

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209512Orig1s000

OTHER REVIEW(S)

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

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

Memorandum

Date: May 30, 2017

To: Nina Mani
Regulatory Project Manager
Division of Antiviral Products

From: Wendy Lubarsky, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion

Subject: NDA 209512 – NORVIR (ritonavir) oral powder
NDA 022417 – NORVIR (ritonavir) tablet, for oral use
NDA 020659 – NORVIR (ritonavir) oral solution

As requested in the Division of Antiviral Products' (DAVP) consult dated December 12, 2016, the Office of Prescription Drug Promotion (OPDP) has reviewed the NORVIR (ritonavir) tablet, for oral use, oral solution, and oral powder prescribing information and patient labeling, and the NORVIR (ritonavir) oral powder instructions for use and carton/container labeling.

OPDP reviewed the proposed substantially complete version of the prescribing information and patient labeling sent via email by Nina Mani on May 16, 2017, and downloaded from link on May 19, 2017. OPDP reviewed the substantially complete version of the carton/container labeling sent via email on May 15, 2017, by Nina Mani and downloaded on May 16, 2017.

OPDP has reviewed the substantially complete prescribing information and carton/container labeling in the attached documents below. We have no comments at this time.

The Division of Medical Policy Programs and OPDP provided a single, consolidated review of the patient labeling and instructions for use under a separate cover on May 30, 2017.

Thank you for your consult. OPDP appreciates the opportunity to provide comments. If you have any questions, please contact Wendy Lubarsky at (240) 402-7721 or wendy.lubarsky@fda.hhs.gov.

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/s/

WENDY R LUBARSKY
05/30/2017

**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 30, 2017

To: Debra Birnkrant, MD
Director
Division of Antiviral Products (DAVP)

Through: LaShawn Griffiths, MSHS-PH, BSN, RN
Associate Director for Patient Labeling
Division of Medical Policy Programs (DMPP)

Barbara Fuller, RN, MSN, CWOCN
Team Leader, Patient Labeling
Division of Medical Policy Programs (DMPP)

From: Morgan Walker, PharmD, MBA, CPH
Patient Labeling Reviewer
Division of Medical Policy Programs (DMPP)

Wendy Lubarsky, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: Review of Patient Labeling: Patient Package Insert (PPI) and
Instructions for Use (IFU)

Drug Name (established name): NORVIR (ritonavir)

Dosage Form and Route: oral powder

Application Type/Number: 209512

Applicant: AbbVie Inc.

1 INTRODUCTION

On December 7, 2016, AbbVie Inc. submitted for the Agency's review a New Drug Application (NDA) 209512 for NORVIR (ritonavir) oral powder. This submission provides for a new dosage form to the existing product line.

NORVIR (ritonavir) Tablets was originally approved on February 10, 2010, NORVIR (ritonavir) Solution was originally approved March 1, 1996, and NORVIR (ritonavir) Capsules, Soft Gelatin was originally approved on June 29, 1999. NORVIR is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

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 Antiviral Products (DAVP) on December 12, 2016, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for NORVIR (ritonavir) oral powder.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and a separate DMEPA review of the IFU was completed on May 16, 2017.

2 MATERIAL REVIEWED

- Draft NORVIR (ritonavir) oral powder PPI and IFU received on December 7, 2016, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on May 16, 2017.
- Draft NORVIR (ritonavir) oral powder Prescribing Information (PI) received on December 7, 2016, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on May 16, 2017.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the PPI and IFU the target reading level is at or below an 8th grade 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 APFont to make medical information more accessible for patients with vision loss. We reformatted the PPI document using the Arial font, size 10.

In our collaborative review of the PPI and IFU we:

- 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 they are 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)
- The enclosed IFU review comments are collaborative DMPP and DMEPA.

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 are 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/

MORGAN A WALKER
05/30/2017

WENDY R LUBARSKY
05/30/2017

BARBARA A FULLER
05/30/2017

LASHAWN M GRIFFITHS
05/30/2017

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: May 16, 2017
Requesting Office or Division: Division of Antiviral Products
Application Type and Number: NDA 209512
Product Name and Strength: Norvir (ritonavir) Powder for Oral Suspension,
100 mg
Applicant/Sponsor Name: AbbVie, Inc.
Submission Date: May 1, 2017 and May 10, 2017
OSE RCM #: 2016-2816-1
DMEPA Primary Reviewer: Valerie S. Wilson, PharmD
DMEPA Team Leader (Acting): Otto L. Townsend, PharmD

1 PURPOSE OF MEMO

The Division of Antiviral Products (DAVP) requested that we review the revised prescribing information, patient information, Instructions for Use, and carton labeling for Norvir Powder for Oral Suspension to determine if it is acceptable from a medication error perspective. The revisions are in response to the recommendations we made during a previous label, labeling, and human factors review^a and recommendations made by DAVP to have the Applicant update labeling to limit the dosage and preparation information related to the Norvir powder for oral suspension to increments of 100 mg.^b Additionally, this memo captures the communication and regulatory history leading up to the May 1, 2017 and May 10, 2017 submissions of the revised materials.

1.1 REGULATORY HISTORY

December 7, 2016

^a Wilson V. Label Labeling and Human Factors Review for Norvir (NDA 209512). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 APR 05. RCM No.: 2016-2816.

^b Murray, J. Information Request for AbbVie Inc: NDA 209512. Silver Spring (MD): FDA, CDER, OND, DAVP (US); 2017 APR 26.

AbbVie submitted proposed container label, carton labeling, a cover note to patients, prescribing information, Instructions for Use (IFU), and Human Factors (HF) validation study results to NDA 209512. On April 5, 2017, DMEPA determined the HF study failures and root cause analyses indicated the user interface did not support the safe and effective preparation of Norvir Powder for Oral Suspension for doses less than 100 mg. DAVP communicated the HF-related (b) (4) deficiencies to AbbVie on April 7, 2017 via an information request, with recommendations to (b) (4) IFU, carton labeling, and cover note.^c

April 20, 2017

AbbVie submitted a response to the April 7, 2017 information request acknowledging our concerns, but stated their belief that modifications to the IFU would not provide significant improvement in a new Human Factors study.^d Also in response to the April 7, 2017 information request, AbbVie submitted the following proposals on April 24, 2017 to:

1. continue the approval process for NDA 209512 for doses greater than 100 mg,
2. update the prescribing information and IFU,
3. (b) (4)
4. (b) (4)

(b) (4)

April 26, 2017

DAVP sent an information request with general concurrence to AbbVie's proposals (b) (4)
(b) (4) DAVP also requested AbbVie resubmit labeling limiting the information related to the pediatric powder formulation to dose increments of 100 mg.

Updated carton labeling, prescribing information, patient information, and Instructions for Use were submitted on May 1, 2017 and May 10, 2017.

^c Mani, N. Information Request for AbbVie Inc: NDA 209512. Silver Spring (MD): FDA, CDER, OND, DAVP (US); 2017 APR 07.

^d AbbVie Inc. Agency Response to April 7, 2017 - Request for Information. North Chicago (IL): AbbVie Inc. 2017 APR 20.

^e Murray, J. Information Request for AbbVie Inc: NDA 209512. Silver Spring (MD): FDA, CDER, OND, DAVP (US); 2017 APR 26.

2 CONCLUSION

We reviewed the revised prescribing information, patient information, Instruction for Use, and carton labeling determined the revised materials are not acceptable from a medication error perspective. Abbvie has revised the majority of the prescribing information, patient information, and Instructions for Use to align with the Agency’s request (b) (4) and preparation information to 100 mg dose increments. However, we identified several areas that could be improved to provide clarity, to prevent dosing and administration errors, and (b) (4) prescribing information to 100 mg dose increments. Additionally, the revised carton labeling is missing required information. Our assessment of the revised materials is as follows:

Prescribing Information

- (b) (4)
- Under section 2.4, under the Dosage and Administration section of the FPI, consideration should be given to provide clarity to the second paragraph, which states “pour and mix the entire contents of each packet...” to state “pour and mix the entire contents of each packet...Use one packet for doses of 100 mg and two packets for doses of 200 mg” to prevent confusion that could lead to wrong preparation or dose errors (see section 3, recommendation #2).

Patient Information

- Consideration should be given to revise the ninth bullet point under the “How should I take Norvir” section which states (b) (4) to provide clarity and align with the preparation

instructions under section 2.4 of the Dosage and Administration section (see section 3, recommendation #3).

Instructions for Use

- We previously recommended AbbVie revise the bullet point stating [REDACTED] (b) (4) [REDACTED] to state “completely tear or cut off the top of the packet and make sure the packet is fully open” based on failures observed during the HF validation study. Participants were observed struggling to tear open or barely opening the Norvir packets during the HF validation study, which lead to some powder being stuck inside the partially sealed packet opening. We recommend AbbVie revise the third bulleted point located under step 4 to prevent underdose errors (see section 4, recommendation #1).

