CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208157Orig1s000

PRODUCT QUALITY REVIEW(S)

Center for Drug Evaluation and Research
Office of Pharmaceutical Quality
Office of Biotechnology Products

LABELS AND LABELING ASSESSMENT

Date of assessment:	June 17, 2019
Assessor:	Scott Dallas, RPh, Labeling Assessor Office of Biotechnology Products (OBP)
Through:	Anjali Shukla, PhD, Product Quality Reviewer OBP/Division of Biotechnology Review and Research II
Application:	NDA 208157
Applicant:	Celerity Pharmaceuticals, LLC
Submission Dates:	April 26, October 26, November 21, 2018; and February 28, March 29, May 15, May 24, and June 17, 2019
Product:	Myxredlin (Insulin Human in Sodium Chloride Injection)
Dosage form:	Injection
Strength and Container-Closure:	100 units/100 mL (1 unit/mL) Intravenous bag
Purpose of review:	The Applicant submitted a new drug application for the Insulin Human Injection in a premixed single-dose GALAXY container.
Recommendations:	The prescribing information, container labels, and carton labeling are acceptable from an OBP labeling perspective.

Materials Considered for this Label and Labeling Assessment	
Materials Assessed	**Appendix Section**
Proposed Labels and Labeling	A
Evaluation Tables	B
Acceptable Labels and Labeling	C

DISCUSSION

We evaluated the proposed labels and labeling for compliance with applicable requirements in the Code of Federal Regulations (see Appendix B).

CONCLUSION

The prescribing information submitted on June 17, 2019 and the container labels, and carton labeling submitted on May 15, 2019 were reviewed and found to be acceptable (see Appendix C) from an OBP labeling perspective.

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

Appendix B: Evaluation Tables
Evaluation Tables: Label[1,2] and Labeling[3] Standards

Container[4] Label Evaluation

Proper Name *(for container of a product capable of bearing a full label)*	**Acceptable**
21 CFR 610.60, 21 CFR 201.50, 21 CFR 201.10	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: March 15, 2019: To Applicant: Please revise the established name to read "Insulin Human in 0.9% Sodium Chloride Injection". Ensure to delete the "[(b) (4)]" reference. Please refer to the USP monographs for the current nomenclature of insulin products. March 29, 2019: The Applicant revised the established name to read "Insulin Human in 0.9% Sodium Chloride Injection". FDA Response: The revision is acceptable.	
Recommended labeling practices (placement of dosage form below the proper name):	✓ Yes ☐ No ☐ N/A

Manufacturer name, address, and license number *(for container of a product capable of bearing a full label)*	**Acceptable**
21 CFR 610.60 (a)(2), 21 CFR 201, 21 CFR 201.1(a), 21 CFR 201.1(h)(5), 21 CFR 201.1(h)(6), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: March 15, 2019: To Applicant: The Manufactured by statement displays the city and zip code for Baxter Healthcare Corporation as Deerfield and 60015. However, the FDA form 356h lists the city and zip code as (b) (4) and (b) (4). Please comment and or revise. Applicant responded on March 29, 2019: Applicant revised the "Manufactured by" city and zip code for Baxter Healthcare Corporation to appear as (b) (4) and (b) (4). This revision is consistent with the Form 356h. FDA Response: The revision is acceptable.	

[1] Per 21 CFR 1.3(b) *Label* means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.
[2] Per CFR 600.3(dd) *Label* means any written, printed, or graphic matter on the container or package or any such matter clearly visible through the immediate carton, receptacle, or wrapper.
[3] Per 21 CFR 1.3(a) *Labeling* includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.
[4] Per 21 CFR 600.3(bb) *Container* (referred to also as "final container") is the immediate unit, bottle, vial, ampule, tube, or other receptacle containing the product as distributed for sale, barter, or exchange.

Recommended labeling practices (using the following qualifying statement "Manufactured by:"):	☐ Yes ☐ No ☒ N/A

Lot number or other lot identification *(container capable of bearing a full label shall bear)*	**Acceptable**
21 CFR 610.60, 21 CFR 201.18, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Expiration date *(container capable of bearing a full label shall bear)*	**Acceptable**
21 CFR 610.60, 21 CFR 201.17	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (the expiration date appears on all aspects of the package):	✓ Yes ☐ No ☐ N/A

Product Strength	**Acceptable**
21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: The letter "U" in the word "units" for the expression of strength is displayed in both capital and lower-case lettering. Please consider revising the word "units" in the expression of strength to appear in all lower-case lettering. Using a lower-case letter "u" may help to provide more of a visual difference between the number "0" and a capital letter "U".

Applicant responded on March 29, 2019:
Applicant revised the presentation of the word "Units" to appears as "units" using a lower-case letter "u" which may provide more of a visual difference between the number "0" and a capital letter "U".

FDA Response: The revision is acceptable.

Recommended labeling practices (expression of strength for injectable drugs): Reference: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 176 USP General Chapters: <7> Labeling	✓ Yes ☐ No ☐ N/A

Multiple dose containers *(recommended individual dose)*	**Acceptable**
21 CFR 610.60, 21 CFR 201.55	☐ Yes ☐ No ☒ N/A

Statement: "Rx only"	**Acceptable**
21 CFR 610.60, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices:	✓ Yes ☐ No ☐ N/A

Medication Guide	**Acceptable**
21 CFR 610.60, 21 CFR 208.24	☐ Yes ☐ No ☒ N/A

No Package for container	**Acceptable**
21 CFR 610.60	☐ Yes ☐ No ☒ N/A

No container label	**Acceptable**
21 CFR 610.60	☐ Yes ☐ No ☒ N/A

Ferrule and cap overseal *(for vials only)*	**Acceptable**
Recommended labeling practices: *United States Pharmacopeia (USP), General Chapters: <7> Labeling (Ferrules and Cap Overseals)*	☐ Yes ☐ No ☒ N/A

Visual inspection *(for vials only)*	**Acceptable**
21 CFR 610.60(e)	✓ Yes ☐ No ☐ N/A

NDC numbers	**Acceptable**
21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: FDA's DMEPA labeling comment to the Applicant: Based on the clarification you provided regarding your packaging, we note that you plan to package cartons containing 1 Galaxy container within a larger carton containing 12 units. We note that the carton containing 12 units of Myxredlin, the labeled carton containing 1 unit of Myxredlin, and the container label each use different NDC package codes. However, the container label for one unit and the carton labeling for 1 unit should have the same NDC package code. Revise the NDC numbers so that the carton labeling for 1 unit and container labels use the same NDC package code.

