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January 30, 2004

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Subject: [Docket No. 2003D-0497]  
Draft Guidance for Industry on Pharmacogenomic Data Submissions  
<http://frwebgate.access.gpo.gov/cgi-bin/leaving.cgi?from=leavingFR.html&log=linklog&to=http://www.fda.gov/dockets/ecomments>.

Quintiles Transnational Corp., a company which provides outsourcing services to pharmaceutical and biotechnology industries, appreciates the opportunity to comment on the above Draft Guidance for Industry, announced in the Federal Register: November 4, 2003 (Volume 68, Number 213) as available and distributed in November 2003 for comment purposes only. The Draft Guidance has been reviewed and discussed by representatives of several areas of Quintiles, including PharmaBio, Product Development, Early Development, Regulatory, and Data Protection.

FDA intends that this Draft Guidance on the Voluntary Genomic Data Submissions (VGDS) process provide recommendations to sponsors holding investigational new drug applications (INDs), new drug applications (NDAs), and biologics license applications (BLAs) on what pharmacogenomic data to submit to the Agency during the drug development process, the format of submissions, and how the data will be used in the regulatory decision-making process. Further, the Agency intends that this Draft Guidance facilitate scientific progress in the area of pharmacogenomics, which should enable the FDA to use pharmacogenomic data in regulatory policies and decision making. Quintiles believes that these are commendable goals, and is providing comment on the Draft Guidance in three sections as follows: **I.** Request for clarification/consideration; **II.** Request whether the Agency concurs with certain statements; and **III.** Requests for response by the Agency on certain views and questions that have been raised by the industry.

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***I. Quintiles requests clarification/consideration of the following issues.***

- Quintiles supports the concept of *voluntary* genomic data submissions. Quintiles plans to offer pharmacogenetic testing to all potential clients. In order to avoid conflicts of interest, Quintiles recommends clarification on how these data will be safeguarded within the Agency and how the Agency plans to safeguard potential discriminatory findings from one sponsor and how it may negatively impact another. For example, Company A voluntarily provides a detailed pharmacogenomic package, which reveals a gene-based defect in how a drug is used. Company B provides data for the same type of drug (same class) without any pharmacogenomic data. Will the data from Company A be used by the Agency with respect to Company B? How will the Intellectual Property be preserved?
- Quintiles asks for clarification regarding the designation of “voluntary” and “mandatory” pharmacogenomic data requirements – how this designation could change from the pre-IND phase through the post-marketing phase of clinical development. We recommend that each designation change should be defined *a priori*, with discussion between the Agency and the sponsor highly encouraged. The designation should be allowed to change during the development process.
- Quintiles requests further clarification when, for example, the validation methods for an exploratory pharmacogenomic (PG) data submission becomes validated. How are these data now out of the “safe harbor” originally provided by the Agency?
- Quintiles urges clarification by FDA as to how the “cross-center Interdisciplinary Pharmacogenomic Review Group (IPRG)” will operate. Quintiles encourages the FDA to include industry representatives in the IPRG, at least in an advisory capacity. Quintiles recommends, in particular, that representatives from industry organizations such as PhRMA, BIO, DIA, as well as the Association of Clinical Research Organizations (ACRO) be included. Quintiles requests that a complete list of proposed participants be made available.
- Quintiles requests that an initiative be implemented by the Agency in order to address and provide specific recommendations for the process of tests for fast and slow metabolizers.
- Quintiles seeks clarification on how data from large non-US databases such as Iceland’s Decode, Estonia’s database, and the Scotland initiative will be received by the Agency.
  - Will these data be perceived differently than those supplied by US databases?
  - The Health Insurance Portability and Accountability Act (HIPAA) privacy regulation applies equal protection to all identifiable health information, including genetic information. However, many consider genetic data as warranting added protections.

For instance, several States have enacted or are enacting laws that apply standards stricter than HIPAA for the protection of genetic data. Compliance with numerous State laws on genetic data may influence the development of pharmacogenomic drugs. As it seems that FDA will occupy the field of pharmacogenomic data submissions, will such State laws be preempted to some extent?

- The European Union (EU) Data Protection Directive has strict rules regarding the transfer of personal data, including sensitive personal data such as identifiable health information, out of the EU to a country without what it regards as an “adequate level of protection.” In contrast to the Directive, which protects all personal data, the US privacy laws are sector specific, such as the HIPAA privacy regulation for the health sector. Accordingly, the EU deems that the US laws do not provide an adequate level of protection to receive personal data, including genetic information. Further, the EU has not set forth uniform standards for de-identification of genetic data. Further, the EU is in the process of developing additional, perhaps stricter, standards for the protection of genetic data, and may further limit the collection or transfer of such data. Depending on the final version of such rules, there could be a negative impact on the development of pharmacogenomic drugs, pharmacogenomic databases, and information sharing. Will FDA provide comment to the EU on these concerns?
- Quintiles regards that clinical, social and ethical issues should be included in the final draft document to provide evidence of the Agency’s thought process for the legal aspects and manifestations of voluntary and mandatory pharmacogenomic data submissions.

***II. Quintiles asks whether the Agency concurs with the following statements***

- Companies find it difficult to interpret their pharmacogenomic data. For labeling claims, data needs to be validated and submitted. However, pharmacogenomic data can also be kept private or may be voluntarily submitted to the Agency. In both cases, data would not be subject to regulatory implications (i.e., companies will not be penalized at a later date for voluntary data submissions). Voluntary data for FDA education would not be made available to the medical reviewer when considering an (NDA/BLA) application, but could be used to prepare the FDA for appropriate evaluation.
- For an IND, pharmacogenomic data would be considered exploratory or of a research nature. No current FDA regulations exist which require such data to be submitted to an NDA or BLA.

*III. Request for consideration of the following views and questions raised by Industry:*

1. It is too risky and costly to submit data in a VGDS format.
2. The standards for data among different companies are not likely to be the same and vary with the technologies used.
3. What happens if a third party develops a pharmacogenomics marker for another company's drug? Who will validate it, and how will the "defending" company get the knowledge and opportunity to review this marker data?
4. Diagnostic companies believe that the FDA's response allows them an opportunity to display the properties of their array plate measures of gene expression.
5. The FDA needs to rationalize data from pharmacogenomic studies and define how the data are abstracted.
6. The FDA needs to define "validated gene markers."
7. Who in the FDA would review the voluntary data? Would any outside experts be allowed to review the data?
8. Will other worldwide regulatory authorities see the voluntary data?
9. How will informed consent issues be handled regarding the possibility that the research subjects' genetic data may be provided to FDA?
10. Of what quality are the current technologies, and what does the data mean?

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Quintiles appreciates the opportunity to provide comment to this Draft Guidance and agrees with many aspects of this Draft Guidance. Quintiles requests clarification and consideration of certain matters and encourages representation from Industry in the Interdisciplinary Pharmacogenomic Review Group (IPRG).

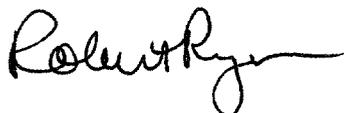
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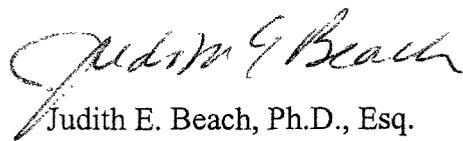
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