Carton Labeling

- An area for the lot and expiration date has not been designated on the immediate carton and is required per 21 CFR 201.17 and 21 CFR 201.10(i)(1), respectively. We provide our recommendation to AbbVie in letter-ready format in section 4, to ensure this information is included on the immediate carton (see section 4, recommendation #2).

We provide recommendations to our assessment of the revised material to DAVP in section 3 and to AbbVie in section 4, in letter-ready format.

3 RECOMMENDATIONS FOR DAVP

1. [REDACTED] (b) (4) of the FPI should be removed as it contains dosing information [REDACTED] (b) (4) [REDACTED]
2. Consider revising the second paragraph under section 2.4 of the Dosage and Administration section to state “Pour and mix the entire content of each packet over soft food or liquid. Use one packet for doses of 100 mg and use two packets for doses of 200 mg.
3. Consider revising the ninth bullet point under the “How should I take Norvir” section of the Patient Information to state [REDACTED] (b) (4) [REDACTED]

4 RECOMMENDATIONS FOR ABBVIE, INC

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

Instructions for Use (IFU)

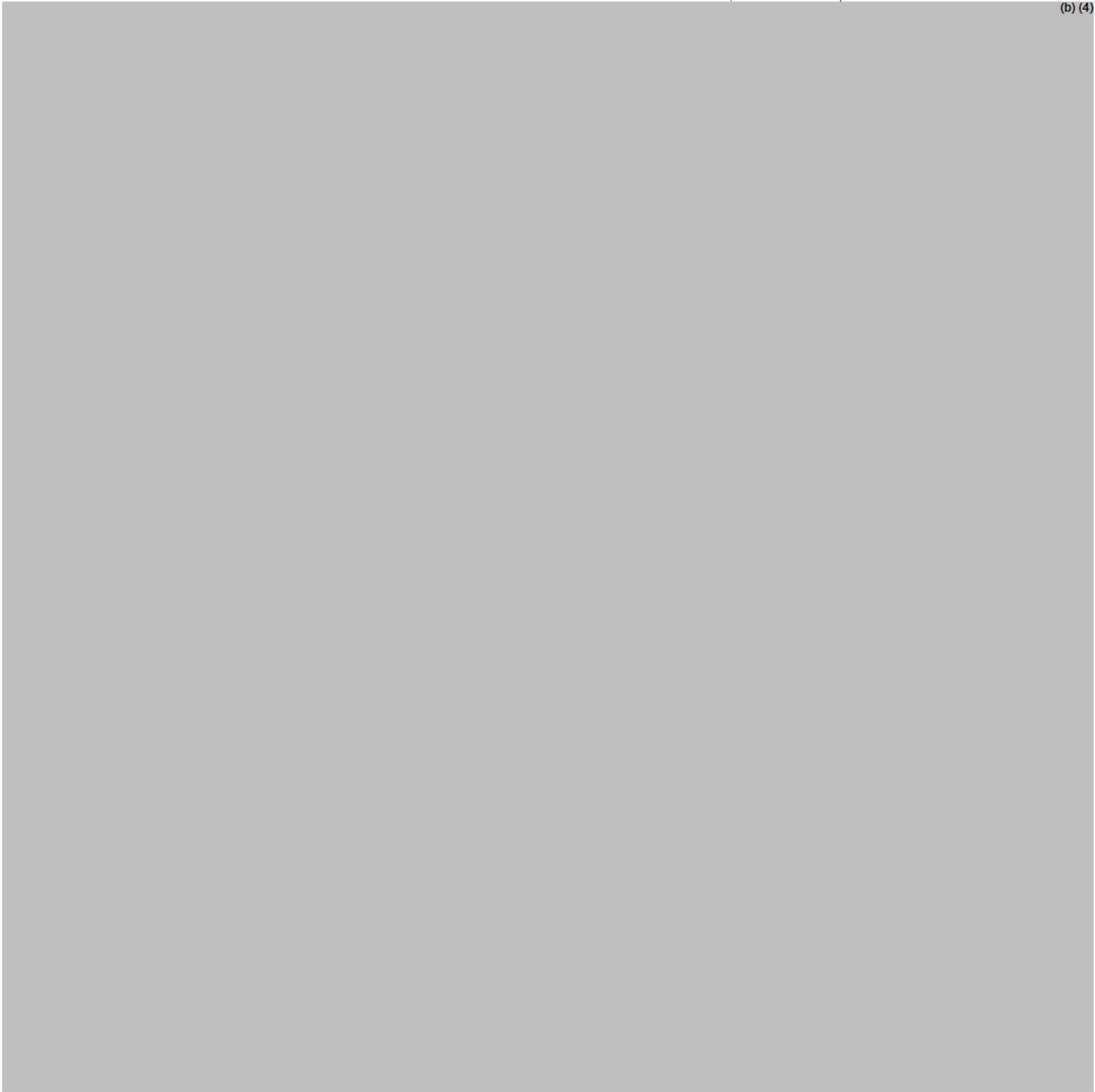
1. Revise the third bulleted point located under step 4 (Open the packet(s)) to read “Completely tear or cut off the top of the packet and make sure the packet is fully open” to prevent underdose errors resulting from powder getting stuck behind a partially sealed opening, as observed during the human factor validation study.

Carton Labeling

2. A section designated for the expiration date and lot number is missing from the immediate carton labeling. Ensure the expiration date and lot number are included on the carton per 21 CFR 201.17 and 21 CFR 201.10(i)(1), respectively.

APPENDIX A. LABEL AND LABELING SUBMITTED ON MAY 10, 2017

Carton Labeling



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/s/

VALERIE S WILSON
05/16/2017

OTTO L TOWNSEND
05/16/2017

LABEL, LABELING, AND HUMAN FACTORS RESULTS 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 5, 2017

Requesting Office or Division: Division of Antiviral Products (DAVP)

Application Type and Number: NDA 209512

Product Name and Strength: Norvir (ritonavir) Powder for Oral Suspension,
100 mg

Product Type: Single ingredient (b) (4)

Rx or OTC: Rx

Applicant/Sponsor Name: AbbVie

Submission Date: December 07, 2016

OSE RCM #: 2016-2816

DMEPA Primary Reviewer: Valerie Wilson, PharmD

DMEPA Team Leader: Vicky Borders-Hemphill, PharmD

DMEPA Associate Director for Human Factors: Quynh Nhu Nguyen, MS

1 REASON FOR REVIEW

Abb-Vie has developed Norvir powder for oral suspension, a new formulation for use in HIV-1 infected pediatric patients. The new formulation does not contain ethanol or propylene glycol

(b) (4)

and has an increased shelf life compared to Norvir oral solution. Doses of Norvir powder for oral suspension require preparation with soft food or liquid prior to administration that is different from Norvir oral solution. Thus, on December 7, 2016, AbbVie submitted to NDA 209512, human factors (HF) validation study results including Knowledge Task Assessment, Instructions for Use (IFU), draft packet label, carton labeling, cover note to patients, and prescribing information (PI).

(b) (4)

We reviewed the submitted materials per DAVP's request.

1.1 REGULATORY HISTORY

1. On June 30, 2014, a Type B Pre-NDA teleconference was held between DAVP and AbbVie. AbbVie concluded from a second formative study

(b) (4)

2. We previously reviewed^{1,2} the HF protocol submitted by AbbVie on September 17, 2015 and identified several deficiencies in the use Failure Mode, Effects, and Criticality Analysis (uFMEA) and human factors validation protocol design. Additionally, we identified areas within the labels and labeling that required revision for clarity. AbbVie accepted all previous recommendations^{1,2,3,4} to revise the uFMEA, HF validation

¹Calderon M. Label and Labeling Review for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2015 Dec 21. 20 p. OSE RCM No.: 2015-2133.

² Calderon M. Review of Response to Agency Comments on Human Factors Validation Protocol for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 Apr 12. 8 p. OSE RCM No.: 2015-2133-1.

³ Calderon M. Review of Response to Agency Comments on Human Factors Validation Protocol for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 Jul 15. 3p. OSE RCM No.: 2015-2133-2.

⁴ Walker M. Patient Labeling Review for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Medical Policy and Initiations, Division of Medical Policy Programs (US); 2015 Nov 24.

protocol, packaging, labels, labeling, (b) (4) and IFU prior to commencement of the HF validation study.

3. On February 23, 2017, we requested a transcript of subjective feedback provided during the validation study and corresponding to Table 18, Table 19, and Table 20 in the HF validation study results report. Additionally, we requested root-cause analysis for the failures observed during the Knowledge Task Assessment study. AbbVie in turn provided subjective feedback for Tables 18, 19, and Table 20 and risk assessment of failures for the Knowledge Task Assessment study (Appendix F).

