

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

202860Orig1s000

OTHER REVIEW(S)

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
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:	December 17, 2019
Requesting Office or Division:	Division of Cardiovascular and Renal Products (DCRP)
Application Type and Number:	NDA 202860
Product Name and Strength:	Genosyl (nitric oxide) for inhalation, concentration up to 800 ppm (b) (4)
Applicant/Sponsor Name:	Vero Biotech
OSE RCM #:	2019-1334-1
DMEPA Safety Evaluator:	Ebony Whaley, PharmD, BCPPS
DMEPA Team Leader:	Lolita White, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted the revised Prescribing Information (PI), quick reference guide (QRG), and Operator's Manual received on December 12, 2019 and the revised carton and container labeling received on December 13, 2019 for Genosyl. The Division of Cardiovascular and Renal Products (DCRP) requested that we review the revised PI, QRG, Operator's Manual, and carton and container labeling for Genosyl (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.^a

2 CONCLUSION

The Applicant implemented all of our recommendations for the PI, QRG, Operator's Manual, carton labeling, and container label, and we have no additional recommendations at this time from a medication error perspective.

^a Whaley. Human Factors Validation Study Results and Label and Labeling Review for Genosyl (NDA 202860). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 NOV 14. RCM No.: 2019-1334; 2019- 1336.

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FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

******Pre-decisional Agency Information******

Memorandum

Date: November 15, 2019

To: Brian Proctor, RAC, Senior Regulatory Health Project Manager
Division of Cardiovascular and Renal Products (DCRP)

Michael Monteleone, Associate Director for Labeling, (DCRP)

From: Zarna Patel, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for Genosyl (nitric oxide) gas, for inhalation

NDA: 202860

In response to the DCRP consult request dated November 14, 2019 (replacing the August 2018 consult request which was closed out), OPDP has reviewed the proposed product labeling (PI), carton and container labeling, and the user manual for Genosyl delivery system for the original NDA submission for Genosyl (nitric oxide) gas, for oral inhalation.

PI and User Manual: OPDP has reviewed the attached PI and the user manual. We do not have any additional comments at this time.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on June 21, 2019, (emailed to OPDP by DCRP on November 15, 2019) and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Zarna Patel at (301) 796- 3822 or zarna.patel@fda.hhs.gov.

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HUMAN FACTORS VALIDATION STUDY RESULTS AND LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	November 14, 2019
Requesting Office or Division:	Division of Cardiovascular and Renal Products (DCRP)
Application Type and Number:	NDA 202860
Product Name and Strength:	Genosyl (nitric oxide) for inhalation, concentration up to 800 ppm (b) (4) [REDACTED]
Product Type:	Combination product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Vero Biotech
FDA Received Date:	June 21, 2019; August 8, 2019
OSE RCM #:	2019-1334; 2019-1336
DMEPA Safety Evaluator:	Ebony Whaley, PharmD, BCPPS
DMEPA Team Leader:	Lolita White, PharmD
DMEPA Associate Director for Human Factors:	QuynhNhu Nguyen, MS

1 REASON FOR REVIEW

This review evaluates the human factors (HF) validation study results report and labels and labeling submitted as part of a Class 2 resubmission under NDA 202860 for Genosyl (nitric oxide) for inhalation.

1.1 PRODUCT DESCRIPTION

Genosyl is a nitric oxide (NO) gas delivery system that is intended to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents (see Appendix A). Genosyl is generated from liquid dinitrogen tetroxide/nitrogen dioxide (N₂O₄/NO₂) by the Genosyl (b) (4) Delivery System (Genosyl (b) (4)). The Genosyl (b) (4) delivers NO into a ventilator circuit or manual ventilation bag.

The main components of the Genosyl (b) (4) are:

- Consoles: There are two consoles—the primary console and the standby console. The consoles comprise one of the two main sub-systems that convert dinitrogen tetroxide/nitrogen dioxide (N₂O₄/NO₂) liquid into nitric oxide gas. The console is a software-controlled electro-mechanical system that controls and monitors the generated nitric oxide and ensures that nitrogen dioxide (NO₂) levels are at safe levels.
- Cassette: One cassette is inserted into each Genosyl (b) (4) console. The cassettes contain the liquid N₂O₄/NO₂ (b) (4), the conversion cartridges, and the inerting material required to generate nitric oxide gas from N₂O₄/NO₂ cartridges.

