July 18, 2003

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GlaxoSmithKline

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Re: NAS 0; Not Product Specific
General Correspondence
Medical Devices: Draft Guidance for Industry and FDA Reviewers; Multiplex Tests for Heritable DNA Markers, Mutations, and Expression Patterns; Availability. (Docket No. 03D-0120, CDRH 200316)

Dear Sir or Madam,:

We welcome the opportunity to dialogue with the Agency regarding the basic framework for the types of data and regulatory issues that should be addressed in a multiplex device submission.

GlaxoSmithKline is committed to discover, develop and deliver new medicines to address medical needs. GlaxoSmithKline is using information gleaned from the human genome throughout the drug discovery and development process to identify novel ways to combat disease, to predict toxicology and to identify genetic patterns to help determine how individual patients will respond to medicines (pharmacogenetics and pharmacogenomics). We support development of this timely guidance. As members of the Pharmaceutical Research and Manufacturers of America (PhRMA), GlaxoSmithKline has actively reviewed and contributed to the comments on this guidance submitted by PhRMA on July 11, 2003. We are in agreement with those comments. Additionally, given our interest in the interface between studies in clinical drug development and the use of multiplex assays, we wish to offer additional comments. These apply both to the guidance under current consideration and to companion documents that may be under development (http://www.fda.gov/bbs/topics/news/2003/beyond2002/report.html).

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Section I: Purpose, penultimate paragraph. We commend the suggestion that sponsors may submit "pre-IDE protocols". We suggest that when such consultation will impact both the conduct of the IDE study and the application of the resulting data to a drug development program, then the model for these consultations and their documentation would be the Pre-IND meeting guidance included in CDER guidance 2125 (Formal Meetings with Sponsors and Applicants for PDUFA products), and CDER MAPP 4512.1 (Formal Meetings Between CDER and CDERs External Constituents). If an alternate CDRH model or process is to be adopted, this should be specifically stated. The consultation would lead to generation of FDA minutes and correspondence that could be referenced by the sponsor(s) and both Centers during future interactions.

6. **Literature and Appendix 1, point 1:** This section identifies the use of literature to supplement or substitute for clinical performance studies. The draft would be more instructive if the Agency were to identify specific types of data that could potentially be supported by literature and what type of literature might be considered relevant by the Agency.

IV. B. Clinical Validation and Appendix 1, points 6 & 8: The guidance would benefit from greater detail regarding the precise nature and quantity of ethnicity data (as it relates to allelic frequency variation) required in the submission. We suggest that the bridging study approach described in International Conference on Harmonization (ICH) guidance E5: Ethnic Factors in the Acceptability of Foreign Clinical Data (June 1998) for extrapolating clinical data to new geographical regions, might also be applied to allelic frequency. Specifically the ICH guidance proposes that the authority should request only those additional data necessary to assess the ability to extrapolate and that the amount of data required be related to the impact of ethnic factors.

Need for Cross-Center agreements/processes: It is evident that multiplex tests will be used within the industry throughout the discovery and development process. It is currently unclear from the draft guidance how multiplex data will be reviewed across the Centers and Divisions of the FDA. For example, how would pharmacogenetic/pharmacogenomic multiplex data generated as part of an NDA be reviewed by CDER vs. data for a disease test submitted to CDRH? We believe that it will be important to ensure that the expectations of all Centers are harmonized with respect to submission and review of these data and therefore we request that comments arising on Docket No. 03D-0120 are shared with CDER/CBER as well as the CDRH authors of this guidance.

This submission is provided in paper via duplicate copies with an additional copy on diskette (Word 97) and an electronic copy via email according to the instructions provided at Http://www.accessdata.fda.gov/scripts/oc/dockets/commentdocket.cfm

Please contact me at (919) 483-4483, or my colleague Dr. Sue Hall at (919) 483-6159, if you require clarification of any of these comments. Thank you for your consideration.

Sincerely,

Alison Bowers
Director
Regulatory Affairs