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
FDA Adverse Event Reporting System (FAERS)*	E (N/A)
Dose Accuracy Analysis	F
Labels and Labeling	G
Information Requests	H

N/A=not applicable for this review

*We do not typically search FAERS for our 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 (HF) VALIDATION STUDY RESULTS

The proposed Norvir Powder for Oral Suspension IFU includes a set of instructions to prepare exactly 100 mg and 200 mg doses (b) (4)

The HF validation study focused on preparation of Norvir doses (b) (4) by 36 untrained participants (18 healthcare providers (HCP) and 18 caregivers (CG) of pediatric patients). (b) (4)



3.1.1. Simulated Use

We provide a summary table of failures, failure description, associated clinical consequences, participant feedback, and root causes identified by AbbVie for each failed subtask and provide recommendation to mitigate the user interface, in this section. We note multiple participants failed the same task more than once. Additionally, we note AbbVie did not provide additional mitigations to address any failures seen during the simulated use study. We also provide our detailed analysis and recommendations subsequent to each summary table.



Task 2.5 Failures to open 1 packet and pour the powder into the mixing cup (n=92) - may result in wrong dose errors due to creating a Norvir stock concentration that is not 100 mg/10 mL.			
Subtask	# of participant who failed/close call (# of failures for specified task)	Description of use errors/use difficulties (e.g. issues)/associated clinical consequences/participant feedback (if provided)	Root Cause Analysis (AbbVie)
2.5.1 Tap the packet to move all the powder to the bottom	4CG (n=5)	Step ignored or deemed not required. One CG relied on the pictures in the IFU and did not fully read the instructions to perform this step, which resulted in error for 2.5.1 through 2.5.3.c.	Participants failed to notice the step or believed the step was not required
2.5.2 Tear or cut off the top and make sure the packet is fully open	1 HCP and 1 CG (n=4)	Participants observed struggling to tear open the packet or barely opening. Some obtained scissors but failed to cut all the way across. Powder may be stuck inside partially sealed opening.	Many participants required scissors to cut open the packet. Packets are difficult to tear open because of tear force balanced with being child tamperproof.
2.5.3 Pour all powder into the mixing cup a. 1 packet used b. No trouble opening the packet	a. No errors b. 2 CG had trouble opening the packet (n=2)	One CG struggled to tear the Norvir packet open and stated she would use scissors to open the packet if she were at home. One participant did not cut the packet all the way across, which allowed powder to be stuck behind the partially sealed opening.	
(b) (4)			
2.5.4 Tap the packet again and look inside to make sure there is no powder left	13 HCP and 12 CG (n=41)	Step ignored or not deemed required. Residual or tiny amount of powder left in packet.	Too "fiddly" to empty into cup or not worthwhile to perform as packet appeared empty. Participants failed to notice step or believed the step was not required.

We determined the IFU did not include specific instructions for users to obtain a pair of scissors under the heading "Gather items" to aid users in fully opening the top of the packet. Scissors should be added to the list of items in the "Gather items" section of the IFU (see recommendation #8 in section 4.2).

Additionally, the second bullet point for step 6 (b) (4) in the IFU, which corresponds to task 2.5, can be revised to read, for example "Completely tear or cut off the top of the packet." This change requires validation, as ensuring all powder from the packet is emptied into the mixing cup is critical to creating a Norvir 100 mg /10 mL suspension(see recommendation #9 in section 4.2).

We note that the IFU provides two bullet points of instructions listed under step 6 (b) (4) for the participant to tap the packet to move all powder to the bottom prior to opening and to tap the packet to make sure there is no powder remaining after pouring contents into mixing cup. We find these instructions acceptable from a medication error perspective.

(b) (4) the correct prescribed dose is critical to ensuring patients receive the correct dose (see recommendation #1 in section 4.2).

3.1.2 Knowledge Task Assessment Study Results

Our assessment of the Knowledge Task Assessment Study results focuses on the failures identified by incorrect responses to the questions as they relate to the specific step or section in the IFU tested. We reviewed the IFU to determine if vulnerabilities to confusion are present that could have led the participants to answer the assessment questions incorrectly. We note that AbbVie recognized that caregivers (CG) as a group had lower health literacy scores and tended to have more incorrect responses than healthcare providers (HCP). AbbVie identified Questions 1, 5, 8, and 10 were identified as questions CG had the most difficulty answering. Questions 3, 6, 8, and 11 (see Table 18 in Appendix C) were identified as questions HCP had the most difficulty answering, with question 11 receiving the most number of incorrect responses.

Knowledge Task Question	# of participant who failed/close call (# of failures for specified task)	Correct Response/ Failed participant responses	Root Cause Analysis (AbbVie)
1. Imagine your dose is 75mg, which set of instructions would you follow to prepare your dose?	5 CG incorrectly answered and 1 CG was a close to answering the question after further reviewing the IFU		(b) (4)

Our evaluation determined that the inability to identify the set of instructions needed to prepare a prescribed dose (b) (4)

(b) (4)

We have provided specific recommendations in section 4.2 to relocate the section “ (b) (4) ” along with corresponding table to appear before the (b) (4) ” to help users more readily identify that there are two sets of instructions and recognize the set of instructions pertinent to the dose being prepared (see recommendation #12 in section 4.2). Additionally, each side of the leaflet should be clearly labeled to provide adequate differentiation of the different instructions

(b) (4)

The IFU used a negative statement (b) (4)

This is not aligned with FDA’s best practices. From a medication error’s perspective, the statement can be revised to prevent confusion as the word ‘not’ is easily overlooked and to reduce clutter to prevent distraction from more important information such as, “Preparing doses exactly 100 mg and 200 mg”. In addition, AbbVie can consider bolding the statements (b) (4) to help further mitigate risks associated with users preparing doses using the wrong set of instructions, as well as, incorporating a similar statement should be on the opposite of the IFU for instances when the user opens the IFU to the side that indicates (b) (4)

Knowledge Task Question	# of participant who failed/close call (# of failures for specified task)	Correct Response/ Failed participant responses	AbbVie’s Risk Assessment
2. How soon must you give the (b) (4) dose of the medicine (b) (4)	3 CG	Correct answer: ‘within 2 hours’ (b) (4) Participant responses (failures): a. “10 minutes” b. “right away” c. “11 minutes and 30 seconds”	For all responses a through c, AbbVie identified no harm is to be expected as responses were within the allowed 2 hours that is within the instructed limit for normal use of the product.

No response exceeded 2 hours, the max time allowed to administer the medicine (b) (4) is located in the “Important Information” sections on the both sides of the IFU. (b) (4)

We find the way in which this information is presented acceptable.

Knowledge Task Question	# of participant who failed/close call (# of failures for specified task)	Correct Response/ Failed participant responses	AbbVie's Risk Assessment
3. Imagine you are preparing a 200mg dose, which set of instructions would you follow to prepare your dose?	2 HCP and 3 CG	<p>Correct answer: Correct answer is 'Preparing doses exactly 100 mg or 200 mg.'</p> <p>Participant responses (failures):</p> <ul style="list-style-type: none"> a. Indicates light green side. "I'd follow same instructions only adding another 100 mg." b. 2 packets (participant referred to light green side, then looks at dark green side. Flips back and forth) "You make it same one. Use two packets instead of 1 packet." c. "same one" [referring to light green side] d. "Still follow this one [referring to the light green side] but double it to 200, (participant referred to light green side but then refers to "important information section" and to the dark green side) Use two packages of the medicine" e. "This one again. I would use two packages." [referring to the light green side] 	(b) (4)

This knowledge task is also illustrates the failures associated with selecting the wrong side of the IFU ((b) (4) 100 mg or 200 mg doses).

Knowledge Task Question	# of participant who failed/close call (# of failures for specified task)	Correct Response/ Failed participant responses	AbbVie's Risk Assessment
4. How many packets do you need to use (b) (4)	1 CG/1 CG was a close call	<p>Correct answer: 1 packet.</p> <p>Participant response (failures):</p> <ul style="list-style-type: none"> a. "None, only 100 mg doses" <p>Participant response (close call):</p> <ul style="list-style-type: none"> b. "two packets, no, only one" 	(b) (4)

We note the section entitled "How you prepare your dose of Norvir depends on the dose you are prescribed" provides instructions for determining how many packets are needed to prepare a prescribed dose. Additionally, the section entitled "Gather items" provides a diagram of items needed to prepare doses, including 1 packet of 100 mg Norvir oral powder (see recommendations 3, 12, 13, and 14).

