TABLE OF CONTENTS

1. INTRODUCTION

Before following this Standard Operating Procedure (SOP), you must familiarize yourself with applicable content located in the Amgen BlueBook, which contains compliance requirements related to Promotional and Non-Promotional Material Review.

For the current version of any Global Corporate Compliance Policy (GCCP), the Amgen BlueBook, SOPs, or other compliance documents, please visit the Worldwide Compliance and Business Ethics (WC&BE) function page on MyAmgen.

Submission, review, approval, release, dissemination or withdrawal of materials governed by the Materials Approval and Compliance (MAC) Grid, must follow this SOP.

Materials relating to products that may be co-marketed in the U.S. by Amgen and another company will be subject to specific review, approval, release, dissemination and withdrawal processes agreed to and set forth in writing by the parties.

Certain capitalized terms used in this SOP are defined in the Healthcare Compliance Glossary**.**

2. ROLES AND RESPONSIBILITIES

Responsible Party	Responsibility
U.S. Commercial Director	• Attending all MAC meetings for materials sponsored by the Commercial organization. Attending MAC meetings are optional for materials sponsored by the Medical Communications organization. • Ensuring that only quality materials are submitted to review • Providing priority designations to MCM in the prioritization process • Encouraging a team atmosphere of cooperation and constructive issues resolution • Determining in conjunction with the Sponsor if Agency representation is required and managing the behavior of the Agency at meetings • Holding MAC Team members and Sponsors accountable for previous direction given unless there has been a change to the external or internal environment which can be clearly articulated • Ensuring the materials sponsored by the Commercial function meet the business needs of Amgen
File Standards	• The purpose of the File Standards is to ensure quality and consistency in Amgen's approved MAC files • The File Standards outline the minimum file specification requirements for submission and can be found here.

Responsible Party	Responsibility
Medical	• Providing a strategic medical perspective and ensuring the adequacy of medical data to support proposed claims
Medical Communications (MedCom)	• Checking all medical content for data accuracy, reference appropriateness, and scientific accuracy
Law	• Identifying and evaluating legal risks associated with MAC material submissions (e.g., FDCA, anti-kickback, etc.), interpreting laws, and providing privileged legal advice
MAC Business Process Owner (BPO)	• The MAC BPO consists of the head of Regulatory Promotion and Material Compliance Group and is responsible for: ○ Owning the MAC process ○ Responding to observations and enforcements ○ Implementing appropriate corrective actions associated with the process ○ Determining review caps and MAC meeting time
MAC Reviewers	• MAC Reviewers include US Medical Affairs, Law, Medical Communications, and Regulatory Promotion
MAC Team	• The MAC Team consists of the MAC Reviewers, the Commercial Director, the Material Compliance Manager, and the Materials Compliance Associate
Materials Compliance Manager (MCM)	• Continuity of the MAC process • Chair for the organization and flow of MAC meetings • Managing the prioritization process
Material Compliance Associate (MCA)	• Quality check submissions against File Standards and Grid requirements. • Provides editorial corrections on MAC files.

Responsible Party	Responsibility
Regulatory Promotion	• Identifying and evaluating regulatory risks associated with MAC material submissions (e.g., applicable FDA laws, the product label, regulations, enforcements, advisory comments, and guidance documents) • Interpreting regulations, and providing regulatory insight and direction • Assigning the labeling and managing label change updates, FDA Form 2253 status, expiration date, verifies the Material Class, and putting the material on FDA or Office of Prescription Drug Promotion (OPDP) /Advertising and Promotional Labeling Branch (APLB) Hold if appropriate via the electronic review and approval system • Responsible for Health Authority promotion submission records.

Sponsor	• Creating material reviewed through the MAC process
	• Submitting materials to MAC for review and approval
	• Coordinating the production of approved material
	• Ensuring that updates to materials are made according to the MAC Reviewers' comments
	• Managing the MAC lifecycle timeline of his/her materials with support from the MCA
	• Sponsor must not be:
	  ○ Field-based Amgen staff with Account Management Roles
	  ○ Commercial Field Staff below the level of Regional Sales Director
	• Commercial Field Staff members who are on a rotation in-house may be granted temporary access to sponsor and submit materials through the MAC process after contacting the appropriate MAC MCM

3. GENERAL BUSINESS RULES

All materials submitted for MAC Review within the scope of this SOP must comply with the following:

3.1. Materials Provided to U.S. Healthcare Community Require MAC Review

Materials with the purpose of promoting, advertising, and providing reimbursement, or providing disease state information about Amgen's products must be reviewed and approved by the appropriate MAC Reviewers, as identified in the MAC Grid, prior to publication or dissemination. The MAC Grid can be found here.

