POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Risk Evaluation and Mitigation Strategies Modifications and Revisions

Table of Contents

PURPOSE

- The purpose of this MAPP is to describe the policies and procedures that Center for Drug Evaluation and Research (CDER) staff will follow to:
  - Notify an application holder that a risk evaluation and mitigation strategy (REMS) modification is required
  - Process REMS revisions and modifications
  - Coordinate the review time frames and action on proposed REMS modifications between offices
  - Post revised and modified REMS documents and REMS materials on the FDA's website.[1]

[1] See https://www.fda.gov/drugs/drug-safety-and-availability/postmarket-drug-safety-information-patients-and-providers.

- This MAPP applies to the following CDER offices:
  - Office of New Drugs (OND)
  - Office of Generic Drugs (OGD)
  - Office of Surveillance and Epidemiology (OSE)
  - Division of Information Disclosure Policy (DIDP) in the Office of Regulatory Policy
  - Office of Communications (OCOMM)
- This MAPP also applies to changes to a REMS that is part of a shared system[2] (hereafter, a **shared system (SS) REMS**)[3]

BACKGROUND

- Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizes FDA to require holders of applications for drug and biological products[4] to submit a proposed REMS if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh its risks.
- Application holders can propose changes to an approved REMS at any time. Additionally, FDA can require a REMS modification based on the determination that a modification is necessary to ensure the benefits of the drug outweigh its risks, to minimize the burden on the health care delivery system of complying with the REMS, or to accommodate different, comparable aspects of the elements to assure safe use (ETASU) for a drug that is the subject of an application under section 505(j), and the applicable listed drug. The guidance for industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions* describes how changes to REMS are categorized and the specific types of REMS changes.[5] **REMS revisions** are changes that can be implemented following notification to

[2] For the purposes of this MAPP, *a shared system REMS* is a program that encompasses multiple prescription products and is developed and jointly implemented by two or more application holders. A shared system REMS includes a single, shared system REMS as defined in section 505-1(i)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

[3] Terms bolded at first use are defined in the Definitions section.

[4] Applications covered under section 505-1 of the FD&C Act are new drug applications, abbreviated new drug applications, and biologics license applications. For the purposes of this MAPP, all of the products approved under these applications are referred to as *drugs*.

[5] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

FDA. All other changes are REMS *modifications*, defined in the guidance as **minor and major REMS modifications**.

POLICY

- CDER will follow the statutorily mandated time frames for review of and action on proposed REMS modifications.[6]

- REMS revisions will be received as a REMS Revision submission (not a supplement). REMS revisions do not require CDER approval and can be implemented upon submission.

- Proposed minor REMS modifications will be received as a changes-being-effected (CBE)-30 supplement, which can be implemented 30 days after receipt, but are not final until approved.

- Proposed major REMS modifications will be received as a prior approval supplement (PAS) and require CDER approval before implementation.

- Proposed **REMS modifications to conform to approved or ordered safety labeling changes** will be received as a PAS and require CDER approval before implementation.

  – CDER will distinguish REMS modifications to conform to approved safety labeling changes from those that are not considered conforming,[7] and act on the proposed changes within the corresponding time frames.

  – If the REMS modification supplement is submitted either with the safety labeling changes supplement or during the review of the labeling supplement, and no additional changes to the REMS are needed, CDER may approve the REMS modifications at the same time as the labeling supplement.

  – When the REMS modification is due to safety labeling changes and is for an SS REMS that includes abbreviated new drug applications (ANDAs), CDER will generally instruct the application holders in the SS REMS to submit the

[6] See section 505-1(h)(2)(A) of the FD&C Act. See also the guidance for industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions* and Attachment 1, Time Frame for Acting on REMS Revisions and Modifications, of this MAPP.

[7] See the definition for *REMS modifications due to safety labeling changes* in the Definitions section.

proposed REMS modification submission after the class safety labeling changes are approved (or ordered).[8]

- CDER will review and act on submissions that contain more than one type of REMS change based on the time frame for the change with the longer review clock.

