OFFICE OF THE CENTER DIRECTOR

Joint Safety Meetings Between OND and OSE

CONTENTS

PURPOSE

This MAPP describes the policies and procedures for the Office of New Drugs (OND) and the Office of Surveillance and Epidemiology (OSE) to conduct joint meetings to provide a forum for the exchange of scientific and administrative information regarding postmarket safety-related issues associated with drugs and therapeutic biologics. These Joint Safety Meetings are held between an OND review division and OSE staff involved in postmarket safety-related issues for products handled by that review division.

Specifically, this MAPP covers the following points:

- Roles and responsibilities of OND and OSE regarding the joint meetings
- Meeting participants, including participants other than OND and OSE
- Recommended frequency for the joint meetings
- Examples of agenda topics

BACKGROUND

OND and OSE share responsibility for the review of postmarket safety information. OND has the primary responsibility for the review of periodic safety reports and most other clinical regulatory submissions. OSE has the primary responsibility for the review of 15-day alert reports, direct reports of adverse drug experiences, and reports of medication errors, and has the authority to grant waivers of postmarket safety reporting requirements. OND and OSE both have responsibilities for the review of proposed Risk Evaluation and Mitigation Strategies (REMS) and the evaluation and modification of existing REMS. OND, through its Offices and Divisions, has signatory authority for biologics licensing applications (BLAs) and new drug applications (NDAs) assigned to it for review.

Because of the joint responsibilities regarding postmarket safety-related issues with drugs and therapeutic biologics, OND and OSE agree that there is a fundamental need for regularly scheduled interactions to exchange information. Joint Safety Meetings are intended to provide a routine forum for such communication. These meetings will also be used to gather information from and engage with other FDA components to best support the review of postmarket safety information (e.g., Office of Compliance, Office of Biostatistics, and Office of Clinical Pharmacology).

When new significant safety issues emerge, a Safety Issues Team is established to manage the evaluation of the safety issue and make regulatory decisions. The Joint Safety Meetings are not intended to replace the Safety Issues Teams' meetings; however, there will be times when a safety issue is discussed in detail at a Joint Safety Meeting for educational purposes, or to get broader input into the issue from the attendees of the Joint Safety Meeting.

REFERENCES

- MAPP 6010.1 - NDAs: Preapproval Safety Conferences
- MAPP 6700.1 - Risk Management Plan Activities in the Office of New Drugs and the Office of Drug Safety
- MAPP 6700.4 – Tracking of Marketed Drug Safety Issues – Use of the DARRTS Safety Issue Application
- Memorandum of Agreement Between the Office of New Drugs and the Office of Surveillance and Epidemiology on the Management of Significant Safety Issues Associated with Pending and Approved Drug Products (June 16, 2008). (http://www.fda.gov/CDER/drug/DrugSafety/OSE_OND_MOA.pdf)

DEFINITIONS

- **DARRTS (Document Archiving Reporting and Regulatory Tracking System):** A CDER information technology (IT) platform intended to replace many of CDER's core tracking systems, including components of the Center-wide Oracle-based Management Information System (COMIS), the Division File System (DFS), and CDER Standard Letters and Forms (CSL).
- **DARRTS Safety Issue application:** An FDA-sponsored application created for the purpose of tracking and archiving regulatory activities associated with a significant safety issue related to a marketed prescription or over-the-counter drug.

POLICY

- Each OND review division will conduct Joint Safety Meetings with the OSE staff involved in postmarket safety-related issues for products handled by that review division. The meetings will provide a regularly scheduled forum for the exchange of scientific and administrative information regarding postmarket safety-related issues involving drugs and therapeutic biologics. These meetings will be held at least every other month, or more frequently as needed to provide an adequate forum for communication about postmarket safety issues.

- The Joint Safety Meetings will focus on safety issues of joint interest to the OND review division and OSE. The meetings will include scientific discussion of specific postmarket safety issues and updates on the status of reviews in progress. Lengthy discussions of specific issues will generally be held separately. Additional meetings may be needed for time-sensitive issues.

