



**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research**

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**To:** To File (BLA STN **125587/0**)

**From:** Yonggang Wang, Ph.D., Staff Fellow, CBER/OTAT/DPPT

**Through:** Michael C. Kennedy, Ph.D., Team Leader, CBER/OTAT/DPPT

**CC:** Mark Levi, CBER/OTAT/DRPM/RPMBII

**Applicant:** Octapharma Pharmazeutika Produktionsges. M.b.h.

**Product:** Immune Globulin Intravenous, Human 10% (Panzyga®)

**Subject:** Final Review: Resubmission of the original BLA,– stability section

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**RECOMMENDATION**

Approval with the following Postmarketing commitments:

1. Octapharma commits to submitting information on the stability study I7P012, annually as a “Postmarketing commitment – Status Update”. The final stability reports will be submitted as a “Postmarketing Commitment – Final Study Reports” by Oct 30, 2020. Octapharma will also report any confirmed out-of-specification results at the recommended storage conditions from the stability monitoring to the Agency within 45 days of the event(s).

**EXECUTIVE SUMMARY**

This review covers the product stability section submitted by Octapharma in response to the Complete Response (CR) letter, issued to their original Biological License Application (BLA). In the original BLA, the stability studies for the following four materials were reviewed and the proposed storage conditions were found to be acceptable, i.e., (b) (4) (Drug

Substance), and Final container product (Drug Product). In this resubmission, the following changes were proposed and found to be supported by the updated stability data:

1. During the shelf life of 24 months at the storage condition (2-8 °C), the product can be stored for up to 9 months instead of 6 months.

(b) (4)

The proposed dating period of each material was evaluated and found to be acceptable, based on the data from clinical lots, and the updated data from conformance lots, consistency lots, and new conformance lots, and summarized as follows:

| Materials                         | Proposed by Sponsor   | Recommended by Agency |
|-----------------------------------|---|-----------------------|
| (b) (4)                           | (b) (4)   | Acceptable            |
| (b) (4)                           | (b) (4)   | Acceptable            |
| Drug Substance<br>(b) (4)         | (b) (4)   | Acceptable            |
| Drug Product<br>(Final Container) | 5 ± 3°C for up to 24 months; within its shelf life, the product was proposed to be stored at ≤ 25 °C for up to 9 months | Acceptable            |

## **BACKGROUND INFORMATION**

Panzyga is a 10% human normal IgG for intravenous administration (IGIV) in a liquid preparation, indicated for the treatment of primary humoral immunodeficiency and chronic immune thrombocytopenic purpura in adults.

During manufacturing of Panzyga, (b) (4) storable intermediates, i.e., (b) (4) (Drug Substance), were produced. The final product (Drug Product) can be filled in configuration of 10 mL, 25 mL, 50 mL, 100 mL, 200 mL and 300 mL solution, supplied in (b) (4) glass vials with bromobutyl rubber stopper and aluminum flip off cap. Totally (b) (4) clinical batches (manufactured from 2007 to 2011), (b) (4) conformance batches (manufacture in 2013), and (b) (4) consistency batches (manufactured in 2014) were placed under stability studies.

Original BLA was issued a CR letter on Feb 10, 2016.

## **CMC REVIEW SUMMARY**

1. The resubmission was received on Jan 31, 2018. This review mainly covered review of Final container product (drug product) stability studies conducted for the new conformance batches 2017 (17P012), and the updated ongoing stability studies from conformance batches 2013 (13P003), and consistency batches 2014 (14P022) (see table 1 for all batches under stability studies). Sponsor proposed to change Panzyga's shelf life to the following:

*Store Panzyga for 24 months at 2-8 °C (36-46 °F) from the date of manufacture. Within its shelf life, the product may be stored at ≤ 25 °C (77 °F) for up to 9 months. After storage at ≤ 25 °C the product must be used or discarded.*

2. Study 13P003 – (b) (4) Conformance lots

- 1) Long-term studies at 2-8 °C: up to (b) (4) months' data for all batches are available, and the data were all within the limits of specifications, except for "Measles Ab" of batch (b) (4), which were below the specification at (b) (4) months storage.
- 2) Temperature excursion study: (b) (4)

*Reviewer's assessment: No Out of Specification (OOS) was noticed within (b) (4) months, which covered at least 7 months of storage at 25 °C, and longer storage than 24 months at 2-8 °C. The Measles' assay variation may have contributed to the OOS results at (b) (4) months' time-point.*

3. Study 14P022 – (b) (4) consistency lots

- 1) Long-term studies at 2-8 °C: up to (b) (4) months' data for all batches are available, and the data were all within the limits of specifications, except for "Measles Ab" of batch (b) (4), which was below the specification at 18 months storage but returned to normal levels at 24, (b) (4) months.
- 2) Temperature excursion study A: (b) (4)

*Reviewer's assessment: No OOS results were noticed within (b) (4) months, which covered (b) (4) months of storage at 25 °C.*

- 3) Temperature excursion study B: (b) (4)

(b) (4)

*Reviewer's comments:* No OOS was noticed within (b) (4) months, which covered (b) (4) months of storage at 25 °C.

4. Study 17P012 – (b) (4) months data are available.

- 1) Long-term studies at 2-8 °C: up to 6 months' data for all batches are available, and the data were all within the limits of specifications, except for measles Ab of batch (b) (4), which was below the specification at 0 months storage but return to normal level at 3 and 6 months.
- 2) Temperature excursion study: (b) (4)

*Reviewer's assessment:* As "Fragement" appears to be the only limiting factor in the stability monitoring (sections 2 and 3 above), the available 6 months data were compared with the corresponding data from studies 13P003 and 14P022. The range of "Fragement" was found to be 1.0% -2.3% for study 13P003 and 1.0% - 1.8% for Study 14P022. The new conformance batches (17P012) has a range of 1.2%-1.3%, which is within the ranges defined from previous studies, indicating the new batches are comparable to the previous batches.

5. In this resubmission, Octapharma also proposed the following changes which was found to be acceptable:

(b) (4)

