CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202832Orig1s000

SUMMARY REVIEW

SUMMARY REVIEW FOR REGULATORY ACTION

Date	January 6, 2012
From	Lydia Gilbert-McClain, MD
Subject	Summary Review
NDA#	202,832
Applicant Name	Medefil, Inc.
Date of Submission	January 31, 2011
PDUFA Goal Date	January 7, 2012
Proprietary Name/Established (USAN) Name	None/Sodium chloride Injection, USP, 0.9%
Dosage forms/Strength	Solution in pre-filled plastic syringes for single use for injection/0.9%
Proposed Indication (s)	1. Dilution or dissolution of drugs for intravenous (IV), intramuscular (IM) or subcutaneous (SQ) injection
Recommended Action	*Approval*

Materials Reviewed/Consulted OND Action Package, including:	Names of Discipline reviewers
Medical Officer Review	Xu Wang, MD, PhD
Cross Discipline Team Leader Review	Alan Schroeder, PhD
CDRH consult	Kevin Marin

CDTL = Cross Discipline Team Leader

1. Introduction

This is the summary review for this NDA for sodium chloride injection, USP, 0.9% in pre-filled syringes. This summary review is primarily administrative in nature as no studies were conducted to support this application. There are multiple manufacturers of normal saline solution, and similar products have been cleared by CDRH as devices for use as saline flushes. The Agency made the administrative decision that normal saline as a diluent for drugs should be regulated as a drug, hence this product was submitted to CDER under the 505(b)(2) route for approval. The application was initially submitted to the Division of Gastroenterology and Inborn Errors Products on January 31, 2011 but the acceptance of the application for filing was not done until several weeks later because of a question regarding user fees. The Agency did not receive a user fee at the time of submission of the NDA on January 31, 2011 however, the requirement for payment of a user fee was waived on March 7, 2011 and the application was

accepted as of March 7, 2011. Therefore, the PDUFA goal date for this application will be January 7, 2012, based on a standard 10-month review clock.

As a 505(b)(2) application the reference listed product is Sodium chloride injection, 0.9% from Hospira Worldwide, Inc (NDA 18-803). The other products cited in the application sodium chloride 0.9% by Hospira [NDA 19-217] and (b) (4) [ANDA 88-912] contain supportive information.

2. Background

Normal saline in pre-filled syringes are currently marketed based on CDRH clearance as devices. The labeling for devices is for use for maintaining the patency of indwelling intravenous access devices (IVAD). The manufacturer Medefil, Inc proposes labeling the product for use as a diluent for diluting or dissolving drugs for IV, IM, or SQ injection. It was determined that this diluent indication should be regulated by the Agency in CDER as a drug indication as opposed to the device indication of IV flushes for intravenous tubing and/or indwelling access devices, however the products are exactly the same. The applicant received feedback from the Agency in the form of written pre-meeting comments in July 2008 in response to a granted preNDA meeting (the applicant cancelled the preNDA meeting upon receiving the Agency's preliminary comments). The applicant was told that non-clinical and clinical studies would not be required for the NDA and that the proposed product did not raise any pharmacokinetic issues. This interaction took place under the purview of the Division of Gastroenterology and Inborn Error Products[formerly the Division of Gastroenterology Products].

3. CMC

The proposed product in this NDA is pre-filled syringes of 0.9% normal saline in single-use disposable plastic syringes. The drug formulation only contains sodium chloride. The drug product presentations are 1, 2, 2.5, 3, 5, mL each in a 6 mL syringe, and 3, 5, and 10 mL each in a 12 mL syringe. The syringe is made of clear (b) (4) and it contains a luer-lock (b) (4)

CDRH was consulted during the review cycle for evaluation of the performance, robustness, and manufacturability of the device as appropriate. The consult review recommended that a human factors/usability validation study be performed or justification for the lack of such an assessment should be provided. This issue was discussed and addressed during the mid-cycle meeting. Of note, Sodium chloride 0.9% in pre-filled syringes have been on the market and available for a long period of time and performance of a human factors evaluation for this NDA would not affect the use of the product. Given this background, a human factors evaluation is not necessary for this NDA.

There are no outstanding CMC issues regarding the drug substance or drug product that will affect approvability. All manufacturing sites have been recommended as acceptable by the office of compliance.

4. Nonclinical Pharmacology/Toxicology

No non-clinical pharmacology/toxicology studies were required or submitted with this application

5. Clinical Pharmacology/Biopharmaceutics

No clinical pharmacology/biopharmaceutics studies were required or submitted with this application

6. Clinical Microbiology

Not applicable

7. Clinical/Statistical- Efficacy

No clinical studies were required to support the application as discussed in Section 2

8. Safety

No clinical studies were required to support the application as discussed in Section 2

9. Advisory Committee Meeting

An advisory committee meeting was not necessary for this application.

10. Pediatrics

As a diluent for diluting or dissolving drugs the product can be approved without age restriction. There are no safety concerns for the pediatric population with the use of 0.9% normal saline as a diluent or for dissolving drugs. Furthermore, this application does not trigger PREA. The PREA group clarified that this application is for a drug-device combination, not a drug-drug combination. The PREA trigger would have been for a new combination that's a new active ingredient, meaning that it's two active ingredients that have never been combined before. Therefore the application does not trigger PREA.

11. Other Relevant Regulatory Issues

Data Quality, Integrity, and Financial Disclosure

Not applicable as no clinical studies were performed for this application.
Financial disclosure statements were not included and were not necessary for this NDA since no clinical studies were conducted.

12. Labeling

Proprietary name

The applicant initially proposed the proprietary name (b) (4) but this name was not approved by the DEMEPA. The applicant withdrew the name and has decided to forgo a

tradename for this product. The product will be marketed without a tradename and this is acceptable because this 0.9% sodium chloride product is the same product that is currently in the market as cleared by CDRH under the device regulations for use as an IV flush. Having the same product in the market under a unique tradename could create confusion. It is important to keep in mind that the products cleared by CDRH and these products under NDA are the same. The distinction between the two is purely regulatory in terms of which center has regulatory purview over the stated indication in the labeling.

Physician labeling

The applicant submitted a label in the Physician's Labeling Rule Format. The main concern during the labeling review was regarding (b) (4) . From the standpoint of the healthcare provider, it would make sense to have both labeling statements on the same piece of paper since the product is exactly the same for both indications. Based on discussion within the division and feedback from within OND, I have concluded that inclusion of both labeling statements on the same labeling document (with the front portion containing the CDER drug indication statement and the back portion containing the CDRH device intended use and instructions) is acceptable.

Carton and Immediate Container Labels

The carton and immediate container labels were reviewed in consultation with DMEPA and DDMAC and there are no outstanding issues.

Patient Labeling and Medication Guide

There is no separate patient labeling and medication guide for this product

13. Action and Risk Benefit Assessment

Regulatory action

The regulatory action of the application is approval for marketing with the agreed-upon labeling text. We will acknowledge in the action letter that the entire CDRH-cleared intended use and instructions for the normal saline flush syringe used to maintain the patency of in-dwelling intravenous access devices (IVDAs) will be printed on the reverse side of the enclosed agreed-upon labeling.

Risk Benefit Assessment

The overall risk and benefit assessment of the product is favorable.

Postmarketing Risk Management Activities

None

Postmarketing Study Commitments/Requirements

None

APPEARS THIS WAY ON ORIGINAL

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/s/

LYDIA I GILBERT MCCLAIN
01/06/2012
Deputy Division Director