- The Joint Safety Meetings will be co-chaired by the OSE Safety Evaluator Team Leader (SE TL) associated with the review division or designee and the OND review division's Deputy Director for Safety (DDS) or designee. The DDS presides on behalf of the entire review division, and the OSE SE TL presides on behalf of the entire OSE. The co-chairs will attend each meeting. If one of the co-chairs cannot attend, that co-chair's division or office will send an appropriate substitute, but such occurrences should be kept to a minimum. These meetings should be viewed as high priority meetings.

PROCEDURES

Expected Attendees:

OND:
- DDS
- OND Safety Regulatory Project Manager (SRPM)
- Division Director
- Deputy Division Director, if other than the DDS
- Medical officer(s) and clinical team leader(s)
- OND Regulatory Project Managers (RPMs)

OSE:
- OSE SE TL assigned to the OND review division
- OSE RPM assigned to the OND review division
- OSE SEs assigned to the OND review division
- OSE drug use analyst assigned to the OND review division
- Division directors and/or deputy directors of the five OSE review divisions:
  - Division of Pharmacovigilance I (DPVI)
  - Division of Pharmacovigilance II (DPVII)
  - Division of Medication Error Prevention and Analysis (DMEPA)
  - Division of Epidemiology (DEPI)
  - Division of Risk Management (DRISK)
- OSE risk management coordinator
- DMEPA Rapid Response Safety Evaluator
- Other OSE reviewer(s) assigned to the safety issue(s) on the agenda and their team leaders
- Other OSE management as needed

OC:
- Division of Compliance Risk Management and Surveillance staff

Optional Invitees

- All OND review division staff and all OSE staff interested in the agenda are encouraged to attend

- OND office directors and deputies, as appropriate
- Office of Clinical Pharmacology (OCP) and Office of Biometrics (OB) division directors and team leaders or their designees
- Office of Compliance (OC) Director and division directors or their designees
- Other relevant CDER staff including, but not limited to the following:
  - Additional OSE and OND management
  - Quantitative Safety and Pharmacoepidemiology Group in OB
  - Pediatric and Maternal Health Staff in OND
  - Division of Drug Marketing, Advertising, and Communication staff
  - Office of Counter-Terrorism and Emergency Coordination staff
  - Controlled Substances Staff
  - Office of Generic Drugs staff

Agenda Format

The agenda should include the following sections (the items in bold print should be discussed at every meeting):

- **Selected topic(s) for discussion (X minutes)**
- **Brief discussion of new and emerging issues (X minutes)**
  - OSE
  - OND
- Other updates (e.g., upcoming Advisory Committee meetings, BPCA due dates) (X minutes)
- Project Highlights (X minutes)
  - Pending Projects (X minutes)
  - Completed Actions since last meeting (X minutes)
- **Safety issues needing public communications (X minutes)**
- **Recap of action items**

Agenda Items

The agenda should include a few select issues that merit scientific discussion. Administrative agenda items (e.g., status of each active safety review) should be presented in a summarized fashion, such as a listing attached to the agenda, with only highlights addressed at the meeting.

A report of the Division's DARRTS Safety Issue applications may serve as a starting point in formulating the agenda. In addition, the meeting agenda from the preceding meeting can be modified to cover the new items.

Potential agenda items include the following:

Topics for scientific discussion

- Emerging safety signals, including OSE-initiated safety reviews being contemplated

- A discussion of a premarket safety issue arising in an NDA or BLA under review that may benefit from OSE input, such as consideration of the need for a postmarket epidemiology study or REMS
- Completed OSE safety reviews involving the division's products but requested by parties outside of the review division (e.g., reviews of pediatric safety as mandated by the Best Pharmaceuticals for Children Act; requests from the Centers for Disease Control and Prevention (CDC), requests from the European Medicines Agency (EMEA))
- Methodological or statistical inferential issues in the design, analysis, or interpretation of randomized clinical trials, pharmacoepidemiological studies, or meta-analyses