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3.3 Container labeling

The net quantity statement is in close proximity to the printed strength on the principal display panel (PDP) which could lead to misinterpretation as the strength. The net quantity statement can be relocated away from the strength (see recommendation #18 in section 4.2)

3.4 Instructions for use (IFU)

The IFU is large at a size of ~3'x2'. AbbVie noted several participants did not read or use the IFU during the simulated use study. We considered whether the large size of the IFU contributed to participants not using the IFU. The size of the IFU can be reduced to improve accessibility (see recommendation #17 in section 4.2).

3.5 Cover note to patients

[REDACTED] (b) (4)

3.6 Prescribing Information

In the Dosage and Administration section of the FPI, [REDACTED] (b) (4)

[REDACTED]

4. CONCLUSION & RECOMMENDATIONS

The HF validation study results showed multiple failures across multiple critical tasks and across the two user groups that could result in medication errors. These results and associated root cause analyses indicate that the user interface does not support safe and effective [REDACTED] (b) (4)

[REDACTED] We note AbbVie did not implement any additional mitigations to address failures observed during the HF validation study. Given the that this is an antiviral product, [REDACTED] (b) (4) In addition, the pediatric patient population represents a more vulnerable population, we recommend AbbVie to further optimize the product user interface by implementing additional mitigations and provide additional HF validation data to support that the proposed product can be used safely and effectively by lay caregivers and HCPs [REDACTED] (b) (4)

Additionally, we determined the Instructions for Use, carton label, cover note to patients, and prescribing information can be improved [REDACTED] (b) (4). We provide recommendations to the Division in section 4.1 and recommendations in section 4.2 in letter-ready format to be communicated to the Applicant.

4.1 RECOMMENDATIONS FOR THE DIVISION

1. [REDACTED] (b) (4)

4.2 RECOMMENDATIONS FOR ABBVIE

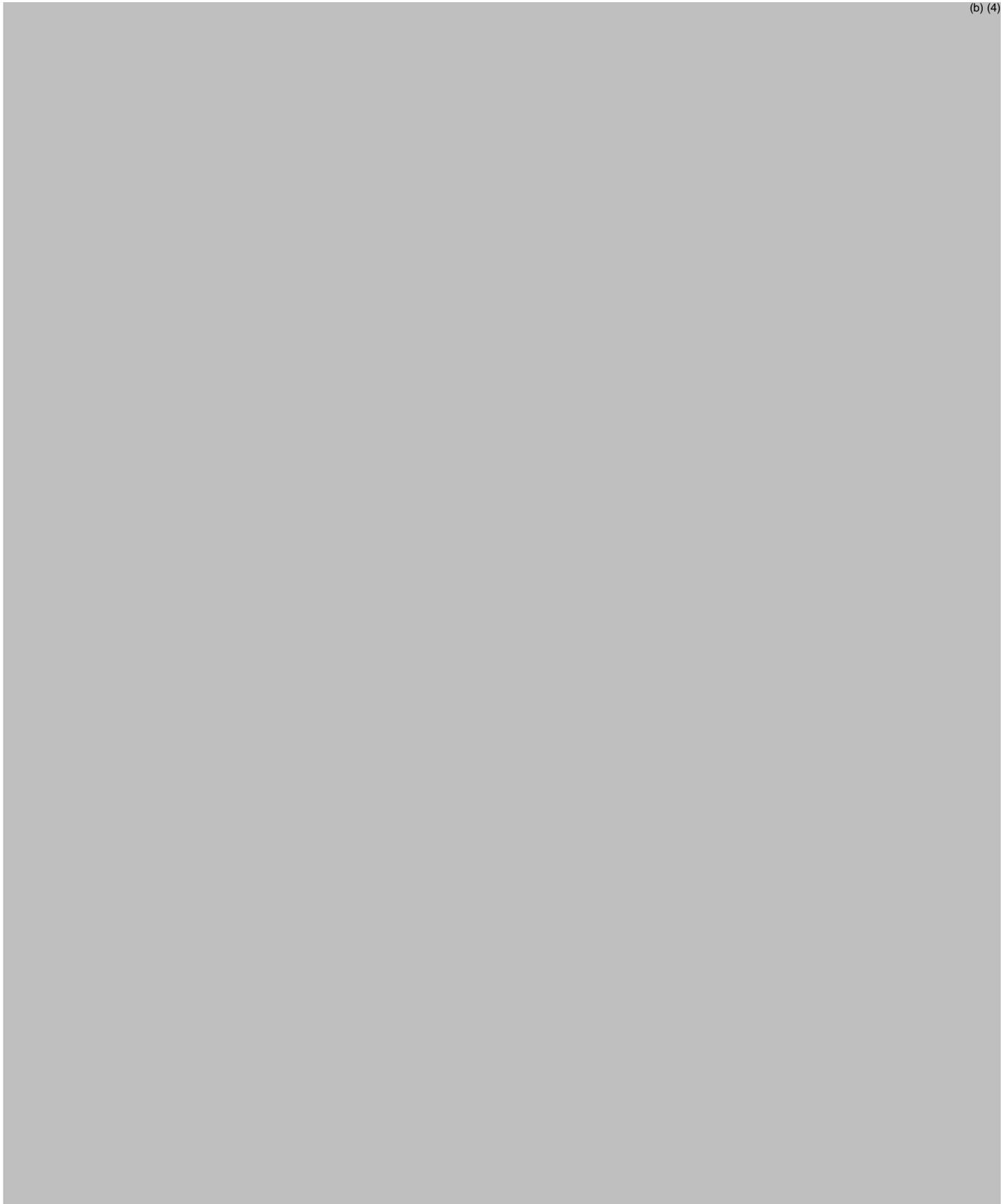
The human factors validation study results showed multiple failures across multiple critical tasks and across the two user groups (b) (4). These results and associated root cause analyses indicate that the user interface does not support safe and effective (b) (4). We note you did not implement any additional mitigations to address failures observed during the HF validation study. We recommend you to further optimize the product user interface by implementing additional mitigations and provide additional HF validation data to support that the proposed product can be used safely and effectively by lay caregivers and HCPs (b) (4)

Simulated Use - HF Validation Study

We have identified a product design concern related to (b) (4)

(b) (4)

(b) (4)



Please also address the following regarding the proposed product's carton labeling and cover note.

Carton Labeling

18. Relocate the net quantity statement to appear away from the product strength, for example to the bottom of the principal display panel (PDP), to mitigate the risk of numerical confusion between the strength and net quantity which increases when the net quantity statement is located in close proximity to the strength statement.

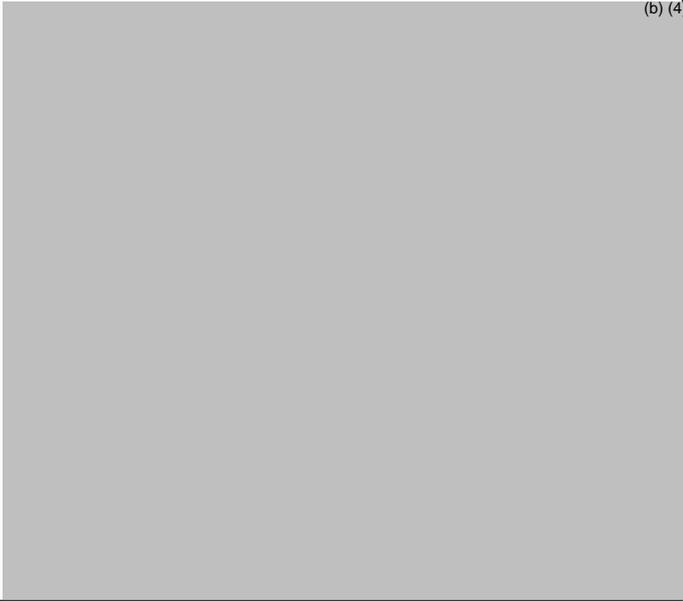
Cover Note

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Norvir that AbbVie submitted on December 7, 2016, and the listed drug (LD).

