POLICY AND PROCEDURES

OFFICE OF STRATEGIC PROGRAMS

Preparation of Topics and Nomination of Experts For Development and Harmonization of International Scientific and Technical Guidelines

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PURPOSE

This MAPP establishes the process and defines the roles and responsibilities in preparing topics and nominating experts for development and harmonization of international scientific and technical guidelines for pharmaceutical products regulation. The policies and procedures described will further enable CDER to foster uniform and scientifically driven standards for global development of medical products. This MAPP supports implementation of Section 1123 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), *Optimizing Global Clinical Trials* (see Pub.L.112-144).

BACKGROUND

The increasing globalization of the pharmaceutical industry prompts enhancement of CDER's policies related to harmonization of international guidelines for drug development and regulation. To uphold CDER's commitment to ensuring that pharmaceutical products available in the United States are developed according to sound scientific principles and manufactured in quality systems,

CDER staff collaborates with international organizations and regulatory authorities of other countries to develop and harmonize internationally acceptable scientific and technical guidelines.

One venue for development and harmonization of such guidelines is FDA's participation in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Under the ICH procedures, Expert Working Groups (EWG) and Implementation Working Groups (IWG) are assembled to develop guidelines. These groups include expert representatives from drug regulatory agencies and industry. Since its inception in 1990, ICH has produced over 60 guidelines establishing globally consistent approach to various aspects of pharmaceutical development including product quality, safety, efficacy, and standards for regulatory submissions.

Over the past two decades, CDER staff has been participating in development, harmonization, and implementation of ICH guidelines. To continue meeting the complex demands of the globalized regulatory environment and to ensure consistent and effective engagement in global regulatory activities, CDER is implementing the strategic approach outlined in this MAPP. The described policies, the procedures, and the respective roles and responsibilities apply to all CDER offices and super offices and may be used by other FDA Centers.

POLICY

- Each topic proposed by CDER for international guideline development and harmonization will support CDER's mission of protecting and promoting public health.
- Each topic proposed for international guideline development and harmonization will go through a managed process of rigorous scientific discussions and approval by the Scientific Technical Group (STG) Chair, the lead office and super office directors, the International Strategy Council (ISC), and CDER Director.
- Each proposal for development and harmonization of international scientific or technical guidelines will be documented on the International Proposal Form (IPF). (See Sample, Attachment 1.)
- CDER Subject Matter Experts (SMEs) will be nominated by their offices or STGs and appointed by the ISC to participate in international guideline development and negotiations.
- CDER staff approved for participation in international engagements will be appropriately prepared for meeting participation and will provide debriefings upon return from international meetings.

RESPONSIBILITIES

Scientific Technical Group (STG)

An STG meeting is a forum for detailed discussion of a proposed topic. An STG may be an existing group within an office in CDER or a new group formed to address specific issues within one discipline or across disciplines. Upon discussion of the topic, an STG will:

For new topics:

1. Determine the proposal's scientific merit, regulatory relevance, feasibility for development of international guidelines, and support to CDER's mission.
2. Identify other offices within and outside of CDER whose input would be important for development of new or revised guidelines in the proposed area.
3. Identify and nominate the lead SMEs for the proposed topic.
4. Prepare SMEs for international discussions and negotiations based on the current scientific and technical knowledge in the field.
5. Identify the lead office and super office for the proposed topic.
6. If needed, provide suggestions for formation of additional CDER interoffice working groups for further topic development.

For ongoing harmonization projects:

1. Discuss progress of the guidelines that are currently in development, as well as points of negotiation and contention with outside parties.
2. Provide suggestions for resolution of issues related to ongoing harmonization efforts.

Subject Matter Experts (SMEs)

SMEs will:

1. Discuss topics for development of international guidelines with the STG.
2. Complete the IPF, obtain signatures from the STG chair or the lead office director and the lead super office director, and route the IPF to the ISC manager.
3. Present new topic proposals to the ISC.
4. Represent CDER and FDA at international meetings. Become part of ICH EWG or IWG.
5. Provide debriefings to the STG and the ISC upon return from international meetings.
6. Provide periodic updates to their respective STG and the ISC on the ongoing international harmonization efforts.