  – For submissions containing REMS modifications of any type *and* REMS revisions, CDER may instruct the application holder to submit the REMS revisions in a separate submission to allow for their immediate implementation

- CDER will review and act on REMS modifications that are submitted as part of a chemistry, manufacturing, and controls (CMC) supplement or an efficacy supplement according to the time frame for that supplement. REMS modifications submitted as part of an efficacy or CMC supplement cannot be implemented until approved.

- CDER will review proposed REMS modifications of any type that are submitted with a scheduled REMS assessment[9] concurrently with the assessment. CDER will act on the proposed REMS modifications following CDER's review of the REMS assessment. The modifications cannot be implemented until approved.

- For REMS that comprise multiple application holders, including SS REMS, CDER will generally act on REMS modification submissions for all application holders on the same day.

- When CDER requires a REMS modification, CDER will issue a REMS modification notification letter that includes the basis for the required modification and specifies the type of change and submission type.

- If a REMS modification submission is not complete, CDER will instruct the application holder to submit the additional information needed for review. If CDER does not receive the necessary information in sufficient time to review, CDER may issue a complete response (CR) letter.

[8] This instruction helps to ensure that FDA has the necessary information to assess the REMS modification supplements and act on them in a timely manner, consistent with any priority review designation that may apply to the supplements. See MAPP 5240.3 Rev.5 *Prioritization of the Review of Original ANDAs, Amendments, and Supplements*. MAPPs can be found on the Manual of Policies and Procedures web page at https://www.fda.gov/about-fda/center-drug-evaluation-and-research/cder-manual-policies-procedures-mapp.

[9] REMS assessments must be submitted at the times specified in the REMS timetable for submission of assessments (section 505-1(g)(2)(B) of the FD&C Act).

- The REMS Revision Processing Team (RRPT), consisting of representatives from the OND Immediate Office and the OSE Division of Risk Management (DRISK), will process all REMS revisions.

- A multidisciplinary team comprised of relevant staff from OND, OSE, OGD, the Office of Compliance, and other divisions and offices as appropriate (e.g., Office of Scientific Investigations) will review proposed REMS modification submissions and, as appropriate, discuss proposed major REMS modifications with the REMS Oversight Committee.

RESPONSIBILITIES AND PROCEDURES[10]

Because SS REMS comprise multiple types of applications and application holders, the procedures for management of and action on modifications of SS REMS differ from those for non-SS REMS (i.e., REMS for individual applications). In brief:

- OND and OGD have primary responsibility for the management of and action on proposed REMS modification submissions to new drug applications (NDAs)/biologics license applications (BLAs) and ANDAs, respectively.

- DRISK has primary responsibility for the review of the content of proposed REMS modification submissions for both SS and non-SS REMS.

  – Staff from other relevant disciplines (e.g., OND clinical reviewers) may also review the content of the proposed modification submissions, depending on the nature of the proposed REMS change

- The OND and OSE project management staff[11] and the OGD REMS coordinator staff have responsibilities for proposed REMS modification submissions depending on whether the changes are to an SS REMS or a REMS for an individual product (see Attachment 2, OND/OSE Project Manager and OGD REMS Coordinator Responsibilities).

Specific responsibilities and procedures are outlined in the following sections.

1. Requiring a REMS Modification

The **multidisciplinary review team** will:

- Determine that a REMS modification is necessary

[10] This MAPP does not discuss additional responsibilities and procedures applicable to modifications to SS REMS that use a drug master file for REMS submissions.

[11] For the purposes of this MAPP, OND and OSE project management staff are defined as the regulatory health project manager and safety regulatory health project manager.