March 29, 2019: The Applicant revised the NDC numbers so that the carton labeling for 1 unit and container labels use the same NDC package code.

FDA Response: The revision is acceptable.

Route of administration	**Acceptable**
21 CFR 201.5, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices: route of administration statement to appear after the strength statement on the principal display panel	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
DMEPA was ok with the location of the ROA statement from a safety perspective. Thus, OBP labeling will not provide a comment.

Preparation instructions	**Acceptable**
21 CFR 201.5	☐ Yes ☐ No ☒ N/A
Recommended labeling practices: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430)	☐ Yes ☐ No ☒ N/A

Package type term	**Acceptable**
Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use. USP chapter <659> Packaging and Storage Requirements	✓ Yes ☐ No ☐ N/A

Misleading statements	**Acceptable**
21 CFR 201.6	✓ Yes ☐ No ☐ N/A

Prominence of required label statements	**Acceptable**
21 CFR 201.15	✓ Yes ☐ No ☐ N/A

Spanish-language (Drugs)	**Acceptable**
21 CFR 201.16	☐ Yes ☐ No ☒ N/A

FD&C Yellow No. 5 and/or FD&C Yellow No. 6	**Acceptable**
21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Phenylalanine as a component of aspartame	**Acceptable**
21 CFR 201.21	☐ Yes ☐ No ☒ N/A

Sulfites; required warning statements	**Acceptable**
21 CFR 201.22	☐ Yes ☐ No ☒ N/A

Bar code label requirements	**Acceptable**
21 CFR 201.25, 21 CFR 610.67	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: FDA's DMEPA labeling comment to Applicant: The barcode is denoted by a placeholder on the labels and labeling. Therefore, we request you add the product's linear barcode to each Myxredlin carton and container label as required per 21CFR 201.25(c)(2). In addition, ensure that that the barcode is surrounded by sufficient white space to allow scanners to correctly read the barcode in accordance with 21 CFR 201.25(c)(i). Please resubmit for review.

March 29, 2019: The Applicant added a linear bar code to the back of the container.

FDA Response: The revision is acceptable.

Recommended labeling practices: *Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011* *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786)* **Comment/Recommendation:**	✓ Yes ☐ No ☐ N/A
Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products)	**Acceptable**
21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A
Net quantity	**Acceptable**
21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: March 29, 2019: The Applicant revised the net quantity statement from "1 GALAXY Single Dose Container" to read "1 Single-Dose GALAXY container" to be consistent with the carton labeling. FDA Response: The revision is acceptable.	
Recommended labeling practices: *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463)* *Guidance: Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products, June 2015 (line 68, 93-99)* *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	✓ Yes ☐ No ☐ N/A
Usual dosage statement	**Acceptable**
21 CFR 201.55, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Inactive ingredients	**Acceptable**
21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Please revise your active and inactive ingredient statements to read: Each mL contains: 1 unit Insulin Human, USP; 0.412 mg Dibasic Sodium Phosphate Anhydrous, USP; 0.29 mg Monobasic Sodium Phosphate Monohydrate, USP; 9 mg Sodium Chloride, USP; and Water for Injection, USP. This revision lists the inactive ingredients in alphabetical order per USP <1091> Labeling of Inactive Ingredients. Please note the addition of the word "Anhydrous".

March 29, 2019: The Applicant revised the list of inactive ingredients as requested above.

FDA Response: The revision is acceptable.

Recommended labeling practices: USP General Chapters <1091> Labeling of Inactive Ingredients	✓ Yes ☐ No ☐ N/A

Storage requirements	**Acceptable**
Recommended labeling practices: *USP General Chapters <7> Labeling* *USP General Chapters <659> Packaging and Storage Requirements*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Please consider revising the statements "Use carton to protect contents from light until administration" and "Refrigerate at (36°F - 46°F) 2°C - 8°C" to read "Store refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light until administration. Do Not Shake. Do Not Freeze." However, ensure to add the phrases "Do Not Shake" and "Do Not Freeze" to the label.

Please consider revising the "May store at room temperature…." statements to read "If needed, may store MYXREDLIN at room temperature up to 77°F (25°C) up to 30 days in the original carton. Discard after 30 days if stored at room temperature."

March 29, 2019: The Applicant revised the storage and handling statements as requested above.

FDA Response: The revisions are acceptable.

Dispensing container	**Acceptable**
21 CFR 201.100	☐ Yes ☐ No ☒ N/A

Package[5] Label Evaluation

Proper name	**Acceptable**
21 CFR 610.61, 21 CFR 201.50, 21 CFR 201.10	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Please revise the established name to read "Insulin Human in 0.9% Sodium Chloride Injection". Ensure to delete the (b) (4)]" reference. Please refer to the USP monographs for the current nomenclature of insulin products.

March 29, 2019: The Applicant revised the established name to read "Insulin Human in 0.9% Sodium Chloride Injection".

FDA Response: The revision is acceptable.

Manufacturer name, address, and license number	**Acceptable**
21 CFR 610.61, 21 CFR 201.1(a), 21 CFR 201.1(h)(5), 21 CFR 201.1(h)(6), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: The Manufactured by statement states the city and zip code for Baxter Healthcare Corporation as Deerfield and 60015. However, the FDA form 356h lists the city and zip code as (b) (4) and (b) (4) Please comment and or revise.

March 29, 2019: The Applicant revised the "Manufactured by" city and zip code for Baxter Healthcare Corporation to appear as (b) (4) and (b) (4). This revision is consistent with the Form 356h.

FDA Response: The revision is acceptable.