In addition, the SMEs may:

1. Have additional responsibilities per outside organizations' procedures (e.g., regulatory chair for ICH EWG).

2. Be trained in international organizations' procedures as well as in international negotiation and facilitation skills.

STG Chair or Lead Office Director
The STG Chair or the Lead Office Director will:

1. Lead the STG meeting forums.
2. Advise on channels for development of international guidelines in their area of expertise.
3. Sign IPFs, either approving or disapproving proposals, as per STG recommendations.
4. Ensure that SMEs from their office appointed to represent FDA are trained and adequately prepared before participation in international meetings.

Lead Super Office Director
The Lead Super Office Director will:

1. Provide oversight for the activities related to international guideline development within the super office.
2. Coordinate with the STG Chair or the Lead Office Director, as appropriate.
3. Sign IPFs originating from their super office.
4. When relevant, determine if a new STG should be assembled.

International Strategy Council (ISC)
Upon vetting topics and appointing experts, the ISC will:

1. Review, prioritize, and approve proposals for international guideline development and harmonization based on public health needs and CDER's strategic goals.
2. Appoint the STG-nominated CDER staff to serve as SMEs for development and harmonization of international guidelines.
3. In consultation with the CDER Executive Committee, provide advice and guidance to the appointed staff on the boundaries of negotiations at ICH and at other international meetings.
4. Provide guidance to CDER offices and staff on the appropriate international channels or organizations to be engaged to negotiate guidelines in development.
5. Serve as the focal point for resolution of disagreements between CDER offices on issues related to international activities.
6. Receive debriefings from SMEs following ICH and other international meetings.

ISC Manager
When working with the proposed topics, the ISC manager will:

1. Receive proposed topics from CDER staff and route proposals to the ISC.
2. Maintain a portfolio of all topics proposed or discussed by CDER staff.

3. Maintain an inventory of all international organizations with which CDER collaborates, and of the extent of CDER's participation in their proceedings.
4. Maintain a portfolio of the international guidelines in development and other documents, as appropriate.
5. Notify Office of Regulatory Policy (ORP) of the proposals approved by CDER for international harmonization and guideline development.
6. Coordinate activities with the ICH Secretariat.
7. Route submissions with topic proposals from regulated industry to the relevant STG or office and super office.

ISC Chair

For the topics proposed to the ISC, the ISC Chair or their designated alternative will:

1. Lead the ISC discussion of the proposed topics.
2. Signs IPFs with proposals approved or disapproved by the ISC.

CDER Director

For each topic proposal approved by the ISC, CDER Director will:

1. Make the final determination whether to put the proposal forward for international harmonization and guideline development.
2. Sign IPF approving or disapproving the proposal.

PROCEDURES

The process for vetting harmonization-related topics and nominating experts to participate in international guideline development and negotiations is shown in Attachment 2. Proposals for international harmonization may originate from a variety of sources, including staff from CDER and other FDA Centers (e.g., CBER), the regulated industry, outside organizations, or other regulatory agencies. All external proposals are initially sent to the ISC manager in the Office of Strategic Programs in CDER for routing to the appropriate office, super office, or STG.

1. All proposals with topics for international harmonization and guideline development will be routed to and discussed by an appropriate STG within CDER. If an STG with the needed expertise does not exist, the proposal will be routed to the senior leadership of the relevant super office or office to determine if assembling a new group is warranted.
2. The STG will discuss a proposal and nominate SMEs for participation in development and harmonization of international guidelines. Following discussion at the STG meeting, proposals may be approved or disapproved by the STG chair, or the lead office director, and the lead super office director.
3. Each proposal and the respective decision will be documented on the IPF to be signed by the STG chair (or, alternatively, the lead office director) and the lead super office director.

