



June 20, 2023

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Sent electronically to <https://www.regulations.gov>

**Re: Pharmacogenomic Data Submissions, Guidance for Industry: Draft
Guidance Docket No. FDA-2022-D-2856**

Dear Dr. Pacanowski and Mr. Ripley:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group that convenes more than 220 institutions from across the health care spectrum to promote the understanding and adoption of personalized medicine concepts, services, and products for the benefit of patients and health systems, thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the *Draft Guidance on Pharmacogenomic Data Submissions*. We understand that the draft guidance outlines FDA's expectations for the submission of data from pharmacogenomic (PGx) studies in investigational new drug applications (INDs), new drug applications (NDAs), and biologics license applications (BLAs), replacing the previous *Pharmacogenomic Data Submissions* final guidance published in 2005. PMC's comments below express support for the agency's efforts to update its guidance on PGx data submissions. We also offer suggestions on how to best characterize some types of PGx information and how to standardize the location of PGx information submitted in applications.

Personalized medicine is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients. Personalized medicine is playing an important role in transforming care and patient outcomes for a range of serious and life-threatening diseases and conditions, helping to shift patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions.

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PGx testing is a cornerstone of personalized medicine, providing a way to guide treatment and prevention strategies based on individual patient characteristics. The use of diagnostic tests to detect drug-gene associations can play an important role in avoiding adverse events, optimizing drug dosing, and identifying patients who will or will not respond to certain medications.

PMC and FDA share the goal of achieving better health outcomes for patients by improving treatment safety and efficacy. Clear FDA guidance on how PGx data should be submitted in new drug and biologics applications will help achieve this goal. Since the previous guidance was published, many significant technological advances in genomics research and PGx have occurred. We applaud FDA for providing updated guidance so that stakeholders can better understand and navigate data submissions to the agency in the modern landscape. We believe the new draft guidance helps clarify when and how to submit required PGx data in INDs, NDAs, and BLAs, as well as FDA's expectations regarding the format for reporting of this data. However, to facilitate clearer and more consistent labeling for new products with PGx implications, we encourage FDA to more thoroughly standardize the placement of PGx information within submissions and standardize the types and categories of metabolic PGx information to be submitted.

Statement of Neutrality

Many of PMC's members will present their own responses to the *Draft Guidance on Pharmacogenomic Data Submissions* and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance. These comments are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the initial guidance and/or any that follows.

Location of PGx Information Within IND, NDA, and BLA Submissions

The draft guidance proposes that sponsors provide PGx study findings when they support the use of a genomic biomarker in the design, conduct, or analysis of a planned clinical trial either under the "Previous Human Experience" section of the IND, NDA, or BLA, in the meeting package, or in clinical study protocols or reports. Other PGx study findings must be described in *Annual Reports*, such as those pertaining to studies that identify significant predictors of treatment response, findings related to pharmacokinetics, or results from completed clinical trials where the biomarker was integral to the design, conduct, or analysis of the study and are relevant to understanding the drug's actions. Additionally, PGx findings that identify predictors of adverse events with the potential to pose significant risks are required to be submitted in the *Safety Report* for INDs. NDA and BLA sponsors must also submit a detailed report with subject-level data when the genomic biomarker study results are proposed for inclusion in labeling, including for determining dosing and administration or informing drug-drug interactions. The draft guidance also notes that synopses or detailed reports should be referenced within relevant sections of the submission. Additionally, the draft guidance states that FDA encourages sponsors to summarize these data in relevant submission summaries such as the *Integrated Summary of Safety or Effectiveness*.

Considering all the various PGx-related data that sponsors may need to include in multiple sections of a submission, including additional findings that may be included in annual reports, we recommend that the agency provide clear standards regarding what types of information go into which sections of a submission and under what circumstances this information is required. We also recommend that submissions require addition of a standard “pharmacogenomic information summary,” to include all PGx information included within the submission, to be completed when applicable. This will allow sponsors and reviewers to access PGx information more easily and will provide more clarity on when and how this information may apply to treatment dosing and administration. This will be especially useful when submitting annual reports during drug development. This also could help facilitate, at the time of approval, drug labeling in a more standardized way that most clearly indicates PGx interactions and recommendations for testing.

Metabolic Phenotypic Categories

We recommend that the draft guidance consistently note currently recognized categories for PGx information and consider stating that current PGx concepts should be reflected within submissions. For example, since therapy recommendations relevant to PGx testing are often based on metabolic phenotype categories for many genes, we recommend in the section about detailed reports that FDA add “metabolic phenotype distributions for relevant genes” after “genotype/haplotype distributions.”

Additionally, FDA should specify that in PGx studies, the translation of diplotypes to phenotypes should be included according to recognized PGx standards such as through the Clinical Pharmacogenetics Implementation Consortium (CPIC) tables (www.cpicpgx.org). If different translations of diplotypes to phenotypes are used, these should be clearly described. This information will provide helpful clarity.

Finally, since most laboratories performing PGx testing use high-throughput microarray technology, it might be beneficial for FDA to state “high-throughput microarray and DNA sequencing” in the background description on Page 2.

Conclusion

PMC appreciates FDA’s commitment to ensuring better health outcomes through improved safety and efficacy of treatments with consideration of PGx information. As the agency finalizes the *Guidance on Pharmacogenomic Data Submissions*, we encourage FDA to consider our comments regarding standardization of data submissions that may help facilitate clearer treatment recommendations. If you have any questions about the content of this letter, please contact Daryl Pritchard, PMC’s Senior Vice President for Science Policy, at dpritchard@personalizedmedicinecoalition.org, or David Davenport, PMC’s Manager of Public and Science Policy, at ddavenport@personalizedmedicinecoalition.org.

Sincerely,



Daryl Pritchard, Ph.D.
Senior Vice President, Science Policy