

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209359Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



PIND 106980

MEETING MINUTES

Hospira, Inc.
Attention: Mr. Fred Fantozzi
275 N. Field Drive
Bldg. H2-2, Dept. 0389
Lake Forest, IL 60045

Dear Mr. Fantozzi:

Please refer to your Pre-Investigational New Drug Application (PIND) file for Epinephrine Injection USP.

We also refer to the Pre-NDA meeting held via teleconference between representatives of your firm and the FDA on December 14, 2015. The purpose of the meeting was to discuss your plans to submit a 505(b)(2) NDA.

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

If you have any questions, please contact:

Quynh Nguyen, Pharm.D., RAC
Regulatory Health Project Manager
(301) 796-0510

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: December 14, 2015 at 11:00 AM – 12:00 PM ET
Meeting Location: via Teleconference

Application Number: PIND 106980
Product Name: Epinephrine Injection USP
Indication: To increase mean arterial pressure in hypotension associated with septic shock.
Sponsor/Applicant Name: Hospira, Inc.

Meeting Chair: Norman Stockbridge, M.D., Ph.D.
Meeting Recorder: Quynh Nguyen, Pharm.D., RAC

FDA ATTENDEES

Center for Drug Evaluation and Research

Office of New Drugs, Office of Drug Evaluation I, Division of Cardiovascular and Renal Products

Norman Stockbridge, M.D., Ph.D.	Director
Shari Targum, M.D.	Clinical Team Leader
Martin Rose, M.D.	Clinical Team Leader
Fortunato Fred Senatore M.D., Ph.D., FACC	Clinical Reviewer
Thomas Papoian, Ph.D.	Pharmacology Team Leader
Rama Dwivedi, Ph.D.	Pharmacology Reviewer
Brian Proctor	Regulatory Project Manager
Bridget Kane	Regulatory Project Manager
Quynh Nguyen, Pharm.D., RAC	Regulatory Project Manager

Office of Clinical Pharmacology, Division of Clinical Pharmacology I

Sudharshan Hariharan, Ph.D.	Clinical Pharmacology Reviewer
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Office of Pharmaceutical Quality

Office of New Drug Products, Branch I

Mohan Sapru, Ph.D.	CMC Lead for Cardiovascular and Renal Products (Acting)
Mariappan Chelliah, Ph.D.	Product Quality Reviewer

Office of New Drug Products, Division of Biopharmaceutics

Gerlie Gieser, Ph.D.	Biopharmaceutics Reviewer
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Office of Compliance, Division of New Drugs and Labeling Compliance, Prescription Drugs Team
Astrid Lopez-Goldberg, J.D. Regulatory Counsel

Drug Shortage Staff
Jeannie David, M.S. Senior Program Management Officer

Center for Devices & Radiological Health

*Office of Device Evaluation, Division of Anesthesiology, General Hospital, Respiratory, Infection Control,
& Dental Devices, General Hospital Devices Branch*
Kathleen Fitzgerald Nurse consultant

SPONSOR ATTENDEES

Representing Hospira, Inc.

Mary Baker, Pharm.D., M.B.A.
Gao Dong, Ph.D., DABT
Louis Amari, Ph.D.

Eric Zhang, Ph.D.

Laurie Wojtko, M.B.A.
Xifeng Zhang, M.S.
Fred Fantozzi, M.S.
Brian McHugh, M.B.A.

Lisa Zboril, R.Ph.