The IPF will be routed to the ISC manager. Approved proposals will be put forward for consideration and discussion by the ISC. Proposals from other FDA Centers may also be documented on the IPF and sent to the ISC for consideration. When proposals from other FDA Centers are vetted, representatives from the respective Center will be invited to the ISC meetings.

4. The ISC will review and prioritize submitted proposals in consultation with the CDER Executive Committee. For all proposals approved by the ISC, the Council will appoint SMEs to participate in further development of international guidelines. Proposals that have not been approved by the ISC will be recorded by the ISC manager.
5. The appointed SMEs will be trained and provided guidance on the points of negotiation and position statements by the ISC and the respective STG before participation in international meetings.
6. The appointed SMEs will provide debriefings to the appropriate STGs, the lead office and super office directors, and to the ISC upon return from the international meetings. SMEs also will provide periodic updates related to any ongoing international activities in which they are participating.

The timeline for pre-meeting preparations and post-meeting debriefings is shown in Attachment 3. The timeline represents a 6-month cycle scheduled around biannual ICH meetings. Meetings with other international organizations may follow similar or modified timelines, depending on the organization's proceedings. Any of the listed activities may occur at any time but should occur no later than the indicated time points, unless a proposal of high priority to public health is considered. All CDER offices and super offices are expected to adhere to the provided timeline.

REFERENCES

1. FDA, 2012, Food and Drug Administration Safety and Innovation Act.
2. FDA Staff Manual Guide 9100.1, 2012, Development and Use of Standards.
3. International Conference of Harmonization, 2010, The Value and Benefits of ICH to Drug Regulatory Authorities - Advancing Harmonization for Better Health.

DEFINITIONS

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH): an organization that brings together the regulatory authorities and pharmaceutical industry of Europe, Japan, the US, and other countries to discuss scientific and technical aspects of drug registration and to develop guidelines and harmonize requirements for registration of pharmaceuticals for human use.

International Proposal Form (IPF): a form used by FDA staff to document proposals for international harmonization, including development and revision of international scientific and technical guidelines. A fillable electronic copy of the IPF may be obtained from the ISC manager.

International Strategy Council (ISC): a subcommittee of the CDER Executive Committee responsible for establishing objectives and strategy for CDER's collaboration with international organizations and international drug regulatory authorities.

Subject Matter Experts (SMEs): CDER staff with scientific, regulatory, technical, or other expertise relevant to the topic for which international guidelines are developed or other international collaboration is needed.

Scientific Technical Group (STG): an internal group of FDA staff with relevant expertise that meets to discuss issues related to pharmaceutical product development and regulation.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
9/24/13	Initial	n/a.

ATTACHMENT 1: International Proposal Form

International Proposal Form (Page 1 of 3)

1. Topic Description (1 paragraph to 1 page)

Explanation of the subject or area for harmonization with focus on the following:

i) Why is this important for international harmonization?
ii) How would a harmonized approach to this subject advance CDER's mission?
iii) Is the proposal in alignment with the current US regulations?

Explain topic description here (1 paragraph to 1 page in length).

International Proposal Form (Page 2 of 3)

Concept Paper (ICH format) attached: Yes ☐ No ☐

Topic proposed by (specify):

☐ Industry _____

☐ FDA _____

☐ Other Regulatory Agency _____

☐ Other Organization _____

2. Lead Office and Scientific Technical Group

The proposal has been discussed at _____ Scientific Technical Group meeting

Lead Office _____

Lead Super Office _____

Lead Experts _____

3. Other offices and super offices involved (include offices with relevant expertise for topic development, offices that have a stake in the outcome and whose work will be affected by new international guidelines). Select each office and super office that is a stakeholder for this topic.

