Safety Requirements Appendix

Safety Requirements for Market Research (MR) Programs

This Safety Requirements for MR Programs Appendix ("**Appendix**") supplements (and is not intended, and shall not be interpreted, to limit the terms of the Agreement) and is governed by the terms and conditions of the Agreement to which it is attached. Any defined terms not otherwise defined herein shall have the meanings set forth in the Agreement. The term Amgen as used herein shall mean the Amgen entity identified in the Agreement, or as applicable, the Order governing the Services to which this Appendix applies. The safety reporting obligations related to Reportable Events in this Safety Requirements Appendix will remain effective for so long as Provider (or Subcontractor if applicable) provides services to Amgen and/or interacts directly or indirectly with Market Research participants using Amgen products and/or services.

Amgen, as the Marketing Authorization Holder (MAH), is responsible for regulatory and legal obligations related to Reportable Event (as defined below) reporting to (a) protect the health and safety of patients and (b) continually assess the safety of Amgen's products and devices. To enable compliance with applicable regulations, Provider conducting business on Amgen's behalf, must comply with all applicable local laws and regulations related to Reportable Event reporting in addition to the requirements set forth in this Appendix.

Effective Date: 31st March 2023

1. Definitions

a. Adverse Event

An Adverse Event (AE) is any untoward medical occurrence in a patient administered an Amgen product and which is not necessarily caused by the Amgen product. An AE can therefore be any unfavorable and unintended sign (i.e. an abnormal laboratory finding), symptom, or disease temporally associated with the use of an Amgen product, combination product, or medical device, whether or not considered related to the product. This includes:

- Any clinically significant worsening of a pre-existing condition;
- An AE that has been associated with the discontinuation of the use of a product

b. Amgen Reference ID

A unique identification code generated by Amgen's system that corresponds with the specific Reportable Event submitted. This unique number will be provided by Amgen to the reporter via email upon successful submission of the Reportable Event (i.e. XX-XXXXXXX, AGS-US-EMAIL-XXXXXX-XXXXXX-XX, etc).

c. Amgen Safety Reporting Portal (ASRP)

Web-based reporting tool that allows the Provider to submit Reportable Events to Amgen electronically. Upon each submission, ASRP generates a unique Amgen Reference ID, which is emailed to the Provider immediately, allowing for real time (in-line) reconciliation.

d. Date of Awareness

Date of Awareness (also referred to as Initial Receipt Date) is defined as the earliest date that the Provider, or any Subcontractor, receives information that constitutes a Reportable Event (i.e. the earliest date any verbal communication (e.g., face to face, telephone call or voicemail, etc.), fax, email, text, mail or any other type of communication is received by the Provider or Subcontractor. For the purpose of Amgen regulatory reporting, the Date of Awareness (day zero) must be captured by the Provider and transferred to Amgen with the Reportable Event.

e. Organization Code

A unique code assigned by Amgen to identify a specific Provider (i.e. PMR-XXXXX). The Organization Code is not the same value as the Vendor Reference ID/Respondent ID or the Project ID.

f. Other Safety Findings

Other Safety Findings (OSFs) include the following, regardless of whether they are associated with an AE and they must be reported to Amgen:

- Use of an Amgen product while pregnant and/or breast feeding (includes pregnancies in women whose sexual partner took, or is taking, an Amgen product)
- Medication Errors
- Overdose
- Underdose
- Misuse
- Abuse
- Addiction
- Unexpected therapeutic benefit
- Transmission of an infectious agent through an Amgen product
- Accidental exposure
- Occupational exposure
- Lack or loss of therapeutic effect/efficacy
- Missed dose
- Reports of patient “death” after exposure to an Amgen’s product
- Off label use of an Amgen product

g. Product Complaints

Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a drug, combination product, or device after it is released for distribution to market or clinic by either Amgen or by distributors or partners for whom Amgen manufactures the material. This includes all components distributed with the drug, such as packaging, drug containers, delivery system, labelling, and inserts. Potential sources of product complaints may include Software as a Medical Device (SaMD) provided by Amgen; examples include, but are not limited to Medication Reminders, disease/symptom trackers, etc.