All materials will be assigned a class designation for identifying how a material may be used. Commercial material class designations are found here. Non-commercial material class designations are found here.

All class designations are owned by the MAC BPO, or their designate. Materials contained in the MAC Grid must be reviewed and approved through the system of record prior to release.

3.2. MAC Reviewers Must be Qualified

MAC Reviewers must be appropriately qualified, by education, training and/or experience, to evaluate the content of submitted material(s) and have the authority to approve or reject materials.

3.3. Materials Must be Approved and Released Prior to Dissemination

All material must be approved and released for use within the system of record prior to dissemination for use.

3.4. Promotional Materials Must Be Submitted to the OPDP/APLB

The following materials must be submitted to the OPDP/APLB prior to release:

- Direct-to-Consumer Broadcast Television Advertising: New direct-to-consumer (DTC) broadcast television advertisements must be sent to the OPDP/APLB for Advisory Comments prior to release.
- Products under accelerated approval (21 CFR 601 Subpart E or 21 CFR 314 Subpart H) or when human efficacy studies are not ethical or feasible (21 CFR 601 Subpart H)
    - Unless otherwise informed by the agency, promotional materials must be submitted to OPDP/APLB for Advisory Comments prior to release.
- Materials Subject to OPDP/APLB Form 2253 Submission: All materials requiring OPDP/APLB Form 2253 reporting must be submitted to the OPDP/APLB by the Regulatory Promotion group prior to release.

3.5. Changes to Approved or Released Materials Must Be Re-Reviewed

Materials that include changes after release must be re-reviewed and approved by MAC. Approved non-material changes are allowed after release if the changes are on the approved Non-Material Change list which can be found within the File Standards

4. PROCEDURES

The following are the detailed activities to submit, review, approve, release, track and withdraw materials in the MAC process:

Hold Office Hours	Submit Material for MAC Review	Review and Approve Material	Submit Material to OPDP/ APLB	Submit FDA Form 2253	Release Material	Track and Update Material	Withdraw Materials

4.1. Hold Office Hours

4.1.1. Office hours are used at the discretion of the Sponsor in order to obtain high level guidance/guardrails on proposed promotional content.

4.1.2. The MCM manages the meeting.

4.1.3. Required attendees at Office Hours are the Law, Regulatory Promotions, and Medical Communications reviewers. U.S. Medical Affairs may be invited as needed.

4.2. Submit Material for MAC Review

4.2.1. The Sponsor submits review-ready materials to MAC.

4.2.2. The MCA performs quality check of the intended use, target audience, and purpose into the system of record.

4.2.3. The MCA and/or the Sponsor ensure that the Material meets the MAC File Standards including:

- Citing medical references and sources
- Being void of content or claims that were previously rejected by MAC
- Having been properly proofread

4.3. Review and Approval Material

4.3.1. The MCM facilitates the weekly prioritization process to help prioritize which materials will be reviewed for the upcoming week.

- Required participants in the weekly prioritization process are the Commercial Director, the Regulatory Promotion Reviewer, and the MCM.
- The Commercial Director is responsible for Prioritization.
- Materials not scheduled for review in a given week are scheduled for a later review cycle

4.3.2. MAC Reviewers are assigned based on the job type as noted in the MAC Grid.

- A MAC Reviewer may not approve his/her own material. If an assigned MAC Reviewer is the material's Sponsor, the Sponsor must delegate his/her MAC Reviewer duties with respect to review of the specific material.
- A primary MAC Reviewer can remove himself/herself from the review but must assign a new primary MAC Reviewer within his/her discipline through the MAC system.
- The Commercial Director does not review or approve materials sponsored by the Medical Communications organization.

4.3.3. Each MAC Reviewer documents his/her comments, if any, on the materials within the system of record.

4.3.4. The MAC Reviewers complete their reviews and designate their decisions.

4.3.5. Any MAC Team member may request an Elevation Meeting to escalate a question or concern to more senior leaders. There are three levels of elevations as outlined here. The levels do not need to be followed sequentially. The MAC system of record will track elevations.

4.3.6. After the MAC Review, the Sponsor ensures all required changes are made to the material and the updated materials are uploaded to the electronic review and approval system.

4.3.7. The system of record routes approved materials that require Check Change to the MCA team where any MCA can perform the Check Change review.

