

UNITED STATES PUBLIC HEALTH SERVICE
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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INTERNAL MEMORANDUM

DATE: Jan 6, 2012

FROM: Jan Simak, Ph.D.
Visiting Scientist, Laboratory of Cellular Hematology

THROUGH: Jaroslav Vostal, M.D., Ph.D.
Chief, Laboratory of Cellular Hematology

TO: Iliana Valencia
Regulatory Project Manager

SUBJECT: Filing Memorandum

Submission type: NDA
BN 090067/0011 Amendment- Response to Non-
Approval Letter dated Feb 4, 2011.

Product Name: Isoplate Solution in the 500 mL EXCEL Container

Applicant/Manufacturing Site: B. Braun Medical Inc., Irvine, CA

CBER Rec. Date: 11/10/2011

Conclusion and Recommendation:

My recommendation is that the submission is sufficiently complete to permit a substantive review. The goal date is May 11, 2012.

Background Summary:

CBER issued a Non-Approval Letter of BN 090067 on Feb. 4, 2011.
CBER received on November 10, 2011, resubmission of the NDA and considers this a complete, class 2 response to February 4, 2011, Action Letter. Therefore, the goal date is May 11, 2012.

Submission Content:

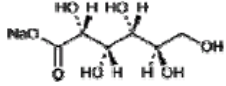
In support of the complete response, the following information is enclosed:

1. In Module 1 are enclosed- the 356h form, cover letter, and response to non-approval letter, and FDA non-approval letter dated February 4, 2011.
2. In Module 2, 2.7.6 Synopses of Individual Studies.
3. In Module 1.14.1, the revised container label and amended Physician's Labeling Reference (PLR).
4. In Module 3.2.S.6, details on the container closure system (i.e., materials of composition, suitability, and quality control) for the following drug substances: sodium chloride, sodium acetate trihydrate, potassium chloride, magnesium chloride, sodium phosphate dibasic heptahydrate, and monobasic potassium phosphate.
5. In Module 5.3.5.1 are enclosed Protocol II and III Clinical Report and statistical calculations.
6. In Module 5.3.5.1.25.3 are enclosed the raw data and calculations for Protocol II and III Clinical Report in SAS, .xpt, and Excel format.

Drug description

The Isoplate Solution is identical to the Isolyte[®] S, pH 7.4 (Multi-Electrolyte Injection) is a FDA approved sterile, nonpyrogenic intravenous injection packaged in B. Braun's EXCEL[®] Container and approved, as of September 29, 1989 (ANDA 19-696), for the following indication: For use in adults as a source of electrolytes and water for hydration, and as an alkalinizing agent.

Isolyte S has the following approved formulation:

Ingredients	Formula	Amount (Each 100 mL contains)
ACTIVE INGREDIENTS (electrolytes)		
Sodium Chloride USP	NaCl	0.53g
Sodium Acetate Trihydrate USP	$C_2H_3NaO_2 \cdot 3H_2O$	0.37g
Potassium Chloride USP	KCl	0.037g
Magnesium Chloride Hexahydrate USP	$MgCl_2 \cdot 6H_2O$	0.03g
Dibasic Sodium Phosphate Heptahydrate USP	$Na_2HPO_4 \cdot 7H_2O$	0.012g
Monobasic Potassium Phosphate NF	K_2HPO_4	0.00082g
Sodium Gluconate USP		0.5g
INACTIVE INGREDIENTS		
Water for Injection USP	H_2O	q.s.
Glacial Acetic Acid USP	$C_2H_4O_2$	adjustment for pH
Sodium Hydroxide NF	NaCl	adjustment for pH

Isoplate Solution Indication for Use

Indicated as a platelet additive solution for the storage of leukoreduced hyperconcentrated apheresis platelets.

NDA review team

Review Discipline	Reviewer Name
Regulatory	Iliana Valencia (OBRR/DBA/RPMB)
Clinical	Jan Simak (OBRR/DH/LCH)
Pharmacology	Yolanda Branch (OBRR/DH/
Statistical	Chinying Wang (OBE/DB/TEB)
CMC/CDER	Minerva Hughes (OPS/ONDQA/NDQAII/Branch IV)
DMPQ	Nawab Siddiqui (OCBQ/DMPQ/BII)
Labeling	Lore Fields (OBRR/DBA/BPB)
BIMO	Anthony Hawkins (OCBQ/DIS/BMB)
Epidemiology	Faith Barash (OBE/DE/TBSB)
PNR Review	Dana Martin (OCBQ/DCM/APLB)

Review progress

Fileability: Yes, the application was found sufficiently complete to permit a substantive review. The review classification for this application is Standard. Therefore, the user fee goal date is May 11, 2012.

PREA: No, as assessed for the original submission, this application similarly to BN080041 does not trigger PREA (21 U.S.C. 355c) requirements because it does not include new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration. (email from Nisha Jain of 6/29/2010)

BIMO: Clinical Investigator Inspection of the additional clinical site Dr. Cancelas-Perez, Hoxworth Blood Center requested (email from Anthony Hawkins 11/29/2011)

DMPQ: Company should submit the Categorical exclusion under 21 CFR 25.31(a). They have submitted Categorical exclusion under 21 CFR 25.31(J). This does not apply to this NDA. No other issues for the response to CR letter. (email from Nawab Siddiqui 11/18/2011)

Epidemiology: No comments on the response to CR letter. (email from Faith Barash of 11/18/2011)

CDER consult CMC review: The Applicant's response is complete for filing from the CMC (i.e., CDER consulted CMC) perspective. Of note, all review comments regarding labeling from the CDER consult final discipline review were not conveyed to the applicant in the CR letter, and we can work to resolve the remaining labeling concerns during the review period. (email from Minerva Hughes of 11/18/2011)

Pharm./tox review: The nonclinical responses to CR letter were sufficient. (email from Yolanda Branch of 11/18/2011)