Genosyl (b) (4) is designed to deliver NO gas into a mechanical ventilator circuit or a manual ventilation bagging system. The Genosyl (b) (4) is intended for use by pediatric and/or neonatal respiratory therapists in a neonatal intensive care unit (NICU) in a hospital.

1.2 REGULATORY HISTORY RELATED TO THE PROPOSED PRODUCT'S HUMAN FACTORS DEVELOPMENT PROGRAM

On July 23, 2018, the Applicant submitted an HF validation study results report for their proposed Genosyl (b) (4) as a part of their 505(b)(2) resubmission for NDA 202860. We reviewed the HF validation study results^a and concluded that the study results did not provide sufficient evidence to demonstrate that the proposed product could be used safely and effectively by the

^a Stewart J. Human Factors Results and Label and Labeling Review for Genosyl NDA 202860. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 JAN 4. RCM No.: 2018-1578 and 2018-1579.

intended users for its intended uses and use environments. In addition, we determined that the HF study methodology and study implementation had flaws that limited the utility and interpretation of the results. We also noted that the Applicant made post-validation revisions to the user interface that were not further validated. We recommended that the Applicant evaluate the use-related errors observed in the HF study, employ additional mitigation strategies, update their use-related risk analysis, and conduct another HF validation study using appropriate study methodology. Subsequently, the Agency issued a Complete Response that contained the HF deficiencies along with two other issues related to facility inspection and device engineering.

On February 27, 2019, the Applicant submitted their HF validation study protocol for an additional HF validation study and we provided recommendations to the Applicant.^b On June 21, 2019, the Applicant submitted the results of the HF validation study testing as part of a Class 2 resubmission for NDA 202860.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Background Information Previous HF Reviews (DMEPA and CDRH)	B
Background Information on Human Factors Engineering (HFE) Process	C
Human Factors Validation Study Report	D
CDRH Human Factors Consult Review	E
Information Requests Issued During the Review	F – N/A
Labels and Labeling	G

N/A=not applicable for this review

3 OVERALL ASSESSMENT OF MATERIALS REVIEWED

^b Stewart J. Human Factors Protocol Review for Genosyl IND 109066. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 APR 25. RCM No.: 2019-451.

The sections below provide a summary of the study design, errors observed, and our analysis to determine if the results support the safe and effective use of the proposed product.

We also consulted CDRH Human Factors team to review the study report, and the team did not identify any deficiencies.^c

3.1 SUMMARY OF STUDY DESIGN

The HF validation study included 15 respiratory therapist study participants. The study participants attended a one-day training and familiarization session and there was a 16—24 hour training decay period. We acknowledge that variability in the training decay period may confound the data; however, it did not preclude our review of the study results. Following the training decay period, the participants returned to complete validation testing as follows:

A. Simulated use scenarios

1. Use Genosyl to set up the system and its connections, and then turn on and start up the system.
2. Use Genosyl to calibrate air, NO, and NO₂ gases.
3. Use Genosyl to administer simulated NO to a simulated patient.
4. Use Genosyl to adjust the dose of the NO administration (wean).
5. Use Genosyl to administer NO with manual ventilation.
6. Use Genosyl to transition over to the standby console.
7. [Alarm Scenario 1] Use Genosyl to address a “Cassette Removed” alarm by using the standby console as a backup system to restore NO delivery.
8. [Alarm Scenario 2] Use Genosyl to address a “Low NO” alarm condition.
9. [Alarm Scenario 3] Use Genosyl to address a “Line Occlusion” alarm condition.
10. [Alarm Scenario 4] Use Genosyl to address a “Water Trap Not Detected” alarm condition.
11. [Alarm Scenario 5] Use Genosyl to address a “Hi NO” alarm condition
12. [Alarm Scenario 6] Use Genosyl to address a “Hi NO₂” alarm condition
13. Powering Down the System
14. Remove, Empty and Replace Water Trap

B. Knowledge Task Questions

1. Find and understand instructions to contact technical support if battery needs to be replaced.
2. Find and understand cassette storage instructions
3. Find and understand cassette troubleshooting instructions.
4. Understand proper delivery system cleaning technique
5. Understand the cassette cannot be reused once it becomes inerted.