Recommended labeling practices: OPQ-OBP-RP-014	☐ Yes ☐ No ☒ N/A

Lot number or other lot identification	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Expiration date	**Acceptable**
21 CFR 610.61, 21 CFR 201.17	✓ Yes ☐ No ☐ N/A

[5] Per 21 CFR 600.3(cc) *Package* means the immediate carton, receptacle, or wrapper, including all labeling matter therein and thereon, and the contents of the one or more enclosed containers. If no package, as defined in the preceding sentence, is used, the container shall be deemed to be the package. Thus, this includes the carton, prescribing information, and patient labeling.

Preservative	**Acceptable**
21 CFR 610.61	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:
This is an NDA product so the labeling does not need to comply.

Number of containers	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Revise the net quantity statement from "1 GALAXY Single Dose Container" to read "1 Single-Dose GALAXY container".

March 29, 2019: The Applicant revised the net quantity statement from "1 GALAXY Single Dose Container" to read "1 Single-Dose GALAXY container".

FDA Response: The revision is acceptable.

Strength/volume	**Acceptable**
21 CFR 610.61, 21 CFR 201.10, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices: *Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 176* *USP General Chapters: <7> Labeling*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

March 15, 2019: To Applicant: The letter "U" in the word "units" for the expression of strength is displayed in both capital and lower-case lettering. Please consider revising the word "units" in the expression of strength to appear in all lower-case lettering. Using a lower-case letter "u" may help to provide more of a visual difference between the number "0" and a capital letter "U".

March 29, 2019: The Applicant revised the presentation of the word "Units" to appears as "units" using a lower-case letter "u" which may provide more of a visual difference between the number "0" and a capital letter "U".

FDA Response: The revision is acceptable.

Storage temperature/requirements	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: On the back panel consider revising the statements "Use carton to protect contents from light until administration" and "Refrigerate at (36°F - 46°F) 2°C - 8°C" to read "Store refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light until administration. Do Not Shake. Do Not Freeze." However, ensure to add the phrases "Do Not Shake" and "Do Not Freeze" to the labeling.

Please consider revising the "May store at room temperature…." statements to read "If needed, may store MYXREDLIN at room temperature up to 77°F (25°C) up to 30 days in the original carton. Once stored at room temperature, do not place back in the refrigerator. Discard after 30 days if stored at room temperature."

March 29, 2019: The Applicant revised the storage statements as requested above.

FDA Response: The revisions are acceptable.

Recommended labeling practices: USP General Chapters: <7> Labeling	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Please consider revising the statements "(b) (4) :" to read similar to: "Discard 30 days after storing at room temperature. Discard after:" The remainder of the box area is acceptable.

March 29, 2019: The Applicant revised the storage statements as requested above.

FDA Response: The revision is acceptable.

Handling: "Do Not Shake", "Do not Freeze" or equivalent	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
A Do Not Shake and a Do Not Freeze statement were added to the storage comment above.

Multiple dose containers (recommended individual dose)	**Acceptable**
21 CFR 610.61	☐ Yes ☐ No ☒ N/A

Route of administration	**Acceptable**
21 CFR 610.61, 21 CFR 201.5, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (route of administration statement recommended locations):	✓ Yes ☐ No

	☐ N/A

Known sensitizing substances	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Inactive ingredients	**Acceptable**
21 CFR 610.61, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Please revise your active and inactive ingredient statements to read: Each mL contains: 1 unit Insulin Human, USP; 0.412 mg Dibasic Sodium Phosphate Anhydrous, USP; 0.29 mg Monobasic Sodium Phosphate Monohydrate, USP; 9 mg Sodium Chloride, USP; and Water for Injection, USP. This revision lists the inactive ingredients in alphabetical order per USP <1091> Labeling of Inactive Ingredients. Please note the addition of the word "Anhydrous".

March 29, 2019: The Applicant revised the ingredient statement as requested above.

FDA Response: The revision is acceptable.

Recommended labeling practices: *USP General Chapters <1091> Labeling of Inactive Ingredients* *USP General Chapters <7> Labeling*	✓ Yes ☐ No ☐ N/A

Source of the product	**Acceptable**
21 CFR 610.61	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
The source is not a safety factor.

Minimum potency of product	**Acceptable**
21 CFR 610.61	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:
This is an NDA product. The regulation does not apply.

Rx only	**Acceptable**
21 CFR 610.61, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Recommended labeling practices:	✓ Yes ☐ No ☐ N/A

Divided manufacturing	**Acceptable**
21 CFR 610.63 (Divided manufacturing responsibility to be shown)	☐ Yes ☐ No ☒ N/A

Distributor	**Acceptable**
21 CFR 610.64 (Name and address of distributor)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:
This product was filed as an NDA and this regulation does not apply.

Bar code	**Acceptable**
21 CFR 610.67, 21 CFR 201.25	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: The barcode is denoted by a placeholder on the labels and labeling. Therefore, we request you add the product's linear barcode to each Myxredlin carton and container label as required per 21CFR 201.25(c)(2). In addition, ensure that that the barcode is surrounded by sufficient white space to allow scanners to correctly read the barcode in accordance with 21 CFR 201.25(c)(i). Please resubmit for review.

March 29, 2019: The Applicant added a linear bar code as requested above.

FDA Response: The revision is acceptable.

Recommended labeling practices: *Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011* *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786)*	✓ Yes ☐ No ☐ N/A

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products)	**Acceptable**
21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A

NDC numbers	**Acceptable**
21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: FDA's DMEPA's labeling comment to Applicant: Based on the clarification you provided regarding your packaging, we note that you plan to package cartons containing 1 Galaxy container within a larger carton containing 12 units. We note that the carton containing 12 units of Myxredlin, the labeled carton containing 1 unit of Myxredlin, and the container label each use different NDC package codes. However, the container label for one unit and the carton labeling for 1 unit should have the same NDC package code. Revise the NDC numbers so that the carton labeling for 1 unit and container labels use the same NDC package code.