Use Error is a situation in which the outcome of device use was different than intended, but not due to malfunction of the device. The error may have been due to a poorly designed device, or it may have been used in a situation that promoted incorrect usage. Use errors are considered product complaints.

h. Project ID

A unique code assigned by Amgen for a specific MR project. The Project ID is not the same value as the Organization Code or the Vendor Reference ID/Responent ID.

i. Reportable Event

An Adverse Event (AE), Other Safety Finding (OSF) and Product Complaint (PC) are collectively known as Reportable Events. All Reportable Events must be submitted to Amgen regardless of whether or not they are stated to be related to, or caused by, an Amgen product, combination product or device.

j. Source Document

A Source Document is the original document, image of the source document, data, or record in which information collected for a Reportable Event (verbatim term/description) is first recorded.

k. Subcontractor

Any person or entity that has been retained to perform all or a portion of Provider's obligations set forth in the Agreement. Provider will not delegate or subcontract any of its duties under this Appendix without the prior written consent of Amgen. Any permitted delegation or subcontract shall be pursuant to an appropriate written agreement between Provider and such Subcontractor containing obligations consistent with the requirements of the Agreement and this Appendix. Provider shall be responsible for (i) all conduct, actions and omissions of Provider's Subcontractors; (ii) compliance by each of Provider's Subcontractors with the requirements of the Agreement and this Appendix; and (iii) management, oversight, and coordination of the performance of all such Provider's Subcontractors. Any breach of the terms or conditions of the Agreement or this Appendix by any Provider Subcontractors shall be deemed a direct breach by Provider of such terms or conditions.

l. Vendor Reference ID/Respondent ID

A unique ID code originating internally from the Provider that corresponds with the case specific Reportable Event being submitted to Amgen Safety. This ID number is how the Provider would search for the Reportable Event within their system and must be entered in the "Vendor Reference ID/Respondent ID" field on ASRP or the backup reporting form. The Vendor Reference ID/Respondent ID is not the same value as the Organization Code

2. Reporting Procedures

a. Identification and Reporting

A Reportable Event must be identified and reported by the Provider from all potential sources that result from exchange of information with participants, or their Health Care Professional (HCP). The Provider is required to systematically review all potential sources of Reportable Events relevant to the project. Examples of potential sources of Reportable Events include, but are not limited to, reports, letters, voicemails, call center notes/recordings, verbal communications such as face to face or telephone call/logs, forms, customers surveys, nurse visit notes, clinical/office charts, hospital/medical records, insurance forms/benefit verification, returned mail, emails (including no-reply emails), SMS/text messages, data collected through chatbots, and social media, data collected via systems/websites/portals/apps (e.g. WhatsApp, GroupMe, WeChat, etc.).

With respect to each Reportable Event, the Provider must (a) collect all necessary information for the Reportable Event in accordance with the requirements set forth in this Appendix (**see section 2e**), (b) explain to the project participants, the importance of capturing and sending Reportable Event data to Amgen, (c) seek to obtain each participant's consent to enable Amgen to follow up with the participant and or, as appropriate, the participant's HCP (**see section 2f**).

If applicable, Source Document(s) relevant to the Reportable Event, must be submitted together with the Reportable Event irrespective of the reporting channel used for transmission of Reportable Events to Amgen (**see section 2b**). Provider must comply with all applicable local laws and regulations related to redaction (removal) of identifiable personal information/data from the Source Document to protect patients' privacy rights. Depending on local requirements examples of personal information (data) that require redaction include but are not limited to:

- First and Last Name
- Social Security Numbers, National Insurance Number, or local equivalent
- Medical record numbers (including prescription number)
- Health plan beneficiary numbers
- Photographic images of patient and/or insurance cards

b. Transmission of Reportable Events to Amgen

Note: In order to protect confidentiality, integrity, and availability of Reportable Event information, secure email exchange (i.e. Transport Layer Security (TLS) encryption) must be established between the Provider and Amgen prior to sending proprietary/personal information via email.

The reporting channel(s) relevant to the project and any necessary reporting form/e-form for the program will be communicated to the Provider by the Amgen designated contact (the "Amgen Contact") at the beginning of the project.

The Provider must clearly state the specific reporting channel(s) in their written procedures for the project i.e. work/client instructions or operating guidance (see section 3b). The Provider must provide this document to Amgen when requested.

The Provider must also have a mechanism in place to generate and provide a unique *Vendor Reference ID*/Respondent ID (i.e. database record ID, interaction ID, etc.) with each report submitted to Amgen. Both, *Amgen Reference ID* and *Vendor reference ID*/Respondent ID must be retrievable, when requested, in the Provider's system (i.e. in a form of a project specific listing), to allow for reconciliation (**see section 2d**) and monitoring/Quality Control activities (**see section 3e**).

Regardless of reporting channel, the Provider will always receive a unique *Amgen Reference ID* for each report submitted with the exception of fax. This *Amgen Reference ID* must be retained by the Provider as acknowledgement of receipt of the submitted Reportable Event. Until the Provider is in receipt of an *Amgen Reference ID*, the Provider should not consider the Reportable Event to be successfully transferred to Amgen Safety. If the *Amgen Reference ID* has not been received within 1 hour of the submission, the Provider must resubmit the report within the same business day. For fax method, the Provider must retain the fax acknowledgement message as verification of successful submission.

