# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 208437Orig1s000

# 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:** | July 19, 2017 |
| **Requesting Office or Division:** | Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) |
| **Application Type and Number:** | NDA 208437 |
| **Product Name and Strength:** | Lonhala Magnair (Glycopyrrolate) Solution for Inhalation 25 mcg per vial |
| **Applicant/Sponsor Name:** | Sunovion Respiratory Development Inc. |
| **Submission Date:** | June 15, 2017 |
| **OSE RCM #:** | 2016-1847-1 and 2016-2100-1 |
| **DMEPA Primary Reviewer:** | Lissa C. Owens, PharmD |
| **DMEPA Team Leader:** | Sarah K. Vee, PharmD |

## 1 PURPOSE OF MEMO

Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) requested that we review the finalized container labels and carton labeling for Lonhala Magnair (Appendix A) to determine if it is acceptable from a medication error perspective. This application received a complete response (CR) on May 26, 2017 due to deficiencies relating to the biocompatibility testing for the PARI eFlow closed system nebulizer. The application was resubmitted on June 15, 2017. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

## 2 CONCLUSION

We note that all of the revised container labels and carton labeling submitted do not contain the complete proposed proprietary name 'Lonhala Magnair' in the full presentation as conditionally approved. There are some label and labeling that contain 'Lonhala' only and some that contain 'Magnair' only. We make recommendations in Section 3.

[a] Owens, L Label and Labeling Review for Lonhala Magnair (NDA 208437). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 APR 14. RCM No.: 2016-1847 and 2016-2100

## 3 RECOMMENDATIONS FOR SUNOVION RESPIRATORY DEVELOPMENT INC.

We recommend the following be implemented prior to approval of this NDA:

### A. All Labels and Labeling

1. The conditionally acceptable proprietary name is, 'Lonhala Magnair. You have labeled some labels and labeling as 'Lonhala' only or 'Magnair' only. Update the labels and labeling to include the full conditionally acceptable name 'Lonhala Magnair' and resubmit for review.

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/s/

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LISSA C OWENS
07/19/2017

SARAH K VEE
07/19/2017

# MEMORANDUM

**REVISED REVIEW OF HUMAN FACTORS AND 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)

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|---|---|
| **Date of This Memorandum:** | May 26, 2017 |
| **Requesting Office or Division:** | Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) |
| **Application Type and Number:** | NDA 208437 |
| **Product Name and Strength:** | Lonhala Magnair (Glycopyrrolate) Solution for Inhalation 25 mcg per vial |
| **Applicant/Sponsor Name:** | Sunovion Respiratory Development Inc. |
| **Submission Date:** | July 29, 2016 and March 31, 2017 |
| **OSE RCM #:** | 2016-1847 and 2016-2100 |
| **DMEPA Primary Reviewer:** | Lissa C. Owens, PharmD |
| **DMEPA Team Leader (Acting):** | Sarah K. Vee, PharmD |
| **DMEPA Associate Director Human Factors:** | QuynhNhu Nguyen, MS |

## 1 PURPOSE OF MEMO

On March 17, 2017, an Information Request (IR) was sent to clarify the potential risks for harm (which includes compromised medical care) for several use errors and difficulties listed in the human factors report that may result in the device being unable to deliver medication, including difficulty inserting the drug vial into the medicine cap, and on March 31, 2017, Sunovion responded to the IR (see Appendix A).

On May 23, 2017, DMEPA and CDRH discussed the IR response internally and agreed to send another IR requesting that Sunovion: 1) submit an updated risk analysis which includes an analysis of the underdosing risk and describe existing mitigations that are built into the product design to address this risk; 2) indicate if additional mitigations are necessary and submit a description of the proposed modifications, including an assessment of whether additional human factors validation data are needed (See Appendix A). However, per the DPARP clinical team, "the issue of underdosing is not a safety concern as the product is not used for acute

treatment of symptoms…[if] a patient continues making the error repetitively, [they] will see their physician with a complaint that their medication is not working". This is in alignment with our initial assessment for these errors in our review dated 04/14/2017[a]. DPARP finds that the residual risk may be managed through labeling and human factors will not be listed as a deficiency in the pending Complete Response (CR) for this application. Therefore, the IR was not sent.

## 2 CONCLUSION

Based on the clinical information DPARP provided, we agree that no further information is required at this time from Sunovion regarding the potential under-dosing errors associated with vials that are pierced open prior to inserting the aerosol head but are not empty, and agree that human factors is not included in the CR letter for this application.

