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PŘÍLOHA C/ EXHIBIT C
SAFETY REPORTING REQUIREMENTS

1. DEFINITIONS

1.1 "ADVERSE EVENT" OR "AE"

An adverse event is any untoward medical occurrence in a patient or clinical investigation subject administered a Company medicinal product and which is not necessarily caused by this treatment. An adverse event can therefore be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.
The definition of an adverse event includes:

- Worsening of a pre-existing condition or underlying disease
- Events associated with the discontinuation of the use of a medicinal product(s), (e.g., appearance of new symptoms)

1.2 "ADVERSE DEVICE EFFECT" OR "ADE"

Adverse device effect is any adverse event related to the use of a Company combination product or medical device. Adverse device effects include adverse events resulting from insufficient or inadequate instructions for use, adverse events resulting from any malfunction of the device, or adverse events resulting from use error or from intentional misuse of the device.

The detection and documentation procedures for adverse device effects described in this exhibit apply to all Company medical devices

1.3 "CAUSALITY"

Causality refers to the possible relationship of an Adverse Event to a Company product as determined by a healthcare professional ("HCP").

1.4 "DATE OF AWARENESS"

The Date of Awareness is the date that the Physician or their delegate receives notification of information that constitutes a Reportable Event (i.e., the date the fax, mail, or telephone call is received by Physician or their delegate).

This date must be captured by the Physician and clearly communicated or recorded on any safety information transmitted to Company.

1.5 "OTHER SAFETY FINDINGS"

Other safety findings include the following, whether or not such event is associated with an AE:

- Use of a Company product while pregnant and/or breast feeding. This includes pregnancies in women whose sexual partner took, or is taking, a Company product.
- Medication errors
- Overdose
- Underdose
- Misuse
- Abuse
- Addiction
- Transmission of an infectious agent through a contaminated Company product
- Accidental Exposure
- Occupational Exposure
- Lack or loss of therapeutic efficacy

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- Missed dose, if not taken prior to the next scheduled dose
- Reports of patient “death” after exposure to Company’s product where no other details are provided (e.g., fatal outcomes)

1.6 "PRODUCT COMPLAINT" OR “PC”

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: (1) Amgen or (2) distributors or partners for whom Amgen manufactures the material. This includes all components distributed with the drug, such as packaging, drug containers, delivery system, labeling, and inserts.
Examples include:

- Device that is damaged or broken
- Bent or blunt needles
- Missing or illegible labeling
- Inability of customer to administer the product
- Product with an unexpected color, appearance, or particles
- User error (i.e, an act or omission of an act that results in a different combination product or medical device response than intended by the manufacturer or expected by the user, where the user attempted to use the combination product or medical device in good faith and experienced difficulty or deficiency administering the product).

Reports of misuse of a combination product or medical device (i.e, the intentional and improper use of a combination product or medical device not in accordance with the authorized product information) are not considered Product Complaints.

1.7 "REPORTABLE EVENT"

A “Reportable Event” is an Adverse Event (AE), Adverse Device Effect (ADE), Other Safety Finding (OSF) or a Product Complaint (PC). All Reportable Events must be submitted to Company regardless of whether or not they are stated to be related to, or caused by, a Company product, combination product or device.

2 REPORTING OBLIGATIONS AND PROCEDURES

2.1 COLLECTION AND REPORTING OF REPORTABLE EVENTS

Each Reportable Event (AE, ADE, Other safety finding and PC) shall be reported to Company by Physician or its delegate within one (1) business day of Date of Awareness.

The Physician or its delegate will report AEs, ADEs and Other safety findings to Amgen Safety by completing a Reporting Form provided by Amgen ("Expanded Access Reporting Form") and transmitting the completed Expanded Access Reporting Form to Company using the contact information (e.g., fax number/email address) provided on the Expanded Access Reporting Form.

The Physician or its delegate will report Product Complaints to Amgen Quality by completing a Product Complaint form provided by Amgen and transmitting the completed Product Complaint Form to Company using the contact information email address provided on the Product Complaint Form.

Reportable Events must be transmitted to Company regardless of the amount of information available. However, for each Reportable Event, Physician will capture as much information as is available (e.g., details regarding the AE, ADE, Other Safety Finding or Product Complaint, Lot number, serial number of Company product)

The information provided should be sufficient to provide a true and comprehensive description and medical confirmation of the AE, ADE, Other Safety Finding, or Product Complaint, as it is understood at the time. If available, information should include a summary of the relevant critical data found in medical records (e.g., applicable discharge summaries, lot numbers, relevant laboratory and scan data, autopsy reports).

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Physician shall forward all additional follow-up information to Company within the same timeframes that Physician is required to provide initial reports, i.e., one business day of Day of Awareness.