Safety Requirements Appendix

Safety Requirements for tezepelumab (Tezspire) Market Research

This Safety Requirements Appendix ("**Appendix**") for tezepelumab (the "Product") Market Research Projects (the "MR") supplements that certain Order (e.g. Statement of Work) entered into by and between Amgen and Provider dated [insert date] (the "Order"). This Appendix is not intended, and shall not be interpreted, to limit the terms of the "Order" and shall be governed by the terms and conditions in the Order. Any defined terms not otherwise defined herein shall have the meanings set forth in the Order. The term Amgen as used herein shall mean the Amgen entity identified in the Order governing the Services to which this Appendix applies. The safety reporting obligations related to Reportable Events in this Appendix will remain effective for so long as Provider (or Subcontractor if applicable) provides services to Amgen and AstraZeneca and/or interacts directly or indirectly with tezepelumab Market Research Project participants using the Product and/or Product related services.

The signatories to this Appendix acknowledge and agree that AstraZeneca AB ("AstraZeneca") is the Marketing Authorization Holder for the Product and is responsible for regulatory and legal obligations related to Reportable Events (as defined in this Safety Resaquirements Appendix) reporting to (a) protect the health and safety of patients and (b) continually assess the safety of the Product and associated devices. Further, the signatories acknowledge and agree that Amgen is the lead for tezepelumab Market Research in the United States.

To enable compliance with applicable regulations, Provider conducting business on Amgen's and AstraZeneca'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: 28 September 2023

1. Definitions

a. Adverse Event

Any untoward medical occurrence in a patient who has been administered the Product. For purposes of this definition, "untoward" means unfavorable, negative or harmful.

It is not necessary that the occurrence have a causal relationship to the use of the Product by the patient. Adverse Events (AE) therefore include any unfavorable and unintended sign, symptom or disease temporally associated with the use of the Product. AEs can arise from any use of the Product (including off-label use or use in combination with another drug) and from any route of administration, formulation or dose, including overdose.

AEs also include: (1) any clinically significant worsening of a pre-existing condition; and (2) an untoward medical occurrence associated with discontinuing use of the Product. For purposes of this Agreement, any doubt as to whether information constitutes an AE shall be resolved by treating it as an AE.

b. AstraZeneca MR Program Number

The AstraZeneca Program Number is unique code assigned for the specific MR (i.e. 12345). The AstraZeneca Program Number is not the same value as the Local Reference ID.

c. AstraZeneca Reference ID

A unique identification code generated by AstraZeneca's system that corresponds with the specific Reportable Event submitted via CHAMPion. This unique number will be provided by AstraZeneca via email to the reporter upon successful submission of the Reportable Event.

d. AstraZeneca Reporting Portal (CHAMPion)

The CHAMPion portal is a web-based reporting tool that allows the Provider to submit Reportable Events to AstraZeneca electronically.

e. Date of Awareness

Date of awareness is defined as the earliest date that the Provider, or any persons contracted by the Provider, 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 person contracted by the Provider) and is not the date when the Provider, or any person contracted by the Provider, first views the information. For the purpose of AstraZeneca's regulatory reporting, the date of awareness (day zero) must be captured by the Provider and transferred to AstraZeneca with the Reportable Event.

f. Local Reference ID

A unique ID code originating internally from the Provider that corresponds with the case specific Reportable Event being submitted to AstraZeneca. This ID number is how the Provider would search for the Reportable Event within their system and must be entered in the "Local Reference ID" field in CHAMPion or, on the backup reporting form. The Local Reference ID is not the same value as the Program Number. The Local Reference ID and AstraZeneca Reference ID number must then be stored together for inspection readiness by both AstraZeneca and the Provider.

g. Product Complaints

Product Complaints (PC) are defined as 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 and 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.

A 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. Reportable Event

A "Reportable Event" is an Adverse Event (AE), Special Situations, or a Product Complaint (PC). All Reportable Events must be submitted to AstraZeneca regardless of whether or not they are stated to be related to, or caused by, the Product, combination product or associated device.

i. 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.

j. Special Situations

Special situations are situations of relevance for monitoring the safety of the Product and which may or may not be associated with an AE. These special situations must be collected/received, even if no AE occurred and they must be reported to AstraZeneca:

- Drug Exposure during pregnancy
- Exposure during Breast Feeding/Lactation
- Drug Overdose
- Drug Abuse

- Misuse
- Off Label Use with associated AE
- Medication Error/Potential Medication Error
- Occupational Exposure
- Lack of Efficacy and disease progression
- Exposure to an Infectious Agent
- Drug Interaction
- Death, including Death Cause Unknown
- Suicide or Attempted Suicide
- Unexpected Benefit

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 and AstraZeneca. 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.

