development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products for human use among regulators around the world. The six founding members of the ICH are: The European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; CDER and CBER, FDA; and the Pharmaceutical Research and Manufacturers of America. The Standing Members of the ICH Association include Health Canada and Swissmedic. Any party eligible as a Member in accordance with the ICH Articles of Association can apply for membership in writing to the ICH Secretariat. The ICH Secretariat, which coordinates the preparation of documentation, operates as an international nonprofit organization and is funded by the Members of the ICH Association. The ICH Assembly is the overarching body of the Association and includes representatives from each of the ICH members and observers.

In the **Federal Register** of December 24, 1997 (62 FR 67377), FDA published a notice announcing the availability of the ICH guidance for industry entitled ''Q3C Impurities: Residual Solvents.'' The guidance makes recommendations as to what amounts of residual solvents are considered toxicologically acceptable for some residual solvents. Upon issuance in 1997, the text and appendix 1 of the guidance contained several tables and a list of solvents categorizing residual solvents by toxicity, classes 1 through 3, with class 1 being the most toxic. The ICH Quality Expert Working Group (EWG) agreed that the PDE could be modified if reliable and more relevant toxicity data were brought to the attention of the group and the modified PDE could result in a revision of the tables and list.

In 1999, ICH instituted a Q3C maintenance agreement and formed a maintenance EWG (Q3C EWG). The agreement provided for the revisitation of solvent PDEs and allowed for minor changes to the tables and list that include the existing PDEs. The agreement also provided for new solvents and PDEs that could be added to the tables and list based on adequate toxicity data. In the **Federal Register** of February 12, 2002 (67 FR 6542), FDA briefly described the process for proposing future revisions to the PDE. In the same notice, the Agency announced its decision to delink the tables and list from the Q3C guidance and create a stand-alone document entitled ''Q3C: Tables and List'' to facilitate making changes recommended by ICH, available at *https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073395.pdf.* The ''Q3C: Tables and List'' has been updated as of January 2017 to include the recommended PDE for triethylamine and methylisobutylketone.

In the **Federal Register** of October 16, 2015 (80 FR 62537), FDA published a notice announcing the availability of draft recommendations for the PDEs for two solvents, trimethylamine and methylisobutylketone, according to the maintenance procedures for the guidance entitled ''Q3C Impurities: Residual Solvents,'' available at *https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm073394.pdf.* The notice gave interested persons an opportunity to submit comments by December 15, 2015. After consideration of the comments received and revisions to the guidance, a final draft of the recommendations was submitted to the ICH Assembly and endorsed by the regulatory agencies in November 2016.

The guidance provides a new PDE for the solvent trimethylamine and a revised PDE for the solvent methylisobutylketone. In addition, the data used to derive the PDEs are summarized. Revisions made to the final guidance as a result of comments include a modification of the PDE for methylisobutylketone from 22.6 milligrams (mg)/day to 45 mg/day based on reconsideration of the severity of effects identified in rat studies and the human relevance of effects identified in mouse carcinogenicity study. The recommendation to place methylisobutylketone into class 2 remains. The ''Q3C: Tables and List'' has been updated as of January 2017 to include the recommended PDE for triethylamine and methylisobutylketone.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on ''Q3C Impurities: Residual Solvents.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Electronic Access

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

Dated: July 18, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

[FR Doc. 2017–15537 Filed 7–24–17; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2015–D–3235]

M4E(R2): The Common Technical Document—Efficacy; International Council for Harmonisation; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a guidance entitled ''M4E(R2): The CTD—Efficacy.'' The guidance was prepared under the auspices of the International Council for Harmonisation (ICH), formerly the International Conference on Harmonisation. The guidance revises the ICH guidance ''M4E: The CTD—Efficacy'' (M4E guidance). The revised guidance standardizes the presentation of benefit-risk information in regulatory submissions, providing greater specificity on the format and structure of benefit-risk information. This revision is intended to facilitate communication among regulators and industry.

DATES: Submit either electronic or written comments on Agency guidance's at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the

instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*

• If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

• *Mail/Hand delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

• For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2015–D–3235 for ''M4E(R2): The Common Technical Document—Efficacy; International Council for Harmonisation; Guidance for Industry; Availability.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

• Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002, or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 240–402–8010. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: Pujita Vaidya, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 1144, Silver Spring, MD 20993–0002, 301–796–0684; or Steve Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

Regarding the ICH: Amanda Roache, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 1176, Silver Spring, MD 20993–0002, 301–796–4548.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products for human use among regulators around the world. The six founding members of the ICH are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; CDER and CBER, FDA; and the Pharmaceutical Research and Manufacturers of America. The Standing Members of the ICH Association include Health Canada and Swissmedic. Any party eligible as a Member in accordance with the ICH Articles of Association can apply for membership in writing to the ICH Secretariat. The ICH Secretariat, which coordinates the preparation of documentation, operates as an international nonprofit organization and is funded by the Members of the ICH Association.