March 29, 2019: The Applicant revised the NDC numbers so that the carton labeling for 1 unit and container labels use the same NDC package code.

FDA Response: The revision is acceptable.

Preparation instructions	**Acceptable**
21 CFR 201.5	☐ Yes ☐ No ☒ N/A

Recommended labeling practices: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430) USP General Chapters <7> Labeling	☐ Yes ☐ No ☒ N/A

Package type term	**Acceptable**
Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use. USP chapter <659> Packaging and Storage Requirements	✓ Yes ☐ No ☐ N/A

Misleading statements	**Acceptable**
21 CFR 201.6	☐ Yes ☐ No ☒ N/A

Prominence of required label statements	**Acceptable**
21 CFR 201.15	✓ Yes ☐ No ☐ N/A

Spanish-language (Drugs)	**Acceptable**
21 CFR 201.16	☐ Yes ☐ No ☒ N/A

FD&C Yellow No. 5 and/or FD&C Yellow No. 6	**Acceptable**
21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Phenylalanine as a component of aspartame	**Acceptable**
21 CFR 201.21	☐ Yes ☐ No ☒ N/A

Sulfites; required warning statements	**Acceptable**
21 CFR 201.22	☐ Yes ☐ No ☒ N/A

Net quantity	**Acceptable**
21 CFR 201.51	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
March 15, 2019: To Applicant: Revise the net quantity statement from "1 GALAXY Single Dose Container" to read "1 Single-Dose GALAXY container".

March 29, 2019: The Applicant revised the net quantity statement from "1 GALAXY Single Dose Container" to read "1 Single-Dose GALAXY container".

FDA Response: The revision is acceptable.

Recommended labeling practices: *Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463)*	✓ Yes ☐ No ☐ N/A

Usual dosage statement	**Acceptable**
21 CFR 201.55, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Dispensing container	Acceptable
21 CFR 201.100	☐ Yes ☐ No ☒ N/A

Medication Guide	Acceptable
21 CFR 610.60, 21 CFR 208.24	☐ Yes ☐ No ☒ N/A

Other	Acceptable
	☐ Yes ☐ No ☒ N/A

Prescribing Information

PRESCRIBING INFORMATION

Highlights of Prescribing Information	
PRODUCT TITLE	**Acceptable**
21 CFR 201.57(a)(2)	✓ Yes ☐ No ☐ N/A
Comment/Recommendation: Team commented to the applicant to revise the established name to be in agreement with formatting described in the draft Product Title Guidance. May 24, 2019: The Product Title reads: MYXREDLIN™ (insulin human in sodium chloride injection), for intravenous use FDA Response: The revised Product Title is acceptable.	
Recommended labeling practices: *Draft Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format Guidance for Industry (January 2018)*	✓ Yes ☐ No ☐ N/A
DOSAGE AND ADMINISTRATION	**Acceptable**
Recommended labeling practices: USP nomenclature for diluents and intravenous solutions	☐ Yes ☐ No ☒ N/A

DOSAGE FORMS AND STRENGTHS	**Acceptable**
21 CFR 201.57(a)(8), 21 CFR 201.10, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: Please revise to include the dosage formulation per 21 CFR 201.57(a)(8).

Internal labeling discussions between the Associate Director of Labeling (ADL), DMEPA and OBP Labeling agreed to present the statement as:

Injection: 100 units insulin human in 100 mL of 0.9% sodium chloride (1 unit/mL) in a single-dose container (3)

June 17, 2019: The applicant revised the statement as requested above.

FDA Response: The applicant's revision is acceptable.

Recommended labeling practices: *Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)* *USP chapter <659> Packaging and Storage Requirements* *Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 176* *USP General Chapters: <7> Labeling*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: Please add the appropriate package type terminology, "single-dose" per the Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)

Internal labeling discussions between the Associate Director of Labeling (ADL), DMEPA and OBP Labeling agreed to present the package type statement as "single-dose container".

June 17, 2019: The applicant revised the statement as requested above.

FDA Response: The applicant's revision is acceptable.

Full Prescribing Information	
2 DOSAGE AND ADMINISTRATION	**Acceptable**
21 CFR 201.57(c)(3)(iv)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Internal labeling discussions between the Associate Director of Labeling (ADL) and OBP Labeling aligned that the statement "Inspect MYXREDLIN visually before use. It should appear clear and colorless. Do not use MYXREDLIN if particulate matter or coloration is seen." was adequate and the statement "(b) (4) per 21 CFR 201.57(c)(3)(iv) was not necessary.

Dr. Shukla indicated both a Do not Freeze and a Do not Shake statement are acceptable for this product.

May 24, 2019: Section 2.1 of the prescribing information contains the 3 statements described in this section.

FDA Response: The applicant's proposed wording is acceptable.

Recommended labeling practices: *USP nomenclature for diluents and intravenous solutions*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
This product is prepared in 0.9% Sodium Chloride Injection, USP which was reviewed as part of the finished drug product. The solution is acceptable.

To Applicant: Please include a "discard unused portion" statement to help prevent the misuse of the product.

May 24, 2019: The applicant agreed to include a "Discard any unused portion" statement in section 2.1.

FDA Response: The applicant's revision is acceptable.

3 DOSAGE FORMS AND STRENGTHS	**Acceptable**
21 CFR 201.57(c)(4)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

To Applicant: Please revise to include the dosage formulation and the identifying characteristics per 21 CFR 201.57(c)(4).

Dr. Shukla confirmed the identifying characteristics for the product are clear, colorless, and also free of visible particulate matter.

Internal labeling discussions between the Associate Director of Labeling (ADL), DMEPA and OBP Labeling agreed to present the statement as:

Injection: 100 units insulin human in 100 mL of 0.9% sodium chloride (1 unit per mL) as a clear, colorless solution in a single-dose container.

June 17, 2019: The applicant revised the statement as requested above.

FDA Response: The applicant's revision is acceptable.

