Governors Take Aim At FDA For Not Releasing Follow-On Biologics Guidances

A bipartisan group of four governors are accusing FDA of violating the Administrative Procedure Act by not issuing guidance documents on therapeutically equivalent versions of insulin and human growth hormone products.

“FDA’s unsubstantiated decision was arbitrary and capricious and in violation of the Administrative Procedure Act,” an Aug. 3 citizen petition filed on behalf of Governors James Douglas (R-Vt.), Jim Doyle (D-Wisc.), Tim Pawlenty (R-Minn.) and Kathleen Sebelius (D-Kans.) states. The petition calls for FDA to “publish specific requirements for applications seeking approval to market therapeutically equivalent versions of insulin and human growth hormone.”

“Despite the fact that FDA staff have drafted these documents and FDA officials repeatedly have indicated that these documents will be forthcoming, the agency has abandoned the product-specific guidance documents and apparently has decided to address the approval process for therapeutically equivalent insulin and HGH only in the context of guidance for all therapeutically equivalent biologic products,” the petition states.

“This new undertaking is a vastly broader endeavor...and a dramatically different class of biologics, which, at the current pace, will take many years to complete.”

FDA planned to issue product specific guidances but then changed course in favor of creating “more broadly applicable” guidance for follow-on biologics (“The Pink Sheet” April 10, 2006, p. 13).

Sen. Orrin Hatch (R-Utah), Rep. Henry Waxman (D-Calif.) and Sen. Hillary Clinton (D-N.Y.) have also pressed FDA for the release of the guidances.

The governors’ citizen petition refers to a Supreme Court ruling in Motor Vehicle Manufacturers Association of the U.S. v. State Farm in which the court held that “an agency must cogently explain why it has exercised its discretion in a given manner.”

“The agency has given no cogent explanation...for its failure and refusal to issue the guidance documents for insulin and HGH and to permit therapeutically equivalent versions of those products,” the citizen petition states.

The governors are requesting the release of the documents to facilitate the availability of more affordable and “therapeutically equivalent” versions of insulin and HGH in order to “help states reduce the burden of excessive pharmaceutical costs.”

The petition states that “having market competition for insulin and increased market competition for HGH products could save the American health care system hundreds of millions of dollars annually.”

“Based on previous experience with what occurs in price and savings when generic drugs [enter] the market, we can apply this to what could occur with insulin,” according to Sebelius’ office.

“Assuming a conservative 30% savings, the state of Minnesota and other purchasers could save $12.5 mil. per year from the use of generic insulin,” Pawlenty’s office said.

However, the price erosion assumptions that the governors use are at odds with other estimates of the potential impact of follow-on biologics.

Novartis, whose Sandoz subsidiary received U.S. approval for its HGH follow-on Omnitrope in June, has said that follow-on biologics will be priced at a discount to the brand, but not as low as for small molecule generics (“The Pink Sheet” May 1, 2006, p. 15). The company has not announced a U.S. price for Omnitrope but said the product will be sold in Europe at a 25% discount to the reference product.

Henry Grabowski, David Ridley and Kevin Schulman (Duke University) echo Novartis’ position on pricing in their forthcoming paper, “Entry and Competition in Generic Biologics.”

“Generic biologics will have high fixed costs from clinical testing and from manufacturing, so there will be less entry than would be expected for generic pharmaceuticals. With fewer generic competitors, generic biologics will be relatively close in price to branded biologics,” the paper states.
The governors did not include a formal economic impact analysis since such information “is to be submitted only when requested by the Commissioner following review of the petition,” the document states.

The petition also asks the agency to “commit to working with drug companies developing such products and to expediting the application process so that these products may be approved and made available to patients as quickly as possible.”

The petition recounts FDA’s actions over the past five years in developing the documents as evidence that “FDA is ready to issue regulatory guidance.”

The governors criticized FDA’s eventual decision to pursue broader guidance for being “dramatically different from the previous statements made by the agency indicating its intent to issue promptly guidance documents for insulin and HGH.”

The petition contends that there are no legal obstacles to the approval of follow-on versions of insulin or HGH, referring to their unique regulation under the FD&C Act and citing the recent approval of Omnitrope as evidence that approval of such products is legally possible.

The petitioners also maintain that there are no scientific barriers to approving follow-ons of insulin and HGH since “both drugs are widely acknowledged to be well-characterized, meaning that it is possible to fully understand and to document their different components and characteristics.”

“Resolution of the issues raised by the larger initiative may take several years because they involve newer, potentially more complex and less understood products.”

“If the scientific issues pertaining to insulin and HGH have been resolved, as appears to be the case, then the guidance documents should be released.”

According to Pawlenty, this is the first time a group of governors has submitted a citizen petition to the FDA. However, the Administrative Procedure Act has previously been used as a tool in the follow-on biologics debate to support arguments against approving an HGH follow-on.

In a citizen petition opposing the Omnitrope application—a follow-on to Pfizer’s Genotropin—Pfizer argued that FDA was in violation of APA by not relying on propriety Genotropin data to support the Omnitrope approval (“The Pink Sheet” June 7, 2004, p. 6). ♦ ♦