Table 2. Relevant Product Information for Norvir and the Listed Drug		
Product Name	Norvir	Norvir
Initial Approval Date	N/A	March 1, 1996
Active Ingredient	Ritonavir	Ritonavir
Indication	In combination with other antiretroviral agents for the treatment of pediatric HIV-1 infection.	Treatment of HIV-1 infection (adults and children greater than one month of age) in combination with other antiretroviral agents.
Route of Administration	Oral	Oral
Dosage Form	Powder for Oral Suspension	Oral Solution
Strength	100 mg	80 mg/mL

Dose and Frequency*	Adults: 600 mg twice daily	Adults: 600 mg twice daily																																								
	Pediatric:  (b) (4)	Pediatric: Table 1. Pediatric Dosage Guidelines for Oral Solution*																																								
		<table border="1"> <thead> <tr> <th>Body Surface Area (m²)</th> <th>Twice Daily Dose 250 mg per m²</th> <th>Twice Daily Dose 300 mg per m²</th> <th>Twice Daily Dose 350 mg per m²</th> <th>Twice Daily Dose 400 mg per m²</th> </tr> </thead> <tbody> <tr> <td>0.20</td> <td>0.6 mL (50 mg)</td> <td>0.75 mL (60 mg)</td> <td>0.9 mL (70 mg)</td> <td>1.0 mL (80 mg)</td> </tr> <tr> <td>0.25</td> <td>0.8 mL (62.5 mg)</td> <td>0.9 mL (75 mg)</td> <td>1.1 mL (87.5 mg)</td> <td>1.25 mL (100 mg)</td> </tr> <tr> <td>0.50</td> <td>1.6 mL (125 mg)</td> <td>1.9 mL (150 mg)</td> <td>2.2 mL (175 mg)</td> <td>2.5 mL (200 mg)</td> </tr> <tr> <td>0.75</td> <td>2.3 mL (187.5 mg)</td> <td>2.8 mL (225 mg)</td> <td>3.3 mL (262.5 mg)</td> <td>3.75 mL (300 mg)</td> </tr> <tr> <td>1.00</td> <td>3.1 mL (250 mg)</td> <td>3.75 mL (300 mg)</td> <td>4.4 mL (350 mg)</td> <td>5 mL (400 mg)</td> </tr> <tr> <td>1.25</td> <td>3.9 mL (312.5 mg)</td> <td>4.7 mL (375 mg)</td> <td>5.5 mL (437.5 mg)</td> <td>6.25 mL (500 mg)</td> </tr> <tr> <td>1.50</td> <td>4.7 mL (375 mg)</td> <td>5.6 mL (450 mg)</td> <td>6.6 mL (525 mg)</td> <td>7.5 mL (600 mg)</td> </tr> </tbody> </table>	Body Surface Area (m ²)	Twice Daily Dose 250 mg per m ²	Twice Daily Dose 300 mg per m ²	Twice Daily Dose 350 mg per m ²	Twice Daily Dose 400 mg per m ²	0.20	0.6 mL (50 mg)	0.75 mL (60 mg)	0.9 mL (70 mg)	1.0 mL (80 mg)	0.25	0.8 mL (62.5 mg)	0.9 mL (75 mg)	1.1 mL (87.5 mg)	1.25 mL (100 mg)	0.50	1.6 mL (125 mg)	1.9 mL (150 mg)	2.2 mL (175 mg)	2.5 mL (200 mg)	0.75	2.3 mL (187.5 mg)	2.8 mL (225 mg)	3.3 mL (262.5 mg)	3.75 mL (300 mg)	1.00	3.1 mL (250 mg)	3.75 mL (300 mg)	4.4 mL (350 mg)	5 mL (400 mg)	1.25	3.9 mL (312.5 mg)	4.7 mL (375 mg)	5.5 mL (437.5 mg)	6.25 mL (500 mg)	1.50	4.7 mL (375 mg)	5.6 mL (450 mg)	6.6 mL (525 mg)	7.5 mL (600 mg)
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How Supplied	100 mg, single-use packets, cartons of 30 packets	Bottles of 240 mL																																								
Storage	Store at or below 30°C (86°F)	Store at room temperature 20°-25°C (68°-77°F). Do not refrigerate.																																								
Container Closure	Foil/laminate, child-resistant packets																																									

* Clinically, ritonavir is no longer utilized as a treatment option in combination with other antiretroviral agents but is instead most often prescribed for use as a pharmacokinetic (PK) enhancer to boost the serum concentrations of other HIV protease inhibitors in pediatric and adult patients. Dependent on the protease inhibitor it is co-administered with, ritonavir doses range 200 mg or less, once or twice daily. Dosing for ritonavir as a PK enhancer is provided within the individual FPIs of the protease inhibitor it is boosting and not within the Norvir FPI.

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On February 14, 2017, we searched the L:drive and AIMS using the terms, Norvir to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified three previous reviews^{5,6,7}, and we confirmed that our previous recommendations were implemented.

⁶ Calderon M. Review of Response to Agency Comments on Human Factors Validation Protocol for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 Apr 12. 8 p. OSE RCM No.: 2015-2133-1.

⁷ Calderon M. Review of Response to Agency Comments on Human Factors Validation Protocol for Norvir (IND 43718). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 Jul 15. 3p. OSE RCM No.: 2015-2133-2.

APPENDIX C. HUMAN FACTORS STUDY

C.1 Study Design

Simulated Use Study

Aimed to test participants' ability to follow the information in the IFU which covered (b) (4) preparation of doses exactly 100 mg or 200 mg (b) (4)

Knowledge Task Assessment Study

Aimed to further test participants' ability to find and understand critical task information and other key information in the IFU.

Study Participants

Total: 36 participants

18 Caregivers

- Subcategorized as:
 - 9 caregivers caring for children with HIV or who care for chronically ill children
 - 9 caregivers caring for healthy children
- Minimum age of 18 years
- Responsible for children less than 18 years old but greater than 1 month old
- Literacy score Range:
 - Caregivers caring for children with HIV or who care for chronically ill Children: 1-6
 - Caregivers caring for healthy children: 2-6

18 Healthcare Providers (HCP) specializing in HIV care

- Literacy Score Range: 4-6

Training

Training was not provided to the participants for the simulated-use test. However, a role-play session with the moderator portraying an HCP was included to mimic the discussion that will occur with a caregiver/patient or another HCP when antiretroviral therapy is initiated that reinforces the importance of reading and following the instructions to obtain an accurate dose.

(b) (4)

Table 19. HCP Results of Analysis of Human Factors Validation Test (continued)

Use Task	Fpts #. (# of Trials) (1) - One Trial, (2) - Both Trials	# of Use Errors	Task Failure (n=36 trials)		Risk Analysis		Possible Root Cause	Possible Risk Control	Revised Risk Analysis: Redesign needed?	
			Observations of User(s) (Guides)	Comment by User(s) (Debrief)	Clinical Consequence (UFMEA)	Potential Harm (SRA)				
2.5 Open 1 packet and pour powder into mixing cup	2.5.1 Tap the packet to move all the powder to the bottom	N/A	0	None	N/A	N/A	N/A	IFU Step 6	No	
	2.5.2 Tear or cut off the top and make sure the packet is fully open	25(2)	2	Packet barely opened	None	Underdose (powder spilled due to small opening)	Disease progression	Unable to fully tear open packet and scissors not used Instructions not followed	IFU Step 6	No
	2.5.3. Pour all powder into the mixing cup a. 1 packet used	N/A	0	None	N/A	N/A	N/A	N/A	IFU Important information section, IFU Gather items section, IFU Step 6	No

Table 19. HCP Results of Analysis of Human Factors Validation Test (continued)

Use Task		Ppts #. (# of Trials) (1) – One Trial, (2) – Both Trials	# of Use Errors	Task Failure (n=36 trials)		Risk Analysis		Possible Root Cause	Possible Risk Control	Revised Risk Analysis: Redesign needed?
				Observations of User(s) (Guides)	Comment by User(s) (Debrief)	Clinical Consequence (UFMEA)	Potential Harm (SRA)			
2.5 Open 1 packet and pour powder into mixing cup	2.5.3. Pour all powder into the mixing cup b. No trouble opening the packet	N/A	0	None	N/A	N/A	N/A	N/A	IFU Step 6	No
	2.5.3. Pour all powder into the mixing cup c. No powder spilt	5(1), 9(1), 12(2), 18(1), 19(1), 25(2), 27(2), 28(1), 29(2), 30(2), 34(2), 36(2), 38(1)	20	Very small amounts of powder spilt either when opening packet and pouring powder or when placing "empty" packet on table	None	Underdose	Disease progression	Small amounts of powder aerosolize when pouring and residual powder emitted from packets when placed on table	IFU Step 6	No

Table 19. HCP Results of Analysis of Human Factors Validation Test (continued)

Use Task		Ppts #. (# of Trials) (1) – One Trial, (2) – Both Trials	# of Use Errors	Task Failure (n=36 trials)		Risk Analysis		Possible Root Cause	Possible Risk Control	Revised Risk Analysis: Redesign needed?
				Observations of User(s) (Guides)	Comment by User(s) (Debrief)	Clinical Consequence (UFMEA)	Potential Harm (SRA)			
2.5 Open 1 packet and pour powder into mixing cup	2.5.4 Tap the packet again and look inside to make sure there is no powder left	12(1), 16(1), 18(1), 19(1), 24(2), 25(2), 27(2), 28(2), 29(1), 30(2), 34(2), 36(2), 38(2)	21	Residual or tiny amount of powder left in packet	None	Underdose	Disease progression	Residual powder left in packets, not tapped possibly too fiddly to empty into cup or not worthwhile exercise as packet appears empty	IFU Step 6	No

(b) (4)

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APPENDIX D. ISMP NEWSLETTERS

D.1 Methods

On February 14, 2017, we searched the Institute for Safe Medication Practices (ISMP) newsletters using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newsletter(s)	Acute Care, Community, and Nursing
Search Strategy and Terms	Match Exact Word or Phrase: Norvir

D.2 Results

Our search retrieved zero relevant cases.