The **DRISK members of the multidisciplinary review team** will:

- Before the REMS modification notification letter is issued, finalize and archive their review that describes the rationale for the REMS modification

The **OND regulatory health project manager (RPM)/safety regulatory health project manager (SRPM)** and/or **OGD REMS coordinator** (see Attachment 2) will:

- Draft and (as applicable) initiate clearance of the REMS modification notification letter to the applicant(s). The letter should include:
  - A description of and the rationale for the required REMS modification
  - The type of modification required and, based on the type of modification, the type of submission required (CBE-30 or PAS)
  - The time frame within which the application holder must submit the REMS modification, generally 120 days or an otherwise reasonable time from the date of the REMS modification notification letter
- *For required modifications of SS REMS,* also prepare a general, nonapplicant-specific copy of the REMS modification notification letter and provide it to the OSE SRPM
- Issue the REMS modification notification letter to the application holder(s)

The **OSE SRPM** will:

- *For required modifications of SS REMS,* provide the general, nonapplicant-specific copy of the REMS modification notification letter to the point of contact (POC) for the **Industry Working Group (IWG)** only. The OSE SRPM will provide this letter to the **IWG POC** only after the REMS modification notification letters have been sent to individual application holders.

The **deputy director for safety (DDS)** will:

- Oversee the OND review division activities regarding REMS modification notifications
- *As applicable*, complete a REMS memorandum to document the rationale for the addition or removal of REMS elements and/or changes to the REMS goals
- Be the signatory authority for REMS modification notification letters for NDA/BLA products

The **OGD Director of Office of Bioequivalence (or designee)** will:

- Oversee the OGD activities regarding REMS modification notifications
- Be the signatory authority for REMS modification notification letters for ANDA products

2. Processing Submissions for REMS Changes[12]

REMS revision submissions

The **RRPT** will:

- Within 5 days of receipt, determine if the changes proposed by the application holder meet the criteria for REMS revisions

If the REMS revision criteria are met

The **RRPT** will:

- Send the PDF document (containing the REMS document[13] and REMS materials) to:
  - The DIDP mailbox, copying the OND RPM, OND SRPM, DDS, DRISK risk management analyst (RMA) team leader (TL), OSE SRPM, and OGD REMS coordinator (if appropriate)
  - The FDA REMS web page mailbox,[14] and summarize the revisions to the REMS

The **DIDP** will:

- Review and redact the documents and place them in the FOIREAD folder for the Division of Drug Information in OCOMM

[12] Procedures for processing REMS modifications due to safety labeling changes are described separately in section 3, Processing Submissions for REMS Modifications Due to Approved or Ordered Safety Labeling Changes, of this MAPP.

[13] Before the revised REMS document and REMS materials are sent to DIDP, the RRPT should update the "Last modified/revised date" on the top left side of the first page of the REMS document to the date the submission was received by FDA.

[14] FDAREMSwebsite@fda.hhs.gov

If the REMS revision criteria are not met

The **RRPT** will:

- Notify the OND RPM, OND SRPM, DDS, DRISK RMA TL, and OSE SRPM and OGD REMS coordinator (if appropriate)

The **DDS** and **DRISK RMA TL** will:

- Determine the appropriate type of modification (minor or major)

The **OND RPM/SRPM** will:

- Inform the document room staff that the submission should be recoded as a REMS modification (minor or major)

- Notify the application holder that the submission type has been changed from revision to modification by issuing the appropriate supplement acknowledgment letter

The **OGD REMS coordinator** will:

- Inform the document room staff that the submission should be recoded as a REMS modification (minor or major)

- Notify the application holder that the submission has been recoded as a REMS modification (minor or major)

Minor REMS modification (CBE-30 supplement) and major REMS modification (PAS) submissions

The **DDS** and **DRISK RMA TL** will:

- Within 14 days of receipt, determine if the proposed modification meets the criteria for minor or major REMS modifications

The **OND RPM/SRPM** will:

If modification criteria (major or minor) are met

- Within 14 days of receipt of the submission, issue a supplement acknowledgment letter to the application holder(s)

  – Minor modifications: Acknowledge CBE supplement

  - Major modifications: Acknowledge PAS

- Include the action date in the supplement acknowledgment letter and, if applicable, instructions to submit additional information needed for review

If modification criteria (minor or major) are not met

- Within 14 days of receipt of the submission, issue a supplement acknowledgment letter to inform the application holder of the appropriate REMS modification category and why; include the appropriate action date