^c Brooks, M. Human Factors Review for Genosyl NDA 202860. Silver Spring (MD): FDA, CDRH, OHT3, DHT3C, THT3C4 (US); 2019 SEP 27. ICC1900691.

6. Find and understand labeling regarding factory service schedule
7. Find and understand Warnings regarding gas lines from another device.
8. Find and understand storage information
9. Find and understand critical alarm information (Low NO...at (b) (4))
10. Find and understand Calibration required alarm
11. Find and understand Hardware failure alarm
12. Find and understand Battery error alarm
13. Find and understand Cassette Not Operational alarm
14. Find and understand Low NO, empty cassette alarm

3.2 RESULTS AND ANALYSES

Table 2 describes the errors observed with critical and essential tasks in the HF validation study, Applicant's analyses of the results, and DMEPA's analyses and recommendations.

Table 2. Summary and analyses of errors with critical and essential tasks during HF validation testing

Tasks	Number of, Description of, and Subjective Feedback for Failures/ Use Errors, Close Calls and Use Difficulties	Applicant's Root Cause Analysis	Applicant's Discussion of Mitigation Strategies	DMEPA's Analysis and Recommendations
Check the expiration date for each cassette and the Iso-Gard filter, to ensure use is within the expiration date [Essential Task]	<i>Failure</i> n = 1 - One participant (b) (6) checked the expiration date on the cassette but failed to check the expiration date on the filter. The participant stated they "Lost focus and forgot to check the expiration date during set up".	The Applicant stated that after checking the date on the cassette, the participant's focus was on setting up the circuit and they neglected to also check the expiration date on the filter.	The Applicant stated that the expiration dates for accessories are checked at multiple points in time within the hospital setting and that the practice of checking labeling with Genosyl is documented properly in the quick reference guide (QRG) and Operator's Manual (OM) and is consistent with expectations on similar products in the clinical space. The Applicant noted that all user interface education, training, and instructions associated with the Genosyl (b) (4) explicitly identify the task of checking the expiration date of the Iso-guard filter as important and that the expiration date is prominently labeled.	Based on the Applicant's use-related risk analysis (URRA), if this task is not performed correctly and an expired filter is used, there is risk of shortened usable life span of the filter which could lead to temporary injury or impairment not requiring medication intervention. The Iso-Gard filter is used to filter air from the mixer. Our review of the study results did not identify subjective feedback indicating confusion with the labels and labeling.

Table 2. Summary and analyses of errors with critical and essential tasks during HF validation testing

Tasks	Number of, Description of, and Subjective Feedback for Failures/ Use Errors, Close Calls and Use Difficulties	Applicant's Root Cause Analysis	Applicant's Discussion of Mitigation Strategies	DMEPA's Analysis and Recommendations
			The Applicant determined that no additional mitigation is either possible or necessary at this time. The Applicant determined the residual risk is acceptable.	Our review of the Iso-Gard filter container label notes that the expiration date is not preceded by the term "expiration date" or "exp date" but instead preceded by an hourglass symbol, which per the CDRH HF reviewer, is a recognized symbol per ISO (b) (4). As such, based on the overall assessment of the study results participant subjective feedback and adequacy of the presentation of the expiration date on the labels and labeling, we find the residual risk acceptable and have no

Table 2. Summary and analyses of errors with critical and essential tasks during HF validation testing