Safety review status updates

- OND-requested safety reviews currently in progress in OSE
- OSE-initiated safety reviews being conducted
- OND response to recently completed safety reviews by OSE
- NME Postmarket Safety Evaluations

Risk management and risk communication

- A discussion of which safety issues would benefit from communication to health care providers and/or the general public
- REMS issues, including data collection, completeness, status of a REMS evaluation, or update reports
- Topics for the Drug Safety Newsletter

Other updates

- New or pending safety labeling supplements
- Upcoming dates and actions of safety interest (i.e., expected approvals, preapproval safety conferences, advisory committee meetings, scientific rounds, safety evaluator/epidemiology forums)
- Other safety topics of interest

RESPONSIBILITIES:

In preparation for the meeting (see **Attachment** for schematic of meeting planning timeline)

The OND SRPM will:

- Schedule meetings with expected OND and OSE attendees at least every other month or more frequently as needed. Additional attendees (e.g., OB, OC, and OCP) will be invited to individual meetings by the Agenda Lead as appropriate based on the agenda items.
- Ask the OND clinical staff for potential agenda items 2 weeks before the scheduled meeting, and request responses within 3-5 calendar days
- Alternate serving as the Agenda Lead with the OSE RPM

The OSE RPM will:

- Act as back-up to the OND SRPM to ensure that the meetings are scheduled

- Ask OSE staff for potential agenda items 2 weeks before the scheduled meeting, and request responses within 3-5 calendar days
- Alternate serving as the Agenda Lead with the OND SRPM

The Agenda Lead RPM will:

- Following receipt of agenda items from OND and OSE staff, collaborate with the non-agenda lead RPM at least 9 calendar days before the meeting to prepare the draft agenda
- Indicate the priority of the items
- Include proposals for any additional staff to be invited. Additional staff are only to be invited when the agenda includes substantive discussion of the safety issue, not for a brief status update.
- Notify proposed additional invitees of upcoming meeting so they can tentatively block their schedules
- Notify Division of Compliance Risk Management and Surveillance staff of compliance-related issues to be discussed, so that they may contact any additional relevant Office of Compliance staff
- Forward the draft agenda to the meeting co-chairs (DDS and the OSE SE TL) for review and concurrence on agenda item prioritization and attendees at least 5 calendar days before the meeting; copy the non-agenda lead RPM on the e-mail
- Following concurrence from the co-chairs, confirm additional staff invitations as needed
- Suggest to the co-chairs any late-breaking items to be added to the agenda as needed
- Send the meeting agenda 3 calendar days before the meeting to the attendees and additional invitees
- Ensure the set-up of any equipment for the meeting (e.g., laptop computer and projector) that will be needed by staff and coordinate the preparation of meeting materials (e.g., handouts) with appropriate staff

OND Clinical Staff will:

- Review all active DARRTS Safety Issue applications to which they are assigned when prompted for potential agenda items
- As needed, suggest agenda items and participants to the OND SRPM within 3-5 calendar days of being requested

OSE Staff will:

- Review all active OSE projects for the relevant OND division when prompted for potential agenda items
- As needed, suggest agenda items and participants to the assigned OSE RPM within 3-5 calendar days of being requested

The DDS and OSE SE TL will:

- Consider whether additional management from OSE and OND should be included in the meeting
- Concur with or modify attendee list
- Review the planned meeting agenda for the following:
    - Completeness
    - Prioritization of issues
    - Addition of late-breaking items

    - Time allotment for the scientific discussion and other agenda items
- Forward the final agenda to the OSE RPM and the OND SRPM within 2 days of receipt of the proposed agenda or sooner to ensure that the agenda can be circulated to attendees 3 calendar days before the meeting

Flexibility in agenda-related time frames and responsibilities

In some divisions, the OND SRPM, DDS, OSE PM, and OSE SE TL meet as a group to plan the agenda. In those cases, additional time for review and concurrence by the DDS and OSE SE TL does not have to be scheduled, and the other time frames can be adjusted accordingly with the goal of distributing the agenda 3 calendar days before the meeting.

