OFFICE OF THE CENTER DIRECTOR

Processing and Reviewing Voluntary Genomic Data Submissions (VGDSs)

CONTENTS

PURPOSE

This MAPP explains how the Center for Drug Evaluation and Research (CDER) will process and review voluntary genomic data submissions (VGDSs) to the Food and Drug Administration (FDA).

BACKGROUND

The Agency has issued its final guidance on *Pharmacogenomic Data Submissions*, which encourages the voluntary submission of genomic data to the Agency. The guidance describes how the Agency will handle voluntary submissions (i.e., submissions that are not required as part of a regulatory submission). The guidance emphasizes that data submitted voluntarily will be used to help the Agency gain an understanding of genomic data while not being used as part of the regulatory decision making process. This MAPP explains how VGDSs will be received, reviewed, and maintained by the Agency.

The concept of voluntary data submission has been created with the goal of gaining access to drug development data that are vital for future reviews of drug applications containing genomic information. Therefore, CDER's goal in reviewing VGDSs is not only to understand them, but also to ensure that the *lessons learned* are communicated to all interested parties, in particular the review divisions, within the FDA.

REFERENCES

- Guidance for industry, *Pharmacogenomic Data Submissions*
- CDER MAPP 4180.2, Establishment of the Interdisciplinary Pharmacogenomic Review Group (IPRG)
- 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

GDS: A Genomic Data Submission

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

Stand-alone VGDS: 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: A voluntary GDS that is submitted to an existing application (e.g., investigational new drug application (IND) (also pre-INDs), new drug application (NDA), biologics licensing application (BLA), or supplement). Such VGDSs will be submitted to the existing application, but will not be used by FDA in the process of regulatory decision making regarding the existing application.

Required GDS: A GDS that is required 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 the usual standards for routine application submissions.

IPRG: Designation for Interdisciplinary Pharmacogenomic Review Group. The IPRG will review all VGDSs submitted to the Agency (see MAPP 4180.2, describing the formation and responsibilities of the IPRG) and consult, on request, on the required GDSs.

GENERAL POLICY

- VGDSs will be sent to and reviewed by the IPRG; they will not be sent to or reviewed by the review divisions.
- The IPRG will send a summary of its report to the sponsor.
- The IPRG will send a copy of its report to the appropriate review division.
- The FDA will not use information submitted through the voluntary process for regulatory decision making.
- The IPRG will be available, as needed, to respond to consults from the reviewing divisions on required GDSs submitted with an application.

PROCEDURES FOR RECEIPT AND PROCESSING VGDSs

Receipt

- All VGDSs must be accompanied by the *Voluntary Genomic Data Submission* cover sheet to ensure processing according to this MAPP. If not identified appropriately, the submission may be processed according to standard processing for routine application submissions.
- All VGDSs will be received and processed by the Central Document Room staff. Voluntary submissions will be identifiable by the *Voluntary Genomic Data Submission* cover sheet (see Attachment B).
- If a VGDS is submitted to a Division Document Room, it will be identifiable by the *Voluntary Genomic Data Submission* cover sheet (see Attachment B), and forwarded to the Central Document Room for processing.

Submission Processing

1. Stand-alone VGDSs (not submitted to an existing application):

- Upon receipt of any submission accompanied by the VGDS cover sheet, the Central Document Room Staff will:
  - Stamp the submission with the receipt date.
  - Establish a pre-IND number for the submission.
  - Perform data entry in the corporate database for document tracking.
  - Identify the submission by putting it in the IPRG jacket.
  - Deliver the submission, using a courier, to the IPRG for review.

2. Associated VGDSs (submitted to a previously established application):

Note: Voluntary submissions to existing applications can be received, processed, archived, and reviewed regardless of the status of the application. For example, a sponsor can submit a voluntary submission to a withdrawn application. Such submissions will not change the status of the application.

- Upon receipt of any submission accompanied by the VGDS cover sheet, the Central Document Room staff will:
  - Stamp the submission with the receipt date.
  - Perform data entry in the corporate database for document tracking.
  - Identify the VGDS by putting it in the IPRG jacket.
  - Deliver the VGDS, using a courier, for review to the IPRG.

  The IPRG will maintain a log of VGDS sent to the IPRG for review.