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.) or any other generic social media asset owned by the Provider that is part of the project.

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 AstraZeneca, (c) seek to obtain each participant's consent to enable AstraZeneca to follow up with the participant and or, as appropriate, the participant's HCP (**see section 2f**).

The AstraZeneca unique MR Program Number for the project must be properly entered in CHAMPion and noted on the source documents (i.e. reporting e-form, call notes, etc.) to ensure that Amgen and AstraZeneca are able to associate the Reportable Event with the project.

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:

- 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

Provider will promptly notify the Amgen Contact of any deviations from the reporting process for Reportable Events.

b. Transmission of Reportable Events

Note: 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, AstraZeneca 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 project 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 standard operational documentation for the project (i.e. work/client instructions or operating guidance). The Provider must provide this document to Amgen when requested.

AstraZeneca Reporting Portal - CHAMPion*

* AstraZeneca's reporting method

Upon becoming aware of a Reportable Event, the Provider must complete and submit the e-form(s) available using the CHAMPion portal in accordance with project specific training provided by Amgen. Immediately after submission of a Reportable Event to CHAMPion portal, the Provider will receive a unique *AstraZeneca Reference Number* for that report (confirming receipt), which will be visible on screen and sent to Provider via email. This unique *AstraZeneca Reference ID* must be retained by the Provider as acknowledgement of receipt of the submitted Reportable Event. Until the Provider is in receipt of a *AstraZeneca Reference ID*, the Provider should not consider the Reportable Event to be successfully transferred. If the *AstraZeneca Reference ID* has not been received within 1 hour of the CHAMPion submission, the Provider must resubmit the report within the same business day via CHAMPion. If re-submission via CHAMPion is not successful, then Provider must follow the back-up/contingency reporting process defined below.

Back-up/Contingency Reporting Form (Email)

CHAMPion is always to be utilized by the Provider for reporting. *Project specific CHAMPion back-up reporting* form will be supplied to the Provider prior to project start. The use of back-up paper form is only allowed, after confirmation has been received by AstraZeneca to implement if the CHAMPion portal is down for **more than 24 hours**. It should not be used for any intermittent issues.

If the Provider becomes aware of a Reportable Event and is unable to access CHAMPion (or if the Reference Number is not immediately received from the CHAMPion portal **after re-submission**) then the Provider shall use the back-up CHAMPion paper form to report AEs/PCs/Special Situations to AstraZeneca at ae.us@astrazeneca.com.

***Note**:* If email is used to submit a Reportable Event, the Provider will not receive a unique *AstraZeneca Reference ID*. The email sent to AstraZeneca (ae.us@astrazeneca.com) must be retained by the Provider as verification of successful submission

In addition, the Provider must report the issue by emailing the AZ Systems Team at: US-MA-Patient-Safety-Systems@astrazeneca.com
***Note**:* This email address is for technical issues only, do not report AEs/PCs/Special Situations to this mailbox.

Applicable to all reporting channels
The Provider must have a mechanism in place to generate and provide a unique *Local Reference ID* (i.e. Provider database record ID, respondent ID etc.) with each report submitted. Both the *AstraZeneca Reference ID* and the *Local Reference 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 3d**).

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

- **For Amgen product only:**

Any potentially reportable events suspected to be related to any Amgen medicinal product (non-tezepelumab Amgen product) should 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 suspected to be related to any Amgen medicinal product 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 or the Marketing Authorization Holder (MAH) in line with the local country requirements.

c. Reporting timeframe

All Reportable Events must be reported to AstraZeneca's CHAMPion Safety Reporting Portal within one (1) business day of the Provider's Date of Awareness (**see section 1c)**. Provider must have processes, 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. For late reports through CHAMPion portal, AstraZeneca will reach out to the Provider for the corrective and preventative action for the late case. AstraZeneca will request this information as part of ongoing monitoring and compliance activities.