Director Medical Services
Associate R & D Fellow, Preclinical Development
Director, Research & Development, US Marketed
Product Support
Associate Research Fellow, Global Research &
Development
Associate Director, Global Regulatory Affairs
Sr. Associate, Global Regulatory Affairs
Sr. Manager, Global Regulatory Affairs
Program Manager, Specialty Injectable
Pharmaceuticals
Vice President, Global Regulatory Affairs

1.0 BACKGROUND

Hospira, Inc. is the sponsor of PIND 106980 for Epinephrine Injection USP, 0.1 mg/mL, Abboject™ Single-Use Syringe, which is a marketed, but unapproved product. A Pre-NDA Meeting was previously held between Hospira and the Division on January 25, 2010 regarding submission of a (b) (4) 505(b)(2) application to bring Epinephrine Injection USP for (b) (4) several interactions followed the Pre-NDA Meeting. The Division had indicated (b) (4) . Subsequently, however, in an Advice/Information Request Letter dated December 13, 2010, the Division indicated that it was possible to gain approval of a (b) (4) application for Hospira's product for the indication of increasing (b) (4) arterial blood pressure in (b) (4) hypotensive (b) (4) . Consequently, Hospira modified the indication it was pursuing to hypotensive shock.

Belcher Pharmaceuticals, LLC obtained approval of NDA 205029 for Epinephrine Injection USP, 1 mg/mL, Single-Dose Ampuls on July 29, 2014. Accordingly, Hospira intends to use Belcher's product as the Reference Listed Drug (RLD). Because of the time which has elapsed since the January 25, 2010 Pre-NDA meeting and the approval of Belcher's Epinephrine Injection USP product, Hospira has requested this follow-up Pre-NDA meeting to discuss their plans to submit a 505(b)(2) NDA, which is planned for February 2016.

FDA sent Preliminary Comments to the sponsor on December 11, 2015. During the teleconference, the Preliminary Comments to Questions 3, 4 and 5 regarding (b) (4) were discussed.

2. DISCUSSION

2.1. Regulatory

Question 1:

On July 29, 2014, Belcher Pharmaceuticals obtained approval of NDA 205029 for Epinephrine Injection USP, 1 mg/mL, Single-Dose Ampuls for the indication and route of administration currently being sought by Hospira. Accordingly, Hospira would like to use Belcher's product as our RLD. The proposed product qualifies for submission as a 505(b)(2) application due to the differences in form of the active ingredient and strength (concentration) from the RLD (see differences italicized and highlighted in Table 1).

Hospira intends to submit a 505(b)(2) application to gain approval of the subject product and to use Belcher's 1 mg/mL Epinephrine Injection product approved under NDA 205029 as the Reference Listed Drug. Does the Agency agree?

FDA Response to Question 1:

Yes, a 505(b)(2) application appears acceptable, at this time, based on the information available. For information for sponsors considering the submission of an application through the 505(b)(2) pathway, please see section 7.0 of this document.

Discussion:

The sponsor accepted FDA's response; no discussion occurred.

Question 2:

Although the concentration in Hospira's marketed product container is different than the proposed RLD's (1 mg/10 mL for Hospira's product and 1 mg/mL for Belcher's product), Hospira's epinephrine delivers the same amount of drug to the patient (see Table 1). When diluted in 1000 mL of a dextrose containing solution, the concentration of the Hospira product is (b) (4) mcg/mL compared (b) (4) mcg/mL for Belcher's product. This difference is not significant since the drug is titrated to effect.

Hospira's proposed product contains excipients which are not present in Belcher's product (see Table 1). Sodium Metabisulfite NF functions as (b) (4) in the formulation; Citric Acid, Anhydrous USP, and Sodium Citrate Dihydrate USP are pH buffering agents. The proposed drug product is intended for administration by intravenous infusion and the all excipient concentrations are either less than those in the currently approved Epinephrine products or within the amounts listed in the FDA's Inactive Ingredient Database for that route of administration. Therefore, the formulation differences would not be expected to affect product safety and efficacy. Most importantly, the proposed excipient differences in the formulation are required (b) (4) of Hospira's product and are justified in Section 10 below. Consequently, Hospira proposes to use Belcher's package insert to support its application without further preclinical or clinical investigation.

Hospira intends to reference the non-clinical and clinical data contained in NDA 205029, such that no further non-clinical and clinical assessment is necessary. Does the Agency concur?

