CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217338Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 105403

MEETING MINUTES

RB Health (US) LLC
Attention: Ebru Unver Kulak
Senior Regulatory Manager
399 Interpace Parkway
Parsippany, NJ 07054

Dear Mrs. Kulak:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for guaifenesin, dextromethorphan hydrobromide, and naproxen sodium 12-Hour extended-release tablet, 600 mg / 30 mg / 110 mg.

We also refer to the video conference between representatives of your firm and the FDA on Monday, June 5, 2023. The purpose of the meeting was to discuss NDA format and content, proposed indications, age restrictions, and dosing recommendations for your proposed product.

A copy of the official minutes of the video conference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have questions, call Shannon Liu, DPT, Regulatory Project Manager at (240) 402-2484, or email shannon.liu@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Martha Lenhart, MD, PhD
Deputy Director
Division of Nonprescription Drugs I
Office of Nonprescription Drugs
Office of New Drugs
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM OF MEETING MINUTES

Meeting Type:	Type B
Meeting Category:	Pre-NDA
Meeting Date and Time:	June 5, 2023, 2:00 p.m. – 3:00 p.m. Eastern Time
Meeting Location:	Videoconference
Application Number:	IND 105403
Product Name:	guaifenesin, dextromethorphan hydrobromide, naproxen sodium 12-hour extended-release tablet, 600 mg / 30mg / 110 mg
Indication:	(b) (4) cough, (b) (4), minor aches and pains, headache, fever; temporarily relieves the intensity of coughing and the impulse to cough to help you get to sleep; helps loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and make coughs more productive
Sponsor Name:	RB Health (US) LLC
Regulatory Pathway:	505(b)(2) of the Federal Food, Drug, and Cosmetic Act
Meeting Chair:	Martha Lenhart, MD, PhD, Deputy Director, Division of Nonprescription Drugs I
Meeting Recorder:	Shannon Liu, DPT, Regulatory Project Manager, Division of Regulatory Operations for Nonprescription Drugs

Office of New Drugs, Office of Nonprescription Drugs (ONPD), Division of Nonprescription Drug Products I (DNPD I)
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Martha Lenhart, MD, PhD, Deputy Director
Oritsematosan Oruwariye, MD, Clinical Reviewer
Teresa Podruchny, MD, Clinical Reviewer
Michelle Walker, PhD, Interdisciplinary Scientist
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Tanvir Bell, MD, Clinical Team Leader

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Swapan De, PhD, Senior Pharmaceutical Quality Assessment Lead

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Office of New Drugs (OND), Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORDPURM), Division of Pediatric and Maternal Health (DPMH)
Amy Taylor, MD, MHS, Clinical Reviewer

Office of Regulatory Operations (ORO), Division of Regulatory Operations for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (DRORDPURM)
Heather Buck, MS, MBA, Senior Regulatory Project Manager

Office of Surveillance and Epidemiology (OSE), Office of Medication Prevention and Risk Management (OMEPRM), Division of Medication Error Prevention and Analysis (DMEPA)
Grace Jones, PharmD, Safety Evaluator

SPONSOR ATTENDEES
Julia Kim, PhD, RPh, Head of Regulatory Health NA
Michael Cammarata, RPh, Regulatory Director
Ebru Unver Kulak, Senior Regulatory Manager
Madhavi Allam, PhD, MS, Senior Regulatory Manager, CMC

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Tim Shea, Senior Medical Scientist, R&D
Ernie Woodhouse, MS, Senior Associate, R&D, Cough Respiratory
AnnMarie Matei, PhD, MS, DABT, RPh, OTC Safety Manager
Liam Kennedy, MS, Head of Statistics and Data Management
(b) (4)
(b) (4)
Paul Hatswell, R&D Method Development Manager
Martha Salazar, MChem, MS, R&D Analytical Associate
(b) (6)

1.0 BACKGROUND

Per the Sponsor's meeting package, RB intends to submit an NDA pursuant to section 505(b)(2) and plans to rely on FDA's previous findings of efficacy and safety for Aleve 220 mg tablets (NDA 020204), Mucinex DM extended-release bi-layer tablets (NDA 021620), and the Cold, Cough, Allergy, Bronchodilator, and Anti-asthmatic Drug Products for Over-the-Counter Human Use OTC Monograph.

On June 5, 2009, RB opened IND 105403 with a pilot Phase 1 study. RB's initial efforts were focused on the development of a modified-release bi-layer tablet, but RB shifted its focus to the development of (b) (4) to overcome challenges pertaining to the pharmacokinetic (PK) release profile of the bi-layer tablet.