- Inform the document room staff that the submission should be recoded CBE or PAS, as appropriate

If modification criteria are not met and the proposed changes meet criteria for REMS revisions

- Send the submission to the RRPT mailbox[15] (see REMS revision submissions in section 2)

- Upon confirmation of submission type from the RRPT, issue an Acknowledge and Retain Information Incorrectly Submitted as Supplement letter to notify the application holder that the changes are considered REMS revisions and can be implemented immediately

- Notify the review team and the OGD REMS coordinator (as applicable) that the submission type is incorrect

The **OGD REMS coordinator** will:

If minor modification criteria are not met and the proposed modifications meet the criteria for major modifications

- Issue a CBE denied letter. This automatically withdraws the CBE-30 supplement and instructs the applicant to resubmit the REMS modifications as a PAS.

If major modification criteria are not met and the proposed modifications meet the criteria for minor modifications

- Notify the application holder via email, and request that the document room staff recode the submission as a CBE-30 supplement

[15] REMSRevisionProcessing@fda.hhs.gov

If major or minor modification criteria are not met and the proposed modifications meet the criteria for REMS revisions

- Notify the application holder via email that the changes are considered REMS revisions and can be implemented immediately; request that the document room staff recode the submission as a REMS revision

- For ANDA-only shared system REMS: Send the submission to the RRPT mailbox[16] (see REMS revision submissions in section 2)

3. Processing Submissions for REMS Modifications Due to Approved or Ordered Safety Labeling Changes

The **DDS** and **DRISK RMA TL** will:

- Within 14 days of receipt of the submission, determine if the proposed changes are conforming[17] or nonconforming[18]

The **OND RPM/SRPM** will:

If the proposed REMS modifications are submitted at the same time as the proposed safety labeling changes

- Ensure that the REMS modification and safety labeling changes are in separate supplements

- Verify that the separate supplements are correctly coded in CDER's electronic document archiving system

- After the safety labeling changes are approved or ordered:

  – Ensure the pending REMS modification supplement is amended by the application holder, as needed, to reflect the approved or ordered safety labeling changes

  – Enter an FRM-ADMIN-65 Memo to File into CDER's electronic document archiving system and link it to the corresponding REMS modification

[16] REMSRevisionProcessing@fda.hhs.gov

[17] REMS modifications that transfer new labeling language that is approved or ordered into the existing REMS and/or REMS materials are considered conforming.

[18] Overall design, programmatic, and/or implementation changes to the REMS that result from approved or ordered safety labeling changes are not considered conforming REMS modifications.

supplement to open the 60- or 180-day goal date for the REMS modification due to safety labeling changes supplement[19]

If the proposed REMS modifications are submitted after approval of the proposed safety labeling changes

- Enter an FRM-ADMIN-65 Memo to File into CDER's electronic document archiving system and link it to the corresponding REMS modification supplement to open the 60- or 180-day goal date for the REMS modification due to safety labeling changes supplement

The **OGD REMS coordinator** will:

- Ensure that the application holder has submitted a REMS modification supplement or amendment to the pending REMS modification that reflects the approved or ordered safety labeling changes

- Verify that the supplement is correctly coded in CDER's electronic document archiving system

4. Reviewing REMS Modification Submissions

The **OND RPM/SRPM**, **OGD REMS coordinator**, or **OSE SRPM**[20] (see Attachment 2) will:

- Notify members of the multidisciplinary team of the REMS supplement

- Send consult requests to other offices/centers, as necessary

- Schedule meetings (within the review team and/or with the application holder or IWG) as needed to discuss the supplement

- Act as POC for communicating with applicant(s) and/or IWG during the review of the REMS modification submission

- Promptly communicate any questions and/or concerns from the multidisciplinary team to the application holder (or IWG, if applicable) during the review

[19] The 60- or 180-day goal date is not opened (and the Memo to File is not entered) until CDER receives the REMS modification to conform or align to the approved safety labeling changes or the labeling changes in a safety labeling changes order letter. Even if a REMS modification due to safety labeling changes supplement is submitted at the same time as the corresponding proposed safety labeling changes, or after submission but before the approval of the labeling supplement, the 60- or 180-day goal date does not begin until the associated labeling supplement is approved or ordered and the REMS modification supplement is amended to accurately reflect the approved labeling.