Offices who are stakeholders and in agreement with this proposal: (To select more than one office **hold Ctrl** key)

Select Office(s)
Office of Compliance
Office of Unapproved Drugs and Labeling Compliance
Office of Science Investigations
Office of Manufacturing and Product Quality
Office of Drug Security, Integrity, and Recalls
Office of Regulatory Policy
Office of Medical Policy
Office of Prescription Drug Promotion
Office of Medical Policy Initiatives
Office of Translational Sciences
Office of Biostatistics
Office of Clinical Pharmacology
Office of Computational Science
Office of Strategic Programs
Office of Program and Strategic Analysis
Office of Business Informatics Data Standards Program
Office of Surveillance and Epidemiology
Office of Medication Errors Prevention and Risk Management
Office of Pharmacovigilance and Epidemiology
Office of New Drugs
Office of Drug Evaluation I
Office of Drug Evaluation II
Office of Drug Evaluation III
Office of Antimicrobial Products
Office of Drug Evaluation IV
Office of Hematology Oncology Products
Office of Pharmaceutical Science
Office of Generic Drugs
Office of New Drug Quality Assessment
Office of Testing and Research
Office of Biotechnology Products

☐ **Other Office** (within or outside CDER)

_____

Offices who are stakeholders and in disagreement with this proposal: (To select more than one office **hold Ctrl** key)

Select Office(s)
Office of Compliance
Office of Unapproved Drugs and Labeling Compliance
Office of Science Investigations
Office of Manufacturing and Product Quality
Office of Drug Security, Integrity, and Recalls
Office of Regulatory Policy
Office of Medical Policy
Office of Prescription Drug Promotion
Office of Medical Policy Initiatives
Office of Translational Sciences
Office of Biostatistics
Office of Clinical Pharmacology
Office of Computational Science
Office of Strategic Programs
Office of Program and Strategic Analysis
Office of Business Informatics Data Standards Program
Office of Surveillance and Epidemiology
Office of Medication Errors Prevention and Risk Management
Office of Pharmacovigilance and Epidemiology
Office of New Drugs
Office of Drug Evaluation I
Office of Drug Evaluation II
Office of Drug Evaluation III
Office of Antimicrobial Products
Office of Drug Evaluation IV
Office of Hematology Oncology Products
Office of Pharmaceutical Science
Office of Generic Drugs
Office of New Drug Quality Assessment
Office of Testing and Research
Office of Biotechnology Products

☐ **Other Office** (within or outside CDER)

_____

International Proposal Form (Page 3 of 3)

4. Clearance

Chair of the Scientific Technical Group or Lead Office Director: ☐ Approved ☐ Not Approved _____ Date

Signature _____

Comments _____

Lead Super Office Director: ☐ Approved ☐ Not Approved _____ Date

Signature _____

Comments _____

Chair of the International Strategy Council: ☐ Approved ☐ Not Approved _____ Date