PROCEDURES FOR REVIEWING VGDSs

Procedures

- The IPRG is responsible for reviewing all VGDSs and is the primary point of contact for the sponsor during and after the review process on matters relating to voluntary submission of pharmacogenomic data.
- The IPRG meets monthly to discuss VGDS-related issues.
- Reviewers from CDER, CBER, and CDRH are appointed by the respective Center Delegates to ensure adept review of the submission.
- To facilitate the review process, the IPRG can meet with the sponsor (refer to the section on meetings).
- The IPRG will write a VGDS report. The Chair of the IPRG and the Director of the Office of Clinical Pharmacology and Biopharmaceutics (OCPB) or his/her designee are responsible for documenting concurrence or any differences of opinion regarding the report and the interpretation of the data and how such differences were resolved.
- The IPRG is responsible for entering the report into DFS with copies to all IPRG members and the Chief of the Project Management Staff in the appropriate review division.
- A summary report of the VGDS review will be sent to the sponsor.
- The IPRG intends to review a VGDS as soon as possible, with a target timeline of no longer than 6 months from receipt of the VGDS to the sponsor's receipt of the IPRG's summary.
- If the IPRG determines that the VGDS data are applicable to the regulatory review of a drug that is the subject of an investigational or marketing application, the IPRG will notify the sponsor and ask that the information be submitted to the relevant application as a required submission.
- If it is unclear whether a submission is voluntary or required, the IPRG can convene a meeting (or telecon) with the sponsor and representative(s) from the relevant review division to help determine the status of the submission in question.
- The IPRG will organize educational seminars and workshops (internal and public) and advisory committee meetings to discuss findings based on VGDSs. The IPRG will ensure that data presented at such public meetings are appropriately redacted or that permission to present the data is obtained from the sponsor.
- The IPRG will store all VGDS documents (electronic and paper).

Meetings Relating To VGDSs

- **Presubmission Meeting with IPRG**

A pre-VGDS meeting can be requested by a sponsor wishing to discuss aspects of a VGDS. See the guidance for industry on *Formal Meetings with Sponsors and Applicants for PDUFA Products* for procedures on requesting and granting meetings.

Note: Although PDUFA regulations do not apply to pre-VGDS meetings, the goal is to follow the procedures laid out in the guidance, using type B meeting timelines.

- **VGDS Meeting with IPRG**

During the review process, one or more meetings between the IPRG and the sponsor may be held. Meetings can be requested by a sponsor or the FDA.

- **Postreport Meeting**

A meeting with the IPRG can be requested by the sponsor to discuss the findings in the report.

RESPONSIBILITIES

Central Document Room Staff

- Receive and process voluntary submissions
- Establish a pre-IND application if a submission is a stand-alone VGDS
- Enter data into the corporate database for tracking
- Distribute all submissions (paper and electronic) to the IPRG

Division Document Room

- Forward submissions accompanied by the VGDS cover sheet to the CDR for processing

IPRG

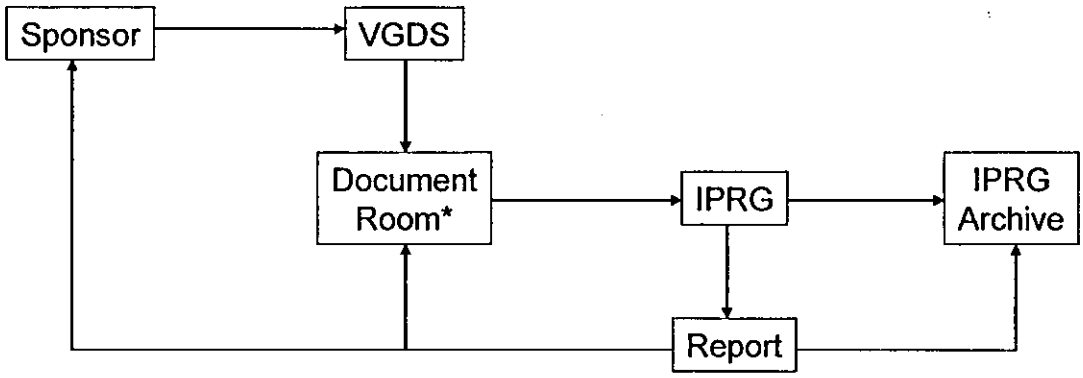
- Maintain a log of VGDSs reviewed by the IPRG
- Review all written VGDS reports
- Send a summary report to the review divisions and the sponsor and file reports in DFS
- Meet with the sponsor and applicable review division as needed
- Store all VGDS documents (paper and electronic)
- Coordinate communications with sponsors and interested parties on issues related to VGDSs

For more detail on the constitution and functions of the IPRG, see MAPP 4180.2

EFFECTIVE DATE

This MAPP is effective upon date of publication.