- The designated MCA reviewer reviews the material to ensure all agreed upon blackline changes have been incorporated into the material, and that no material changes have been made. MAC Approved non-material changes are allowed between the MAC review and Check Change review phase. The approved Non-Material Change list can be found within the File Standards.
- If needed, the MCA reviewer coordinates with the Sponsor until the material is appropriately edited and ready for release.
- If material changes have been made, the Sponsor must submit the material for re-review by the MAC Reviewers

4.4. Submit Materials to OPDP/APLB for Pre-Clearance (if required)

4.4.1. If a material requires OPDP/APLB Advisory Comments or Pre-clearance, the Regulatory Promotion Reviewer places the material on an OPDP/APLB or FDA Hold during his/her review.

4.4.2. Once the material is preliminarily approved by the MAC Reviewers and the Check Changes process is complete, the Regulatory Promotion group sends the material to the OPDP/APLB.

4.4.3. The Regulatory Promotion Reviewer notifies the MAC Team of the next steps required prior to final approval, as applicable.

4.4.4. Upon the completion of any required changes the Regulatory Promotion Reviewer removes the OPDP/APLB, or FDA Hold and the material continues through the approval, Check Changes, OPDP/APLB Form 2253 submission, and release procedures.

4.5. Submit FDA Form 2253 (if required)

4.5.1. The Regulatory Promotion group performs processing of all materials deemed 2253 reportable in accordance with industry best practices for OPDP/APLB submission.

4.5.2. The Submission Publishing group archives the complete OPDP/APLB submission, including confirmation of submission, in the Regulatory system of record per department governance requirements

4.6. Release Material

4.6.1. For materials that do not require OPDP/APLB Submission, the MAC system of record releases approved materials as designated on the MAC Grid, upon the upload of the final approved material and completion of the Check Changes review, if applicable.

4.6.2. Materials requiring submission to the OPDP/APLB for Advisory Comments, Pre-clearance, or FDA Form 2253 cannot be used until all required actions are taken, and the Regulatory Promotion group releases the material.

4.6.3. Unless otherwise specified by the Regulatory Reviewer all materials are released for use for a period of 36 months or less. At the 36-month timepoint, materials automatically expire, and re-use of expired material requires a new routing.

4.7. Track and Update Material (if required)

4.7.1. All materials, proof of review and approval, withdrawals, and updates (if required) are tracked in the system of record.

4.7.2. The material's Sponsor and distribution vendor receives notification of release.

4.7.3. Amgen personnel may use each released material for its MAC approved use until the material expires or is withdrawn.

4.7.4. Amgen's system of record will send the Sponsor automated notifications if their material needs to be updated.

- A Sponsor may elect to not make any required changes and withdraw the material from use.
- If a change is required, Sponsors will need to follow update instructions and timing per the required change.

4.8. Withdraw Materials

4.8.1. The system of record will notify the Sponsor and vendor of any changes to expiration date.

4.8.2. Materials may be withdrawn by the material's Sponsor or by the Regulatory Promotion group.

4.8.3. Notification must be sent to the Sponsor and distribution vendor to cease distribution and use of the material.

4.8.4. The system of record will notify the applicable Amgen staff to discontinue use of the material.

5. DOCUMENT RETENTION

Staff members must comply with the Amgen Information Classification and Records Management Policy (POL-401247) and review the Amgen Records Retention Schedule and applicable Hold Orders to determine retention requirements.

6. REPORTING AND DISCIPLINE

Questions/Assistance: To report a concern or ask a question, contact the Business Conduct Hotline. Other resources are your Compliance Leads, Human Resources or your manager.

Reporting: If you are aware of a situation that you believe may be a violation of this SOP or may be otherwise unlawful or unethical, you can contact the Business Conduct Hotline at (888) 376-5574 or via the internet at https://amgenbch.ethicspoint.com at any time of day or night. Reports can be made anonymously, except where limited by law. Amgen maintains a strict Non-retaliation Policy, so concerns that are raised in good faith can be reported without fear of retribution or reprisal.

Discipline: If Amgen determines that any Amgen staff has violated the SOP, applicable laws or regulations, appropriate disciplinary measures will be taken. The following is a non-exhaustive list of possible disciplinary measures to which Amgen staff members may be subject: oral or written warning; suspension; removal of job duties/responsibilities or demotion; reduction in compensation; and termination of employment.

Amgen reserves the right to take whatever disciplinary measure(s) it determines in its sole discretion to be appropriate in any particular situation, including disclosure of the wrongdoing to governmental authorities. Nothing in the SOP changes the at-will nature of employment at Amgen, its affiliates or subsidiaries, where applicable.

Document Approvals for SOP-434364, V2.0

Approved Date: 30 May 2023

Owner Approval Outcome: Approve	Ben Salazar Owner 30-May-2023 19:12:55 GMT+0000