[20] SS REMS only.

- Before the action letter is issued, confirm that the DRISK review is finalized and archived in the CDER electronic document archiving system

The **DRISK RMA TL** will:

- Assign the RMA and other necessary DRISK staff to review the REMS modification submissions
- Oversee timely completion of REMS modification supplement reviews by DRISK staff

The **multidisciplinary review team** will:

- Within 45 days (minor modifications) or 160 days (major modifications) of receipt of the supplement, discuss any questions and/or concerns about the proposed modifications with the application holder (or IWG, if applicable)

The **DRISK RMA** will:

- Write the REMS modification supplement review and incorporate into the review (as necessary) information from disciplines consulted by DRISK
- Ensure clearance of the REMS document and materials via established procedures (as applicable)
- Provide the OND RPM/SRPM (and if applicable, OGD REMS coordinator and OSE SRPM) with the final version of the modified REMS document

The **DDS** will:

- Work with the OND RPM/SRPM (and if applicable, OGD REMS coordinator and OSE SRPM) to ensure timely OND review of and action on REMS modification submissions
- *For modifications of REMS that comprise only ANDAs and if applicable,* work with the OND SRPM to coordinate OND review activities with OGD
- *For major modifications and if applicable*, before the action letter is issued, complete a REMS memorandum to document the rationale for the addition or removal of REMS elements and/or changes to the REMS goals[21]

[21] The DDS will write a REMS memo for only NDA/BLA products. A REMS memo is not written by OGD for ANDA products.

The **OGD Director of Office of Bioequivalence (or designee)** will:

- Work with the OGD REMS coordinator to ensure timely OGD review of and action on REMS modification submissions

5. Acting on REMS Modification Submissions

The **OND RPM/SRPM** and/or **OGD REMS coordinator** will:

- Work with the DDS to ensure a REMS memorandum is written and archived, as needed

- Draft the action letter(s) to the applicant(s) upon completion of the multidisciplinary review

- *For modifications of SS REMS*, also prepare a general, nonapplicant-specific copy of the action letter and provide it to the OSE SRPM.

- No less than 1 week before the action goal date, initiate clearance of the draft action letter(s), and the REMS memo as applicable, via established CDER procedures (as applicable)

- Obtain the final version of the modified REMS document from the DRISK RMA

- Issue a supplement approval or CR letter within 60 days (minor modifications or conforming REMS modifications) or 180 days (major modifications or nonconforming REMS modifications) of receipt of the supplement

  – Ensure coordinated issuance of action letters across OND review division(s) and OGD, as applicable

The **DDS/OND signatory authority** will:

- Be the signatory authority for REMS modification action letters for NDA/BLA products

The **OGD Director of Office of Bioequivalence (or designee)** will:

- Be the signatory authority for REMS modification action letters for ANDA products

The **OSE SRPM** will:

- *For modifications of SS REMS*, provide the general, nonapplicant-specific copy of the action letter to the POC for the IWG only after the letters have been sent to individual application holders (i.e., a courtesy copy of the action letter)

6. Posting the Approved Modified REMS on the FDA Website

The **DIDP** will:

- Receive documents related to REMS revisions from RRPT
- *For REMS modifications for NDAs/BLAs*, receive approval letters for REMS modification supplements (with the attached REMS document and REMS materials) through CDER's electronic document archiving system
- *For REMS modifications for ANDAs*, receive the REMS document and REMS materials from the OGD RPM/REMS coordinator
- Promptly redact the aforementioned REMS-related documents
- Promptly place the REMS document and appended materials in an electronic folder for access by the Division of Drug Information

The **OCOMM Division of Drug Information** will:

- Post the revised REMS on the FDA website within 14 business days of FDA's receipt of the submission
- Post the approved modified REMS on the FDA website within 3 business days of the approval date

REFERENCES

1. Postmarket Drug Safety Information for Patients and Providers web page (https://www.fda.gov/drugs/drug-safety-and-availability/postmarket-drug-safety-information-patients-and-providers)
2. Guidance for industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions* (https://www.fda.gov/regulatory-information/search-fda-guidance-documents)

DEFINITIONS

Industry Working Group (IWG) — A group of application holders who participate in an SS REMS. In addition to working together to develop the shared program, the IWG coordinates modifications of the SS REMS across the participating application holders and submissions of proposed REMS modifications to FDA.

Industry Working Group Point of Contact (IWG POC) — The single representative for the IWG who facilitates communications between FDA and the IWG about the SS REMS.

Major REMS modifications — Changes that have a substantial effect on (1) the information contained in the REMS document and/or REMS materials about the serious risk or safe use of the drug; and/or (2) the actions application holders, patients, health care providers, or other stakeholders must take to comply with the REMS, or the REMS materials that support those actions.

Minor REMS modifications — Changes that have a limited effect on (1) the information contained in the REMS document and/or REMS materials about the serious risk or safe use of the drug; and/or (2) the actions application holders, patients, health care providers, or other stakeholders must take to comply with the REMS, or the REMS materials that support those actions.

REMS modifications due to safety labeling changes — REMS modifications that transfer new labeling language that is approved or ordered into the existing REMS and/or REMS materials are considered *conforming*. Overall design, programmatic, and/or implementation changes to the REMS that result from approved or ordered safety labeling changes are not considered conforming REMS modifications.

REMS revisions — Changes that do not affect (1) the information contained in the REMS document and/or REMS materials about the serious risk or safe use of the drug; and/or (2) the actions application holders, patients, health care providers, or other stakeholders must take to comply with the REMS, or the REMS materials that support those actions.

Shared system (SS) REMS — For the purposes of this MAPP, a REMS program in which more than one application holder in a class of drugs uses the same program to implement elements to assure safe use, including a single shared system REMS as defined in section 505-1(i)(1) of the FD&C Act.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
7/10/19	Initial	
6/29/20		None identified.
7/1/25		Document recertified. No updates incorporated.

ATTACHMENT 1: Time Frame for Acting on REMS Revisions and Modifications

The following table summarizes the types of changes to an approved risk evaluation and mitigation strategy (REMS), how these changes are to be submitted to FDA, and FDA's time frames for processing of REMS revisions, and action on proposed REMS modifications.

Proposed REMS Changes	**REMS Submission Classification**	**Time Frame**
REMS revisions	REMS revisions	Processed within 14 days
Minor modifications	CBE-30[1]	60 days from receipt date
Major modifications	PAS[1]	180 days from receipt date
Modifications due to SLC[1]	PAS (separate from SLC supplement)	Conforming modifications — 60 days from receipt date of the modifications that conform to the SLC
		Modifications not considered conforming — 180 days from receipt date of the modifications that align with the SLC
Minor and major modifications[2]	PAS	180 days from receipt date
Minor modifications and REMS revisions[2]	CBE-30	60 days from receipt date
Major modifications and REMS revisions[2]	PAS	180 days from receipt date
REMS modifications included in a REMS assessment submitted according to the timetable	CBE-30 **or** PAS	Modification will be reviewed and acted upon following the complete review of the REMS assessment
REMS modifications included in an efficacy or CMC[1] supplement	Submitted as part of the efficacy or CMC supplement	Modification will be reviewed and acted upon as part of the efficacy or CMC supplement

[1] CBE-30 = changes being effected; PAS = prior approval supplement; SLC = safety labeling changes; CMC = chemistry, manufacturing, and controls

[2] Supplements that contain more than one type of a proposed REMS change will be reviewed according to the proposed change that has the longer review time frame.

