Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling.'' This guidance should help sponsors, researchers, and other interested persons engaged in new drug development in evaluating how variations in the human genome, specifically DNA sequence variants, could affect a drug's pharmacokinetics, pharmacodynamics, efficacy, or safety. The guidance provides recommendations on when and how genomic principles should be considered and applied in early-phase clinical studies to address questions arising during drug development and regulatory review. The guidance does not address trial design or statistical analysis considerations for later-phase randomized controlled clinical trials that are intended to draw definitive conclusions about treatment effects in a genomic subgroup or codevelopment of a drug and in vitro diagnostic. Rather, the considerations here are more relevant for exploratory and observational studies intended to generate genomic hypotheses that may then be tested in confirmatory trials.

Drug development is commonly described in ''phases'' (21 CFR 312.21). The first two phases provide initial information about safety and efficacy, and ideally examine a broad range of doses, so that the larger, later adequate, and well-controlled trials (phase 3) that are needed to support marketing approval can be efficiently designed. Across the drug development continuum, genomic data may be used for several purposes, including: (1) Identifying the basis for PK outliers and intersubject variability in clinical response; (2) ruling out the role of polymorphic pathways as clinically significant contributors to variable PK, PD, efficacy, or safety; (3) estimating the magnitude of potential drug-drug interactions; (4) investigating the molecular or mechanistic basis for lack of efficacy or occurrence of adverse reactions; and (5) designing clinical trials to test for greater effects in specific subgroups (i.e., use in study enrichment strategies).

On February 18, 2011 (76 FR 9583), FDA issued a draft of this guidance to solicit comments from the public. After carefully reviewing received comments and in light of increased regulatory experience and the evolution of the science, FDA has revised the guidance. In addition to making clarifying changes, FDA added content to describe when pharmacogenomics (PGx) studies are warranted, including circumstances when full sample ascertainment is expected to evaluate a specific hypothesis. In addition, a number of topics were further elaborated, including targeted sample collection, sample retention, genotyping approaches, pooled analyses, dedicated prospective PGx studies, genetic substudies, and safety PGx.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on conducting pharmacogenomic studies in early-phase clinical studies. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information have been approved under OMB control numbers 0910–0014 and 0910–0572.

III. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances, http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm* or *http://www.regulations.gov.*

Dated: January 22, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–01638 Filed 1–25–13; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–D–0128; Formerly Docket No. 2007D–0396]

Detecting and Evaluating Drug-Induced Liver Injury; What's Normal, What's Not, and What Should We Do About It?; Public Conference; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public conference; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public conference entitled ''Detecting and Evaluating Drug-Induced Liver Injury; What's Normal, What's Not, and What Should We Do About It?'' This conference will be cosponsored with the Critical Path Institute (C-Path) and the Pharmaceutical Research and Manufacturers of America. Its purpose is to discuss, debate, and build consensus among stakeholders in the pharmaceutical industry, academia, health care providers, patient groups, and regulatory bodies on how best to detect and assess the severity, extent, and likelihood of drug causation of liver injury and dysfunction in people using drugs for any medical purpose.

DATES: The public conference will be held on March 20, 2013, from 8 a.m. to 6 p.m. and March 21, 2013, from 8 a.m. until 4 p.m.

ADDRESSES: The conference will take place at the Marriott Inn & Conference Center, University of Maryland University College, 3501 University Blvd., East Hyattsville, MD 20783.

FOR FURTHER INFORMATION CONTACT: Lana L. Pauls, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4307, Silver Spring MD 20993–0002, 301–796–0518, *lana.pauls@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

In July 2009, FDA announced the availability of guidance for industry entitled ''Drug-Induced Liver Injury: Premarketing Clinical Evaluation'' (74 FR 38035; July 30, 2009). This guidance explained that drug-induced liver injury (DILI) was the most frequent cause of safety-related drug marketing withdrawals for the past 50 years and that hepatotoxicity has limited use of many drugs that have been approved and prevented the approval of others. It

discusses methods of detecting DILI by periodic tests of serum enzyme activities and bilirubin concentration, and how changes in the results of those laboratory tests over time, along with symptoms and physical findings, may be used to estimate severity of the injury. It suggests some ''stopping rules'' for interrupting drug treatment, and the need to obtain sufficient clinical information to assess causation. FDA published a draft of this guidance in 2006, and comments on the draft were taken into consideration when issuing the final guidance in July 2009 (*http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM174090.pdf*.). FDA is now interested in obtaining stakeholder input on the issues addressed in this guidance, including comments regarding potential revisions to the guidance.