ATTACHMENT A: Procedure for Receipt and Processing of VGDS



ATTACHMENT B: Voluntary Genomic Data Submission Cover Sheet

Send all CDER voluntary genomic data submissions to the following address accompanied by this coversheet:
FDA/CDER
Central Document Room (CDR)
5901-B Ammendale Road
Beltswille, MD 20705-1266

Attention!

This is a

Voluntary
Genomic Data Submission

Application number _____ (leave blank if this is the first submission for a stand-alone VGDS)

_____Initial Submission

_____Subsequent Submission

Please route directly to the IPRG (HFD-850) After processing in the CDR!

Genomics at FDA

Regulatory Information

As part of an agency-wide initiative to speed development of new medical products, the Food an Drug Administration (FDA) issued today the final guidance titled "Pharmacogenomic Data Submissions." Pharmacogenomics holds the promise to tailor medicines to individuals, often referred to as "personalized medicine." The guidance and this Web page are part of a broad effor by the FDA to foster the use of pharmacogenomics during drug development. Please visit this Web site again soon; we will be updating it as information becomes available.

Press Release

- FDA Works to Speed the Advent of New, More Effective Personalized Medicines (3/22/2005)

Guidance

- Pharmacogenomic Data Submissions [HTML] or [Word] or [PDF] (3/22/2005)
  - Examples of Voluntary Submissions or Submissions Required Under 21 CFR 312, 314, or 601 [HTML] or [Word] or [PDF] (3/22/2005)

Manual of Policy and Procedures (MaPP)

- Management of the Interdisciplinary Pharmacogenomics Review Group (IPRG) MaPP 4180.2
- Processing and Reviewing Voluntary Genomic Data Submissions (VGDSs) MaPP 4180.3

Contact Information

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FDA News

FOR IMMEDIATE RELEASE
P05-12
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Media Inquiries: Susan Cruzan
301-827-6242
Consumer Inquiries: 888-INFO-

FDA Works to Speed the Advent of New, More Effective Personalized Medicines

As part of an agency-wide initiative to speed development of new medical products through the science of pharmacogenomics, the Food and Drug Administration (FDA) today issued a final guidance titled "Pharmacogenomic Data Submissions."

Pharmacogenomics allows health care providers to identify sources of an individual's profile of drug response and predict the best possible treatment option for this individual. For example, genomic tests are helping to identify cancers that have a good chance of responding to a particular medication or regimen. This technology has enabled the development of targeted therapies like Herceptin for metastatic breast cancer, Gleevec for chronic myeloid leukemia and Erbitux for metastatic colorectal cancer.

"FDA's efforts will bring us one step closer to 'personalizing' medical treatment," explained Janet Woodcock, M.D., Acting Deputy Commissioner for Operations, FDA. "This new technology will allow medicines to be uniquely crafted to maximize their therapeutic benefits and minimize their potential risks for each patient."

Instead of the standard hit-or-miss approach to treating patients, where it can take multiple attempts to find the right drug and the right dose, doctors will eventually be able to analyze a patient's genetic profile and prescribe the best available drug therapy and dose from the start. Both the guidance and a new Web page are part of a broad effort underway at FDA to foster pharmacogenomics during drug development.

FDA also recently approved the first laboratory test, the Amplichip Cytochrome P450 Genotyping Test, which will enable physicians to use genetic information to select the right doses of certain medications for cardiac, psychiatric diseases and cancer.

"We hope ultimately to bring pharmacogenomics, a way in which to foster the personalizing of medicine, to every healthcare professional's prescription pad for the benefit of their patients and U.S. consumers," said Dr. Woodcock.

The guidance "Pharmacogenomic Data Submissions," clarifies how pharmacogenomic data will be evaluated. The final guidance describes what data will be needed during the marketing application review process, the format for submissions, and the data that will be used during regulatory decision making. The guidance also explains a new mechanism for industry to voluntarily submit research data to further the scientific exchange of information as we move into more advanced areas of pharmacogenomic research. The voluntary data, which will be reviewed by an internal, agency-wide group and will not be used for regulatory decision making, will help FDA and industry gain valuable experience as this new field continues to evolve.

FDA believes this approach will save time and resources and eliminate possible delays in the application review process because parties will be able to familiarize themselves with novel pharmacogenomic approaches as they evolve.

FDA's new pharmacogenomics Web page is available at http://www.fda.gov/cder/genomics/default.htm. The Web site ("Genomics at FDA") will be useful to industry because it includes detailed information on submitting genomic data, including a decision tree to simplify data submissions, relevant regulatory information, and FDA contact information.