FDA Response to Question 2:

We agree with your plan to rely upon NDA 205029 for non-clinical information.

Include in the NDA a request to waive the requirement to conduct an *in vivo* bioequivalence study of your proposed drug product and the Listed Drug(s). To support the biowaiver request, submit a side-by-side comparison of the chemical compositions of the proposed and the listed drug product(s), and the justification for why you believe that any differences in configuration/presentation, excipients, physicochemical properties (e.g., pH, osmolality), etc. would not impact the disposition, efficacy and safety of your proposed drug product. Note that the acceptability of the biowaiver request will be a review issue under the NDA.

Alternatively, if you wish to rely on published PK and other information, submit the supportive literature in the NDA. Include a justification for your reliance on such literature and include information to support a bridge between your proposed drug product and the products used in the literature studies.

Discussion:

The sponsor accepted FDA's response; no discussion occurred.

Question 3:

The Pediatric Research Equity Act (PREA) requires all applications submitted under section 505 of the Act for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration contain a pediatric assessment unless the applicant has obtained a waiver or deferral. Hospira's proposed product does not satisfy any of the criteria required for a pediatric assessment. In addition, review of the Summary Basis of Approval for NDA 205029, Belcher's Epinephrine Injection USP, disclosed that Belcher was granted a waiver from the requirements of PREA. The Reviewer stated, "[b]ased on previous literature searches of pressor use in pediatric patients with septic shock, I do not think that it will be easy, practical or feasible for the applicant to conduct a clinical trial of intravenous epinephrine use in this population." She further concluded that there is insufficient information in the literature and Belcher "made a "good faith" attempt to provide literature support for epinephrine use in pediatric patients."

Hospira requests a waiver from the pediatric assessment requirements of PREA. Does the Agency agree?

FDA Response to Question 3:

Yes, the Division agrees with your plan to request a waiver from the pediatric assessment requirements of PREA. Please note that your plan will also need to be reviewed by the Pediatric Review Committee (PeRC) upon submission of an initial Pediatric Study Plan (iPSP). Please see section **3.0 PREA REQUIREMENTS** below regarding submission of the iPSP.

Discussion:

The Division asked when the iPSP would be submitted; Hospira replied that they planned to include the iPSP in the NDA submission. The Division explained that at the time of NDA submission, an "Agreed iPSP" must be submitted, not the proposed iPSP. Therefore, the iPSP would need to be submitted at least 210 days prior to the NDA submission because the review process to reach an Agreed iPSP generally requires 210 days, including reviews by the PeRC. In this case, if the PeRC were to also agree with the sponsor's plan to request a waiver, then the timeframe to reach an Agreed iPSP might take approximately 120 days instead. Based on this information, the sponsor stated that they planned to submit their iPSP in February 2016 and the NDA four months after that.

2.2. Chemistry, Manufacturing and Controls

Question 4:

Belcher's product is currently unavailable for purchase through retail and wholesale sources and Belcher has been unresponsive to Hospira's requests to purchase their product. Due to the unavailability of Belcher's product, Hospira proposes (b) (4) to perform comparative product testing. (b) (4) Does the Agency agree?

FDA Response to Question 4:

We do not agree with your proposal (b) (4). Therefore, in the NDA submission, you should provide a comparison of your product to Belcher's Epinephrine Injection. See also our response to Question #2.

Discussion:

The sponsor stated that they will continue efforts to purchase Belcher's Epinephrine Injection for comparative *in vitro* testing with their product. The sponsor asked if it would be acceptable to provide a side-by-side comparison of their product and Belcher's Epinephrine Injection product (similar to Table 1 of the briefing package) in the event that they were unable to obtain Belcher's product. The table would be expanded to include a column for the justification of why they believe the differences from Belcher's product would not impact the safety and efficacy of their proposed product. The FDA stated that the sponsor's proposal was acceptable. Additionally, the FDA clarified that should it not be feasible to conduct actual *in vitro* comparative testing, it might be acceptable to include in the biowaiver request the physicochemical characteristics, etc. of the Listed Drug based on publicly available information. The acceptability of such information would be a review issue.