On April 12, 2011, a type C meeting was held to discuss the target population, PK program, and PREA requirements.

On July 27, 2015, a type C meeting was held to discuss the development of (b) (4). Based on the feedback RB received from FDA with regard to (b) (4), RB decided to develop an extended-release bi-layer tablet dosage form consisting of an immediate release layer and a modified-release layer.

On March 7, 2016, FDA provided guidance on a proposed bioequivalence study program in a type C Written Response Only.

On August 25, 2022, RB submitted a type B Pre-NDA meeting request to discuss format and content, proposed indications, age restrictions, and dosing recommendations. FDA received the meeting package on April 20, 2023.

FDA sent Preliminary Comments to RB on May 31, 2023.

2.0 DISCUSSION

The Sponsor's questions are **bolded**; FDA's preliminary responses are in normal font; the Sponsor's premeeting responses to FDA's preliminary responses follow in *italics;* and the meeting discussion and postmeeting comments are in ***bold italics***.

2.1. Content of the NDA

Question 1: Does the Agency agree that the content outlined above will be sufficient to support the 505(b)(2) application review?

FDA Preliminary Response to Question 1:

We agree that your proposed content outline appears reasonable for submission of your planned 505(b)(2) NDA. However, there are gaps in the proposed content given several claims (b) (4) included in your proposed label or on the principal display panel (PDP) that are not supported in the labeling of the referenced NDAs.

- As noted in the 2015 meeting communications, the addition of the indication, (b) (4) is not supported by the products cross-referenced NDAs nor by the active pharmaceutical ingredients (APIs) in the proposed product. See also the response to Questions 5 and 6 below.

- We also note the inclusion of (b) (4) as one of the proposed indications for your product. This claim is not supported by the products cross-referenced (as noted in the respective Drug Facts label (DFL) uses). Provide a justification for our review to support this. See also the response to Question 5.

- NDA 020204 (Aleve) language regarding fever is for fever reduction, (b) (4) (b) (4). These are not interchangeable concepts. Address this for our review.

- The proposed combination dosing interval is 2 tablets every 12 hours with not more than 4 tablets in a 24-hour period. Each tablet contains 110 mg naproxen sodium (100 mg naproxen) as Aleve and guaifenesin 600 mg/dextromethorphan bromide 30 mg in Mucinex DM. The proposed dosing interval of single ingredient naproxen tablet, Aleve, 220 mg, allows for use every 8-12 hours. What would a consumer do if the fever increases or symptoms related to the naproxen are not controlled for the 12-hour proposed dosing interval? This may create the need for consumer studies. Address this issue for our review.

Given you propose to rely upon the FDA's previous finding of safety for NDA 020204 (Aleve) and NDA 021620 (Mucinex DM), provide a summary of safety information relevant to your proposed indication in your submission. Also provide discussions and conclusions for your overall safety database and each topic of special interest (such as

stomach bleeding, heart attack and stroke, pregnancy warnings, etc. for naproxen, and abuse potential for dextromethorphan), as well as updated analysis by seriousness, [redacted] and age group if available. Regarding your postmarketing safety data, provide a comprehensive, cumulative review of the safety data from all your clinical trials and any global database (if available) and a summary of the literature review with a risk-benefit assessment covering the last 5 years.

In addition, provide postmarketing safety data for the individual components (naproxen, guaifenesin, and dextromethorphan) using data up to 6 months prior to your planned NDA submission from the following databases: FDA Adverse Reporting System (FAERS), World Health Organization (WHO), National Poison Data System (NPDS) and the Drug Abuse Warning Network (DAWN). If this proposed product is marketed anywhere in the world, provide the labeling in English, describe the marketing status, and include discussion of safety issues. If the proposed product has been withdrawn or discontinued from sale in any world market, provide the reasons why this occurred.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 1:
Topic RB Health would like to discuss in regards to FDA preliminary comments: "The proposed combination dosing interval is 2 tablets every 12 hours with not more than 4 tablets in a 24-hour period. Each tablet contains 110 mg naproxen sodium (100 mg naproxen) as Aleve and guaifenesin 600 mg/dextromethorphan hydrobromide 30 mg in Mucinex DM. The proposed dosing interval of single ingredient naproxen tablet, Aleve, 220 mg, allows for use every 8-12 hours. What would a consumer do if the fever increases or symptoms related to the naproxen are not controlled for the 12-hour proposed dosing interval?"