FDA has already received several pharmacogenomic data submissions through both the regulatory and voluntary processes and will continue to work closely with industry and the healthcare community on this exciting emerging technology.

In addition to announcing the availability of its final guidance and the new pharmacogenomic Web page, the agency also reminded the public of the April 11 to 13 meeting being held at the Mariott Hotel in Bethesda , MD on pharmacogenomics issues. The meeting is being sponsored jointly by FDA and the Drug Information Association. The joint FDA/DIA meeting, "Pharmacogenomics in Drug Development and Regulatory Decision Making" will focus on integrating pharmacogenomics in clinical trials for new drugs, biologics, and associated devices. FDA will also address ways to translate pharmacogenomics into medical product development and clinical practice.

On April 26th at 1:00 p.m. at the Washington Convention Center , the FDA will be presenting a symposium for the public entitled "Personalizing your Healthcare: The Best Consumer is an Educated Consumer." This free session will allow members of the general public the opportunity to hear about the science behind personalized medicine, an issue of critical importance to both consumers and FDA. Presentations will be from experts in the field and there will be time for questions. For more information, please go to: http://www.fda.gov/scienceforum; for public session: http://www.cfsan.fda.gov/~frf/forum05/pubsci.html.

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Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System

Document issued on: March 10, 2005

For questions regarding this document contact Courtney Harper at 240-276-0443 or by email at courtney.harper@fda.hhs.gov.

C·D·R·H
Center for Devices and Radiological Health

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Office of In Vitro Diagnostic Device Evaluation and Safety
Division of Chemistry and Toxicology Devices

Contains Nonbinding Recommendations

Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. Please identify your comments with the Docket No. 2005D-0068. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/cdrh/oivd/guidance/1551.pdf, or to receive this document by your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt, press 1 to order a document. Enter the document number 1551 followed by the pound sign (#). Follow the remaining voice prompts to complete your request. For questions regarding the use or interpretation of this guidance contact: Courtney Harper at 240-276-0443 or by email at courtney.harper@fda.hhs.gov.

Contains Nonbinding Recommendations

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Contains Nonbinding Recommendations

Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the number listed on the title page of this guidance.

1. Introduction

This document was developed as a special control to support the classification of drug metabolizing enzyme (DME) genotyping systems into class II (special controls). A DME genotyping system is a device intended for use in testing DNA to identify the presence or absence of human genotypic markers encoding a drug metabolizing enzyme. This device is used as an aid in determining treatment choice and individualizing treatment dose for therapeutics that are metabolized primarily by the specific enzyme about which the system provides genotypic information.

This guidance is issued in conjunction with a *Federal Register* notice announcing the classification of DME genotyping systems. Any firm submitting a 510(k) premarket notification for a DME genotyping system will need to address the issues covered in the special control guidance. However, the firm need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe should be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the

burden that may be incurred in your attempt to follow the statutory and regulatory criteria in the manner suggested by the guidance and in your attempt to address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the document, "A Suggested Approach to Resolving Least Burdensome Issues." It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html.

2. Background

FDA believes that special controls, when combined with the general controls, provide reasonable assurance of the safety and effectiveness of DME genotyping systems. A manufacturer who intends to market a device of this type should (1) conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the Act), including the premarket notification requirements described in 21 CFR 807 Subpart E, (2) address the specific risks to health associated with DME genotyping systems identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device.

This guidance document identifies the classification regulation and product code for DME genotyping systems. (Refer to Section 4 – Scope.) In addition, other sections of this guidance document list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with the general controls, will generally address the risks associated with these assays and lead to a timely premarket notification [510(k)] review and clearance. This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87 and other FDA documents on this topic, such as the **510(k) Manual - Premarket Notification: 510(k) - Regulatory Requirements for Medical Devices,** http://www.fda.gov/cdrh/manual/510kprt1.html.

As explained in "**The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance**[1]," a manufacturer may submit either a Traditional 510(k) or an Abbreviated 510(k). FDA believes an Abbreviated 510(k) provides the least burdensome means of demonstrating substantial equivalence for a new device, particularly when FDA has issued a guidance document that provides recommendations on what should be addressed in a submission for the device. Alternatively, manufacturers considering modifications to their own cleared devices may lessen the regulatory burden by submitting a Special 510(k).