Recommended labeling practices: *Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)* *USP General Chapters <659>, USP General Chapters <7>*	✓ Yes ☐ No ☐ N/A

11 DESCRIPTION	**Acceptable**
21 CFR 201.57(c)(12), 21 CFR 610.61 (m), 21 CFR 610.61(o), 21 CFR 610.61 (p), 21 CFR 610.61 (q)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Dr. Shukla confirmed there are no safety concerns with Pichia, no antibiotics used in the manufacturing process, the molecular weight is correct, the product is sterile and preservative-free, and the intravenous bag is acceptable. Also, the qualitative and quantitative information is correct.
Each milliliter of solution contains 1 unit Insulin Human, USP; 0.412 mg Dibasic Sodium Phosphate Anhydrous, USP; 0.29 mg Monobasic Sodium Phosphate Monohydrate, USP; 9 mg Sodium Chloride, USP; and Water for Injection, USP.

For the Applicant: Revisions to Section 11 were proposed including the format and nomenclature for the qualitative and quantitative information.

May 24, 2019: The applicant accepted the proposed revisions.

FDA Response: The applicant's revisions are acceptable.

Recommended labeling practices: *USP General Chapters <1091>, USP General Chapters <7>*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: The proprietary name and infusion solution was deleted from the first paragraph because this paragraph discusses the drug substance.

May 24, 2019: The applicant accepted the proposed revisions.

FDA Response: The applicant's revisions are acceptable.

16 HOW SUPPLIED/ STORAGE AND HANDLING	**Acceptable**

21 CFR 201.57(c)(17)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
Dr. Shukla confirmed the fill volume is compliant with USP<1151>. Dr. Shukla confirmed the product should be refrigerated, protected from light until administration, protected from freezing, protected from shaking, protected from heat and no sensitizing substances (latex) are associated with this product.
Dr. Shukla stated the data supports the product may be stored for up to 30 days at 25°C.
To Applicant: Revised to include the strength and identifying characteristics per 21 CFR 201.57(c)(17)

To Applicant: Please delete the reference to the code in this section. It does not provide useful information to the practitioner.

To Applicant: Please create a different National Drug Code for a package of 12 bags. If two or more units are packaged into a single carton then the NDC for the unit and the carton should be different. The NDC presented here is already used to identify an individual bag.

Additional formatting and editorial revisions were proposed in the draft labeling to the applicant.

May 24, 2019: The applicant accepted the proposed revisions.

FDA Response: The applicant's revisions are acceptable.

Recommended labeling practices: to ensure placement of detailed storage conditions for reconstituted and diluted products	✓ Yes ☐ No ☐ N/A

MANUFACTURER INFORMATION	**Acceptable**
21 CFR 201.100(e), 21 CFR 201.1, 19 CFR 134.11	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: Please include a qualifying phrase refer to 21CFR201.1(h)(5) "Manufactured for:"

May 24, 2019: The applicant included a "Manufactured for:" and a "Manufactured by" designation.

FDA Response: The applicant's revisions are acceptable for an NDA product. However, this information may need to be changed when the product is transitioned to be a BLA.

Recommended labeling practices: *21 CFR 610.61 (add the US license number for consistency with the carton labeling), and 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
Note: this is an NDA product and does not have a license number at this time.

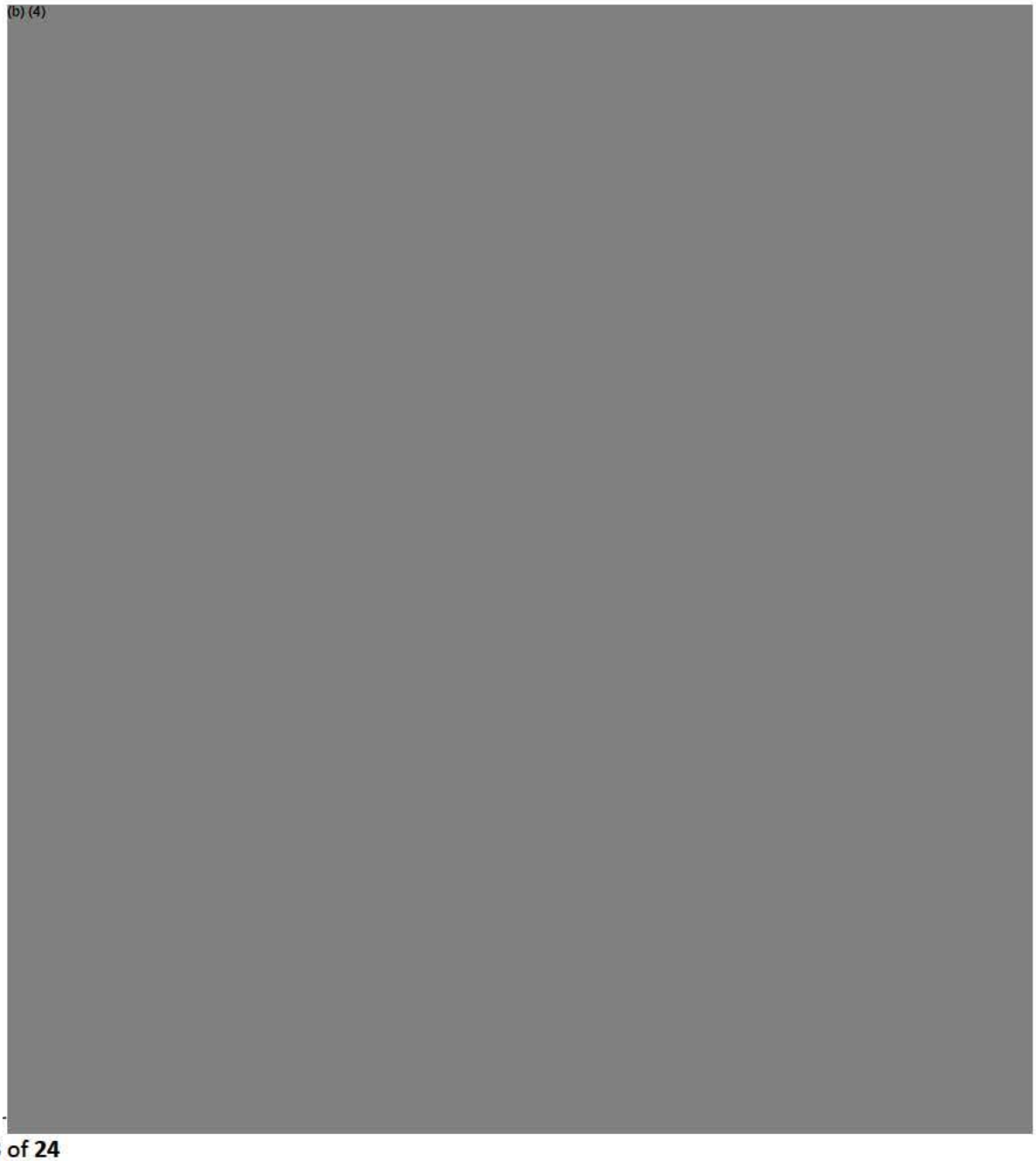
APPENDIX C. Acceptable Labels and Labeling