Question 5:

Hospira has performed extensive development work (b) (4) the proposed formulation, manufacturing process and specifications. A summary of this work is detailed in Section 10 below. Does the Agency concur that Hospira's product is suitable for submission in its 505(b)(2) application for Epinephrine Injection?

FDA Response to Question 5:

You have provided minimal information regarding the design of the device constituent parts of the proposed pre-filled syringe Abboject™ Single-Use Syringe combination product. Within future investigational or marketing applications, the Agency expects that you will provide all necessary information and performance tests to support the safety and functionality of the constituent parts. You are advised to consult the following guidance documents and consensus standards prior to future investigational or marketing applications:

- Guidance Document: Technical considerations for Pen, jet, and Related Injectors Intended for Use with Drug and Biological Products.
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM147095.pdf>
- Draft Guidance Document: Glass Syringes for Delivering Drug and Biological Products: Technical Information to Supplement International Organization for Standardization (ISO) Standard 11040-4
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM346181.pdf>
- FDA Draft Guidance for Industry and Food and Drug Administration Staff (2012): Design Considerations for Devices Intended for Home Use

<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm331681.pdf>

- ISO 11040-4 Prefilled Syringes-Part 4: Glass barrels for injectables.
- ISO 11040-5 Prefilled Syringes-Part 5: Plunger stoppers for injectables.
- ISO 11608-1:2012: Needle-based injection systems for medical use – Requirements and test methods-Part 1: Needle-based injection systems, Part 2: Needles and Part 3: Finished Containers.

If the device will consist of a Sharps Injury prevention feature:

- Guidance for Industry and FDA Staff: Medical Devices with Sharps Injury Prevention Features.
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071663.htm>
- ISO 23908:2011: Sharps injury protection -- Requirements and test methods – Sharps protection features for single-use hypodermic needles, introducers for catheters and needles used for blood sampling.

Additional Comments:

- We do not agree with your proposal of (b) (4)

- In the NDA filing, you must include the release and stability data (long-term and accelerated) for at least one batch of the epinephrine injection product that will be manufactured (b) (4)

If you submit the long-term stability data for only one batch of the drug product (b) (4) in the NDA filing, you must provide a post-approval commitment to evaluate the long-term stability for the first three commercial batches.
- Acceptability of the excipient levels in the drug product is a review matter.
- We recommend that you assess impurities (b) (4) for structural alerts.
- Your proposed shelf-life specification is not the same as the release specification. Please note that the regulatory specification applies through the product shelf-life. Therefore, we consider that the shelf-life specification is the regulatory specification for the drug product, irrespective of whether you have a separate release specification.
- Assay acceptance criteria for batches that will be manufactured (b) (4) must be revised to (b) (4) %.
- The fill volume of the epinephrine injection product listed in table 1 and table 26 do not match. As an additional note, the guidance for excess volume recommended in USP <1151> is not applicable to prefilled syringes. Therefore, adequate justification must be provided for any excess volume in the Abboject pre-filled syringe.
- Since sodium metabisulfite in aqueous solution is known to convert into bisulfite, justify whether the drug product should be tested for metabisulfite or bisulfite.

- Provide extractables and leachables data for any elastomeric component that are used in the Abboject syringe that comes in contact with the drug product (refer to USP <1663> and <1664>).

Discussion:

[REDACTED] (b) (4)

[REDACTED] (b) (4)

[REDACTED] (b) (4)

[REDACTED]. However, the Agency offered some flexibility regarding requirement for stability data at the time of NDA submission. Normally, the Agency requires 12-month long-term and 6-month accelerated stability data for three primary batches of the drug substance and drug product at the time of NDA submission. In this case, the sponsor can submit long-term stability data for one batch [REDACTED] (b) (4) the NDA filing and provide the additional stability data [REDACTED] (b) (4) during the NDA review period. The Agency reiterated that the shelf-life of the commercial product can only be determined based on the quality and quantity of the long-term stability data from the batches [REDACTED] (b) (4).