3. The Content and Format of an Abbreviated 510(k) Submission

An Abbreviated 510(k) submission must include the required elements identified in 21 CFR 807.87, including the proposed labeling for the device sufficient to describe the device, its intended use, and the directions for its use. In an Abbreviated 510(k), FDA may consider the contents of a summary report to be appropriate supporting data within the meaning of 21 CFR

[1] http://www.fda.gov/cdrh/ode/parad510.html

807.87(f) or (g); therefore, we recommend that you include a summary report. The report should describe how this guidance document was used during the device development and testing and the methods or tests used. The report should also include a summary of the test data or description of the acceptance criteria applied to address the risks identified in this document, as well as any additional risks specific to your device. This section suggests information to fulfill some of the requirements of 21 CFR 807.87 as well as some other items that we recommend you generally include in an Abbreviated 510(k).

Coversheet

The coversheet should prominently identify the submission as an Abbreviated 510(k) and cite the title of this guidance document.

Proposed labeling

Proposed labeling should be sufficient to describe the device, its intended use, and the directions for its use. (Refer to Section 10 for specific information that you should include in the labeling for this type of device.)

Summary report

We recommend that the summary report contain the following:

- A description of the device and its intended use. You should also submit an "indications for use" enclosure.[2] (Refer to Section 6 for specific information that you should include in the intended use and device description for this type of device.)

- A description of the device design. We recommend that the description include a complete discussion of the performance specifications and, when appropriate, detailed, labeled drawings of the device.

- Identification of the Risk Analysis method(s) used to assess the risk profile in general, as well as the specific device's design and the results of this analysis. (Refer to Section 5 for the risks to health generally associated with the use of this device.)

- A discussion of the device characteristics that address the risks identified in this class II special controls guidance document, as well as any additional risks identified in your risk analysis.

- A brief description of the test method(s) you have used or intend to use to address each performance aspect identified in Sections 7 and 8 of this guidance document. If you follow a suggested test method, you may cite the method rather than describing it. If you modify a suggested test method, you may cite the method, but should provide sufficient information to explain the nature of and reason for the modification. For each test, you may either (1) present the data resulting from the test in clear and concise form, such as a table, **or** (2) describe the acceptance criteria

[2] Refer to http://www.fda.gov/cdrh/ode/indicate.html for the recommended format.

that you will apply to your test results.[3] (See also 21 CFR 820.30, Subpart C - Design Controls for the Quality System Regulation.)

- If you choose to rely on a recognized standard for any part of the device design or testing, you may include either: (1) a statement that testing will be conducted and meet specified acceptance criteria before the product is marketed, or (2) a declaration of conformity to the standard.[4] Because a declaration of conformity is based on results from testing, we believe you cannot properly submit a declaration of conformity until you have completed the testing the standard describes. For more information, please refer to section 514(c)(1)(B) of the Act and the FDA guidance, **Use of Standards in Substantial Equivalence Determinations; Final Guidance for Industry and FDA**, http://www.fda.gov/cdrh/ode/guidance/1131.html.

If it is not clear how you have addressed the risks identified by FDA or additional risks identified through your risk analysis, we may request additional information about aspects of the device's performance characteristics. We may also request additional information if we need it to assess the adequacy of your acceptance criteria. (Under 21 CFR 807.87(l), we may request any additional information that is necessary to reach a determination regarding substantial equivalence.)

As an alternative to submitting an Abbreviated 510(k), you can submit a Traditional 510(k) that provides all of the information and data required under 21 CFR 807.87 and described in this guidance. A Traditional 510(k) should include all of your methods, data, acceptance criteria, and conclusions. Manufacturers considering modifications to their own cleared devices should consider submitting Special 510(k)s.

The general discussion above applies to any device subject to a special controls guidance document. The following is a specific discussion of how you should apply this special controls guidance document to a premarket notification for DME genotyping systems.

4. Scope

The scope of this document is limited to the following devices as described in 21 CFR 862.3360 (product code NTI):

21 CFR 862.3360 Drug metabolizing enzyme genotyping system

[3] If FDA makes a substantial equivalence determination based on acceptance criteria, the subject device should be tested and shown to meet these acceptance criteria before being introduced into interstate commerce. If the finished device does not meet the acceptance criteria and, thus, differs from the device described in the cleared 510(k), FDA recommends that submitters apply the same criteria used to assess modifications to legally marketed devices (21 CFR 807.81(a)(3)) to determine whether marketing of the finished device requires clearance of a new 510(k).

[4] See Required Elements for a Declaration of Conformity to a Recognized Standard (Screening Checklist for All Premarket Notification [510(K)] Submissions), http://www.fda.gov/cdrh/ode/reqrecstand.html.

