CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75392

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA 75-392 **DRUG PRODUCT:** Propofol Injectable Emulsion (0.025% Sodium Metabisulfite)

FIRM: Gensia Sicor Pharmaceuticals, Inc. **DOSAGE FORM:** IV

STRENGTHS: 10 mg/mL

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable -
See **ESTABLISHMENT EVALUATION REPORT** dated 5/14/99.

BIO INFORMATION: Acceptable -
See bio review, dated 10/30/98.

VALIDATION-(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): Acceptable
Methods validation for drug substance and drug product were performed under ANDA which used the same methods. Only the sodium metabisulfite assay was tested on ANDA 75-102. See methods validation report dated May 26, 1998.

STABILITY: Adequate -
Accelerated (40°±2°C/75±5% RH and Light Box) stability data are provided for lot no. XP7N314F1, tested initially, 1, 2 and 3-month test intervals in the final marketed container/closure system. Controlled room temperature (25°±2°C/60±5% RH) data tested initially, 1, 2 and 3 month intervals are also provided. The data are adequate and within the specified limits.

LABELING: Adequate -
See labeling review dated 11/23/99.

STERILIZATION VALIDATION: Acceptable -
See Microbiology review #1, dated 12/16/99

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?) Adequate -
Bio batch same as exhibit lot no. XP7N314. See size of stability batch below for details. Bulk substance manufacturer is ⌜ ⌟lot no. PL-PROP-4 used. DMF⌜ ⌟found **ADEQUATE**, dated 1/5/00.

SIZE OF STABILITY BATCHES - Adequate -
Executed Batch Record is provided for lot no. XP7N314, which was filled into 20 mL vials (lot no. XP7N314) and 20 mL prefilled

syrings (lot no. XP7N314F1). Documentation from lot #XP7N314 (20 mL vial) is included only to provide the information regarding the compounding and mass balance for the bulk emulsion. A theoretical yield of Liters, actual yield equals Liters. Batch reconciliation indicates the entire batch was packaged. The batch was manufactured using production equipment under production conditions.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY? Yes!

The proposed maximum production batch size is Liters, with equipment specified are provided.

RECOMMENDATION:

APPROVED

/S/

Raymond Brown

4/25/00

Date

cc: HFD-645/RBrown/4/25/00
HFD-645/BArnwine/5/3/00
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F/T by pah/5/4/00

5/11/2000

1. CHEMIST'S REVIEW NO. **2**

2. ANDA #**75-392**

3. NAME AND ADDRESS OF APPLICANT
Gensia Sicor Pharmaceuticals, Inc.
17 Hughes
Irvine, CA 92618-1902

4. LEGAL BASIS FOR ANDA SUBMISSION
Generic version of Zeneca, Ltd., Diprivan® (NDA 19-627). Patent certification and exclusivity statement are provided (pp. 011-014).

5. SUPPLEMENT(s) N/A

6. ESTABLISHED NAME
Propofol Injectable Emulsion (with 0.025% Sodium Metabisulfite)

7. PROPRIETARY NAME
N/A

8. SUPPLEMENT(s) PROVIDE(s) FOR Original ANDA

9. AMENDMENTS AND OTHER DATES

Firm		FDA	
Orig. submission	5/29/98	Phone call	6/18/98
Amendment	6/24/98	Acknowledgment letter	6/26/98
New correspondence	7/8/98		
New correspondence	7/30/98	Bio review	10/30/98
New correspondence	12/1/98	Labeling review	12/11/98
Amendment	12/22/98	Labeling review	4/6/99
Amendment (labeling)	5/7/99	Labeling review	7/12/99
New correspondence	8/18/99		
Amendment (labeling)	8/30/99	Labeling review	10/13/99
Amendment (labeling)	11/12/99	Labeling review	11/30/99
		Deficiency letter	3/1/00
Amendment (FAX)	3/7/00		
Amendment	5/22/00		
Amendment	6/7/00		

This review covers submission dated 3/7, 5/22 and 6/7/00.

10. PHARMACOLOGICAL CATEGORY
Anesthetic - is indicated for both induction and/or maintenance of anesthesia as part of a balanced anesthetic technique for inpatient and outpatient surgery.

11. Rx or OTC

Rx

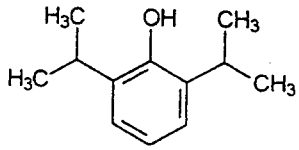
12. RELATED DMF(s)

13. DOSAGE FORM
Emulsion (Intravenous)

14. STRENGTH
10 mg/ml

15. CHEMICAL NAME AND STRUCTURE

Propofol. Phenol, 2,6-bis(1-methylethyl)-. $C_{12}H_{18}O$. 178.27. 2074-54-8. Anesthetic (intravenous).



Drug substance and drug product are not official USP 24 items.

16. RECORDS AND REPORTS None

17. COMMENTS
a. Application is ADEQUATE for approval.
b. Labeling found acceptable, dated 11/30/99.
c. Bio found acceptable, dated 10/30/98
d. DMF found **adequate**, dated 1/5/00.
e. Methods validation for drug substance and drug product found **acceptable**, see ANDA 75-102.
f. Establishment Evaluation Report found **Acceptable**, dated 5/14/99.
g. Microbiology Review found **Acceptable**, dated 12/16/99.

18. CONCLUSIONS AND RECOMMENDATIONS
APPROVED

19. REVIEWER:
Raymond Brown

DATE COMPLETED:
June 13, 2000

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pages of trade

secret and/or

confidential

commercial

information

Chem #2

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38. CHEMISTRY COMMENT TO BE PROVIDED TO THE APPLICANT

ANDA # 75-392 APPLICANT: **Gensia Sicor Pharmaceuticals, Inc.**

DRUG PRODUCT: **Propofol Injectable Emulsion, 10 mg/mL (with 0.025% Sodium Metabisulfite)**

The deficiencies presented below represent FAX deficiencies.

Sincerely yours,

/S/

for Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center of Drug Evaluation and Research