II. The Public Conference

A. Why are we holding this conference?

The purpose of the 2013 conference is to invite participants to present their data and views, and to hold open discussion.

B. Registration, Transcripts, and Additional Information on This Conference and Its Predecessors

A registration fee ($600 for industry registrants and $300 for Federal Government and academic registrants) will be charged to help defray the costs of renting meeting spaces and the meals and snacks provided. The fee will also be used to cover travel costs incurred by invited academic (but not Government or Industry) speakers and other expenses. The registration process will be handled by C-Path, an independent, nonprofit organization established in 2005 with public and private philanthropic support from the southern Arizona community, Science Foundation Arizona, and FDA.

The presentations and discussions will be transcribed and published on the Internet for public availability after minor editing by the organizers of the meeting.

Additional information on the conference, program, and registration procedures may be obtained on the Internet at *http://www.c-path.org*, and also at *http://www.fda.gov* by typing into the search box ''liver toxicity''. (FDA has verified the C-Path Web site address, but is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.) Material presented at past programs (from 1999 to 2012) may be accessed at *www.aasld.org*. Click on Education/Training and then scroll down to ''Drug Induced Liver Injury 2012 Program.''

Dated: January 22, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–01640 Filed 1–25–13; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301–496–7057; fax: 301–402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

SIRT2 Inhibitors as Novel Therapeutics for Myocardial Infarction and Ischemic Stroke and to Prevent Necrosis

Description of Technology: Sirtuin 2 (SIRT2) inhibitors to reduce necrosis and, thereby, as novel therapeutics to treat ischemic stroke and myocardial infarction. Accumulating evidence indicates that programmed necrosis plays a critical role in cell death during ischemia-reperfusion. NIH investigators have shown that the NAD-dependent deacetylase SIRT2 binds constitutively to receptor-interacting protein 3 (RIP3) and that deletion or knockdown of SIRT2 prevents formation of the RIP1–RIP3 complex in mice. These investigators also found that genetic or pharmacological inhibition of SIRT2 blocks cellular necrosis induced by TNF-alpha and RIP1 is a critical target of SIRT2-dependent deacetylation. Further studies also showed that the hearts of *Sirt2*$^{-/-}$ mice, or wild-type mice treated with a specific pharmacological inhibitor of SIRT2, show marked protection from ischemic injury. These results implicate SIRT2 as an important regulator of programmed necrosis and indicate that SIRT2 inhibitors may constitute a novel approach to protect against necrotic injuries, including ischemic stroke and myocardial infarction.

Potential Commercial Applications:

- Novel therapeutics to protect against necrotic injuries.
- Novel therapeutics to treat ischemic stroke and myocardial infarction.
- Novel therapeutics to treat diseases in which necrosis is involved.

Competitive Advantages:

- None of the currently available drugs address the necrotic damage caused due to ischemia and reperfusion.
- Using a SIRT2 inhibitor could limit the damage caused by necrosis and contribute to accelerated recovery in patients suffering from these conditions.

Development Stage:

- Early-stage
- Pre-clinical
- In vitro data available
- In vivo data available (animal)

Inventors: Drs. Nisha Narayan and Toren Finkel (NHLBI)

Publication: Narayan N, et al. The NAD-dependent deacetylase SIRT2 is required for programmed necrosis. Nature. 2012 Dec 13;492(7428):199–204. [PMID 23201684]

Intellectual Property: HHS Reference No. E–003–2013/0—U.S. Application No. 61/723,496 filed 17 Nov 2012

Licensing Contact: Suryanarayana (Sury) Vepa, Ph.D., J.D.; 301–435–5020; *vepas@mail.nih.gov*

Collaborative Research Opportunity: The NHLBI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize retinoid-related orphan receptors (RORs) function in chronic diseases. For collaboration opportunities, please contact Ms. Peg Koelble at *koelblep@mail.nih.gov* or 301–594–4095.

Multivalent Meningiococcal Conjugates and Methods for Preparing Conjugates

Description of Technology: Among 13 isolated meningococcal serogroups, A, B, C, W–135 and Y are the most prevalent. There are three FDA-approved capsular polysaccharide (PS)-based vaccines, one tetravalent PS vaccine, and two tetravalent conjugate vaccines for protection against