A drug metabolizing enzyme genotyping system is a device intended for use in testing DNA to identify the presence or absence of human genotypic markers encoding a drug metabolizing enzyme. This device is used as an aid in determining treatment choice and individualizing treatment dose for therapeutics that are metabolized primarily by the specific enzyme about which the system provides genotypic information.

DME genotyping systems that are multiplex tests may be run on instrumentation for clinical multiplex test systems. Instrumentation for clinical multiplex test systems is regulated under 21 CFR 862.2570. Guidance for such instrumentation is available in the FDA Guidance for Industry and FDA Staff "*Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems.*" If your device includes a DME genotyping assay with instrumentation for clinical multiplex test systems for that assay, you may submit the information for both devices within one 510(k). Although instrumentation for clinical multiplex test systems (a Class II device) may be used with a DME genotyping system, the guidance document, "*Replacement Reagent and Instrument Family Policy*", (available at http://www.fda.gov/cdrh/oivd/guidance/950.pdf) does not apply to DME genotyping systems for use with instrumentation for clinical multiplex test systems.

5. Risks to Health

Failure to correctly identify the DME genotype could result in incorrect patient management decisions. In these situations a patient might be prescribed an incorrect drug or drug dose with concomitant increased risk of adverse reactions due to increased or decreased drug metabolism. Likewise, failure to properly interpret genotyping results could lead to incorrect prediction of phenotype and result in incorrect patient management decisions.

The information provided by this type of genetic test should only be used to supplement other tools for therapeutic decision-making in conjunction with routine monitoring by a physician. The effect that a specific DME allele has on drug metabolism may vary depending on the specific drug, even for drugs within a specific class. Effects of specific alleles on drug metabolism are well-documented for some drugs; for other drugs, they are less well-documented. Therefore, clinicians should use professional judgement when interpreting results from this type of test. In addition, results from this type of assay should not be used to predict a patient's response to drugs in cases where either, 1) the drug metabolizing enzyme activity of the allele has not been determined, or 2) the drug's metabolic pathway has not been clearly established.

In the table below, FDA has identified the risks to health generally associated with the use of DME genotyping systems addressed in this document. The measures recommended to mitigate these identified risks are given in this guidance document, as shown in the table below. We recommend that you conduct a risk analysis, prior to submitting your premarket notification, to identify any other risks specific to your device. The premarket notification should describe the risk analysis method. If you elect to use an alternative approach to address a particular risk identified in this document, or have identified risks additional to those in this document, you should provide sufficient detail to support the approach you have used to address that risk.

Identified risk	Recommended mitigation measures
Failure to correctly identify genotype encoding for a DME	Sections 7, 8, and 9
Failure to properly interpret genotyping results	Section 10

6. Device Description

You should describe the following information in your 510(k).

Intended Use

The intended use should specify the genotype(s) the test is intended to detect, the general clinical utility of detecting the genotype, and the specific populations to which the test is targeted. The intended use should specify the drug metabolizing enzyme encoded by the genotype.
Some tests may have multiple intended uses (e.g., multiple DME's). When separate studies are needed to support the multiple intended uses, you should submit separate 510(k) applications for each intended use. You should consult the appropriate review divisions in OIVD for advice on submitting applications for test systems with multiple intended uses.

Test Methodology

You should describe in detail the methodology used by your device to detect genotypes. For example, you should describe the following elements, where applicable for your device:

- Test platform[5] (e.g., flow cytometry, instrumentation for clinical multiplex test systems).
- Composition and spatial layout of arrays or other spatially fixed platforms.
- Methods used in attaching the probe material to a solid surface, if applicable.
- Sequence or identity of oligonucleotides, primers, probes, or other capture elements.
- Hybridization conditions, washing procedures and drying conditions (e.g., temperature, length of time).
- Specificity of probes for the sequence of interest, especially when pseudogenes or sequence-related genes exist.
- Methodology for DNA extraction that you provide or that you recommend for users.
- Assay components such as buffers, enzymes, fluorescent dyes, chemiluminescent reagents, other signaling and signal amplification reagents, instruments.
- External controls that you recommend or provide to users.
- Any internal controls, including those that mitigate miscalls (inaccurate results) due to genotypes that your device does not detect.

[5] Some of the elements listed in this section are applicable to instrumentation. If you are submitting a separate 510(k) for your instrumentation, you can describe the elements specific for instrumentation in that 510(k).