[a] Owens, Lissa C. Human Factors, Label, Labeling, and Packaging Review for Lonhala Magnair NDA 208437. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Apr 14. RCM No.: 2016-1847 and 2016-2100

## APPENDIX A. OTHER

CDRH Information Request sent on March 17, 2017:

CDRH IR.pdf

Sunovion Response to Information Request, received on March31, 2017:

1.11.1 Quality Info. Amendme...

Draft Information Request Language (not sent):

(b) (5)

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/s/

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LISSA C OWENS
05/26/2017

SARAH K VEE
05/26/2017

QUYNHNHU T NGUYEN
05/26/2017

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

# PATIENT LABELING REVIEW

| | |
|---|---|
| Date: | May 10, 2017 |
| To: | Badrul Chowdhury, MD, PhD<br>Director<br>**Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)** |
| Through: | LaShawn Griffiths, MSHS-PH, BSN, RN<br>Associate Director for Patient Labeling<br>**Division of Medical Policy Programs (DMPP)**<br><br>Marcia Williams, PhD<br>Team Leader, Patient Labeling<br>**Division of Medical Policy Programs (DMPP)** |
| From: | Nyedra W. Booker, PharmD, MPH<br>Patient Labeling Reviewer<br>**Division of Medical Policy Programs (DMPP)**<br><br>Taylor Burnett, PharmD<br>Regulatory Review Officer<br>**Office of Prescription Drug Promotion (OPDP)** |
| Subject: | Review of Patient Labeling: Patient Package Insert (PPI) and Instructions for Use (IFU) |
| Drug Name (established name): | LONHALA MAGNAIR (glycopyrrolate) |
| Dosage Form and Route: | inhalation solution, for oral inhalation use |
| Application Type/Number: | NDA 208437 |
| Applicant: | Sunovion Respiratory Development Inc. |

## 1 INTRODUCTION

On July 28, 2016, Sunovion Respiratory Development Inc. submitted for the Agency's review an original New Drug Application (NDA) 208437 for LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use. The proposed indication for LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use is for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) on August 22, 2016, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and a separate DMEPA review of the IFU was completed on April 14, 2017.

## 2 MATERIAL REVIEWED

- Draft LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use PPI and IFU received on July 28, 2016, revised by the review division throughout the review cycle, and received by DMPP and OPDP on April 18, 2017.
- Draft LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use Prescribing Information (PI) received on July 28, 2016, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 18, 2017.
- Approved SEEBRI NEOHALER (glycopyrrolate) inhalation powder, for oral inhalation use comparator labeling dated January 19, 2017.

## 3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6$^{th}$ to 8$^{th}$ grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8$^{th}$ grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We have reformatted the PPI and IFU document using the Arial font, size 10 and 11 respectively.

In our collaborative review of the PPI and IFU we have:

- simplified wording and clarified concepts where possible
- ensured that the PPI and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI and IFU are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI and IFU meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

## 4 CONCLUSIONS

The PPI and IFU are acceptable with our recommended changes.

## 5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI and IFU is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI and IFU.

Please let us know if you have any questions.

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/s/

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NYEDRA W BOOKER
05/10/2017

TAYLOR B BURNETT
05/10/2017

MARCIA B WILLIAMS
05/10/2017

LASHAWN M GRIFFITHS
05/10/2017

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

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

## Memorandum

**Date:** May 3, 2017

**To:** Sadaf Nabavian, Pharm.D.
Regulatory Project Manager
Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)

**From:** Taylor Burnett, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

**Through:** Puja Shah, Pharm.D., RAC
Regulatory Review Officer
OPDP

**CC:** Kathleen Klemm, Pharm.D., RAC
Team Leader
OPDP

**Subject:** NDA 208437
OPDP labeling comments for LONHALA MAGNAIR (glycopyrrolate) inhalation solution, for oral inhalation use (Lonhala)

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OPDP has reviewed the proposed draft labeling (Package Insert [PI] and Carton and Container Labeling) for Lonhala submitted for consult on August 22, 2016. OPDP's comments on the proposed Patient Package Insert (PPI) and Instructions for Use (IFU) will be provided at a later date under separate cover in collaboration with the Division of Medical Policy Programs (DMPP).