Tasks	Number of, Description of, and Subjective Feedback for Failures/ Use Errors, Close Calls and Use Difficulties	Applicant's Root Cause Analysis	Applicant's Discussion of Mitigation Strategies	DMEPA's Analysis and Recommendations
				recommendations at this time.
Question 14: Transitioning consoles when dosing cassette is getting empty. (Low or empty) “(b) (6) encounters a ‘Low NO’ alarm while the console fuel gauge is showing 0%. What should she do?” Correct answer: You should switch over to	<i>Failure</i> n = 1 - One participant (b) (6) did not respond correctly to the question. The participant located the correct section in the OM to answer the question but referenced the incorrect answer. The participant stated, “My immediate reaction to the question was a leak in the NO injection line (this was the first possible cause in the troubleshooting table in the OM), I did not immediately connect 0% on the fuel gauge with empty cassette.” “Once I connected ‘fuel gauge’ at 0% with an empty cassette I realized	The Applicant stated that this question used a term that is not used in the interface or in the troubleshooting table in question. The term “Cassette” or “Cassette Status Indicator” was not referenced in the test question and the term “fuel gauge” was used instead. The Applicant stated that this participant did not connect the two terms as	The Applicant noted that the proper responses to Low NO alarm condition and transitioning to the back-up console when switching to a new cassette were covered by simulated used scenarios 6, 7, and 8, in which there were no participant user errors observed. The Applicant also noted that in actual use, multiple user interface indicators inform the user of the correct actions, so the ability to correctly identify the applicable information in the manual is not the only source for this information. The Applicant stated that the user feedback on this question indicates a	We note the use of inconsistent terminology in the knowledge task question, which may have introduced study artifact. As such, we have no recommendations at this time.

Table 2. Summary and analyses of errors with critical and essential tasks during HF validation testing

Tasks	Number of, Description of, and Subjective Feedback for Failures/ Use Errors, Close Calls and Use Difficulties	Applicant's Root Cause Analysis	Applicant's Discussion of Mitigation Strategies	DMEPA's Analysis and Recommendations
the new standby console.	the correct answer; transitioning the console."	meaning the same thing.	misunderstanding of terminology used in the question and that the participant indicated clear understanding when the same terminology was used in the debrief discussion. Thus, the Applicant considered this user performance to have a study artifact component. The Applicant did not propose mitigations in response to this failure.	

3.3 ADDITIONAL SUBJECTIVE FEEDBACK DURING PARTICIPANT DEBRIEF

We note that study participants provided general additional subjective feedback during the HF validation study debrief interview that are not specific to specific use tasks. For example, some participants indicated that the stopcocks for Genosyl are different than those on other products they are familiar with and/or the stopcocks might be a source of confusion; or some participants indicated that the manual ventilation process for Genosyl is different than with other products they are familiar with. While we acknowledge this feedback, we also note that there were no associated failures, close calls, or use difficulties in the HF validation study with the aforementioned aspects of the proposed product. As such, we do not have any recommendations at this time; however, we recommend that the Applicant take the study participants' feedback and recommendations into consideration.

4 LABELS AND LABELING - FINDINGS AND RECOMMENDATIONS

Our evaluation of the proposed label and labeling identified areas of vulnerability that may lead to medication errors. Tables 3 and 4 below include the identified medication error issues with the submitted label and labeling, DMEPA's rationale for concern, and the proposed recommendation to minimize the risk for medication error. Table 3 is for the Division and Table 4 is for the Applicant. We ask that the Division convey Table 4 in its entirety to the Applicant so that recommendations are implemented prior to approval of this NDA 202860.

Table 3: Identified Issues and Recommendations for Division of Cardiovascular and Renal Products

Prescribing Information			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
General Issues			
1.	The proposed proprietary name inappropriately uses tall man lettering.	The capital letters "NO" in GeNOSyl is a form of tall man lettering. The tall man lettering technique is reserved for established name pairs with demonstrated name confusion.	We recommend that all instances of tall man lettering in the Prescribing Information are revised so that that the entire proposed proprietary name is presented in title case.
2.	The proposed proprietary name contains non-standard phonetic descriptor.	The presence of the macron above the letter "e" in the proprietary name is non-	We recommend that all instances of the macron in the proposed proprietary name be removed.

		standard and may lead to confusion.	
Full Prescribing Information			
1.	The storage information in Section 16 How Supplied/Storage and Handling does not contain the temperature scale designation (i.e., "°C") after each numerical value.	Lack of clarity regarding product storage might contribute to deteriorated drug product errors.	We recommend revising the phrase "...with excursions permitted to 15– 30°C (59– 86°F)" is revised to "...with excursions permitted to 15°C– 30°C (59°F– 86°F)".
2.	Section 16 does not include the product NDC number.	We are unable to review the intended NDC number for appropriateness.	We recommend the Applicant revise to the PI to include the NDC number.

