Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee February 15, 2023

Location: Please note that due to the impact of this COVID-19 pandemic, all meeting participants will be joining this advisory committee meeting via an online teleconferencing platform

Topic: The committees discussed supplemental new drug application 208411/S–006, for NARCAN (naloxone hydrochloride) nasal spray, 4 mg/0.1 mL, submitted by Emergent BioSolutions Inc. NARCAN is proposed for nonprescription treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. The issues discussed were on the adequacy of the data supporting the nonprescription application. This product represented a potential first in class product in a new therapeutic category for nonprescription drugs.

These summary minutes for the February 15, 2023 joint meeting of the Nonprescription Drugs Advisory Committee (NDAC) and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) of the Food and Drug Administration were approved on March 23, 2023.

I certify that I attended the February 15, 2023 joint meeting of the NDAC and the AADPAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Moon Hee V. Choi, PharmD	Maria C. Coyle, PharmD, FCCP, BCPS, BCACP, CLS
Designated Federal Officer, NDAC	Chairperson, NDAC

Final Summary Minutes of the Nonprescription Drugs Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee Joint Meeting
February 15, 2023

The Nonprescription Drugs Advisory Committee (NDAC) and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on February 15, 2023. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Emergent BioSolutions, Inc. The meeting was called to order by Maria C. Coyle PharmD, FCCP, BCPS, BCACP, CLS (Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Designated Federal Officer). There were approximately 466 people online. There was a total of six Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda:
The committees discussed supplemental new drug application 208411/S–006, for NARCAN (naloxone hydrochloride) nasal spray, 4 mg/0.1 mL, submitted by Emergent BioSolutions Inc. NARCAN is proposed for nonprescription treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. The issues discussed were on the adequacy of the data supporting the nonprescription application. This product represented a potential first in class product in a new therapeutic category for nonprescription drugs.

Attendance:

Nonprescription Drugs Advisory Committee Members Present (Voting): Maria C. Coyle, PharmD, FCCP, BCPS, BCACP, CLS; Stephen C. Clement, MD; Diane B. Ginsburg, PhD, MS, RPh, FASHP; Ruth M. Parker, MD, MACP; Paul Pisarik, MD, MPH, FAAFP; Katalin E. Roth, JD, MD; Leslie Walker-Harding, MD, FAAP, FSAHM

Nonprescription Drugs Advisory Committee Members Not Present (Voting): Elma D. Baron, MD; Tonya S. King, PhD

Nonprescription Drugs Advisory Committee Member (Non-Voting): Mark E. Dato, MD, PhD (*Industry Representative*)

Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Brian T. Bateman, MD, MSc; Mark C. Bicket, MD, PhD, FASA; Jennifer Higgins, PhD, MBA (*Consumer Representative*); Maura S. McAuliffe, CRNA, MSN, MSNA, PhD, FAAN; Mary Ellen McCann, MD, MPH; Timothy J. Ness, MD, PhD; Rebecca Richmond, PharmD, BCPS; Abigail B. Shoben, PhD; Michael Sprintz, DO, DFASAM

Anesthetic and Analgesic Drug Products Advisory Committee Member Not Present (Voting): Maryam Jowza, MD; Sherif Zaafran, MD, FASA

Anesthetic and Analgesic Drug Products Advisory Committee Member Present (Non-Voting): Jay Horrow, MD, MS, FACC (*Industry Representative*)

Temporary Members (Voting): Jordan Marie Ballou; PharmD, BCACP; Jeffrey Brent, MD, PhD; Elizabeth Coykendall, NRP (*Patient Representative*)

FDA Participants (Non-Voting): Theresa Michele, MD; Jody Green, MD; Dorothy Chang, MD; Barbara Cohen, MPA; Millie Shah, PharmD, BCPS

Designated Federal Officer (Non-Voting): Moon Hee V. Choi, PharmD

Open Public Hearing Speakers Present: Bobby Mukkamala, MD (American Medical Association); Bonnie Milas, MD; Jessica Hulsey (Addiction Policy Forum); Terry Wilcox (Patients Rising); Fred Wells Brason II (Project Lazarus); David C. Spangler (Consumer Healthcare Products Association)