A few divisions meet monthly with OSE rather than bimonthly. For divisions meeting monthly, the time frames described above may be shortened to allow the agenda to be maximally inclusive of safety issues that emerge during the month. Every effort should be made, however, to distribute the agenda 2 calendar days before the meeting.

During the meeting

The DDS and OSE SE TL will:

- Co-chair the meeting or assign a designee to co-chair the meeting
- Monitor the discussion so that all agenda items can be addressed
- Engage the relevant OND and OSE staff in discussion of the agenda items

The Agenda Lead RPM will:

- Take meeting notes, with an emphasis on the main discussion points and action items for each agenda item, as appropriate
- Ensure that the appropriate office is identified as the lead in the action items and a target date for follow-up is determined

Following the meeting

The Agenda Lead RPM will:

- Circulate the meeting agenda annotated with the main discussion points and action items from the meeting to the OND division, the relevant OSE staff, and meeting invitees from other offices and/or divisions. If the DARRTS Safety Issue workplans have been modified with action items from the meeting, a DARRTS workplan report for the division may be circulated as an addendum to the annotated meeting agenda.

Meeting Co-chairs (OSE SE TL and DDS) will:

- Ensure that action items are appropriately assigned to OSE and OND staff, with target dates
- Ensure that respective OSE and OND management are informed about safety issue updates, as needed
- Follow up with OSE and OND staff periodically to monitor the completion of assignments

The DDS will:

- Notify the Safety Policy and Communication Staff of any issues for which a risk communication piece may be warranted (based on the discussion at the meeting)

The OND SRPM will:

- Work with the OND reviewers/TLs to address action items, as needed
- Update the DARRTS Safety Issue applications and workplans, as needed
- Notify the OSE RPM about any updated action items and target dates

The OSE RPM will:

- Work with OSE management and staff to address action items, as needed
- Notify the OND SRPM about any updated action items and target dates

The primary OND Medical Officer will:

- Clarify any action items and target dates discussed at the meeting, as needed
- Forward any workplan updates to the OND SRPM
- Address assigned action items

The OND Medical Team Leader will:

- Update proposed OND action items and target dates discussed at the meeting, as needed
- Note the proposed OSE action items for assigned safety issues
- Send the updated OND action items and target dates to the DDS, as needed
- Supervise the OND Medical Officer in addressing action items for assigned safety issues

OSE Staff associated with the issue discussed will:

- Clarify OSE assigned workplan activities discussed at the meeting, as needed
- Note the proposed OND action items of the safety plan and target dates
- Ensure that OSE team leaders are informed of any proposed OSE action items and target dates discussed at the meeting, as needed
- Send the updated OSE action items and target dates to the OSE SE TL and OSE RPM, as needed
- Address action items, as appropriate

OSE Team Leaders will:

- Lead OSE staff in addressing action items, as needed

EFFECTIVE DATE

This MAPP is effective upon date of publication.

Attachment: OND-OSE Joint Meeting Agenda Planning Schedule

	Day -14	**Day -13**	**Day -12**	**Day -11**	**Day -10**	**Day -9**	**Day -8**	**Day -7**	**Day -6**	**Day -5**	**Day -4**	**Day -3**	**Day -2**	**Day -1**	**MTG**	**Post MTG**
1. OSE RPM and OND SRPM solicit respective staffs for agenda items																
2. OSE staff identifies agenda items and notifies OSE RPM																
3. OND staff identifies agenda items and notifies OND SRPM																
4. Draft agenda preparation by Agenda Lead RPM																
5. Review/concurrence of agenda/invitees by co-chairs																
6. Additional staff invited as needed by Agenda Lead RPM																
7. Agenda Lead RPM distributes agenda																
8. Conduct meeting																
9. Agenda Lead RPM distributes action items; DDS contacts SPCS regarding risk communication issues																

Notes:

1. Proposed additional attendees are notified at day -7 (hashed box) that they may be needed at the upcoming meeting so that they can tentatively block their schedules. The need for their attendance is confirmed on day -3.