Meeting Discussion:
RB Health posited the following points:

- ***The labeled dosing directions for Aleve (naproxen sodium) are relatively complex (i.e., take 1 tablet every 8 to 12 hours while symptoms last; for the first dose you may take 2 tablets within the first hour; do not exceed 2 tablets in any 8- to 12-hour period; do not exceed 3 tablets in a 24-hour period).***
- ***Consumers use NSAIDs and acetaminophen as needed, based on the DFL Directions.***
- ***Recurring symptoms are common to all analgesics and consumers are unaware if these symptoms are due to worsening of the disease state or inadequate exposure of the drug product. Class labeling addresses this issue.***
- ***The labeling would advise consumers to stop use and consult a physician if symptoms persist despite self-medication.***
- ***RB Health proposed a conservative dosing strategy for naproxen (i.e., directions for a 12-hour dosing interval (versus 8-hour dosing interval)).***

FDA reiterated its concerns primarily related to the dosing interval of naproxen and related efficacy considerations. FDA noted, as a general matter, that a consumer can obtain active ingredients separately to use per the labeled directions for each respective product, which would, for naproxen, be different from the proposed product's direction to take every 12 hours.

FDA advised RB Health to provide data and information to support the proposed fixed 12-hour dosing interval for naproxen considering the listed drug's dosing interval range.

2.2. Clinical

Question 2: RB Health conducted a PK study as suggested by the Agency. RB Health considers that the planned approach will be adequate to establish a 12-hour dosing regimen. Does the Agency agree?

FDA Preliminary Response to Question 2:

Only the topline results of the PK study RB5-US-1505 were submitted in the meeting package. Acceptability of the results will be considered during review of the NDA.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 2:

- *In the Information Request (IR) dated April 26, 2023, FDA asked RB Health to provide the PK comparison results of dextrorphan (PK parameters and PK profiles) under fasting condition. RB Health provided response to this IR on May 5, 2023. Was the response to the IR acceptable?*
- *Could FDA share initial thoughts on bioequivalence adequacy?*

Meeting Discussion:
RB Health confirmed that dextrorphan plasma concentrations were not measured in the PK study RB5-US-1505. RB Health pointed out that dextrorphan PK measurement was not required by OGD dextromethorphan/guaifenesin drug product-specific guidance. In addition, dextrorphan PK was not measured in NDA 021620 Mucinex DM clinical pharmacology program under 505(b)(2) pathway. FDA acknowledged the mentioned precedents and stated that acceptance of RB Health's clinical pharmacology program without evaluation of dextrorphan PK will be a review issue. FDA added that it may be helpful for further justification if RB Health could include literature results to compare the PK results and pharmacologic activity and potency between dextrorphan and dextromethorphan in the NDA.

RB Health inquired about the adequacy of the bioequivalence results for naproxen, guaifenesin, and dextromethorphan. FDA acknowledged that on face value, the topline PK comparison results of three individual active ingredients

appears reasonable; however, acceptance of the results will be considered during review of the NDA.

Question 3: Does the proposed clinical content of the NDA support eligibility for Hatch Waxman market exclusivity based on this study being a prerequisite for approval?

FDA Preliminary Response to Question 3:

Please be advised that FDA does not make exclusivity determinations pursuant to sections 505(c)(3)(E) and (j)(5)(F) of the Federal Food, Drug, and Cosmetic Act, and 21 CFR 314.108, until after approval of an NDA. As described at 314.50(j), an applicant should include in its NDA a description of the exclusivity to which the applicant believes it is entitled. FDA will consider the applicant's assertions regarding exclusivity in the review of the application.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 3: None.

Meeting Discussion: Not discussed.

2.3. PREA

Question 4: RB Health considers its approach for extrapolating the adult PK data for ages 12-17 years sufficient. Does the Agency agree?

FDA Preliminary Response to Question 4:

Yes, we agree. The proposed plan to extrapolate safety and effectiveness from adult PK data to pediatric patients aged 12 to 17 years appears appropriate.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 4: None.

Meeting Discussion: Not discussed.

2.4. Labeling

Question 5: Does the Agency agree that the annotated DFL, referencing NDA 021620 (Mucinex DM) and NDA 020204 (Aleve), is sufficient to support all drug facts components for the proposed product?

FDA Preliminary Response to Question 5:

We do not agree. See labeling-related comments in preliminary response to Question 1. Additionally, preliminary comments on the proposed draft annotated DFL are provided below.

- On the proposed DFL, under the **Uses** heading, some information is missing that is on the Mucinex DM (NDA 021620) labeling. The bullet on the proposed DFL states the following "temporarily relieves the intensity of coughing and the impulse to cough to help you get to sleep." On the Mucinex DM DFL, the bullet states "temporarily relieves: •cough due to minor throat and bronchial irritation as may occur with the common cold or inhaled irritants; •the intensity of coughing; •the impulse to cough to help you get to sleep." Mirror the language used on the Mucinex DM DFL for this indication.