- Prescribing Information (submitted on June 17, 2019)
  \\cdsesub1\evsprod\nda208157\0020\m1\us\pi-draft-labeling-text-original-draft-v5-c.doc

- Container Labels (submitted on May 15, 2019)

LOT:
EXP:

(b) (4)



1 Page(s) of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

Scott Dallas

Digitally signed by Scott Dallas
Date: 6/17/2019 03:09:17PM
GUID: 508da712000294048aa136a18a6af06a

Anjali Shukla

Digitally signed by Anjali Shukla
Date: 6/17/2019 03:47:21PM
GUID: 57f29f4500712615c8f3d6ddc11716a9

Recommendation:
BLA/NDA: Approval

NDA Number: 208157
Review Number: 02
Review Date: 5/28/2019

Drug Name/Dosage Form	MYXREDLIN / Injectable, Sterile Solution
Strength/Potency	100 Units / 100 mL
Route of Administration	Intravenous Infusion
Rx/OTC dispensed	Rx
Indication	To improve glycemic control in adults and children with diabetes mellitus
Applicant/Sponsor	Celerity Pharmaceuticals, LLC
US agent, if applicable	n/a

Product Overview

MYXREDLIN (regular human insulin) is a two-chain polypeptide hormone consisting of 51 amino acids. The A-chain is composed of 21 amino acids, and the B-chain is composed of 30 amino acids. Insulin Human [USP] is produced in a recombinant *Pichia Pastoris* cell line and has a molecular mass of 5808 Da. MYXREDLIN is a sterile, clear, colorless solution. MYXREDLIN includes regular human insulin in 100 mL of 0.9% Sodium Chloride Injection in a GALAXY plastic container. Each prefilled container contains 100 Units Insulin Human formulated in Sodium Chloride (900 mg), Monobasic Sodium Phosphate, Monohydrate (29.0 mg), Dibasic Sodium Phosphate, Anhydrous (41.2 mg), and Water for Injection, USP. The MYXREDLIN solution has a pH of 6.5-7.2.

Quality Review Team

Discipline	Reviewer	Branch/Division
Drug Substance	Anjali Shukla	OBP/DBRRII
Drug Product		
Labeling	Scott Dallas	OBP/IO
Facility	Laurie Nelson/Peter Qiu	OPF/DIA
Microbiology - DS	Scott Nichols/Patricia Hughes	OPF/DMA
Microbiology – DP	Virginia Carroll/Reyes Candau-Chacon	OPF/DMA
Application Team Lead	William Hallett	OBP/DBRRII
RBPM	Anika Lalmansingh	OPRO

Mutidisciplinary Review Team:

Discipline	Reviewer	Office/Division
RPM	Callie CappelLynch	OND/DMEP
Cross-disciplinary Team Lead	Patrick Archdeacon	OND/DMEP
Medical Officer	Frank Pucino / Patrick Archdeacon	OND/DMEP
Pharm/Tox	Parvaneh Espandiari / Lee Elmore	OND/DMEP
Clinical Pharmacology	Tao Liu / Manoj Khurana	OTS/OCP/DCPII
DMEPA	Ariane Conrad / Hina Mehta	OSE/OMEPRM/DMEPA
DPV	Christine Chamberlain / Christian Cao	OSE/OPE/DPVI

1. Names:
a. Proprietary Name MYXREDLIN

b. Trade Name	MYXREDLIN
c. Non-Proprietary Name/USAN	Regular Human Insulin (rDNA origin) in 0.9% Sodium chloride injection
d. CAS Name:	CAS registry number 11061-68-0
e. Common Name:	none
f. INN Name	Insulin Human [for Drug Substance]
g. Compendial Name	Insulin Human, USP [for Drug Substance]
h. OBP systematic name	RPROT P01308 (INS_HUMAN) Insulin
i. Other names	none

Submissions Reviewed:

Submission(s) Reviewed	Document Date
208157 / 0001	05/04/2018
208157 / 0003	07/17/2018
208157 / 0004 Resubmission	08/22/2018
208157 / 0006	10/26/2018
208157 / 0007	10/31/2018
208157 / 0008	11/21/2018
208157 / 0009	01/17/2019
208157 / 0010	02/28/2019
208157 / 0011	03/01/2019
208157 / 0013	03/29/2019
208157 / 0014	04/12/2019
208157 / 0015	04/24/2019
208157 / Teleconference	05/02/2019
208157 / 0016	05/06/2019
208157 / 0018	05/21/2019

Quality Review Data Sheet

1. Legal Basis for Submission: 505(b)2

2. Related/Supporting Documents:

A. DMFs:

DMF #	DMF Type	DMF Holder	Item referenced	Code[1]	Status[2]	Date Review Completed	Comments
(b) (4)	(b) (4)	(b) (4)	Human insulin drug substance	1	Adequate	5/7/2019	n/a
06344	III	Baxter	Sterile SVP injections in (b) (4) plastic container	1	Adequate	5/7/2019	n/a

1. Action codes for DMF Table: 1- DMF Reviewed; Other codes indicate why the DMF was not reviewed, as follows: 2- Reviewed previously and no revision since last review; 3- Sufficient information in application; 4- Authority to reference not granted; 5- DMF not available; 6- Other (explain under "comments")

2. Adequate, Adequate with Information Request, Deficient, or N/A (There is not enough data in the application; therefore, the DMF did not need to be reviewed.