Signature _____

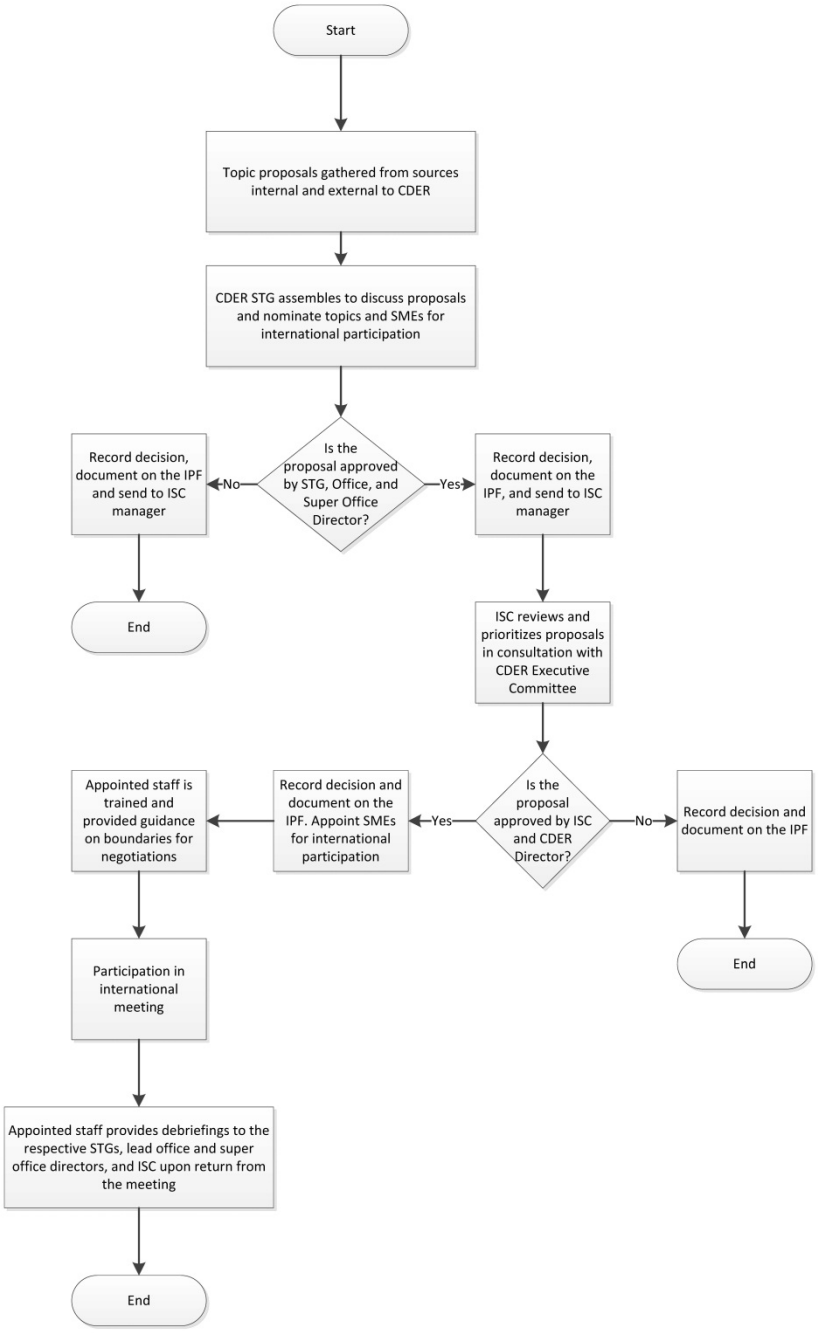
Comments _____

CDER Director / Executive Committee: ☐ Approved ☐ Not Approved _____ Date

Signature _____

Comments _____

ATTACHMENT 2: Process Chart



ATTACHMENT 3: Preparation Timeline

Preparation Timeline

Steps	TIME IN WEEKS											
	BEFORE MEETING										DAYS OF MEETING	AFTER MEETING	
	20 or earlier	18	16	14	12	10	8*	6*	4*	2		2	4
External proposals routed from ISC manager to the relevant super office, office or STG within 4 weeks of receipt.													
Internal proposals are discussed within offices and super offices.													
STG meets to discuss and nominate topics and experts.													
IPF is cleared by the STG chair, or the lead office director, and the lead super office director.													
The completed IPF is routed to the ISC manager.													
The ISC meets, prioritizes topics, approves proposals and appoints SMEs.													
ISC manager notifies ORP of the upcoming guidelines in development.													
The appointed staff is trained in international negotiations skills.													
Pre-meeting discussions within the STG. Preparation of the appointed staff for the meeting.													
Pre-meeting discussions with the ISC. Determination of boundaries for negotiations.													
International meeting													
Post-meeting debriefings with the ISC. Preliminary discussion of directions for the next international meeting.													
Post-meeting debriefings and preliminary discussion of future proposals with STG and appropriate offices.													

*** 4-8 weeks prior to each ICH meeting, the ICH Steering Committee endorses topics to be discussed and EWGs to be invited.**