3.0 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.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End of Phase (EOP2) meeting. In the absence of an End-of-Phase 2 meeting, refer to the draft guidance below. The PSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The PSP 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 PSP, including a PSP 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* at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf>. In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email pdit@fda.hhs.gov. For further guidance on pediatric product development, please refer to: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049867.htm>.

4.0 PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#) including the Pregnancy and Lactation Labeling Rule (PLLR) (for applications submitted on or after June 30, 2015). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) and [Pregnancy and Lactation Labeling Final Rule](#) websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information related to pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.
- FDA’s established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

The application should include a review and summary of the available published literature regarding drug use in pregnant and lactating women, a review and summary of reports from your pharmacovigilance database, and an interim or final report of an ongoing or closed pregnancy registry (if applicable), which should be located in Module 1. Refer to the draft guidance for industry – *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format*

(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425398.pdf>).

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

5.0 ABUSE POTENTIAL ASSESSMENT

Drugs that affect the central nervous system, are chemically or pharmacologically similar to other drugs with known abuse potential, or produce psychoactive effects such as mood or cognitive changes (e.g., euphoria, hallucinations) need to be evaluated for their abuse potential and a proposal for scheduling will be required at the time of the NDA submission [21 CFR 314.50(d)(5)(vii)]. For information on the abuse potential evaluation and information required at the time of your NDA submission, see the draft guidance for industry, *Guidance for Industry Assessment of Abuse Potential of Drugs*, available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM198650.pdf>.

6.0 MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

7.0 505(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), available at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>. 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 <http://www.regulations.gov>).

If you intend to submit a 505(b)(2) application that relies for approval, in part, 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 demonstrate that such reliance is scientifically justified.

If you intend to rely, in part, 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., trade name(s)).

If you intend to rely, in part, 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 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 relies on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature. 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 in your annotated labeling the source(s) of information essential to the approval of your proposed drug that is provided by reliance on FDA's previous finding of safety and efficacy for a listed drug or by reliance on published literature, we encourage you to also include that information in the cover letter for your marketing 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 efficacy 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)
<i>1. Example: Published literature</i>	<i>Nonclinical toxicology</i>
<i>2. Example: NDA XXXXXX "TRADENAME"</i>	<i>Previous finding of effectiveness for indication X</i>
<i>3. Example: NDA YYYYYY "TRADENAME"</i>	<i>Previous finding of safety for Carcinogenicity, labeling section XXX</i>
<i>4.</i>	

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.

8.0 ISSUES REQUIRING FURTHER DISCUSSION

There were no issues requiring further discussion.

9.0 ACTION ITEMS

There were no action items.

10.0 ATTACHMENTS AND HANDOUTS

There were no attachments or handouts for the meeting minutes.

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

/s/

NORMAN L STOCKBRIDGE
01/11/2016

**DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS
FOOD AND DRUG ADMINISTRATION**

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Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardiovascular and Renal Products
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Transmitted via email to: fred.fantozzi@hospira.com

Attention: Mr. Fred Fantozzi

Sponsor: Hospira, Inc.

Phone: (224) 212-4763

Subject: **Pre-NDA Meeting
Minutes**

Date: March 11, 2010

Pages, including this sheet: 8

From: Quynh Nguyen, Pharm.D., RAC

Phone: 301-796-0510

Fax: 301-796-9838

E-mail: quynh.nguyen@fda.hhs.gov

Please note that you are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

Pre-NDA Meeting with Sponsor

Application Number: Pre-IND 106,980
Sponsor: Hospira Inc.
Drug: Epinephrine Injection USP
Type of Meeting: Pre-NDA
Classification: B
Meeting Date: January 25, 2010
Briefing Package Received: December 23, 2009
Confirmation Date: November 5, 2009
Meeting Request Received: October 22, 2009
Meeting Chair: Ellis Unger, M.D.
Recorder: Quynh Nguyen, Pharm.D., RAC