Reporting Channel #1: Amgen Safety Reporting Form (paper)

Project-specific Amgen Safety Reporting Form (ASRF) will be provided to the Provider by the Amgen designated contact (the "Amgen Contact"). Upon becoming aware of a Reportable Event, the Provider must complete Reporting Form provided and transmit it to Amgen using email or fax contact information provided on the Reporting Form.

Note: If email or e-fax is used to submit a Reportable Event, the Provider will receive unique Amgen Reference ID via email (e.g. AGS-US-EMAIL-XXXXXX-XXXXXX-XX). If fax is used to submit a Reportable Event, the Provider will receive an acknowledgement message. This information must be retained by the Provider for either method.

Reporting Channel #2: Amgen Safety Reporting Portal (ASRP)

Upon becoming aware of a Reportable Event, the Provider must complete and submit the e-form(s) available on the ASRP in accordance with project specific training provided by Amgen. The Provider must include the report-specific *Vendor Reference ID*/Respondent ID and Project ID on the e-form and ensure they select the appropriate *Organization Code* (i.e. PMR-XXXXX) within ASRP to associate the Reportable Event correctly.

Immediately after submission of Reportable Event to ASRP, the Provider will receive a unique *Amgen Reference ID* (i.e., XX-XXXXXXX, XX-XXXXXXX-FU-01, etc.) for that report, which will be visible on screen and sent to Provider via email. The email will also display the *Vendor Reference ID*/Respondent ID provided by the Provider when the Reportable Event was submitted. This information must be retained by the Provider.

Please note: It will be communicated to the Provider at the project set-up, how the Provider will submit Reportable Event(s) to Agmen Global Safety. If the project was not issued a project-specific Amgen Safety Reporting From, then any potentially Reportable Event(s) suspected to be related to any Amgen medicinal product, devices or combination products, must be spontaneously reported to Amgen within 1 business day of Provider awareness.

A list of all Amgen medicinal products can be found in the following link:
https://wwwext.amgen.com/amgen-worldwide

To spontaneously report a Reportable Event to Amgen, refer to the following link to locate your Local Amgen contact information by country: https://wwwext.amgen.com/contact-us/product-inquiries

Additional details on what to collect and report to Amgen for the reportable event can be found in the following link: https://wwwext.amgen.com/products/global-patient-safety/adverse-event-reporting

Reportable Events suspected to be related to any non-Amgen medicinal product should be reported to the local authority in line with the local country requirements.

c. Reporting timeframe

All Reportable Events MUST be reported to Amgen within **one (1) business day** of the Provider's Date of Awareness. Provider must have processes, adequate staff, and training in place such that they can ensure the identification of a Reportable Event in a timely manner. If the situation arises that a Reportable Event is submitted late (>1 business day after awareness), a reason for the late submission must be provided by the Provider along with the late submission. Amgen will request this information as part of ongoing monitoring and compliance activities.

d. Reconciliation of Reportable Events

To confirm successful transfer of Reportable Events from the Provider to Amgen, reconciliation is conducted. Only ***Safety reviewed*** projects will be subject to reconciliation process. The Provider will be notified by Amgen Contact, prior to project initiation, if a project is exempt from Safety review. Amgen Contact will provide the Provider with a project-specific Reconciliation Form when applicable.

Project-specific Reconciliation Form will be used by Provider to provide Amgen Safety with a list of all Reportable Events submitted to Amgen during fielding (i.e. all Reportable Events previously submitted as individual reports) or confirmation that no Reportable Events were generated for the project. Provider will submit completed Reconciliation Form to Amgen Safety at the end of each project (within 2 weeks of completion of field work). Following receipt of completed Reconciliation Form(s), Amgen will notify the Provider, within seven (7) business days, of any discrepancies (i.e. missing reports), which will require the Provider to retransmit such Reportable Events to Amgen.

e. Information Collected

Reportable Events must be transmitted by the Provider to Amgen regardless of the amount of information available. For each Reportable Event, the Provider must seek to obtain the following key elements in compliance with the applicable Privacy Laws (please refer to *Privacy and Data Protection Schedule* attached to the Agreement):

- Patient - An actual (i.e. not hypothetical) patient, who can be identified by the Provider. Patient identifiers may include, as permitted by applicable Privacy Laws, a patient's name, initials, date of birth, age, gender or patient identification number
- Product - Details regarding the Amgen medicinal product, combination product or device, together with the Lot number and serial number
- Reporter - An identifiable reporting source (i.e. patient, caregiver, HCP)
- Event - Details regarding the Reportable Event