Table 4: Identified Issues and Recommendations for Vero Biotech (entire table to be conveyed to Applicant)

Operator's Manual			
1.	The proposed proprietary name inappropriately uses tall man lettering.	The capital letters "NO" in GeNOsyl is a form of tall man lettering . The tall man lettering technique is reserved for established name pairs with demonstrated name confusion.	Revise all instances of tall man lettering so that that the entire proposed proprietary name is presented in title case.
2.	The proposed proprietary name contains a non-standard phonetic descriptor.	The presence of the macron above the letter "e" in the proposed proprietary name is non-standard and may lead to confusion.	We recommend that all instances of the macron in the proposed proprietary name be removed.
Container Label - cassette			
1.	The proposed proprietary name inappropriately uses tall man lettering .	The capital letters "NO" in GeNOsyl is a form of tall man lettering. The tall man lettering technique is reserved for established	Revise all instances of tall man lettering so that that the entire proposed proprietary name is presented in title case.

		name pairs with demonstrated name confusion.	
2.	The proposed proprietary name contains a non-standard phonetic descriptor.	The presence of the macron above the letter “e” in the proposed proprietary name is non-standard and may lead to confusion.	We recommend that all instances of the macron in the proposed proprietary name be removed.
3.	The “Rx Only” statement is overly prominent and takes readers attention away from more important product information on the primary display panel (PDP).	The increased prominence of the “Rx Only” statement takes the reader’s attention away from other important information on the PDP such as proprietary name, established name, dosage form statement and strength statement.	Decrease the prominence of the “Rx Only” statement.
4.	The storage information does not contain the temperature scale designation (i.e., “°C”) after each numerical value.	Lack of clarity regarding product storage might contribute to deteriorated drug product errors.	Revise the phrase “...with excursions permitted to 15–30°C (59– 86°F)” is revised to “...with excursions permitted to 15°C– 30°C (59°F– 86°F)”.
5.	The container label does not include a usual dose statement.	A usual dose statement is required per 21 CFR 201.55.	Revise the container label to include the statement “Recommended Dosage: See prescribing information.”
Console package label			
1.	Refer to container label (cassette) recommendations #1—2 and revise accordingly.		
Carton Labeling (cassette package label)			
1.	Refer to container label (cassette) recommendations #1—5 and revise accordingly.		

2.	The carton labeling does not include a 2D barcode.	In September 2018, FDA released draft guidance on product identifiers required under the Drug Supply Chain Security Act. ^d The Act requires manufacturers and repackagers, respectively, to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce beginning November 27, 2017, and November 27, 2018, respectively.	We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling.
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^d The draft guidance is available from: <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf>

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 5 presents relevant product information for Genosyl that Vero Biotech submitted on August 8, 2019.

Table 5. Relevant Product Information for Genosyl	
Initial Approval Date	N/A
Active Ingredient	nitric oxide
Indication	to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents
Route of Administration	inhalation
Dosage Form	for inhalation
Strength	available at concentrations up to 800 ppm (b) (4)
Dose and Frequency	The recommended dose of Genosyl is 20 ppm. Maintain treatment up to 14 days or until the underlying oxygen desaturation has resolved and the neonate is ready to be weaned from Genosyl therapy.
How Supplied	Genosyl (b) (4) drug product cassettes contain at least 216 liters at STP of nitric oxide gas in 800 ppm (b) (4). The main components of the Genosyl (b) (4) are the consoles and the cassette.
Storage	Store at 25°C (77°F) with excursions permitted between 15–30°C (59–86°F) [see USP Controlled Room Temperature].

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On October 1, 2019, we searched the L:drive and AIMS using the term, Genosyl, to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified four previous relevant reviews, and we confirmed that our previous recommendations were implemented or considered.

Table 5. Summary of Previous DMEPA Reviews for Genosyl		
OSE RCM #	Review Date	Summary of Recommendations
2016-1312 ^e	10/18/2016	<i>HF protocol review</i> A. Validating product for conditions of clinical study: We recommended that the Sponsor conduct HF testing prior to starting clinical study. B. Validating product for commercialization: We recommended the Sponsor provide summary of formative HF studies and a revised FMEA. Also provided several recommendations for HF study protocol.
2017-1616 ^f	9/6/2017	<i>HF protocol review</i> Our review of the human factors validation study protocols identified several areas of concern where additional clarification, changes, or additional information is necessary. We recommended that the protocols be revised to address our concerns and to ensure that the methodology is acceptable.
2018-1578 and 2018-1579 ^g	1/4/2019	<i>HF results review</i> We concluded that the HF study did not provide sufficient evidence to demonstrate that the proposed product could be used safely and effectively by the intended users for its intended uses and use environments. The HF study methodology and study implementation had notable flaws that

^e Lowery, A. Human Factors Protocol Review for Genosyl IND 109066. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 OCT 18. RCM No.: 2016-1312.

