DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food & Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

From: Tao Pan, Ph.D., CBER/OCBQ/DBSQC

Subject: Review Memo for Biological License Application for human fibrinogen (Intravenous), Fibryna®, from Octapharma

To: STN: 125612

Through: Lokesh Bhattacharyya, Ph.D., Lab Chief, CBER/OCBQ/DBSQC

William M. McCormick, Ph.D., Director, CBER/OCBQ/DBSQC

Recommendation: Approval

Summary of Review:

The BLA was submitted by Octapharma to seek approval for Fibryna®, a human fibrinogen, drug product for intravenous administration. In this memo, the following analytical methods and their validations have been reviewed for the release of drug product: (b) (4), water content, glycine content, citrate content, chloride content, L-arginine HCl content, (b) (4).

Based on the information provided in this submission, all the above-mentioned assays have been validated adequately for their intended use in lot release testing of drug product. Approval is recommended for these assays.

Submitted Information reviewed:

125612
- 3.2.S. Drug Substance [Substance – Manufacturer]
  - -3.2.S. Human Fibrinogen - Octapharma
    - -3.2.S.4. Control of Drug Substance
      - -3.2.S.4.1. Specification
        - -Specifications
        - -(b) (4) Specification
      - -3.2.S.4.2. Analytical Procedures
        - -Analytical Procedures
        - -(b) (4) Test Method
    - -3.2.S.4.5. Justification of Specification
      - -Justification of Specification
- 3.2.S. Drug Product [Product-Dosage Form-Manufacturer]
  - -3.2.P. Fibryna-Powder for Solution for Injection -Octapharma
    - -3.2.P.5. Control of Drug Product
      - -3.2.P.5.1. Specification
        - -Specification
      - -3.2.P.5.2. Analytical Procedures

-Anlytical Procedure
-(b) (4) Test Method, 130SOP028/05
-(b) (4) Test Method, 130SOP008/03
-Water Test Method, 130SOP086/06
-(b) (4) Test Method, 130SOP184/01
-(b) (4) Test Method, 130SOP149/14
-Glycine Test Method, 130SOP161/03
-Citrate Test Method, 130SOP032/05
-Chloride Test Method, 130SOP131/07
-Arginine Test Method, 130SOP160/03
-(b) (4) Test Method, 130SOP153/04
-(b) (4) Test Method, 130SOP090/07

-3.2.P.5.3. Validation of Analytical Procedures
-Validation of Analytical Procedures
-(b) (4) Validation, #000VAL028FC347348/01.rep
-(b) (4) Validation, 000VAL008FC34x/01.rep
-Water Validation, 000VAL086FC34X/00
-(b) (4) Validation, 000VAL184FC347/01
-(b) (4) Validation, 000VAL149 FC 347 348/00
-Glycine Validation, 000VAL161FC34X/00
-Citrate Validation, 000VAL032FC34X/00
-Chloride Validation, 000VAL131FC34x/01
-Arginine Validation, 000VAL160FC34x/00
-(b) (4) Validation, 000VAL153FC34X/00
-(b) (4) Validation, 000VAL090FC34x/02

-3.2.P.5.6. Justification of Specifications
-Justification of Specification

125612/0.36
- 1.2. Cover Letters
– Cover Letters
- Outstanding Response to FDA information request – Dec 21, 2016
- 3. 2.P.5.3. Validation of Analytical Procedures
- (b) (4) Validation, 000VAL184 FC 34x/02.rep

125612/0.48
- 1.2. Cover Letters
– Cover Letters
- Response to FDA information request – Mar 21, 2017
- 3. 2.P.5.3. Validation of Analytical Procedures
- (b) (4) Validation, 000VAL149 FC 347 348/02

Review Narrative:

1. (b) (4)