List of Attendees:

Food and Drug Administration

Office of New Drugs, Office of Drug Evaluation I

Ellis Unger, M.D. Deputy Director

Office of New Drugs, Division of Cardiovascular and Renal Products

Norman Stockbridge, M.D., Ph.D. Director
Abraham Karkowsky, M.D., Ph.D. Clinical Team Leader
Shari Targum, M.D. Clinical Team Leader
B. Nhi Beasley, Pharm.D. Clinical Reviewer
Patricia Harlow, Ph.D. Pharmacology Team Leader (Acting)
Edward Fromm, R.Ph., RAC Chief, Project Management Staff
Quynh Nguyen, Pharm.D., RAC Regulatory Health Project Manager

Office of Clinical Pharmacology, Division of Clinical Pharmacology I

Rajnikanth Madabushi, Ph.D. Clinical Pharmacology Team Leader
Robert Kumi, Ph.D. Clinical Pharmacologist

Office of Biostatistics, Division of Biometrics I

Fanhui Kong, Ph.D. Statistician

Office of New Drug Quality Assessment, Division of Pre-Marketing Assessment I

Don Henry Project Manager

Office of New Drugs, Guidance and Policy Team

Sally Loewke, M.D. Unapproved Drugs Coordinator

Office of Compliance, Division of New Drugs and Labeling Compliance, Prescription Drugs Team

Astrid Lopez-Goldberg, J.D. Regulatory Counsel

Hospira Inc.

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BACKGROUND

Hospira Inc. requested this meeting via teleconference to discuss the requirements for submission of a 505(b)(2) NDA for Epinephrine Injection USP. (b) (4)

as the Reference Listed Drugs. The Division's Preliminary Responses were sent to the sponsor on January 19, 2010. Only Question 3 was discussed as noted below.

DISCUSSION

(b) (4)

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(b) (4)

4. Does the Agency concur with Hospira's proposed product labeling strategy for the 505(b)(2) application for epinephrine products?

Preliminary Response

This merits discussion at the time a set of indications can be supported.

5. Does the Agency concur that Hospira's proposed formulations and manufacturing processes are suitable for submission in the 505(b)(2) application for epinephrine products?

Preliminary Response

Please refer to the Pre-NDA Meeting Preliminary Responses from the Division of Pulmonary and Allergy Products (DPAP) on this CMC-related question.

6. Does the Agency concur that Hospira's proposed specifications and test methods are suitable for submission in the 505(b)(2) application for epinephrine products?

Preliminary Response

Please refer to the Pre-NDA Meeting Preliminary Responses from DPAP on this CMC-related question.

7. Does the Agency concur with Hospira's proposed stability data package to support requirements for the 505(b)(2) application for epinephrine products?

Preliminary Response

Please refer to the Pre-NDA Meeting Preliminary Responses from DPAP on this CMC-related question.

CONCLUSION

The sponsor's plans for submission of a 505(b)(2) application for epinephrine was discussed.

(b) (4)

The Division encouraged the sponsor to request a subsequent meeting with the Division, to focus on the specific indication the sponsor plans to pursue.

Minutes preparation: Quynh Nguyen, Pharm.D., RAC

Concurrence, Chair: {See appended electronic signature page}
Ellis Unger, M.D.

Rd:

E Unger 3/8/10; 3/10/10
N Stockbridge 3/6/10; 3/10/10
E Fromm 3/1/10

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A Karkowsky	3/1/10
S Targum	3/1/10
N Beasley	2/25/10
P Harlow	2/25/10
F Kong	2/25/10
R Madabushi	2/23/10
R Kumi	2/23/10

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-106980	GI-1	HOSPIRA INC	Epinephrine Injection USP

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/s/

ELLIS F UNGER
03/11/2010