APPENDIX F. DOSE ACCURACY ANALYSIS

(b) (4)



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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

OTTO L TOWNSEND on behalf of VALERIE S WILSON
04/05/2017

OTTO L TOWNSEND on behalf of BRENDA V BORDERS-HEMPHILL
04/05/2017

QUYNHNHU T NGUYEN
04/05/2017

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 209512	NDA Supplement #: S- BLA Supplement #: S-	Efficacy Supplement Category: <input type="checkbox"/> New Indication (SE1) <input type="checkbox"/> New Dosing Regimen (SE2) <input type="checkbox"/> New Route Of Administration (SE3) <input type="checkbox"/> Comparative Efficacy Claim (SE4) <input type="checkbox"/> New Patient Population (SE5) <input type="checkbox"/> Rx To OTC Switch (SE6) <input type="checkbox"/> Accelerated Approval Confirmatory Study (SE7) <input type="checkbox"/> Labeling Change With Clinical Data (SE8) <input type="checkbox"/> Manufacturing Change With Clinical Data (SE9) <input type="checkbox"/> Animal Rule Confirmatory Study (SE10)
Proprietary Name: Norvir Established/Proper Name: ritonavir Dosage Form: Powder for suspension Strengths: 100 mg Route(s) of Administration: Oral		
Applicant: AbbVie, Inc. Agent for Applicant (if applicable):		
Date of Application: December 7, 2016 Date of Receipt: December 7, 2016 Date clock started after Unacceptable for Filing (UN): N/A		
PDUFA Goal Date: June 7, 2017	Action Goal Date (if different):	
Filing Date: February 5, 2017	Date of Filing Meeting: January 18, 2017	
Chemical Classification (original NDAs only) : <input type="checkbox"/> Type 1- New Molecular Entity (NME); NME and New Combination <input type="checkbox"/> Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination <input checked="" type="checkbox"/> Type 3- New Dosage Form; New Dosage Form (b) (4) <input type="checkbox"/> Type 4- New Combination <input type="checkbox"/> Type 5- New Formulation or New Manufacturer <input type="checkbox"/> Type 7- Drug Already Marketed without Approved NDA <input type="checkbox"/> Type 8- Partial Rx to OTC Switch <input type="checkbox"/> Type 9-New Indication or Claim (will <u>not</u> be marketed as a separate NDA after approval) <input type="checkbox"/> Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)		
Proposed indication(s): NORVIR is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients greater than one month of age.		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:	<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)	
<i>If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment” review found at:</i> http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499 .		
Type of BLA <i>If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team</i>	<input type="checkbox"/> 351(a) <input type="checkbox"/> 351(k)	

Review Classification:		<input type="checkbox"/> Standard <input checked="" type="checkbox"/> Priority <input type="checkbox"/> Pediatric WR <input type="checkbox"/> QIDP <input type="checkbox"/> Tropical Disease Priority Review Voucher <input type="checkbox"/> Pediatric Rare Disease Priority Review Voucher			
The application will be a priority review if: <ul style="list-style-type: none"> • A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH) • The product is a Qualified Infectious Disease Product (QIDP) • A Tropical Disease Priority Review Voucher was submitted • A Pediatric Rare Disease Priority Review Voucher was submitted 					
Resubmission after withdrawal? <input type="checkbox"/>		Resubmission after refuse to file? <input type="checkbox"/>			
Part 3 Combination Product? <input type="checkbox"/> If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults OPQ RBM sent the following consults to CDRH: <ul style="list-style-type: none"> • Technical Review • Office of Compliance 		Convenience kit/Co-package <input type="checkbox"/> Pre-filled drug delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Pre-filled biologic delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Device coated/impregnated/combined with drug <input type="checkbox"/> Device coated/impregnated/combined with biologic <input type="checkbox"/> Separate products requiring cross-labeling <input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Possible combination based on cross-labeling of separate products <input type="checkbox"/> Other (drug/device/biological product)			
<input type="checkbox"/> Fast Track Designation <input type="checkbox"/> Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i> <input type="checkbox"/> Rolling Review <input checked="" type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC Other:		<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <ul style="list-style-type: none"> <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies (FDCA Section 505B) <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42) 			
Collaborative Review Division (if OTC product):					
List referenced IND Number(s): 043718					
Goal Dates/Product Names/Classification Properties		YES	NO	NA	Comment
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.		<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Are the established/proper and applicant names correct in electronic archive? If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into electronic archive.		<input checked="" type="checkbox"/>	<input type="checkbox"/>		

Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? <i>Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at: http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm</i> <i>If no, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Application Integrity Policy	YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If yes, explain in comment column.				
If affected by AIP, has OC been notified of the submission? If yes, date notified:	<input type="checkbox"/>	<input type="checkbox"/>		
User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		Orphan designation was granted on Jan 11, 2017. Updated Form 356H can be found in the 1/19/17 submission.
<u>User Fee Status</u> <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>	Payment for this application (<i>check daily email from UserFeeAR@fda.hhs.gov</i>): <input checked="" type="checkbox"/> Paid <input checked="" type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>	Payment of other user fees: <input checked="" type="checkbox"/> Not in arrears <input type="checkbox"/> In arrears			
<u>User Fee Bundling Policy</u> <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf</i>	Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
505(b)(2) (NDAs/NDA Efficacy Supplements only)	YES	NO	NA	Comment
Is the application a 505(b)(2) NDA? (<i>Check the 356h form, cover letter, and annotated labeling</i>). If yes , answer the bulleted questions below:	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	<input type="checkbox"/>	<input type="checkbox"/>		

<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)]. 	<input type="checkbox"/>	<input type="checkbox"/>																		
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]? <p><i>If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.</i></p>	<input type="checkbox"/>	<input type="checkbox"/>																		
<ul style="list-style-type: none"> Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If yes, please list below:</p>	<input type="checkbox"/>	<input type="checkbox"/>																		
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 25%;">Application No.</th> <th style="width: 30%;">Drug Name</th> <th style="width: 25%;">Exclusivity Code</th> <th style="width: 20%;">Exclusivity Expiration</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>	Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																	
<p><i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity and GAIN exclusivity will extend both of the timeframes in this provision by 6 months and five years, respectively. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i></p>																				
<ul style="list-style-type: none"> If FDA has approved one or more pharmaceutically equivalent (PE) products in one or more NDAs before the submission date of the original 505(b)(2) application, did the applicant identify one such product as a listed drug (or an additional listed drug) relied upon and provide an appropriate patent certification or statement [see 21 CFR 314.50(i)(1)(i)(C) and 314.54]? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If no, include template language in the 74-day letter.</p> <p>Failure to identify a PE is an approvability issue but not a filing issue [see 21 CFR 314.125(b)(19)]</p> <p><i>Note: Pharmaceutical equivalents are drug products in identical dosage forms and route(s) of administration that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates.</i></p>	<input type="checkbox"/>	<input type="checkbox"/>																		

Exclusivity	YES	NO	NA	Comment
Does another product (same active moiety) have orphan exclusivity for the same indication? <i>Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(14)]? <i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
NDA/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? If yes, # years requested: <i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
NDA only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
If yes , did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? <i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? <i>If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager</i> <i>Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Format and Content				
<p><i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i></p>	<input type="checkbox"/> All paper (except for COL) <input checked="" type="checkbox"/> All electronic <input type="checkbox"/> Mixed (paper/electronic) <input type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
<p>If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?</p>				
Overall Format/Content	YES	NO	NA	Comment
<p>If electronic submission, does it follow the eCTD guidance?¹ If not, explain (e.g., waiver granted).</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<p>Index: Does the submission contain an accurate comprehensive index?</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>Is the submission complete as required under 21 CFR 314.50 (<i>NDA</i>s/<i>NDA efficacy supplements</i>) or under 21 CFR 601.2 (<i>BLA</i>s/<i>BLA efficacy supplements</i>) including:</p> <p><input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain.</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>BLAs only: Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Forms and Certifications				
<p><i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included.</i> Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</p>				
Application Form	YES	NO	NA	Comment
<p>Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?</p> <p><i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i></p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<p>Are all establishments and their registration numbers listed on the form/attached to the form?</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