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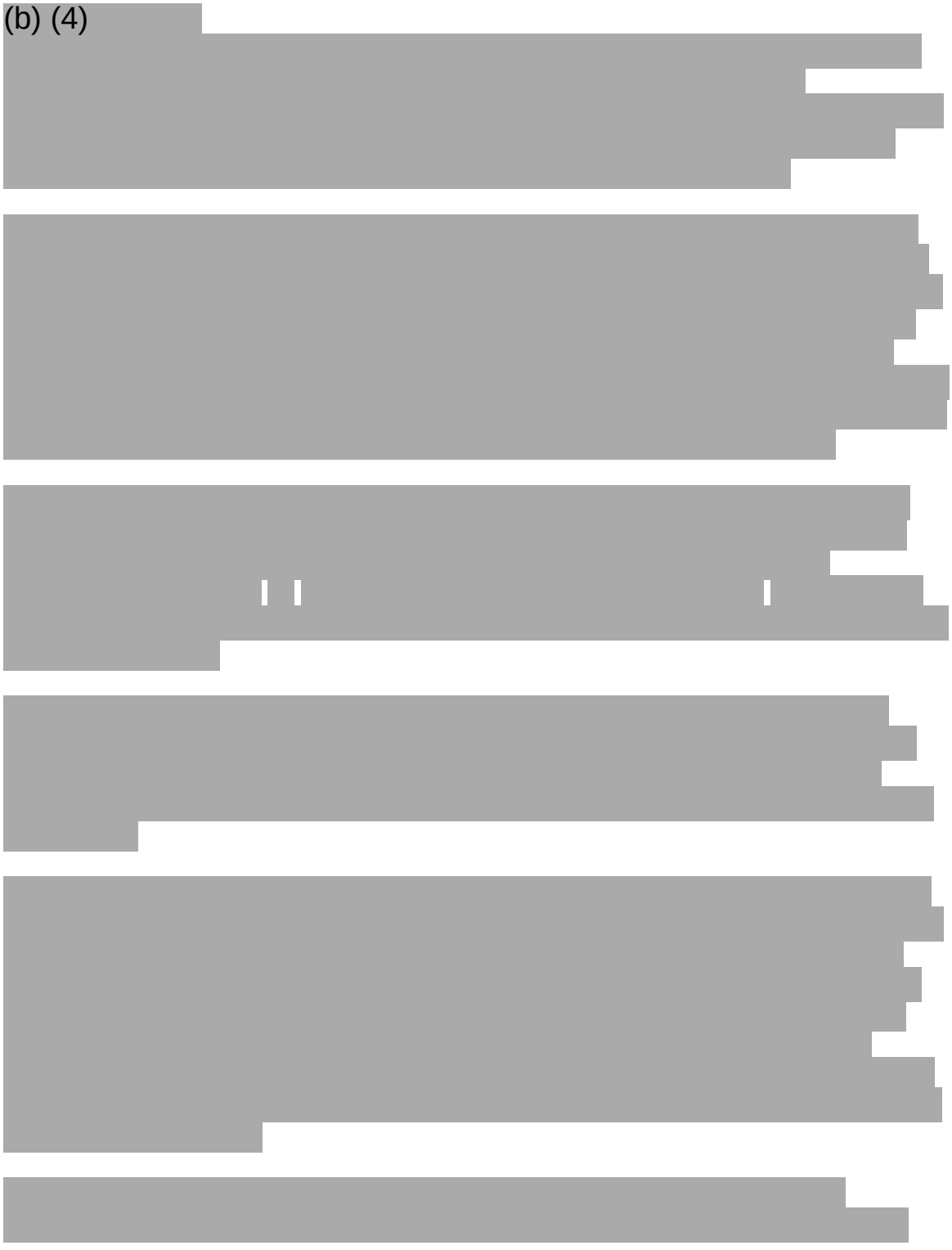
(b) (4)



3. Water content

The water content of lyophilized Fibryna® drug product is determined by (b) (4) method. The specification is (b) (4) for a final container vial with 1g lyophilized powder.

Method

The assay procedures for the determination of water content in lyophilized Fibryna® final container were described in details in document #130SOP086/06, in which the water content in the lyophilized drug product is (b) (4) . Sufficient information has been provided in the document, with details on the calibration of the equipment, the preparation of the samples and controls, the execution of the method, validity criteria of the assay result, and the generation of the reportable result.

Method Validation

(b) (4)

(b) (4)

Based on the data on the validation of accuracy, specificity, precision, linearity, range, LOQ, and robustness, this method has been validated for the release of fibrinogen drug product.

4. (b) (4)

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(b) (4)

6. Glycine content

The content of glycine in the Fibryna® drug product is determined using a (b) (4)

The specification for the reconstituted drug product is (b) (4).

Method

(b) (4)

Method Validation

(b) (4)

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(b) (4)

Based on the data on the validation of accuracy, specificity, precision, linearity, range, and robustness, this method has been validated for the release of fibrinogen drug product.

7. Citrate content

The content of citrate in the Fibryna® drug product is determined using an (b) (4) . The specification for the reconstituted drug product is (b) (4).

Method

(b) (4)

Method Validation

(b) (4)

(b) (4)

Based on the data on the validation of accuracy, specificity, precision, linearity, range, and robustness, this method has been validated for the release of fibrinogen drug product.

8. Chloride content

The content of chloride in the Fibryna® drug product is determined using (b) (4) method. The specification for the reconstituted drug product is (b) (4) .

Method

1 page has been determined to be not releasable: b(4)

(b) (4)

Based on the data on the validation of specificity, accuracy, precision, linearity, range, and robustness, this method has been validated for the release of fibrinogen drug product.

9. Arginine content

The content of arginine in the Fibryna® drug product is determined using a (b) (4) method following (b) (4). The specification for the reconstituted drug product is (b) (4).

Method

(b) (4)

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(b) (4)

Based on the data on the validation of accuracy, specificity, precision, linearity, range, and robustness, this method has been validated for the release of fibrinogen drug product.

10. (b) (4)

4 pages have been determined to be not releasable: b(4)

Based on the information provided in the BLA submission STN125612 and Amendments 0.36 and 0.48, the following analytical methods: (b) (4), water content, glycine content, citrate content, chloride content, L-arginine HCl content, (b) (4) have been validated adequately for the release of Fibryna drug product.