



FOOD AND DRUG ADMINISTRATION

Center For Biologics Evaluation and Research

MEMORANDUM

Date: November 12, 2007

APPROVED

By Elena Karnaukhova on 11/12/07

From: Elena Karnaukhova, Ph.D.; HFM-343; LBVB, DH,
OBRR, CBER; (301) 402-4635, FAX (301) 402-2780

Subject: NDA 70012/0.0; Final review memo for the
original NDA for 6% hydroxyethyl starch
(HES) 130/0.4 in 0.9% NaCl infusion (Voluven®),
submitted by Carolina Research Group on behalf
of Fresenius Kabi Deutschland GmbH; Module 3:
Quality (analytical method validation)

APPROVED

By Abdu Alayash on 11/12/07

Through: Abdu Alayash, Ph.D., Chief; HFM-343, LBVB, DH,
OBRR, CBER; (301) 827-3813, FAX (301) 435-4034

To: Franklin Stephenson, RPM; HFM-380, RPMB, DBA,
OBRR, CBER; (301) 827-3524, Fax (301) 827-3535

To the file: NDA 70012

Action recommended: Approval

SUMMARY

Submission date: 2-28-2007

CBER receipt date: 3-1-2007

DATS Log #: 412822

Sponsor: Fresenius Kabi Deutschland GmbH (FK)

US Agent: Carolina Research Group, Inc. (CRG)

Type of submission: Original NDA BN070012/0

Product: 6% HES 130/0.4 in 0.9% NaCl infusion (Voluven®)

Indications: treatment and prophylaxis of hypovolemia

Administration: i.v.

Module 3 (Quality), STN BN070012/0, and Master Files, STN

██████████ provide the manufacture data for:

DRUG SUBSTANCE (HES 130/0.4 powder) and

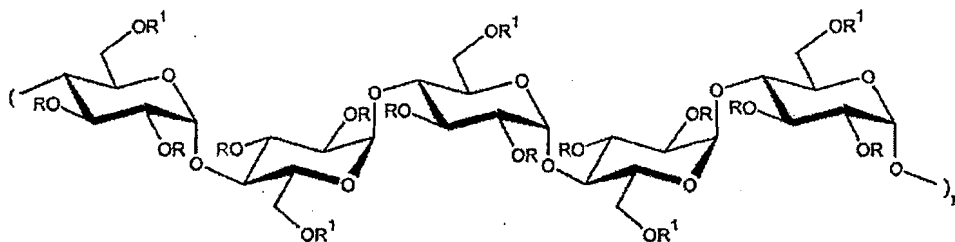
DRUG PRODUCT (Voluven 6% solution for infusion)

This memo is a review of analytical methods validation.

Background

The Fresenius Kabi's 6% HES 130/0.4 in 0.9% NaCl infusion (Voluven®) is a new plasma volume substitute that is indicated for the treatment and prophylaxis of hypovolemia. The active component of Voluven, HES 130/0.4, is a new specification of hydroxyethyl starches which is characterized by a medium molecular weight (MW) and degree of molar substitution (MS) on the glucose units of the starch. Voluven was initially approved for marketing in Germany in 1999 and currently is marketed in 66 countries.

HES 130/0.4 is a polymeric glucose derivative (amilopectine) that mainly consists of α -1,4-connected glucose units with several α -1,6-branches, also containing a small amount of amylase. Hydroxyls at the 2,3 and 6 positions of glucose are subject of partial derivatization to hydroxyethyl groups.



$R = -H, -CH_2CH_2OH$

$R' = -H, -CH_2CH_2OH$ or glucose units

Molecular weight (MW) limits for HES 130/0.4 are:

Weight average MW: 130,000 \pm 20,000 Dalton

██

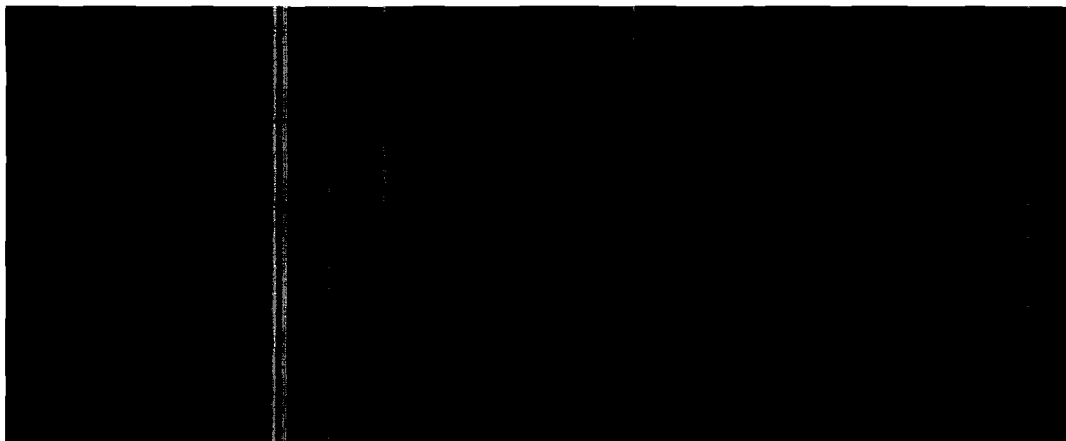
Molar substitution (MS), the ratio of hydroxyethyl groups to glucose units is 0.38-0.45.

12 PAGES

DETERMINED NOT

TO BE

RELEASABLE



Reviewer's comment: the response is adequate.

COMMENTS

Based on the CMC review of product quality/analytical methods, 6% hydroxyethyl starch 130/0.4 in 0.9% NaCl infusion (Voluven®) is approvable.