OPDP's comments on the PI are provided directly in the marked-up document attached (see below) and are based on the proposed draft marked-up labeling available via SharePoint at:

http://sharepoint.fda.gov/orgs/CDER-ODEII-DPARP/RPM/Sadaf/NDA 208437_Glycopyrrolate_Sunovion/Labeling/11413-proposed-track-changes7apr17.doc

OPDP has no comments on the proposed carton and container labeling at this time.

Thank you for the opportunity to comment on the proposed labeling.

If you have any questions, please contact Taylor Burnett at (240) 402-1349 or taylor.burnett@fda.hhs.gov.

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TAYLOR B BURNETT
05/03/2017

**HUMAN FACTORS RESULTS, LABEL, LABELING, AND PACKAGING 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:** | April 14, 2017 |
| **Requesting Office or Division:** | Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) |
| **Application Type and Number:** | NDA 208437 |
| **Product Name and Strength:** | Lonhala Magnair (Glycopyrrolate) Solution for Inhalation 25 mcg per vial |
| **Product Type:** | Drug-Device Combination Product |
| **Rx or OTC:** | Rx |
| **Applicant/Sponsor Name:** | Sunovion Respiratory Development Inc. |
| **Submission Date:** | July 29, 2016 |
| **OSE RCM #:** | 2016-1847 and 2016-2100 |
| **DMEPA Primary Reviewer:** | Lissa C. Owens, PharmD |
| **DMEPA Team Leader (Acting):** | Sarah K. Vee, PharmD |
| **DMEPA Associate Director for Human Factors:** | QuynhNhu Nguyen, MS |

# 1 REASON FOR REVIEW

This review responds to a request from the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) to review the Human Factors (HF) validation study report, proposed container label, carton labeling, and Prescribing Information (PI) submitted on July 29, 2016 as a 505(b)(2) submission under NDA 208437. As part of the approval process Lonhala Magnair, we reviewed the HF validation study report and proposed labeling for any vulnerability from a medication error perspective

# 2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

**Table 1. Materials Considered for this Label and Labeling Review**

| Material Reviewed | Appendix Section (for Methods and Results) |
|---|---|
| Product Information/Prescribing Information | A |
| Previous DMEPA Reviews | B |
| Human Factors Study | C |
| ISMP Newsletters | D-N/A |
| FDA Adverse Event Reporting System (FAERS)* | E-N/A |
| Other | F |
| Labels and Labeling | G |

N/A=not applicable for this review
*We do not typically search FAERS for label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

# 3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

## 3.1 HUMAN FACTORS VALIDATION STUDY

A total of 91 participants (45 trained and 46 untrained) participated in the Human Factors validation study. The study evaluated the following three critical tasks: Deliver a treatment and prepare device for storage which includes the subtasks: device assembly, treatment delivery, and device cleaning, Use easycare for weekly maintenance of aerosol head, and IFU interpretation exercise. DMEPA previously reviewed the HF protocol found the protocol acceptable under OSE RCM 2013-2728[a] . We note that the study was conducted by a test team (b) (4) ) and then further evaluated by Sunovion.

Task 1: Deliver a Treatment and Prepare Device for Storage (includes device assembly, treatment delivery, and device cleaning)

Overall 86 out of 91 participants were successful in completing the task. Of the five failures, one was considered related to safety and four were due to test administrator assistance, which are considered as task failures.

[a] Owens, Lissa C. Human Factors Protocol Memorandum for Sun-101 (Glycopyrrolate) IND 110663. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 Jan 10. RCM No.: 2013-2728

Regarding the one safety-related failure, one untrained participant inserted the drug vial before inserting the aerosol head which caused some of the medication to leak out of the drug vial and into the nebulizer. A partial dose would be delivered. The participant recognized the partial dose and referred to the IFU to troubleshoot. The participant determined that the nebulizer ran out of medication early and inserted a new vial correctly and therefore would have given more than one dose of medication. Sunovion believes that there is a low residual risk associated with this use error and does not warrant modifications to the device design. They state that clinical studies have demonstrated the safety and tolerability of single doses up to 20 fold higher than the maximum dose expected to be recommended for the approved product. While we note that this is a safety-related error in which a participant would have received an extra dose, we confirmed Sunovion's claim with the medical officer that no harm would come to the patient with the one extra dose. Sunovion proposed changes to the trouble shooting section of the IFU to address partially delivered vials (see Appendix C2). As the participant consulted the IFU for instructions on how to handle the partial vial, the proposed changes to the trouble shooting section of the IFU will attempt to mitigate these types of errors. In addition, we agree with the proposed changes to the IFU to clarify the prominence of important safety information and illustrations.