Provider will report to Amgen any additional relevent information for the Reportable Event provided by the Provider including but not limited to treatment, concomitant medications, medical history, outcome, etc. (if applicable) and must retain sufficient information to allow for successful reconciliation of Reportable Events (i.e. Amgen product name, date report was submitted to Amgen, *Amgen Reference ID*, *Vendor Reference/Respondent ID*, patient initials or other legally permissible identifiers).

f. Follow Up

With respect to each Reportable Event, the Provider must inform the participant that the information provided will be shared with Amgen and the relevant health authorities. In addition, Provider must seek to obtain the participant's consent, enabling Amgen to follow up directly with them or, as appropriate, the patient's HCP, regarding the Reportable Event should there be a need. If the participant refuses to consent to such follow up, such refusal must be documented and transmitted to Amgen when the Reportable Event is reported.

In case direct interaction for follow up between Amgen and the participant is not possible, but Provider is permitted to continue to interact and follow up with participant to obtain follow up information, this must be documented and transmitted to Amgen when the Reportable Event is reported. In that case Amgen will forward the queries for the Reported Event to the Provider and request that the Provider reach out to participant within three (3) business days of receipt in order to obtain responses to the queries. The Provider is required to submit all responses within one (1) business day of receipt to Amgen. If the

participant withdraws the initial consent to follow up, such withdrawal must be documented and transmitted to Amgen within one (1) business day of Providers awareness.

g. Privacy and Data Protection

Provider shall ensure that the participant receives a privacy notice before or at the time Personal Information is collected for a Reportable Event. Such notice will be in accordance with applicable Privacy Laws and any instruction provided by Amgen.

For Without limiting Provider's obligations under the Privacy and Data Protection Schedule, Provider acknowledges and agrees that with respect to the collection of European Personal Information for a Reportable Event, Provider shall be deemed a "processor" (as such term is defined in the General Data Protection Regulation (GDPR)) of Personal Information relating to such Reportable Event.

Note: The European Union (EU) GDPR applies to a Provider established in the EU or in the case where a Provider offers goods or services to data subjects in the EU and/or monitors behavior of data subjects in the EU. If the United States program(s) are intended for United States residents, then European Union GDPR does not apply.

3. Program Administration and Execution

a. Training

Amgen will provide *Vendor Safety Reporting Training* materials which communicate the safety requirements set forth in this Appendix to the Provider. The Provider is responsible for ensuring all individuals supporting the conduct of Provider's activities are trained using the Amgen-provided training materials. Individual Provider personnel must complete the Vendor Safety Reporting Training before rendering services on any Amgen project and must complete refresher training at least annually thereafter. The Provider must immediately notify Amgen of any Vendor Safety Training non-compliance along with the reason for the non-compliance.

b. Written Procedures

Provider must have written procedures in place, that are version controlled and dated, to support adherence to requirements set forth in this Appendix. The following include but are not limited to, identification and reporting of Reportable Events to Amgen, internal Quality Control and monitoring of performance measures, training plan, business continuity plan and disaster recovery plan.

c. Records Maintenance

The Provider is responsible for maintaining all records pertaining to the administration and execution of the project for a period of at least five (5) years to show compliance with the requirements set forth in this Appendix. This includes documents such as staff CVs (resumes) and original Reporting Forms along with Reportable Event Source Documents (**see Section 2a**).

d. Program Changes and Status Updates

If Provider is submitting Reportable Events to Amgen using ASRP, then the Provider must inform Amgen within five (5) business days of any modification/deactivation of ASRP user accounts.

e. Audits and Inspections

Without limiting Amgen's audit rights under the Agreement, upon provision of prior written notice to the Provider, the Provider will allow access to its premises, systems, personnel and records by Amgen, its

agents and its representatives for the purpose of assessing the Provider's compliance with the Agreement. Such assessments may take the form formal audits by Amgen internal or external auditors, as deemed necessary by Amgen. At Amgen's discretion, such activities may be conducted in-person or virtually.

The Provider will cooperate with Amgen in the conduct of any such audits. When applicable, following an audit, Amgen may request data and records pertaining to the capture of Reportable Events for further review and assessment. Provider agrees to disclose necessary records pertaining to the Provider's staff supporting the conduct of the project such training records, organizational charts, operational procedures etc. to Amgen, and demonstrate through documentation that the Provider staff have the requisite experience and qualification to perform their duties (e.g. resume) to demonstrate compliance with the requirements set forth in this safety Appendix and the applicable regulatory authority standards.

The Provider also agrees to fully cooperate with any inspection of the Provider by a health authority that is related to Provider's administration and execution of the project. In the event of any such health authority inspection, the Provider will notify Amgen in writing within one (1) business day upon receiving notice of such inspection or, if no notice is given by the health authority, upon commencement of the inspection.