^f Lowery, A. Human Factors Protocol Review for Genosyl IND 109066. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 SEP 6. RCM No.: 2017-1616.

^g Stewart J. Human Factors Results and Label and Labeling Review for Genosyl NDA 202860. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 JAN 4. RCM No.: 2018-1578 and 2018-1579.

Table 5. Summary of Previous DMEPA Reviews for Genosyl		
OSE RCM #	Review Date	Summary of Recommendations
		limited the utility and interpretation of the results. Additionally, the study did not adequately evaluate participant ability to detect, comprehend, and implement the appropriate action(s) in response to critical alarms. Furthermore, study interruption and study artifact that occurred during the study confound the interpretation of study results. We also noted that the Applicant made several revisions to the product interface to address use-errors observed in the study; however, these revisions were not validated in a subsequent human factors study to ensure they are effective and do not introduce new use-related risks. We recommended that the Applicant evaluate the use-related errors observed in the HF study, employ additional mitigation strategies, update their use-related risk analysis, and conduct another HF validation study using appropriate study methodology and the finalized intend-to-market user interface.
2019-451 ^h	4/25/2019	<i>HF protocol review</i> Our review of the human factors validation study protocol identified several areas of concern. We provided recommendations for revisions.

^h Stewart J. Human Factors Protocol Review for Genosyl IND 109066. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 APR 25. RCM No.: 2019-451.

APPENDIX C. BACKGROUND INFORMATION ON HUMAN FACTORS ENGINEERING PROCESS

The background information can be accessed in EDR via:

[\\cdsesub1\evsprod\nda202860\0042\m5\53-clin-stud-rep\535-rep-effic-safety-stud\neonateshypoxicrespiratoryfailure\5354-other-stud-rep\ \(b\) \(4\) human-factors-validation-study-protocol-300-375.pdf](\\cdsesub1\evsprod\nda202860\0042\m5\53-clin-stud-rep\535-rep-effic-safety-stud\neonateshypoxicrespiratoryfailure\5354-other-stud-rep\ (b) (4) human-factors-validation-study-protocol-300-375.pdf)

APPENDIX D. HUMAN FACTORS VALIDATION STUDY RESULTS REPORT

The HF study results report can be accessed in EDR via:

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APPENDIX E. CDRH HUMAN FACTORS CONSULT REVIEW



ICC1900691 Vero
Biotech NDA 202860 (

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,ⁱ along with postmarket medication error data, we reviewed the following Genosyl labels and labeling submitted by Vero Biotech.

- Container label (cassette label) received on June 21, 2019
- Container label (Iso-Gard filter) received on June 21, 2019
- Carton labeling (cassette package labeling) received on June 21, 2019
- Console labeling
- Quick Reference Guide (Image not shown) received on August 8, 2019
 - o See EDR link: [\\cdsesub1\evsprod\nda202860\0048\m1\us\114-labeling\114a-draft-label\draft-genosyl-\(b\) \(4\) quick-reference-guide.docx](\\cdsesub1\evsprod\nda202860\0048\m1\us\114-labeling\114a-draft-label\draft-genosyl-(b) (4) quick-reference-guide.docx)
- Operator's Manual (Image not shown) received on August 8, 2019
 - o See EDR link: [\\cdsesub1\evsprod\nda202860\0048\m1\us\114-labeling\114a-draft-label\draft-genosyl-\(b\) \(4\) operators-manual.docx](\\cdsesub1\evsprod\nda202860\0048\m1\us\114-labeling\114a-draft-label\draft-genosyl-(b) (4) operators-manual.docx)
- Prescribing Information (Image not shown) received on August 8, 2019
 - o See EDR link: <\\cdsesub1\evsprod\nda202860\0048\m1\us\114-labeling\114a-draft-label\draft-genosyl-label-rev-c.docx>

ⁱ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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