The participants requiring test administer assistance in Task 1 required assistance to know to use the handset to deliver treatment, insert drug vial into medication cap, and insert connection cord into correct side of controller. These instances are further discussed under the corresponding subtasks listed below

Subtask: Know to use Handset to Deliver Treatment

Two (one trained, one untrained) participants inserted the aerosol head into the easycare, rather than into the handset, while assembling the nebulizer to deliver a treatment. As such, the participants were unable to deliver the treatment using the nebulizer (i.e., did not produce aerosol mist). These participants ultimately required test administrator assistance to know to insert the aerosol head into the handset rather than the easycare. These errors would result in a delay in therapy. Root causes were identified by Sunovion as similar appearance of easycare and handset. One participant pointed out the cropped nature of the illustration on the bottom of the IFU which displays only a portion of the handset. The illustration can be mistaken for the easycare due to its similar shape and size and performance anxiety. Sunovion proposed changes to include the full illustration to address this issue (See Appendix C2). We agree that the proposed changes are acceptable to mitigate the risk of confusing the handset and the easycare. We do not believe the changes made require additional human factor validation testing.

Subtask: Insert Drug Vial into Medication Cap

One untrained participant repeatedly attempted to force the drug vial through the medication cap's top with the drug vial's flat tab first. This participant was unknowingly orienting the medication cap upside-down. As a result, the participant was unaware that he was inserting the drug vial through the medication cap's top, rather than the medication cap's bottom, even though he repeatedly read the IFU instruction. The test team attributed this participant's use error to the fact that a user can insert the drug vial into the medication cap in various orientations and negative transfer from using other nebulizer vials. Sunovion states that this error would result in a delay of therapy and will diminish over time with continued use and utilizing the training materials and help line. We note that the instructions for use are clear in showing the direction

the drug vial is inserted into the medication cap and that no further mitigations are needed at this time.

Subtask: Insert Connection Cord into Correct Side of Controller

One trained participant inserted the connection cord into the controller's gray side and repeatedly attempted to insert the AC adapter into the controller's blue side. When the participant attempted to power on the controller, it produced an error tone because the connection cord was inserted into the wrong side of the controller. The test team attributed this error to the fact that the connection cord fits relatively securely in the controller's gray side by virtue of the secure seal created between the connection cord's rubber rim and the controller's port. As such, this participant likely sensed that the connection cord was inserted securely, which led them to assume they inserted the connection cord correctly. Sunovion states that this error would result in a delay of therapy and will diminish over time with re-reading the instructions, watching the instructional video, or seeking help from the help line. We agree with Sunovion and no further mitigations are needed at this time.

Task 2: Use Easycare for Weekly Maintenance of Aerosol Head

There was one failure due to test administrator assistance. One untrained participant initially struggled to identify the aerosol head among the other nebulizer components. Sunovion states that this use error would result in a delay in performing weekly maintenance of the aerosol head and no effect on the therapy. They proposed changes to the IFU to further clarify the components of the nebulizer (see Appendix C2). We agree that the proposed changes are acceptable to mitigate the risk of confusing the handset and the easycare. We do not believe the changes made require additional human factor validation testing.

Task 3: IFU Interpretation Exercise

There were no errors observed in this task.

Errors with limited potential for harm or negative effect

There were eighteen additional errors by 8 trained and 10 untrained participants that Sunovion determined would have limited potential for harm or negative effect (Appendix C).

We note that all of these errors would result in an underdose, a no dose, or a delay in therapy. However, since Glycopyrrolate is a maintenance medication, a one-time occurrence of an underdose, a no dose, or a delay in therapy will not cause harm to the users. In addition, with repeated use of the nebulizer, we expect that users will become more familiar with the proper use. However, we acknowledge that Sunovion did not provide additional data to support that user difficulties will diminish with repeated use.

## 3.2 LABELS AND LABELING

DMEPA also reviewed the proposed labels and labeling to determine whether there are any significant concerns in terms of safety related to preventable medication errors.

We note that, as agreed upon in the June 2015 Written Response, Sunovion will have the established name on each LDPE vial at launch and the tradename will be added to each vial post-launch.