- For the pregnancy warning, the wording should reflect the Aleve (NDA 020204) DFL as follows: **If pregnant or breastfeeding**, ask a health professional before use. It is especially important not to use naproxen sodium at 20 weeks or later in pregnancy unless directed specifically to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 5: None.

***Meeting Discussion:* Not discussed.**

Question 6: Does the Agency agree that "(b) (4)" is an acceptable claim if the specific symptoms are listed on the Principal Display Panel (PDP)?

FDA Preliminary Response to Question 6:

We do not agree. The claim (b) (4)" suggests that the product (b) (4). None of the active ingredients have the indication of (b) (4) in nonprescription products.

See also the response to Question 1 above.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 6:
Topic RB Health would like to discuss in regards to FDA preliminary comments: "The claim "(b) (4)" suggests that the product (b) (4). None of the active ingredients have the indication of (b) (4) in nonprescription products."

Meeting Discussion:
RB Health noted that (b) (4) RB Health will share a white paper on this subject. RB Health noted that the (b) (4) indication would help direct consumers to the product. RB Health referred to

information submitted in its meeting package as further justification for the claim "(b) (4)." FDA advised that claims listed should match those of the listed drugs and that the listed drugs (b) (4)." RB Health did not think the proposed draft claims were overly broad. Meeting discussion occurred regarding the claim for (b) (4). FDA noted internal discussion is needed and that further information will be provided in a postmeeting comment.

<u>Postmeeting comment</u>:
Your meeting package (p. 21/30) states the following, "Among the many possible combinations of symptoms that may be experienced with the common cold (b) (4), consumers will find RB Health's proposed "(b) (4)" product to be helpful if the Uses match the consumer's needs." These same "many possible combinations of symptoms" could also be symptoms of other (b) (4)

As you note, a consumer can read the label for the symptoms a product treats and determine if that product treats his/her/their symptoms. It is unclear that what you propose would provide additional meaningful information to consumers to change that determination but it may potentially create confusion. Again, we remind you that neither of the marketed products in your proposed product has a (b) (4) claim. It may be challenging to substantiate your proposed claim and PDP wording.

2.5 Chemistry, Manufacturing, Controls

<u>Question 7:</u> Does the Agency agree that the discriminating ability approach of the dissolution method presented in the memorandum document meet the Agency's expectations?

<u>FDA Preliminary Response to Question 7:</u>

On its face, the discriminating ability approach presented in the memorandum document does not meet FDA's expectations. Note that the discriminating ability of the dissolution method is not about the accuracy or linearity of the analytical method. We recommend that you demonstrate the selected dissolution method (specifically the testing parameters i.e., apparatus, rotation speed, medium, volume, etc.) is discriminating against changes in the critical bioavailability attributes (CBAs), which are material attributes, formulation or process variables that are expected to critically impact the bioavailability of a drug product. In general, the testing conducted to demonstrate the discriminating ability of the selected dissolution method should compare the dissolution profiles of the reference (target) product versus the test products that are intentionally manufactured with meaningful variations for the most relevant CBAs (i.e., ± 10-20% change to the specification-ranges of these variables). In addition, if available, submit data showing that the selected dissolution method is able to reject batches that are not bioequivalent.

Note that a complete dissolution method report should be included in your future NDA submission. Refer to the FDA's written response dated March 7, 2016, regarding information that should be included in the report. Alternatively, if you wish to have the aforementioned report assessed prior to NDA submission, you may submit the report as an IND amendment stating in the cover letter that FDA review for acceptability of the dissolution method is being requested. Note that, while acceptability of the dissolution method can be determined during the IND or NDA stage, evaluation of dissolution acceptance criteria will be performed during the NDA review.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 7:
Topic RB Health would like to discuss in regards to FDA's preliminary comments: "On its face, the discriminating ability approach presented in the memorandum document does not meet FDA's expectations."

Meeting Discussion:
RB Health outlined its proposal to address the discriminating ability of the dissolution method. FDA responded that this proposal is different than what was submitted in the meeting package and recommended that the proposal be submitted for review. FDA noted that this proposal could be submitted as an IND amendment or submitted with the NDA. RB Health inquired about review duration, and FDA noted that it usually takes 3 months to review such proposals under an IND.

Question 8: Does the Agency agree that the in vitro dose dumping study results provide sufficient support, and that an in vivo BA study (with alcohol) is not needed?