d. Reconciliation of Reportable Events

In order to confirm successful transfer of Reportable Events from the Provider to AstraZeneca, 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 AstraZeneca Safety with a list of all Reportable Events submitted to AstraZeneca 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 AstraZeneca Safety at the end of each project (within 1 week of completion of field work). Following receipt of the list(s), AstraZeneca will notify the Provider, of any discrepancies (i.e. missing reports), which will require the Provider to retransmit such Reportable Events to AstraZeneca.

e. Information Collected

Reportable Events must be transmitted to AstraZeneca 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:

- 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, age group, gender or patient identification number
- Product – Details regarding the 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 AstraZeneca any additional relevant information for the Reportable Event provided by the Reporter 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. product name, date report was submitted to AstraZeneca, *AstraZeneca Reference ID*, *Local Reference 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 AstraZeneca and the relevant health authorities. In addition, Provider must seek to obtain the participant's consent, enabling AstraZeneca to follow up directly with them or, as appropriate, the participant's HCP, regarding the Reportable Event. If participant consents to such follow up with patient and/or patient's HCP, then obtain relevant contact details (i.e. first name, last name, phone, fax, email, and/or physical mailing address). If the participant refuses to consent to such follow up, such refusal must be documented and transmitted to AstraZeneca via the applicable reporting channel (**See section 2b**).

In case direct interaction for follow up between AstraZeneca 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 AstraZeneca when the Reportable Event is reported. In that case AstraZeneca 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 AstraZeneca. If the participant withdraws the initial consent to follow up, such withdrawal must be documented and transmitted to AstraZeneca within one (1) business day of Provider's 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 and AstraZeneca.

3. Project Administration and Execution

a. Training

Amgen will provide training materials to the Provider which communicate the safety requirements set forth in this Appendix. The Provider is responsible for ensuring all individuals supporting the conduct of Provider's activities for a tezepelumab MR project (including any persons contracted by the Provider) are trained using Amgen-provided training materials that have been developed with AstraZeneca. Individual Provider personnel must complete the training before rendering services on a tezepelumab MR project and must complete refresher training at least annually thereafter.

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. These procedures must include but are not limited to, identification and reporting of Reportable Events to AstraZeneca **(see section 2b),** internal Quality Control and monitoring of performance measures, training plan, business continuity 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), original Reporting Forms (if applicable) along with Reportable Event source documents (**see Section 2a**).

Amgen has the right to request copies of any and all safety reporting records on behalf of AstraZeneca and Provider will submit to Amgen within five business days of such request. In the event that Amgen or AstraZeneca is undergoing a regulatory inspection or audit, Provider will submit requested records as soon as possible and within one business day of such request.

d. Audits, and Inspections

Without limiting any of Amgen's audit rights under the Order or any master purchase 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, its representatives, and AstraZeneca for the purpose of assessing the Provider's compliance with the Order. Such assessments may take the form formal audits by Amgen auditors and AstraZeneca, as deemed necessary by Amgen. At Amgen's discretion, such activities may be conducted in-person or virtually.

The Provider will cooperate with Amgen and AstraZeneca, as deemed necessary by Amgen, in the conduct of any such audits. When applicable, following an audit, Amgen will 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 (including any persons contracted by the Provider), such as training records, organizational charts 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 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 the Amgen Contact 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.

e. Third Party Beneficiary

Provider acknowledges and agrees that it is required to perform in accordance with this Safety Requirements Appendix ("Appendix"), including without limitation the reporting of Reportable Events, to ensure patient safety and to enable AstraZeneca to meet U.S. and Global health authority reporting obligations.

By signing below, Amgen and Provider acknowledge and agree that AstraZeneca is an express, intended third-party beneficiary of this Safety Requirements Appendix, and that AstraZeneca shall be entitled to enforce the obligations of this Appendix against Provider as if AstraZeneca were a party to this Appendix. By AstraZeneca signing below, AstraZeneca acknowledges its rights to enforce the terms of this Appendix as a third-party beneficiary.

[Signatures to follow on next page]

AMGEN INC.

_____
(signature)

By: _____
(print or type name)

Title: _____

Date: _____

ACKNOWLEDGED AS A THIRD PARTY BENEFICIARY: ASTRAZENECA AB

_____
(signature)

By: _____
(print or type name)

Title: _____

Date: _____

[INSERT PROVIDER NAME]

_____
(signature)

By: _____
(print or type name)

Title: _____

Date: _____