
MEMORANDUM
HUMAN FACTORS ADVICE LETTER

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	February XX, 2023
Requesting Office or Division:	Center for Biologics Evaluation and Research (CBER) Division of Clinical Evaluation and Pharmacology/Toxicology (DCEPT)
Application Type and Number:	BLA 125774
Product Name, Dosage Form and Strength:	Vyjuvek (beremagene geperpavec) injection
Applicant/Sponsor Name:	Krystal Biotech, Inc. (Kystal Biotech)
OSE TTT #:	2022-82
DMEPA 1 Team Leader :	Murewa Oguntimein, PhD, MHS, CPH, MCHES
DMEPA 1 Associate Director for Human Factors:	Jason Flint MBA, PMP

1 PURPOSE OF MEMORANDUM

On July 01, 2022, Krystal Biotech, Inc. (the Applicant) submitted a HF validation protocol (PRO-HF-02) as part of their Biologics License Application (BLA) under BLA 125774 for Vyjuvek (beremagene geperpavec) (b) (4) .

2 BACKGROUND AND CONCLUSION

- On November 19, 2020, Kystal Biotech submitted a human factors (HF) validation study protocol to support in-home administration of Vyjuvek by healthcare professionals (HCPs) for the purposes of the clinical trial. We reviewed the protocol and provided recommendations.^a
- On May 17, 2021, Kystal Biotech submitted clarifying questions regarding the acceptability of their HF study methodology. These clarifying questions were in

^a Flint J. Human Factors Protocol Review for B-VEC (IND 18100). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021Jan06. RCM No.: 2020-2502

response to recommendations that we made during our previous HF protocol review.^a We reviewed the questions and responded to the clarifying questions.^b

- On July 16, 2021, the Division of Clinical Evaluation and Pharmacology/Toxicology (DCEPT) provided a letter of agreement to conduct the HF study.^c
- On July 01, 2022, Kystal Biotech submitted their Biologics License Application (BLA) under BLA 125774 that included a HF validation study protocol (PRO-HF-02) to support (b) (4) of the intend-to-market commercial product by HCPs in the intended use environment.
- The BLA application also included Kystal Biotech's proposed prescribing information (PI). We noted the PI section 2 Dosage and Administration stated, "VYJUVEK should be (b) (4) administered by a Healthcare Professional (HCP),". However, Kystal Biotech has not conducted any HF validation study to support the use of the intend-to-market commercial product by the intended users (i.e., HCPs) in the intended use environment. Specifically, Kystal Biotech has not conducted an HF validation study to support (b) (4) of the intend-to-market commercial product by HCPs in the intended use environment. As such, Kystal Biotech will not be able to include the statement, "VYJUVEK should be (b) (4) by a Healthcare Professional (HCP)" in their PI, since the statement has not been validated.
- On October 14, 2022, during the Mid-cycle communication teleconference with Kystal Biotech, we informed Kystal Biotech that they will not be able to include the statement, "VYJUVEK should be (b) (4) by a Healthcare Professional (HCP)" in their PI, since the statement has not been validated. We further clarified that, there are no HF study data that support the HCP (b) (4) of the product since the HF validation study (PRO-HF-02) that is intended to support (b) (4) of the intended-to-market commercial product by HCPs has not been conducted yet. Further, we indicated that all statements in the PI need to be supported by available data. Additionally, we noted that Kystal Biotech submitted an HF validation study protocol (PRO-HF-02) in their BLA to support (b) (4) of the intend-to-market commercial product by HCPs in the intended use environment. However, since Kystal Biotech has not conducted the study at this time, we recommended they withdraw their HF validation protocol (PRO-HF-02) from this BLA submission. We stated that it is not recommended to submit the HF validation study protocol (PRO-HF-02) under the BLA because there is not enough time to conduct the study and submit the study data for FDA to review within the BLA review cycle. We indicated that FDA is willing to provide feedback on the protocol. However, we further reiterated that Kystal Biotech withdraw this protocol from the BLA and submit the revised protocol to the IND after incorporating our comments that would be sent to them as an information request.^d

^b Flint J. Human Factors Advice Clarifying Questions for B-VEC (IND 18100). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021Jun29. RCM No.: 2021-1058

^c Wilson B. Agreement, HF Protocol Assessment for B-VEC (IND 18100). Silver Spring (MD): FDA, CDER, OTAT (US); 2021Jul16

^d Maglalang. R. Midcycle Communication for Vyjuvek (BLA 125774). Silver Spring (MD): FDA, CDER, OTAT (US); 2022Nov10.

- As stated in the midcycle communication summary above, we provide preliminary comments and feedback on the protocol in an information request to Kystal Biotech in section 3 below.

3 RECOMMENDATIONS FOR KRYSTAL BIOTECH, INC. (KYSTAL BIOTECH)

We refer to:

- your Human Factors (HF) Validation Protocol (PRO-HF-02) submitted on July 01, 2022, to your BLA 125774 for Vyjuvek.
- our Mid-Cycle Communication for BLA 125774 Vyjuvek dated October 14, 2022.

We conducted a preliminary review of the HF validation study protocol (PRO-HF-02) and have the following preliminary recommendations.

- The study should assess the entire user interface including the (b) (4) administration with the intend-to-market commercial product by the intended users (HCP) in the intended use environment.
- The study should include an untrained group in the study as this represents a high-risk scenario. We expect the HF study to include this high-risk scenario as we need to understand what use errors might occur.
- If you intend to use training as a risk mitigation, include detailed information about your proposed training program for the trained group.
- Submit five placebo only intend-to-market samples of product that will be tested in the HF validation study.

As we stated in our Mid-Cycle Communication dated October 14, 2022, we recommend you withdraw your HF Validation Protocol (PRO-HF-02) from the BLA submission and resubmit your revised HF validation study protocol to the IND for Agency review and feedback prior to conducting your study.

The requested information should be submitted to the IND in eCTD Section 5.3.5.4 – Other Study reports and related information.