FDA Preliminary Response to Question 8:

We agree that an in vivo study is not needed. In your NDA, for the in vitro alcohol dose dumping study results, report the complete dissolution data (individual, mean, CV%, plots) under all tested conditions, in addition to the f2 values. In the NDA, also report the aqueous solubility (in numerical values) for each drug substance in the physiological pH range.

Sponsor Premeeting Response to FDA Preliminary Comments to Question 8: *None.*

Meeting Discussion: ***Not discussed.***

3.0 OTHER INFORMATION

PREA REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new

indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note your iPSP which was agreed upon on June 1, 2019. We remind you to include the official copy of your agreed iPSP in the appropriate section of an application for marketing approval for dextromethorphan, guaifenesin, and naproxen. Your Agreed iPSP may be amended at your initiative or at FDA's initiative at any time prior to approval of your marketing application. However, FDA must agree to any amendments to an Agreed iPSP. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the draft guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans*.[1] In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email Pedsdrugs@fda.hhs.gov. For further guidance on pediatric product development, please refer to FDA.gov.[2]

505(b)(2) REGULATORY PATHWAY

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the draft guidance for industry *Applications Covered by Section 505(b)(2)* (October 1999).[3] In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions that had challenged the Agency's interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at Regulations.gov.[4]

If you intend to submit a 505(b)(2) application that relies for approval on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to

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[1] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[2] https://www.fda.gov/drugs/development-resources/pediatric-and-maternal-health-product-development
[3] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[4] http://www.regulations.gov

demonstrate that such reliance is scientifically justified.

If you intend to rely on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature or on the other studies is scientifically appropriate. You should include a copy of such published literature in the 505(b)(2) application and identify any listed drug(s) described in the published literature (e.g. by trade name(s)).

If you intend to rely on the Agency's finding of safety and/or effectiveness for a listed drug(s) or published literature describing a listed drug(s) (which is considered to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s)), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that 21 CFR 314.54 requires identification of the "listed drug for which FDA has made a finding of safety and effectiveness," and thus an applicant may only rely upon a listed drug that was approved in an NDA under section 505(c) of the FD&C Act. The regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

If FDA has approved one or more pharmaceutically equivalent products in one or more NDA(s) before the date of submission of the original 505(b)(2) application, you must identify one such pharmaceutically equivalent product as a listed drug (or an additional listed drug) relied upon (see 21 CFR 314.50(i)(1)(i)(C), 314.54, and 314.125(b)(19); see also 21 CFR 314.101(d)(9)). If you identify a listed drug solely to comply with this regulatory requirement, you must provide an appropriate patent certification or statement for any patents that are listed in the Orange Book for the pharmaceutically equivalent product, but you are not required to establish a "bridge" to justify the scientific appropriateness of reliance on the pharmaceutically equivalent product if it is scientifically unnecessary to support approval.

If you propose to rely on FDA's finding of safety and/or effectiveness for a listed drug that has been discontinued from marketing, the acceptability of this approach will be contingent on FDA's consideration of whether the drug was discontinued for reasons of safety or effectiveness.

We encourage you to identify each section of your proposed 505(b)(2) application that is supported by reliance on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature (see table below). In your 505(b)(2) application, we encourage you to clearly identify (for each section of the application, including the labeling): (1) the information for the proposed drug product that is provided by reliance on FDA's finding of safety and/or effectiveness for the listed drug or by reliance on published literature; (2) the "bridge" that supports the scientific appropriateness of such reliance; and (3) the specific name (e.g., proprietary name) of each listed drug named in any published literature on which your marketing application relies for approval. If you are proposing to rely on published literature, include copies of the article(s) in your

submission.

In addition to identifying the source of supporting information in your annotated labeling, we encourage you to include in your marketing application a summary of the information that supports the application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA's previous finding of safety and effectiveness for a listed drug or by reliance on published literature	
Source of information (e.g., published literature, name of listed drug)	**Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)**
(1) Example: Published literature	*Nonclinical toxicology*
(2) Example: NDA XXXXXX "TRADENAME"	*Previous finding of effectiveness for indication A*
(3) Example: NDA YYYYYY "TRADENAME"	*Previous finding of safety for Carcinogenicity, labeling section B*
(4)	

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a "duplicate" of a listed drug and eligible for approval under section 505(j) of the FD&C Act, then it is FDA's policy to refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an Abbreviated New Drug Application (ANDA) that cites the duplicate product as the reference listed drug.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTHA K LENHART
07/05/2023 09:05:59 PM