Sunovion plans to make a demonstration kit available for healthcare providers to demonstrate to patients or for sales representatives to demonstrate to healthcare providers. Sunovion anticipates

the need for placebo refills for these demonstration kits; therefore, a Demonstration Starter Kit and Demonstration Refill Kit are also proposed and labeling submitted.

We note that the proprietary name, Lonhala Magnair, is conditionally acceptable and recommend that the name be included on the labels and labeling.

## 4 CONCLUSION & RECOMMENDATIONS

We find the HF validation study data acceptable. Sunovion has proposed changes to the IFU based on the results of the validation study. We find the changes to the IFU acceptable and do not require additional human factors validation testing of the proposed changes at this time.

We also find the Prescribing Information acceptable from a medication error perspective. However, we make recommendations to the label and labeling in section 4.1.

### 4.1 RECOMMENDATIONS FOR SUNOVION

We recommend the following be implemented prior to approval of this NDA supplement:

**A. All Label and Labeling**

1. Update the placeholder on the labels and labeling to include the conditionally acceptable proprietary name, 'Lonhala Magnair. Ensure that the established name is at least ½ the size of the proprietary name and in accordance with 21 CFR 201.10(g)(2).

## APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

## APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Lonhala Magnair that Sunovion submitted on July 29, 2016.

| **Table 2. Relevant Product Information for Lonhala Magnair** | |
|---|---|
| **Initial Approval Date** | N/A |
| **Active Ingredient** | Glycopyrrolate |
| **Indication** | long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) |
| **Route of Administration** | Oral inhalation |
| **Dosage Form** | Solution for Inhalation |
| **Strength** | 25 mcg per vial |
| **Dose and Frequency** | One vial twice daily using device |
| **How Supplied** | Starter Kit with 30 day supply (30 pouches with 2 vials per pouch) and complete DEVICE nebulizer system<br><br>Refill Kit with 30 day supply (30 pouches with 2 vials per pouch) and DEVICE refill handset |
| **Storage** | 20°-25°C (68°-77°F) [see USP Controlled Room Temperature] |

## APPENDIX B. PREVIOUS DMEPA REVIEWS

### B.1 Methods

On March 8, 2017, we searched the L:drive and AIMS using the terms, Lonhala Magnair to identify reviews previously performed by DMEPA.

### B.2 Results

Our search identified two previous proprietary name reviews that are not relevant to this review.

## APPENDIX C. HUMAN FACTORS STUDY

### C.1 Objective and Study Design

The test's purpose was to confirm that the nebulizer meets users' needs as required by the U.S. Food and Drug Administration's (FDA) Quality System Regulation. The test was designed to determine whether the nebulizer is vulnerable to potentially harmful use errors that could lead to patient injury, serious harm, delays in therapy, or sub-optimal therapy.

The participant could refer to the device's instructional material, which includes the IFU, QRG, instructional DVD, and support line phone number at any time during the tasks. The support line featured actual PARI representatives who were prepared to respond to phone calls from the usability test participants.

Participants:

A total of 92 individuals representing six distinct user groups participated in the summative usability test. We disqualified one individual after she participated in the usability test session.[4] As such, we excluded this participant's data from all test report findings,[5] and this report presents the data from 91 individual test sessions. The sample of intended users included:

- 15 COPD patients who did not receive training on the device prior to the test session
- 15 COPD patients who received training on the device prior to the test session
- 15 caregivers who did not receive training on the device prior to the test session
- 16 caregivers who received training on the device prior to the test session
- 15 healthcare professionals who did not receive training on the device prior to the test session
- 15 healthcare professionals who received training on the device prior to the test session

Method:

Accordingly, half of the test participants received training prior to the usability test session. Layperson test participants (i.e., patients with COPD and caregivers) received training one-on-one with the trainer. HCPs received training either one-on-one or in small groups of up to three participants per group.

All trained individuals participated in the test session after at least one overnight after the associated training session. This training delay appropriately simulated the real world use scenario, in which users might not begin using the device until the day following the training session.

Each usability test session involved one participant and lasted up to 1.5 hours. During each test session, we introduced the participant to the test personnel, oriented him/her to the environment, and described the planned activities. Next, we administered an interview focused on the participant's background (e.g., demographic traits, nebulizer experience) and then instructed participants to perform three tasks (Table 1). After each task, the test administrator conducted a post-task interview including open-ended questions regarding task performance. The post-task interview included questions such as: "Do you recall making any mistakes that could have been hazardous to you / your patient's health while working with the nebulizer?" We recorded objective task performance measures such as instances of test administrator assistance, and we recorded use errors, close calls, and operational difficulties.