The agenda was as follows:

Call to Order	**Maria C. Coyle, PharmD, FCCP, BCPS, BCACP, CLS** Chairperson, NDAC
Introduction of Committee and Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Designated Federal Officer, NDAC
FDA Opening Remarks	**Jody Green, MD** Deputy Director for Safety Division of Nonprescription Drugs I (DNPD I) Office of Nonprescription Drugs (ONPD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Emergent BioSolutions, Inc.**
Introduction	**Manish Vyas, BSc, EMBA** Senior Vice President, Regulatory Affairs Emergent BioSolutions
NARCAN® Nasal Spray 4 mg and the OTC Development Program	**Gay Owens, PharmD, MBA** Global Medical Affairs Lead, Opioid Antidote Emergent BioSolutions

APPLICANT PRESENTATIONS (CONT.)

Medical Need for OTC Nasal Naloxone	**Scott Hadland, MD, MPH, MS** Chief, Division of Adolescent and Young Adult Medicine Massachusetts General Hospital – Harvard Medical School
Human Factors Study	**Sarah Farnsworth, PhD** Vice President, Scientific Affairs PEGUS Research
NARCAN® Benefit-Risk Overview & Conclusion	**Manish Vyas, BSc, EMBA**

Clarifying Questions

BREAK

FDA PRESENTATIONS

Regulatory Overview of Narcan Nasal Spray & Postmarketing Safety Data	**Dorothy Chang, MD** Senior Physician DNPD I, ONPD, OND, CDER, FDA
OTC Naloxone Model Drug Facts Label Comprehension Study	**Barbara Cohen, MPA** Social Science Analyst Division of Nonprescription Drugs II ONPD, OND, CDER, FDA
Human Factors Validation Study	**Millie Shah, PharmD, BCPS** Senior Pharmacist Division of Medication Error Prevention and Analysis II, Office of Surveillance and Epidemiology CDER, FDA

Clarifying questions for FDA

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee	**Jody Green, MD**

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion (cont.)

ADJOURNMENT

Questions to the Committees:

1. **DISCUSSION**: Discuss the safety profile for use of Narcan Nasal Spray (NNS) in the nonprescription setting.

   Committee Discussion*: The committee members agreed the safety profile for use of naloxone nasal spray in the nonprescription setting to be well established without any substantial concerns. One committee member emphasized that the safety profile was favorable enough to include the pediatric population who may need it themselves or may administer it to save a life. Several committee members agreed that even in the setting where naloxone was used but the patient had a different reason for unresponsiveness, naloxone did not affect those situations negatively. One committee member recommended monitoring for unintended consequences of increased naloxone availability, including the risk of greater opioid abuse, but this member acknowledged that there are no data that currently supports this concern. Some committee members expressed disagreement with this concern and stated that the fear of more opioid use due to greater access of naloxone is a common but unfounded fear. Please see the transcript for details of the Committees' discussion.*

2. **DISCUSSION**: Discuss whether the results of the Human Factors validation study (HFVS) support that consumers are able to correctly administer nonprescription NNS in an emergency situation.

   a. Discuss the HFVS study design, and the interpretability of the study.

   b. Discuss the use errors observed in the HFVS where participants started with Step 3 (Call 911) during the simulation and bypassed Steps 1 and 2.

      i. Could the intend-to-market nonprescription carton be further improved to mitigate risk of delayed administration?

Committee Discussion*: Overall, the committee members agreed that the Human Factors validation study (HFVS) design was less than optimal, but they acknowledged its utility in informing the Applicant's newly proposed product packaging. Several committee members agreed that an additional HFVS on the newly proposed packaging and its usability by pediatric population (e.g., ages 10-14 years old) would ideally be conducted, but they also acknowledged that FDA is unable to require that the Applicant conduct these types of studies in the postmarketing phase. Given the public health need, many committee members emphasized that the desire for these additional data should not delay the availability of this product as a nonprescription drug. One committee member noted that the Applicant's newly proposed*

product packaging including the addition of a Quick Start Guide and the placement of the steps for use sequentially all on one panel is unlikely to make users' performance worse and could only help.