ATTACHMENT 2: OND/OSE Project Manager and OGD REMS Coordinator Responsibilities

The following table summarizes the responsibilities of the Office of New Drugs (OND) and Office of Surveillance and Epidemiology (OSE) project management staff, as well as the Office of Generic Drugs (OGD) risk evaluation and mitigation strategy (REMS) coordinator staff, for proposed REMS modification submissions. The responsibilities depend on whether the changes are to a shared system (SS) REMS or a REMS for an individual product.

	Type of REMS/Assigned Role	
Responsibilities[2]	**Non-Shared REMS (i.e., NDA/BLA[1]-only REMS)**	**SS REMS (That Include ANDAs[1])**
General		
Works with other RPMs[1] to identify the necessary members of the multidisciplinary team	OND SRPM[1] or OND RPM	OSE SRPM
Ensures timely multidisciplinary team review of and action on REMS modifications	OND SRPM or OND RPM	OND SRPM OGD RC[1] OSE SRPM
Requiring a REMS modification		
Drafts and issues the REMS modification notification letter	OND SRPM or OND RPM	OND SRPM OGD RC
Processing submissions for REMS revisions and modifications[3]		
Determines if proposed REMS modifications and revisions have been submitted (and coded) correctly or if changes to the type of submission are needed	OND SRPM	OND SRPM OGD RC
Issues supplement acknowledgment letter	OND SRPM or OND RPM	OND SRPM[4]

continued

Table continued

	Type of REMS/Assigned Role	
Responsibilities[2]	**Non-Shared REMS (i.e., NDA/BLA[1]-only REMS)**	**SS REMS (That Include ANDAs[1])**
Review of REMS modification submissions		
Coordinates communication within the review team, including scheduling meetings, as needed to discuss the supplement	OND SRPM or OND RPM	OSE SRPM
Acts as point of contact for communicating with applicant(s) and/or IWG[1] during the review of the REMS modification submission	OND SRPM or OND RPM	OSE SRPM[5]
Sends consult requests to other offices/centers, as necessary	OND SPRM OND RPM OSE SRPM[6]	OSE SRPM

continued

Table continued

	Type of REMS/Assigned Role	
Responsibilities[2]	**Non-Shared REMS (i.e., NDA/BLA[1]-only REMS)**	**SS REMS (That Include ANDAs[1])**
Action on REMS modification submissions		
Works with the DDS[1] to ensure a REMS memorandum is written and archived, as needed	OND SRPM	OND SRPM[7]
Drafts action letter for the REMS modification supplement; initiates clearance of the action letter via established CDER[1] procedures (as applicable)	OND SRPM or OND RPM	OND SRPM and OGD RC
Ensures coordinated issuance of action letters across OND review division(s) and OGD, as applicable	OND SRPM	OND SRPM OGD RC[8]
Sends courtesy copy of the general, nonapplication-specific action letter to the point of contact for the IWG	N/A	OSE SRPM

[1] NDA/BLA = new drug application/biologics license application; ANDA = abbreviated new drug application; RPM = regulatory health project manager; SRPM = safety regulatory health project manager; OGD RC = OGD REMS coordinator; IWG = Industry Working Group; DDS = deputy director for safety; CDER = Center for Drug Evaluation and Research

[2] General communications with individual applicants for single applications will continue to be managed by the project manager or REMS coordinator assigned to the specific application.

[3] Including REMS modifications due to approved or ordered safety labeling changes.

[4] Acknowledgment letters will only be sent to acknowledge receipt of REMS modifications submitted to NDAs and BLAs. OGD currently does not acknowledge ANDA supplements for REMS modifications.

[5] Submission of a supplement that also contains a REMS modification to a single ANDA in an SS REMS will be managed by the OGD REMS coordinator. Subsequent REMS modifications submitted by other members of the SS REMS will be managed by the OSE SRPM.

[6] The OSE SRPM will issue consults requested by the Division of Risk Management.

[7] A REMS memo is written by the OND review division only if there is an NDA/BLA in the SS REMS.

[8] Action letters for REMS modifications submitted to ANDAs generally should be issued on the same day action letters are issued to the reference listed drug.