¹ <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf>

Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? <i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i> <i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature? <i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i> <i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Debarment Certification	YES	NO	NA	Comment
Is a correctly worded Debarment Certification included with authorized signature? <i>Certification is not required for supplements if submitted in the original application; If foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i> <i>Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge..."</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? <i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i> <i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<p>For NMEs: Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?</p> <p><i>If yes, date consult sent to the Controlled Substance Staff:</i></p> <p>For non-NMEs: <i>Date of consult sent to Controlled Substance Staff:</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Pediatrics	YES	NO	NA	Comment
<p><u>PREA</u></p> <p>Does the application trigger PREA?</p> <p><i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i></p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		Since the application has received Orphan designation, PREA is not triggered.
<p>If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)?</p> <p><i>If no, may be an RTF issue - contact DPMH for advice.</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<p>If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application?</p> <p><i>If no, may be an RTF issue - contact DPMH for advice.</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<p><u>BPCA:</u></p> <p>Is this submission a complete response to a pediatric Written Request?</p> <p><i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required³</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

2

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm>

3

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm>

Version: 12/05/2016

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Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted? <i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
REMS	YES	NO	NA	Comment
Is a REMS submitted? <i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
Prescription Labeling	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (Prescribing Information)(PI) <input checked="" type="checkbox"/> Patient Package Insert (PPI) <input checked="" type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input type="checkbox"/> Carton labeling <input type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent labeling <input type="checkbox"/> Other (specify) : Cover note and foil			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format? <i>If no, request applicant to submit SPL before the filing date.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Is the PI submitted in Physician Labeling Rule (PLR) format? ⁴	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	<input checked="" type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input checked="" type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	Sponsor re-submitted in PLLR format on January 19, 2017.
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

⁴ <http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576.htm>

Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (<i>send WORD version if available</i>)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
OTC Labeling	<input checked="" type="checkbox"/> Not Applicable			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify): Cover note and foil.			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>		
Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
All labeling/packaging sent to OSE/DMEPA?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) <i>If yes, specify consult(s) and date(s) sent:</i> January 5, 2017	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	OSI Bioequivalence Audit Request consult
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s):	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): June 30, 2014	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Any Special Protocol Assessments (SPAs)? Date(s):	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

ATTACHMENT

MEMO OF FILING MEETING

DATE: January 18, 2017

BACKGROUND: On December 7, 2016 AbbVie Inc. submitted an NDA for Norvir (ritonavir) powder for oral suspension for use in combination with other ARVs for the treatment of HIV infection. On January 11, 2017 the product received Orphan designation for its use with other ARV agents for the treatment of pediatric HIV-1 infection.

[Redacted] (b) (4)

In June 2014 a pre-NDA meeting was held and the Agency agreed that the Sponsor's new NDA will be based on the demonstration of bioequivalence (BE) of the powder formulation to the currently approved oral solution at a dose of 100 mg. As long as the standard of BE is met the Agency agreed that no new non-clinical or additional clinical studies will be required to demonstrate safety and efficacy of the powder formulation. The Agency also agreed that the powder qualified for a categorical exclusion [Redacted] (b) (4)

Since the Sponsor received Orphan designation the application is not subject to PREA.

For this new formulation the Sponsor has submitted Prescribing Information, Patient Information, and Instructions for Use (IFU) updating the current labeling with Norvir powder information. DMEPA and Patient labeling have been consulted and have previously worked closely with the Sponsor on their three Human Factor studies and one validation study, as well as their IFU.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Nina Mani	Y
	CPMS/TL:	Karen Winestock	Y
Cross-Discipline Team Leader (CDTL)	Shirley Seo		Y
Division Director/Deputy	Debbie Birnkrant/Jeff Murray		Y/Y
Office Director/Deputy			
Clinical	Reviewer:	Regina Alivisatos	Y
	TL:	Adam Sherwat	Y

Social Scientist Review (<i>for OTC products</i>)	Reviewer:		
	TL:		
OTC Labeling Review (<i>for OTC products</i>)	Reviewer:		
	TL:		
Clinical Microbiology (<i>for antimicrobial products</i>)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Su-Young Choi	Y
	TL:	Shirley Seo	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:		
	TL:		

Nonclinical Pharmacology/Toxicology)	Reviewer:	Pritam Verma	Y
	TL:	Hanan Ghantous/Christopher Ellis	N/Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Steve Miller	Y
	RBPM:	Luz Rivera	N
• Drug Substance	Reviewer:	N/A	
• Drug Product	Reviewer:	William McCalmont (Primary) Balajee Shanmugam (Secondary)	Y
			N
• Process	Reviewer:	Sateesh Kumar Sathigari(Primary); Steven Frisbee (Secondary)	Y
			N
• Microbiology	Reviewer:	Sateesh Kumar Sathigari(Primary); Steven Frisbee (Secondary)	Y
			N
• Facility	Reviewer:	Cassandra Abellard (Primary); Derek Smith (Secondary)	Y
			N
• Biopharmaceutics	Reviewer:	Fang Wu	Y
• Immunogenicity	Reviewer:	N/A	
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)			
OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:	Morgan Walker	Y
	TL:	Barbara Fuller	N
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:	Wendy Lubarsky	Y
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:	Valerie Wilson	Y
	TL:	Vicky Border-Hemphill	N
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
<ul style="list-style-type: none"> Discipline CDRH Device Quality/Performance 	Reviewer:	Rong Guo	Y
	TL:		
<ul style="list-style-type: none"> CDRH Facilities: 	Reviewer:	Crystal Lewis	Y
Other attendees	Danyal Chaudhary, OSE RPM Stacey Min, ADL Poonam Mishra, Deputy Director for Safety *For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

<p>GENERAL</p> <ul style="list-style-type: none"> 505(b)(2) filing issues: <ul style="list-style-type: none"> Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? <p>Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Per reviewers, are all parts in English or English translation? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Electronic Submission comments <p>List comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> No comments

<p>CLINICAL</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain:</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</p> <p><i>If no, for an NME NDA or original BLA, include the reason. For example:</i></p> <ul style="list-style-type: none"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CONTROLLED SUBSTANCE STAFF</p> <ul style="list-style-type: none"> Abuse Liability/Potential <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL MICROBIOLOGY</p> <p>Comments: Submission contains no new Clinical Microbiology information; hence, nothing to review</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

<p>CLINICAL PHARMACOLOGY</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>BIOSTATISTICS</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</p> <p>Comments: Submission contains no new Pharm/Tox information; hence, nothing to review</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>PRODUCT QUALITY (CMC)</p> <p>Comments: 3. Kit samples are being requested by the OPQ RBPM, six for CDER/CDRH.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><u>New Molecular Entity (NDAs only)</u></p> <ul style="list-style-type: none"> Is the product an NME? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p><u>Environmental Assessment</u></p> <ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><u>Facility Inspection</u></p> <ul style="list-style-type: none"> Establishment(s) ready for inspection? <p>Comments: CDRH and CDER Office of Compliance reviewers will decide whether the kit packaging facility needs to be inspected. IRs will be handled by OPQ RBPM.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p><u>Facility/Microbiology Review (BLAs only)</u></p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><u>CMC Labeling Review (BLAs only)</u></p> <p>Comments:</p>	<input type="checkbox"/> Review issues for 74-day letter
<p>APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)</p> <ul style="list-style-type: none"> • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days? 	<input checked="" type="checkbox"/> N/A <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • What late submission components, if any, arrived after 30 days? 	None
<ul style="list-style-type: none"> • Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all clinical sites included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO

REGULATORY PROJECT MANAGEMENT

Signatory Authority: Jeffrey Murray, MD, Deputy Director, DAVP

Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V):

21st Century Review Milestones (see attached) (listing review milestones in this document is optional):

Comments:

<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><u>Review Issues:</u></p> <p><input checked="" type="checkbox"/> No review issues have been identified for the 74-day letter. <input type="checkbox"/> Review issues have been identified for the 74-day letter.</p> <p><u>Review Classification:</u></p> <p><input type="checkbox"/> Standard Review <input checked="" type="checkbox"/> Priority Review</p>

ACTION ITEMS

<input checked="" type="checkbox"/>	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
<input type="checkbox"/>	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input checked="" type="checkbox"/>	If priority review, notify applicant in writing by day 60 (see CST for choices)
<input type="checkbox"/>	Send review issues/no review issues by day 74
<input checked="" type="checkbox"/>	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
<input type="checkbox"/>	Update the PDUFA V DARRTS page (for applications in the Program)
<input type="checkbox"/>	Other

Annual review of template by OND ADRAAs completed: April 2016

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NINA MANI
01/25/2017

KAREN D WINESTOCK
01/26/2017

REGULATORY PROJECT MANAGER PHYSICIAN LABELING RULE (PLR) FORMAT REVIEW OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: NDA 209512

Application Type: New NDA

Drug Name(s)/Dosage Form(s): Norvir (ritonavir), powder for suspension

Applicant: AbbVie, Inc.

