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Global Research & Development

July 14, 2003

U.S. Food & Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD, 20852
Fax: 301-827-6870

Re: FDA Docket No. 03D-0120
"Multiplex Tests for Heritable DNA Markers, Mutations and Expression Patterns"

Dear Sir or Madam:

Thank you for the opportunity to comment on the Food and Drug Administration's ("FDA's") Draft Guidance entitled *"Multiplex Tests for Heritable DNA Markers, Mutations and Expression Patterns,"* published in the Federal Register on April 21, 2003. Pfizer submits these comments based on its experience in conducting mutiplex testing, and working to apply this technology to drug discovery and development. Pfizer appreciates the role and efforts of FDA in developing guidance on multiplex test submissions.

Multiplex testing allows the simultaneous assessment of DNA, RNA, or protein within a given sample. This technology increases in the granularity of data available to researchers and has the potential to revolutionize the drug discovery and development process. This innovative technology allows researchers to characterize disease, identify and validate disease targets, differentiate between chemical series, identify and validate safety and efficacy biomarkers, and make predictions on patient disease susceptibility and likelihood of drug response. Since the technology is still in it's infancy, guidance on how it should be applied and the reporting requirements surrounding those applications is an important step towards exploring the potential of this technology.

Studies designed to learn more about a disease, patient disease susceptibility, a compound, or patient response to a compound, are exploratory and should not require detailed reporting as described in Section I of this document. In the situation where there is an already established test used in the decision making process, multiplex data should be treated as part of an exploratory study and decisions continue to be made using the accepted test and criteria. In the event that information obtained during an exploratory study is used to identify a subset of expression patterns whose behavior will drive future decisions, then detailed reporting on that subset of expression patterns is essential.

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Section I.

The level of specificity required in the intended use section has the potential to become quite burdensome if the goal of a study is to identify a set of genes for use as biomarkers of compound efficacy or safety in later studies. When multiplex testing of RNA is being done to identify biomarkers, a least burdensome approach will indicate that the test is intended to measure RNA in order to identify potential biomarkers in a specified target population. Upon the identification of a biomarker, Section I can be applied towards the subset of genes being monitored to either diagnose a disease state or to measure efficacy or safety. This approach will facilitate the use of multiplex technology in both the identification and application of RNA biomarkers.

Section II B.

In instances when the intended use is to conduct a broad search for identifying biomarkers, Section IIB should not apply. However, when the intended use is to measure response or disease progression on the basis of a defined set of genes, this section may be applicable.

Multiplex testing of gene expression requires four major steps, 1) sample collection and processing 2) preparation of probe and hybridization to microarray, 3) image and data acquisition and 4) data analysis and reporting of results. Information that describes the process of sample collection, storage and processing is recommended since changes in these steps can affect the resultant data. Similarly, variations in probe preparation can markedly affect the results and subsequent conclusions drawn from an experiment. As such, validation (quantity of probe generated, acceptable size range of probe, reproducibility of labeling procedure) and reporting of the probe preparation process is extremely important and should be available.

We thank you for the opportunity to comment on the Draft Guidance.

Respectfully,

Pfizer Inc.

Heidi C. Marchand

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