From: Toth-Allen, Jean
Sent: Friday, October 27, 2006 8:38 AM
To: [purged]
Subject: Drug + biomarker

Dear [purged]:

Your inquiry was forwarded to us for response.

As you are most probably aware, development of adequate biomarkers for use at various stages of drug development and/or use is becoming quite common. There are a number of products already on the market (e.g., Herceptin) which were initially approved along with a diagnostic to determine appropriate users. Therefore, it would seem quite feasible that FDA's Center for Drug Evaluation and Research (CDER) would be willing to take another look at a drug such as the one described in your scenario. Personalized medicine, which is a goal for the future, will be built on just such discriminatory use of pharmaceuticals. The manufacturer would need to initiate a discussion in this regard with the CDER review division responsible for the type of drug in question. The manufacturer will need to bring to this discussion both evidence for the selectivity of the biomarker and any and all results regarding the safety profile of the drug in different populations. CDER will need to consider these and all past experience when determining the feasibility of a new clinical trial to support a more defined/restricted use of the drug.

Hope this information is useful. If you need further information and/or have additional questions, please submit them once again to the official GCP mailbox, gcpquestions@oc.fda.gov, in lieu of responding to my personal e-mail address.
Sincerely yours,

Jean Toth-Allen, Ph.D.
Good Clinical Practice Program
OSHC, Office of the Commissioner, US FDA

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [purged]
Sent: Wednesday, October 25, 2006 6:20 PM
To: CDER DRUG INFO
Subject: DrugInfo Comment Form FDA/CDER Site

Name: [purged]

E-Mail: [purged]

Comments: Dear Sir/Madam

I would like to understand the FDA's position on the possibility of drug
rescue please.

Please consider the following scenario in the clinical trials process for DRUG X:
1) In patient population A there is evidence of toxicity, and/or lack of
efficacy
2) Patient population B is populated by non-responders, but they also do
not suffer adverse effects
3)In patient population A there is NO evidence of toxicity, and the drug
proves highly efficacious

But as a consequence of these results, a decision is made not to take the trial forward or the FDA decides not to approve DRUG X. Part of the problem was that there was no biomarker to stratify patients as positive
responders, negative or non-responders etc (or adverse responders).

However, sometime later a biomarker(s) was/were discovered which would serve to enable patient stratification. Would the pharmaceutical/biotechnology company then be allowed (and would the FDA grant permission, especially if the drug had been in phase III stage and
not been approved as an NDA) to undertake retesting of the drug in the patient population which is indicated by the biomarker to consist of positive and non-adverse responders?

This would then mean that drug would have probably have to be sold as a therapeutic medicine in conjunction with a diagnostic test for the biomarker.

Thank you for your immediate attention in this matter.

[purged]