B. Other documents: IND, Referenced Listed Drug (RLD), or sister application.

Document	Application Number	Description
01	NDA 019938	Novolin R – RLD (not reviewed)
02	NDA 208157	NDA

3. Consults: n/a

Executive Summary

I. Recommendations:

A. Recommendation and Conclusion on Approvability:

Recommendation:

The Office of Biotechnology Products, OPQ, CDER, recommends approval of STN 208157 for MYXREDLIN manufactured by Celerity. The data submitted in this application are adequate to support the conclusion that the manufacture of MYXREDLIN is well-controlled and leads to a product that is pure and potent. It is recommended that this product be approved for human use under conditions specified in the package insert.

B. Approval Action Letter Language:

Manufacturing location:

- Drug Substance: [redacted] (b) (4) [redacted]
- Drug Product: Baxter Healthcare Corp, (b) (4) [redacted], (b) (4) [redacted] (b) (4) [redacted]

- Fill size and dosage form 100 Units / 100 mL (1 U/ mL)
- Dating period:
  - Drug Product: (b) (4) [redacted]
  - Drug Substance: (b) (4) [redacted]
  - For packaged products: Not packaged
  - Stability Option:
    - Refer to DMF (b) (4) [redacted]:
    - We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating of your drug product under 21 CFR 601.12.

- Exempt from lot release
  - MYXREDLIN is exempted from lot release because it is a specified product per 601.2(a)

D. Benefit/Risk Considerations:

Regular human insulin is an agonist peptide hormone for the insulin receptor. The data submitted in this application support the conclusion that the manufacture of regular human insulin is well controlled and yields a consistently high-quality product. The conditions used in manufacturing have been sufficiently validated, and a consistent product is prepared from the multiple product runs presented. From a product quality perspective, this product is approvable for human use.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Requirements, Agreements, and/or Risk Management Steps, if approvable:

1. (b) (4) [redacted].

II. Summary of Quality Assessments:

A. CQA Identification, Risk and Lifecycle Knowledge Management
Table 1: Active Pharmaceutical Ingredient CQA Identification, Risk and Lifecycle Knowledge Management

Refer to DMF (b) (4) for CQA Identification, Risk, and Lifecycle Management.

NDA 208157 is submitted under the 505(b)2 pathway with Novolin R as the reference listed drug, which the proposed product relies on for safety and efficacy information. Celerity provided an analytical similarity assessment of MYXREDLIN to Novolin R that included comparisons of the drug products and de-formulated active pharmaceutical ingredients. The analytical similarity data provides assurance critical quality attributes are comparable between Novolin R and MYXREDLIN. Celerity compared the following physico-chemical characteristics using multiple batches of product: primary, secondary, and tertiary structure, molecular size, isoelectric point, particle size, sub-visible particles, intact and reduced mass, aggregates, pH, visual appearance, Insulin Assay [, (b) (4) , Other Related Substances], HMWP, Osmolality, Purity, Insulin Receptor Binding, Mitogenic Potential, Glucose Uptake, and IGF1-Receptor Binding. Refer to the primary technical review for additional details.

B. Drug Substance [Regular Human Insulin] Quality Summary

Refer to DMF (b) (4) for CQA Identification, Risk, and Lifecycle Management.

Drug Product [MYXREDLIN] Quality Summary:

Table 3: Drug Product CQA Identification, Risk, and Lifecycle Management

CQA (type)	Risk	Origin	Control Strategy
Sterility (contaminant)	Safety, Purity, and Efficacy (via degradation or modification of the product by contaminating microorganisms)	Contaminants could be introduced during the manufacturing process or through container closure integrity test failure	(b) (4) [redacted]
Endotoxin	Safety (pyrogenic fever, increased immunogenicity risk) and Purity	Contaminants could be introduced throughout drug product manufacturing or due to container closure integrity failure	

Color and Clarity	Safety and Efficacy	Formulation, Contamination, and Degradation	(b) (4)
Container Closure Integrity	Safety	May be impacted by storage conditions	
Osmolality	Safety, Efficacy (control of degradation through formulation)	Formulation	
pH	Safety and Efficacy	Formulation	
Particulate Matter	Safety / Immunogenicity	Manufacturing Process and Container Closure System	
Fill Volume	Efficacy / Dosing	Manufacturing Process	
Leachables (process-related impurities)	Safety	Manufacturing equipment and CCS	

- Potency and Strength:

MYXREDLIN is supplied at 100 Unites / 100 mL (1 U/mL) in 0.9% sodium chloride in a GALAXY container. Potency of human insulin is determined as a percent UPLC Assay to the human insulin reference standard. The potency assay is the same as described in the drug substance section of this review.

- Summary of Product Design:

MYXREDLIN is provided as a 100 mL (1U/mL) pre-mixed, sterile solution containing regular human insulin in 0.9% sodium chloride injection supplied in a GALAXY plastic bag. The drug product formulation consists of 9.0 mg/mL sodium chloride, 0.290 mg/mL monobasic sodium phosphate, monohydrate, 0.412 mg/mL dibasic sodium phosphate, anhydrous, and water for injection.

- List of Excipients:

Excipients include 9.0 mg/mL sodium chloride, 0.290 mg/mL monobasic sodium phosphate, monohydrate, and 0.412 mg/mL dibasic sodium phosphate, anhydrous.

- Reference Materials:

The reference standard used for testing of the drug product is compendial, USP Human Insulin. The sponsor also used High Molecular Weight Insulin Human USP reference standard for assessment of HWMP.

- Manufacturing process summary:

The drug product manufacturing process consists of (b) (4) Filled GALAXY bags are visually inspected prior to packing into unit pack immediate cartons at 1 bag per carton and 12 individual UPIC per case prior to storage at 2-8°C.