With regard to the use errors observed in the HFVS where participants started with Step 3 (Call 911) during the simulation and bypassed Steps 1 and 2, one member recommended that calling 911 might be a valid first step because a 911 staff member might be able to provide guidance on how to administer the naloxone spray. Another member highlighted that bypassing Steps 1 and 2 could lead to delays in administering naloxone treatment due to 911 wait times. In regard to concerns and improvements involving instructions and placement on the carton, the majority of the members agreed that the Applicant should include all instructions on the back of the package as well as in a package insert. Please see the transcript for details of the Committees' discussion.

c. Discuss the incorrect finger placement on the nasal spray in the HFVS.

    i. Could the pictogram be further improved to optimize correct administration?

d. Discuss whether the HVFS data submitted using the "mock" nonprescription user interface support the safe and effective use of:

    i. the proposed nonprescription NNS and

    ii. the modified intend-to-market user interface.

    If not, what additional data are needed?

***Committee Discussion**: The committee members were strongly in favor of the pictograms and suggested the following enhancements: 1) use of colors to clearly identify different parts of the pictogram with corresponding parts of the device; 2) clear labeling of different device parts (i.e., nozzle and plunger, etc.); and 3) use of an image of the device inside the nostril before the product is to be used. One committee member noted low representation of adults with low literacy or non-native English speakers; however, several committee members noted that pictograms will enhance the instructions for these populations as well as among children. The overall consensus again was that the HFVS design was not perfect, but not concerning enough to require additional data or studies to be conducted that may cause a delay in nonprescription product availability.*

One committee member noted concerns with re-dosing and unclear instructions on how many doses should be administered when someone is not responsive. Another committee member expressed concern with the statement on the package "no training required" and suggested to rephrase the statement as it could be misleading for an inexperienced user. Please see the transcript for details of the Committees' discussion.

3. **DISCUSSION**: Discuss whether there is any additional labeling information that might mitigate risk of use errors.

***Committee Discussion**: The committee members had several recommendations as to whether additional labeling information and/or revisions to the proposed labeling may mitigate risk of use errors. The recommendations made by the committee members included the following: 1) increase the font size of the numerical steps similar to the prescription carton labeling; 2) provide a portal for extra information or a demonstration video (e.g., YouTube) via a QR code; 3) provide access to instructions in multiple languages; 4) provide clear instructions for a 2nd person, if available, to call 911 in concert with administration of NNS; 5)ensure that the Quick Start Guide provides the same content as the DFL, including use of the same color scheme (black/shades of grey/white) so users will understand that it contains the same information; 6) state on the principal display panel that the carton contains two devices; 7) use color carefully to enhance readability; and 8) remove instructions to assess pupil size. One committee member added that although we should not further delay the availability of nonprescription NNS, in the future, it is important to conduct studies in the pediatric population who can also save lives. Please see the transcript for details of the Committees' discussion.*

4. **VOTE**: Is the benefit-risk profile of NNS supportive of its use as a nonprescription opioid overdose reversal agent?

    a. If you vote 'No', what further data should be obtained?

Vote Result: Yes: 19 No: 0 Abstain: 0

***Committee Discussion**: The committee members unanimously agreed that the benefit-risk profile of NNS was supportive of its use as a nonprescription opioid overdose reversal agent. These committee members emphasized that approval of nonprescription naloxone will be an important step from a public health perspective and a key component in addressing the opioid crisis. Committee members reiterated recommendations for improvements to the labeling, suggestions to pursue additional data (e.g., Human Factors) post approval, and recommendations for a postmarketing studies program for nonprescription products. Overall, the consensus from the committee was "don't let perfect be the enemy of good." Please see the transcript for details of the Committees' discussion.*

The meeting was adjourned at approximately 4:15 p.m. ET.