Receipt Date: December 7, 2016

Goal Date: June 7, 2017

1. Regulatory History and Applicant's Main Proposals

AbbVie has developed a new pediatric formulation (b) (4)

This new product has a better shelf-life and the formulation can be mixed with various foods and liquids for ease of administration.

For this new formulation the Sponsor has submitted Prescribing Information, Patient Information, and Instructions for Use (IFU) updating the current labeling with Norvir Powder information. DMEPA and Patient labeling have been consulted and have previously worked closely with the Sponsor on their three Human Factor studies and one validation study, as well as their IFU.

2. Review of the Prescribing Information

This review is based on the applicant's submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements of Prescribing Information (SRPI)" checklist (see Section 4 of this review).

3. Conclusions/Recommendations

No SRPI format deficiencies were identified in the review of this PI.

4. Selected Requirements of Prescribing Information

The Selected Requirement of Prescribing Information (SRPI) is a 41-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Selected Requirements of Prescribing Information

Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

- YES** 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

Comment:

- YES** 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement. Instructions to complete this item: If the length of the HL is one-half page or less, select “YES” in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select “NO” unless a waiver has been granted.

Comment:

- YES** 3. A horizontal line must separate:
- HL from the Table of Contents (TOC), **and**
 - TOC from the Full Prescribing Information (FPI).

Comment:

- YES** 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be **bolded** and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format.

Comment:

- YES** 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix for HL format.

Comment:

- YES** 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

Comment:

- YES** 7. Headings in HL must be presented in the following order:

Heading	Required/Optional
• Highlights Heading	Required
• Highlights Limitation Statement	Required
• Product Title	Required
• Initial U.S. Approval	Required
• Boxed Warning	Required if a BOXED WARNING is in the FPI
• Recent Major Changes	Required for only certain changes to PI*
• Indications and Usage	Required
• Dosage and Administration	Required
• Dosage Forms and Strengths	Required

Selected Requirements of Prescribing Information

• Contraindications	Required (if no contraindications must state “None.”)
• Warnings and Precautions	Not required by regulation, but should be present
• Adverse Reactions	Required
• Drug Interactions	Optional
• Use in Specific Populations	Optional
• Patient Counseling Information Statement	Required
• Revision Date	Required

* RMC only applies to five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

- YES** 8. At the beginning of HL, the following heading, “**HIGHLIGHTS OF PRESCRIBING INFORMATION**” must be **bolded** and should appear in all UPPER CASE letters.

Comment:

Highlights Limitation Statement

- YES** 9. The **bolded** HL Limitation Statement must include the following verbatim statement: “**These highlights do not include all the information needed to use (insert NAME OF DRUG PRODUCT) safely and effectively. See full prescribing information for (insert NAME OF DRUG PRODUCT).**” The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

- YES** 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

- YES** 11. Initial U.S. Approval must be **bolded**, and include the verbatim statement “**Initial U.S. Approval:**” followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

- YES** 12. All text in the BW must be **bolded**.

Comment:

- YES** 13. The BW must have a title in UPPER CASE, following the word “**WARNING**” and other words to identify the subject of the warning. Even if there is more than one warning, the term “**WARNING**” and not “**WARNINGS**” should be used. For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings. The BW title should be centered.

Comment:

YES

Selected Requirements of Prescribing Information

14. The BW must always have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement must be placed immediately beneath the BW title, and should be centered and appear in *italics*.

Comment:

- YES** 15. The BW must be limited in length to 20 lines. (This includes white space but does not include the BW title and the statement “*See full prescribing information for complete boxed warning.*”)

Comment:

Recent Major Changes (RMC) in Highlights

- YES** 16. RMC pertains to only five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the FPI.

Comment:

- YES** 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section’s identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, “Warnings and Precautions, Acute Liver Failure (5.1) --- 8/2015.”

Comment:

- YES** 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

Comment:

Dosage Forms and Strengths in Highlights

- YES** 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

Comment:

Contraindications in Highlights

- YES** 20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word “None.”

Comment:

Adverse Reactions in Highlights

- YES** 21. For drug products other than vaccines, the verbatim **bolded** statement must be present: “**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at**

Selected Requirements of Prescribing Information

(insert manufacturer’s U.S. phone number which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.”

Comment:

Patient Counseling Information Statement in Highlights

- YES** 22. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- See 17 for **PATIENT COUNSELING INFORMATION**

If a product **has (or will have)** FDA-approved patient labeling:

- See 17 for **PATIENT COUNSELING INFORMATION** and **FDA-approved patient labeling**
- See 17 for **PATIENT COUNSELING INFORMATION** and **Medication Guide**

Comment:

Revision Date in Highlights

- YES** 23. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 8/2015**”).

Comment:

Selected Requirements of Prescribing Information

Contents: Table of Contents (TOC)

See Appendix for a sample tool illustrating Table of Contents format.

- YES** 24. The TOC should be in a two-column format.
Comment:
- YES** 25. The following heading must appear at the beginning of the TOC: “**FULL PRESCRIBING INFORMATION: CONTENTS.**” This heading should be in all UPPER CASE letters and **bolded**.
Comment:
- YES** 26. The same title for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.
Comment:
- YES** 27. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.
Comment:
- YES** 28. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (for, of, to) and articles (a, an, the), or conjunctions (or, and)].
Comment:
- YES** 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.
Comment:
- YES** 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading “**FULL PRESCRIBING INFORMATION: CONTENTS***” must be followed by an asterisk and the following statement must appear at the end of the TOC: “*Sections or subsections omitted from the full prescribing information are not listed.”
Comment:

Selected Requirements of Prescribing Information

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

- YES** 31. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. (Section and subsection headings should be in UPPER CASE and title case, respectively.) If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use "Labor and Delivery")
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use "Nursing Mothers")
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

- YES** 32. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, “[*see Warnings and Precautions (5.2)*].”

Comment:

Selected Requirements of Prescribing Information

- YES** 33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

- YES** 34. The following heading “**FULL PRESCRIBING INFORMATION**” must be **bolded**, must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

- YES** 35. All text in the BW should be **bolded**.

Comment:

- YES** 36. The BW must have a title in UPPER CASE, following the word “**WARNING**” and other words to identify the subject of the warning. (Even if there is more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used.) For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings.

Comment:

CONTRAINDICATIONS Section in the FPI

- YES** 37. If no Contraindications are known, this section must state “None.”

Comment:

ADVERSE REACTIONS Section in the FPI

- YES** 38. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.”

Comment:

- YES** 39. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

Comment:

Selected Requirements of Prescribing Information

PATIENT COUNSELING INFORMATION Section in the FPI

- YES** 40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:
- Advise the patient to read the FDA-approved patient labeling (Patient Information).
 - Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
 - Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
 - Advise the patient to read the FDA-approved patient labeling (Medication Guide).
 - Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment:

- YES** 41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) must not be included as a subsection under Section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Selected Requirements of Prescribing Information

Appendix: Highlights and Table of Contents Format

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **PROPRIETARY NAME** safely and effectively. See full prescribing information for **PROPRIETARY NAME**.

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING

See full prescribing information for complete boxed warning.

- Text (4)
- Text (5.x)

RECENT MAJOR CHANGES

Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

INDICATIONS AND USAGE

PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)

Limitations of Use: Text (1)

DOSAGE AND ADMINISTRATION

- Text (2.x)
- Text (2.x)

DOSAGE FORMS AND STRENGTHS

Dosage form(s): strength(s) (3)

CONTRAINDICATIONS

- Text (4)
- Text (4)

WARNINGS AND PRECAUTIONS

- Text (5.x)
- Text (5.x)

ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are text (6.x)

To report **SUSPECTED ADVERSE REACTIONS**, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Text (7.x)
- Text (7.x)

USE IN SPECIFIC POPULATIONS

- Text (8.x)
- Text (8.x)

See 17 for **PATIENT COUNSELING INFORMATION** and FDA-approved patient labeling **OR** and Medication Guide.

Revised: M/201Y

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: TITLE OF WARNING

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 Subsection Title

2.2 Subsection Title

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Subsection Title

5.2 Subsection Title

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Immunogenicity

6.2 or 6.3 Postmarketing Experience

7 DRUG INTERACTIONS

7.1 Subsection Title

7.2 Subsection Title

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation (if not required to be in PLLR format use Labor and Delivery)

8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format use Nursing Mothers)

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Subpopulation X

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

9.2 Abuse

9.3 Dependence

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.4 Microbiology

12.5 Pharmacogenomics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

14.1 Subsection Title

14.2 Subsection Title

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

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/s/

NINA MANI
01/25/2017

KAREN D WINESTOCK
01/25/2017