the FDA has approved the biosimilar as interchangeable or if the physician has provided consent for the switch.</p> <p>Since decisions on <u>interchangeability</u> and <u>substitution</u> are not within the remit of the EMA/CHMP, and <u>interchangeability</u> studies are not part of the EMA registration requirements, such information may not be included in the EPAR.</p> <p>Using this learning and experience, the writers of the U.S. biosimilars legislation added an interchangeability provision to allow the FDA to approve for and advance pharmacy level substitution in the United States. The term “interchangeability” was placed in the BPCIA to allow the FDA to approve a biosimilar that could be substituted by a pharmacist without a physician order. The BPCIA two-tiered system was set up to reflect the needs of the U.S. pharmacy system and the status of biosimilars in Europe at the time, which was over 6 years ago.</p>

**FTC Biosimilars Workshop
FTC Questions / Hospira Responses**

<p>4. Based on the experiences in other countries, does competition from biologics influence investments in research and development for new biologics, improvements to existing biologics, and the timing and rollout of new and/or improved biologics? Does the market experience with generic drugs provide insights into these issues?</p>	<p>Hospira defers to the innovator side of the industry to answer this.</p>
<p>5. What data or empirical evidence exist in Europe or other countries regarding immunogenicity or other serious adverse events, if any, caused by substitution or switching between biosimilar and reference biologics?</p>	<p>Hospira has not experienced any immunogenicity with our biosimilars, nor unexpected adverse events in Europe or Australia. Hospira has instituted robust pharmacovigilance systems for post-market approval surveillance.</p> <p>Pharmacy-level substitution in Europe is not allowed.</p>