CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022462Orig1s000

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

ONDQA BIOPHARMACEUTICS REVIEW

NDA#:	**22-462**
Submission Date:	3/27/09
Drug Name:	Baclofen Injection
Formulation:	intrathecal injection
Strength:	0.05, 0.5, 2 (b) (4) mg/mL
Sponsor:	CNS Therapeutics
Reviewer:	John Duan, Ph.D.
Submission Type:	Biowaiver Request

COMMENTS

The biowaiver may be granted based on the following observations.

1. The product is a solution with similar pH to the listed reference product.
2. The compositions of different strengths are proportionally similar.

(b) (4)

RECOMMENDATION

The biowaiver is recommended to be granted.

_____ _____

John Duan, Ph.D. Date
Reviewer
ONDQA Biopharmaceutics

_____ _____

Patrick Marroum, Ph.D. Date
ONDQA Biopharmaceutics

cc: NDA 22462
Patrick Marroum, John Duan

ATTACHMENT SUMMARY OF THE SUBMISSION

BACKGROUND

Baclofen is approved in the United States for the treatment of spasticity. The approved application for Baclofen Injection is NDA 20-075, which is owned by Medtronic, Inc. Medtronic distributes Baclofen Injection under the trade name, Lioresal®. Medtronic also manufactures and distributes the SynchroMed® II delivery systems that are used for chronic delivery of the drug into the intrathecal space. A second intrathecal pump, the Codman Series 3000, is marketed by Johnson & Johnson and approved for use with baclofen.

The sponsor has developed intrathecal baclofen (b) (4) concentrations, 0.05 mg/mL, 0.5 mg/mL, 2 mg/mL (b) (4) The (b) (4) strengths are quantitatively identical to the corresponding products marketed by Medtronic. By prior agreement with the Agency, they are included in this NDA.

BIOWAIVER REQUEST

The 0.05 mg/mL, 0.5 mg/mL, and 2 mg/mL strengths of baclofen injection are qualitatively and quantitatively identical to the reference listed drug, Lioresal® (baclofen injection). (b) (4) The applicant has submitted a biowaiver request for all product strengths (b) (4)

During the pre-NDA meeting dated April, 30, 2008, the sponsor was advised that a waiver is possible provided the information below is provided.

- Please provide information regarding potential for CSF precipitation of the proposed dosage strength (in vitro study using artificial CSF).

- Provide pH information of your product (all strengths) vs. reference product.

The requested pH comparison and precipitation study results are located in the Pharmaceutical Development section.

Composition of the Drug Product

The formulations of Baclofen Injection (Intrathecal) to be manufactured at the (b) (4) facility are presented in Table 1.

Table 1 - Composition of Baclofen Injection (Intrathecal)

Ingredient	0.05 mg/mL (50mcg/mL) Product Conc.	0.5 mg/mL (500mcg/mL) Product Conc.	2 mg/mL (2000mcg/mL) Product Conc.
Baclofen USP	0.05 g/L	0.50 g/L	2.00 g/L
Sodium Chloride USP	(b) (4)		
Water for Injection USP			

(b) (4)

pH comparison between CNS Baclofen Intrathecal and (RLD) Lioresal®

Testing was conducted at (b) (4) to compare the pH of the (RLD) Lioresal® to CNS intrathecal Baclofen. Lioresal® was purchased from three different lots and triplicate testing was conducted. The table below shows the test results of the purchased Lioresal® and CNS registration batches manufactured by (b) (4)

Test Date	Sample	Lot#	pH Results
7-16-2008	Lioresal® 0.5 mg/mL (10 mg/20 mL)	CS0058A	6.7 – 6.7
7-16-2008	Lioresal® 2 mg/mL (40 mg/20 mL)	DS0028	6.7 – 6.7
7-30-2008	Lioresal® 2 mg/mL (10 mg/5 mL)	BS0046	6.6 – 6.7
12-2-2008	(b) (4) /CNS 0.05 mg/mL (50 mcg/1 mL)	2155-101	6.5 – 6.6
9-3-2008	/CNS 0.5 mg/mL (10 mg/20 mL)	2118-101	6.4 – 6.5

(b) (4)

Precipitation Study

A study was performed to determine if the Baclofen for injection forms a precipitate when injected into cerebrospinal fluid (CSF). (b) (4)

(b) (4)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22462	ORIG-1	CNS THERAPEUTICS INC	BACLOFEN INTRATHECAL INJ 0.05 MG/ML/0.5

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

/s/

JOHN Z DUAN
01/12/2010

PATRICK J MARROUM
01/12/2010