OFFICE OF THE CENTER DIRECTOR

Management of the Interdisciplinary Pharmacogenomics Review Group (IPRG)

CONTENTS

PURPOSE

This MAPP describes

- The role and responsibilities of the Interdisciplinary Pharmacogenomics Review Group (IPRG)
- Procedures to be used in designating members to serve on the IPRG
- The structure and function of the IPRG within the FDA

BACKGROUND

At present, most pharmacogenomic data are of an exploratory or research nature, and FDA regulations do not require that these data be submitted to an investigational new drug application, or that complete reports be submitted to a new drug application or biologics licensing application. However, to be prepared to appropriately evaluate anticipated future submissions, FDA scientists need to develop an understanding of relevant scientific issues, such as:

- The types of genetic loci or gene expression profiles being explored by the pharmaceutical industry for pharmacogenomic testing
- The test systems and techniques being employed
- The problems encountered in applying pharmacogenomic tests to drug development and to clinical outcomes
- The ability to transmit, store, and process large amounts of complex pharmacogenomic data streams with retention of fidelity

As described in the guidance for industry on *Pharmacogenomic Data Submissions*, the FDA is asking sponsors conducting such programs to consider providing pharmacogenomic data to the Agency voluntarily, when such data are not otherwise required by regulation. The guidance also announced the formation of a cross-center Interdisciplinary Pharmacogenomic Review Group (IPRG) to review voluntary pharmacogenomic data submissions (VGDSs) and communicate with sponsors, provide

guidance to the reviewing divisions on required submissions; and work on ongoing pharmacogenomic data submission policy development. This MAPP provides the charter for the IPRG.

REFERENCES

- Guidance for industry*, Pharmacogenomic Data Submissions*
- CDER MAPP 4180.3, Processing and Reviewing Voluntary Genomic Data Submissions
- CBER SOPP 8204, Processing of Voluntary Genomic Data Submissions
- CBER SOPP 8114, Administrative Processing of Documents Received Prior to Submitting Investigational or Marketable Submissions (Pre-Submissions).

DEFINITIONS

IPRG: Designation for Interdisciplinary Pharmacogenomic Review Group. The IPRG will oversee the review of all VGDSs submitted to the Agency and consult, on request, on the GDSs.

GDS: Designation for Genomic Data Submission

Voluntary GDS (VGDS): Designation for Voluntary Genomic Data Submission

Stand alone VGDS: The designation for a voluntary GDS that is not associated with an existing application. Such voluntary submissions will be handled as submissions to a new pre-IND application.

Associated VGDS: The designation for a voluntary GDS that is submitted to an existing application (e.g., investigational new drug application (IND), new drug application (NDA), biologics licensing application (BLA), or supplement). Such information will be submitted to the existing application, but will not be used by FDA in the regulatory decision making process.

Required GDS: The designation for a GDS that is required (per the relevant regulations) to be submitted to, or as part of, an existing application (e.g., IND, NDA, BLA, or supplement) and that will be used during the regulatory decision making process. This MAPP does not address required GDS submissions which will be processed according to standard processing for routine application submissions.

GENERAL POLICY

- The FDA will not use information submitted through the voluntary process for regulatory decision making on investigational and marketing/licensing applications.
- The IPRG will review all VGDSs.
- The reviewing divisions can request a consult with the IPRG on ***required*** GDS submissions.
- Required GDSs will be part of the associated application.
- VGDSs will be received by the Agency, processed, and sent directly to the IPRG.

- The IPRG will be the primary contact (internal and external) for all voluntary submissions, coordinating the communication with sponsors and the FDA regarding all VGDS-related issues.
- When an exploratory biomarker appears to be a probable or known biomarker, the IPRG will initiate a meeting of the Pharmacogenomic Advisory Subcommittee to allow public assessment of the related issues.

ORGANIZATION (See graphic depiction in the Attachment)

- **Oversight** – A senior manager appointed by the FDA Commissioner (***the OC Representative***) and the ***Center Directors of CDER, CBER, and CDRH*** will oversee the IPRG.

- **Location** – Although an interdisciplinary group, the IPRG is located in CDER in the immediate Office of Clinical Pharmacology and Biopharmaceutics.

- **IPRG Members** –
  - ***Chair***, appointed by the OC representative
  - ***CDER, CBER, and CDRH representatives***, appointed by the Center Directors of CDER, CBER, and CDRH. Five representatives are appointed from each center.
  - ***Executive secretary/project manager***, reporting to the Chair

- **Center Experts** – Reviewers, appointed by the CBER, CDER, and CDRH representatives. Experts serve on a temporary basis and are appointed "ad-hoc" depending on the subject matter of the GDS to be reviewed.

- **Advisory Subcommittee** – Advisors to the IPRG will be appointed to a subcommittee (***IPRG Advisory Subcommittee***) under the Drug Safety and Risk Management Advisory Committee. Advisors will be experts in the field and are critical to ensure state-of-the-art scientific evaluation of VGDSs.

RESPONSIBILITIES

The IPRG is the body responsible for reviewing VGDSs. In addition, the IPRG has several responsibilities related to the implementation of genomic review practice within the Agency. In particular, the IPRG will:

General Responsibilities

- Review and evaluate VGDSs
- Meet with sponsors upon request before or after submitting a VGDS (see MAPP 4180.3)
- Consult upon request with review staff on required submissions containing genomic data
- Integrate pharmacogenomics into the regulatory review process and help develop future guidance and review standards
- Harmonize review practices and quality review systems for GDS applications
- Coordinate development of the optimal format for VGDSs, including coordinating electronic formats

- Coordinate among disciplines and organizations in FDA, in particular CBER, CDER, Office of Combination Products (OCP), and CDRH to guarantee the efficient, accurate, and transparent review of genomic data
- Coordinate public discussions and set agendas for advisory committee meetings with regard to "lessons learned" from VGDS review
  - Define key issues to advance the use of rational pharmacogenomic principles in drug development, in particular issues pertaining to the regulatory review process
  - Facilitate FDA internal education regarding pharmacogenomic data, including seminars and printed materials
  - Meet once every month to discuss data submissions and other organizational or policy issues
  - Establish and maintain related policies
  - Establish working groups to facilitate goals of IPRG
  - Bring topics to Drug Safety and Risk Management Advisory Committee

Specific Responsibilities

- OC Representative
  - Appoints Chair of IPRG
  - Updates Office of the Commissioner on IPRG activities

- Center Directors (CDER, CBER, CDRH)
  - Appoint center representatives (max. five representatives per center)

- Chair
  - Coordinates IPRG activities
  - Communicates with sponsors, HHS, industry, and academia
  - Signs off on final reviews of VGDSs
  - Updates OC representative on IPRG activities

- Project Manager/Executive Secretary
  - Track and distribute submissions
  - Set up meetings
  - Document internal and external meetings (meeting minutes)

- Reviewers
  - Provide expertise in highly specialized areas
  - Update center representatives on review activities
  - Review VGDS
  - Request consults
  - Prepare questions for sponsors
  - Recommend new or improved policies
  - Consult with the review divisions upon request for required GDSs
  - Draft VGDS review and/or report

- CDER, CBER, CDRH Representatives
  - Appoint CDER, CBER, CDRH reviewers
  - Disseminate information (submissions, reports, meetings) via appropriate channels within their centers
  - Update Center Directors on IPRG activities

EFFECTIVE DATE

This MAPP is effective upon date of publication.

Attachment

Overview IPRG Organization