After participants completed all three tasks, we administered a post-test interview focused on task performance and the participants' perception of the nebulizer's use-safety.

Critical Tasks:

| # | Task |
|---|---|
| 1 | Deliver a treatment and prepare device for storage[7] |
| 2 | Use easycare for weekly maintenance of aerosol head |
| 3 | IFU interpretation exercise |

## C.2 Results

Overall task step performance by all participants:

| Task # | Task description | Number of participants who performed the task | Overall task pass rate | Safety-related pass rate | Failures due to use errors with limited potential for negative effect | Failures due to safety-related use errors | Failures due to test administrator assistance |
|---|---|---|---|---|---|---|---|
| 1 | Deliver a treatment and prepare device for storage[8] | 91 | n=70 (76.9%) | n=86 (94.5%) | 18 | 1 | 4 |
| 2 | Use easycare for weekly maintenance of aerosol head | 91 | n=90 (98.9%) | n=90 (98.9%) | 0 | 0 | 1 |
| 3 | IFU interpretation exercise | 91 | n=91 (100%) | n=91 (100%) | 0 | 0 | 0 |

### Test administrator assist summary

| Assist description (Required assistance to …) | IDs of participants who required assistance | Task during which the assist occurred |
|---|---|---|
| *Know to use handset to deliver treatment* | PT13, C9 | Task 1 – Deliver a treatment and prepare device for storage[12] |
| *Insert drug vial into medication cap* | P10 | Task 1 – Deliver a treatment and prepare device for storage |
| *Insert connection cord into correct side of controller* | PT12 | Task 1 – Deliver a treatment and prepare device for storage |
| *Know to use easycare for weekly aerosol head maintenance* | C5 | Task 2 – Use easycare for weekly maintenance of aerosol head |

**Use errors**

One participant committed one safety-related use error when performing the tasks.

Eighteen out of 91 participants committed 10 types of use errors with limited potential for harm or negative effect on prescribed therapy. These participants committed 19 use errors in total.

Sixty-five out of 91 participants committed 23 types of use errors with no potential for harm or negative effect on prescribed therapy when performing the tasks. These participants committed 161 use errors in total.

**Participant feedback**

After participants completed all tasks, we asked them to provide their impression of whether the nebulizer is safe to use "as-is," or whether the nebulizer requires modifications to ensure safe use.

Note: We do not cite the following summary of test participants' subjective feedback as evidence of the nebulizer's use-safety, nor as a basis for design validation. Rather, we present the subjective information to provide readers with a more complete picture of participants' experience using the nebulizer.

Eighty-six out of 91 participants considered the nebulizer safe to use "as-is." The five participants who said the nebulizer required modifications to ensure safe use made suggestions such as revising Quick Reference Guide (QRG) "Assemble and use" Step 2B to emphasize the aerosol head, and modifying the controller such that it is rechargeable.

## Changes to be made based on the Validation Study

Since the eFlow CS nebulizer is intended to deliver a maintenance medication, a several minute or even hour delay in therapy resulting from the errors described in Section 6 will not cause harm to users. Furthermore, with respect to the single instance of a safety-related use error of over dosing, users cannot realistically receive a harmful dose of the nebulizer's drug, SUN-101 (glycopyrrolate) Inhalation Solution under normal use. Clinical studies have demonstrated the safety and tolerability of single doses up to 20 fold higher than the maximum dose expected to be recommended for the approved product.

To further improve the usability of the eFlow CS, Sunovion plans to make minor modifications to the IFU as described in Table 16:

## Use Errors with limited potential for harm or negative effect

Table 16: Sunovion's modification plan for the final IFU

| Original Content | Revised Content | Justification |
|---|---|---|
| (b) (4) | | |

| Original Content | Revised Content | Justification |
| --- | --- | --- |
| (b) (4) | | |

**F. Other**


summative-usa...


Lonhala human-factors-...

## 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,[b] along with postmarket medication error data, we reviewed the following Lonhala Magnair labels and labeling submitted by Sunovion on July 29, 2016.

- Carton labeling
- Container label
- Prescribing Information

### G.2 Label and Labeling Images

**Aerosol Head Blister Backing Launch**

(b) (4)

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

14 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

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