The ICH Assembly is the overarching body of the association and includes representatives from each of the ICH members and observers.

In the **Federal Register** of October 2, 2015 (80 FR 59785), FDA published a notice announcing the availability of a draft guidance entitled ''M4E(R2): The CTD—Efficacy.'' The notice gave interested persons an opportunity to submit comments by December 1, 2015.

After consideration of the comments received and revisions to the guidance,

a final draft of the guidance was submitted to the ICH Assembly and endorsed by the regulatory agencies on June 16, 2016.

Regulatory authorities approve drugs that are demonstrated to be safe and effective for human use. The meaning of ''safe'' has historically been interpreted to mean that the benefits of the drug outweigh its risks. This benefit-risk assessment of pharmaceuticals is the fundamental basis of regulatory decision-making. In the last several years, providing greater structure for the benefit-risk assessment has been an important topic in drug regulation. The M4E guidance directs applicants to include their conclusions on benefits and risks in the Clinical Overview of Module 2 of the Common Technical Document (CTD) under section 2.5.6. Although general guidance is provided in the M4E guidance regarding the expected content of section 2.5.6, no further structure is suggested to aid industry in developing the benefit-risk assessment. As a result, regulators observe a high degree of variability in the approaches taken by applicants in presenting this information. This variability may not facilitate efficient communication of industry views to regulators. Although regulators and industry have developed approaches for structured benefit-risk assessment and these approaches may take different forms, there is a common thread evident that can inform harmonization of the format and structure of benefit-risk assessments provided by applicants in their regulatory submissions.

The revised M4E(R2) guidance provides more specific guidance regarding the format and structure of the benefit-risk assessment in section 2.5.6. Section 2.5.6 is divided into four subsections: (1) Therapeutic context, (2) Benefit, (3) Risk, and (4) Benefit-Risk Assessment. Each subsection describes the aspects that are most pertinent to the benefit-risk assessment. This guidance also lists characteristics that should be considered when identifying and describing key benefits and key risks of the medicinal product. Recognizing that there are many reasonable approaches for conducting a benefit-risk assessment, M4E(R2) does not specify a particular approach to be used by industry. However, the document does offer specific guidance on the major elements that should be included in the benefit-risk assessment. Furthermore, the revised guidance does not dictate an approach used by a regulator in conducting a benefit-risk assessment.

This guidance also revises other sections of the guidance for clarification, given the proposed revisions in section 2.5.6. In addition, the revised guidance changes the numbering and the section headings for consistency.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

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 in 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910–0014 and 0910–0001, respectively.

III. Electronic Access

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

Dated: July 18, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

[FR Doc. 2017–15534 Filed 7–24–17; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Office of the Commissioner; Statement of Organization, Functions, and Delegations of Authority

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA), Office of the Commissioner (OC), and Office of Operations (OO) have modified their structures. This new organizational structure was approved by the Secretary of Health and Human Services on January 10, 2017 and effective on February 11, 2017.

FOR FURTHER INFORMATION CONTACT: Segaran Pillai, Ph.D., Director, Office of Laboratory Science and Safety, Office of the Commissioner, Food and Drug Administration, White Oak Bldg. 1, Rm. 2218, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002, 240–402–2856.

SUPPLEMENTARY INFORMATION: Part D, Chapter D–B, (Food and Drug Administration), the Statement of Organization, Functions, and Delegations of Authority for the Department of Health and Human Services (35 FR 3685, February 25, 1970, 60 FR 56606, November 9, 1995, 64 FR 36361, July 6, 1999, 72 FR 50112, August 30, 2007, 74 FR 41713, August 18, 2009, and 76 FR 45270, July 28, 2011) is amended to reflect the reorganization of the Office of the Commissioner and the Office of Operations.

This reorganization establishes the Office of Laboratory Science and Safety, and will authorize the consolidation of the laboratory science, safety functions, and program activities across FDA under one organizational component that will report directly to the Office of the Commissioner. The Employee Safety and Environmental Management Staff will be realigned from the Office of Safety, Security and Crisis Management to the Office of Laboratory Science and Safety. As a result of the staff realignment the Office of Safety, Security and Crisis Management within the Office of Operations will be re-titled to the Office of Security and Emergency Management. The Office of Crisis Management within the newly titled Office of Security and Emergency Management will change its title to the Office of Emergency Management. Additionally, the Office of Security and Emergency Management has established the Emergency Planning, Evaluation, and Exercise Staff, and the Program Operations and Coordination Staff within the Office of Emergency Management.

The Food and Drug Administration, Office of the Commissioner (OC), has been restructured as follows:

DA. ORGANIZATION. The Office of the Commissioner is headed by the Commissioner of Food and Drugs and includes the following organizational units:

Office of the Commissioner (DA)
Office of the Chief Counsel (DAA)
Office of the Executive Secretariat (DAB)
Executive Secretariat Staff (DAB1)
Freedom of Information Staff (DAB2)