The control strategy includes in-process testing of critical and non-critical parameters and release testing of drug product. Critical parameters are selected for routine monitoring related to (b) (4)

All drug product-contact equipment and components are (b) (4) Bioburden is tested during manufacture, and sterility and endotoxin are tested at DP lot release.

- Container closure:

The primary container closure for MYXREDLIN drug product is a Baxter's 100 mL single-port PL2501 GALAXY bag. The film is a (b) (4) that includes product contact layers of (b) (4) polyethylene, (b) (4) and (b) (4). Appropriate compatibility studies were performed for the container closure system. Container closure material suitability includes a safety assessment of the (b) (4) (b) (4) are controlled and monitored through an on-going requalification program. Container closure integrity of the GALAXY bag manufactured by the (b) (4) process has been validated by Baxter over the shelf-life of the system (refer to DMF 6344).

- Dating period and storage conditions:

The dating period for MYXREDLIN drug product is (b) (6) at 2-8°C, protected from light. The product may be removed from 2-8°C and stored at 25°C for up to 30 days, after which the product should be disposed.

C. Novel Approaches/Precedents: None

D. Any Special Product Quality Labeling Recommendations:

Store in a refrigerator at 2°C to 8°C (36°F to 46°F).
Store in product carton until time of use.
Protect from light.
Do not freeze.
Do not shake.
Discard after 30 days if stored at room temperature.

E. Establishment Information:

Overall Recommendation: Adequate					
DRUG SUBSTANCE					
Function	Site Information	FEI Number	Preliminary Assessment	Inspectional Observations	Final Recommendation
CBI- Drug Substance Manufacturing, Packaging, Labeling,	(b) (4)	(b) (4)	High Risk	1. Information discrepancy between DMF (b) (4) and human insulin manufacturing process performed at (b) (4)	Approval

Testing and Release, Stability Testing				Specifically, differences in material product codes. 2. Bacterial endotoxin test method of finished drug product is deficient. 3. Environmental monitoring of clean rooms by microbiological methods is deficient. 4. Laboratory controls failed to ensure that Empower chromatographic system software appropriately reports characteristics of the drug product. 5. Quality unit failed to ensure critical process deviations were documented and investigated. 6. Quality unit failed to ensure that effective systems are used for calibrating critical equipment.	
CTL - Drug Substance Testing (Residual Solvents)	(b) (4)		Medium	n/a	Approval
CTL - Drug Substance Testing (b) (4)			Low	n/a	Approval
CTL - Drug Substance Testing (Microbiological)			Low	n/a	Approval
DRUG PRODUCT					
Function	Site Information	DUNS/FEI Number	Preliminary Assessment	Inspectional Observations	Final Recommendation
SVS - Drug Product Manufacturing, Packaging, Testing and Release, Stability Testing	Baxter Healthcare Corp, (b) (4) (b) (4)	1416980	High	n/a	Approval
CTL - Drug Substance Testing and	(b) (4)		Medium	n/a	Approval

Release, Finished Product Testing and Release, Stability Testing	(b) (4)				

F. Facilities:

Human Insulin API is manufactured at (b) (4) (FEI: (b) (4)). A Prior Approval Inspection was performed at (b) (4) A six-item FDA Form 483 was issued. The firm is acceptable. The DS manufacturing and testing sites were inspected multiple times within recent past, demonstrating acceptable compliance.

G. Lifecycle Knowledge Management:

a. Drug Substance: Refer to DMF (b) (4)

b. Drug Product

i. Protocols approved:
-annual stability protocol
ii. Outstanding review issues/residual risk:
-See Post-Marketing Commitments in Section IB
iii. Future inspection points to consider:
-Evaluate DP PPQ results

Quality Assessment Summary Tables

Table 1: Noteworthy Elements of the Application

#	Checklist		Yes	No	N/A
	Product Type				
1.	Recombinant Product		X		
2.	Naturally Derived Product			X	
3.	Botanical			X	
4.	Human Cell Substrate/source material			X	
5.	Non-Human Primate Cell Substrate/Source Material			X	
6.	Non-Primate Mammalian Cell Substrate/source material			X	
7.	Non-Mammalian Cell Substrate/Source Material		X		
8.	Transgenic Animal source			X	
9.	Transgenic Plant source			X	
10.	New Molecular Entity			X	
11.	PEPFAR drug			X	
12.	PET drug			X	
13.	Sterile Drug Product		X		
14.	Other: [fill in information]			X	
	Regulatory Considerations				
15.	Citizen Petition and/or Controlled Correspondence Linked to the Application [fill in number]			X	
16.	Comparability Protocol(s)			X	
17.	End of Phase II/Pre-NDA Agreements tem			X	
18.	SPOTS (special products on-line tracking system)			X	
19.	USAN assigned name			X	
20.	Other [fill in]			X	
	Quality Considerations				
21.	Drug Substance Overage			X	
22.	Design Space	Formulation		X	
23.		Process		X	
24.		Analytical Methods		X	
25.		Other		X	
26.	Other QbD Elements		X		Design of experiments used in manufacturing process development
27.	Real Time release testing (RTRT)			X	
28.	Parametric release in lieu of Sterility testing			X	
29.	Alternative Microbiological test methods			X	
30.	Process Analytical Technology in Commercial Production			X	
31.	Non-compendial analytical procedures	Drug Product	X		
32.		Excipients		X	
33.		Drug Substance	X		
34.	Excipients	Human or Animal Origin		X	
35.		Novel		X	
36.	Nanomaterials			X	
37.	Genotoxic Impurities or Structural Alerts			X	
38.	Continuous Manufacturing			X	
39.	Use of Models for Release			X	
40.	Other {fill-in}			X	

William Hallett

Digitally signed by William Hallett
Date: 5/30/2019 10:29:27AM
GUID: 5317e2c20000ce395db4bc0c4cf39411
Comments: New version to cover the updates to the PMCs

Patrick Lynch

Digitally signed by Patrick Lynch
Date: 5/30/2019 07:29:30PM
GUID: 54bfb193000693c35f4278034f85d77a