CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-176

ADMINISTRATIVE DOCUMENTS

ANDA APPROVAL SUMMARY

ANDA: 75-176	CHEMIST: Neeru B. Takiar	DATE: February 02, 2000
DRUG PRODUCT: Haloperidol Decanoate Injection		
FIRM: King Pharmaceuticals, Inc.		
DOSAGE FORM: Injectable	STRENGTH: 50 mg/mL and 100 mg/mL (1 mL ampules and 5 mL MDVs)	
cGMP: EER was acceptable on April 08, 1999.		
BIO: The Bio study was acceptable on December 12, 1997; Signed off December 29, 1997		
VALIDATION - *(Description of dosage form same as firm's):* The DS and DP are non compendial items. Method validation results from the district laboratory are satisfactory.		
STABILITY: The firm has provided satisfactory 3 months accelerated and 24 months room temperature stability data for samples stored in vials and ampules. The stability data support an expiration period of 24 months.		
LABELING: Labeling was on August 31, 1999; signed off September 1,1999		
STERILIZATION VALIDATION *(If applicable)*: Sterilization Validation was acceptable on November 19, 1999.		
SIZE OF BIO BATCH *(Firm's source of NDS ok?)*: Size of the bio batch for 1mL ampules (50 mg/mL and 100 mg/mL) is d for 5 mL vials (50 mg/ mL and 100 mg/ mL) The drug substance was manufactured by and was acceptable on April 7, 1999.		
SIZE OF STABILITY BATCHES *(If different from bio batch, were they Manufactured via the same process?):* Size of stability batch is same as that of the bio batch.		
PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?: Size of the proposed production batch size for 1 mL ampules (50 mg/mL and 100 mg/mL) is nd for 5 mL vials (50 mg/ mL and 100 mg/ mL) is he manufacturing process is identical to the exhibit batch.		
Signature of chemist: Neeru B. Takiar 2/4/2000 Neeru B. Takiar/2-2-2000	Signature of supervisor: Dave Gill, Ph.D./ DS Gill 2-2-2000	

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RECORD OF TELEPHONE CONVERSATION

Reference is made to the December 13, 1999 t-con and the firm's amendments dated December 22 and December 28, 1999. OGD's comments to the firm's response were:

1. USP 24 OVI specs: the firm will provide the revised spec. sheet for the drug substance (OVI specs will be included).

2. UNKNOWN impurities: the limit of is for total unknown impurities. The firm will provide limit for individual unknown impurities for drug substance and drug product release and stability. The firm will justify the limits based on observed values of the submission batches and provide the revised spec. sheet.

3. Specific impurity test: the firm will provide a signed statement from the drug substance manufacturer that the impurity is not detectable.

4. Sterilization of tweezers and stoppers: satisfactory. Dr. Andrea High of OGD was consulted and she stated that this is a cGMP issue.

5. Nonaqueous materials/vehicles: satisfactory.

6. Stability protocol and extension of expiration date: Satisfactory

The firm expects to respond by 1/10/2000

DATE
January 3, 2000

ANDA NUMBER
75-176

IND NUMBER

TELECON

INITIATED BY:
FDA

PRODUCT NAME
Haloperidol Decanoate

FIRM NAME
King Pharmaceuticals

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Greg Carrier, David Tegra

TELEPHONE NUMBER
423-989-8166

SIGNATURE
Dave Gill DG 1-6-00
Neeru Takiar N. Takiar 1-6-00
Ruby Yu

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CC:

RECORD OF TELEPHONE CONVERSATION

The applicant was notified by telephone that the endotoxin limits for the subject drug product were high. The applicant was using the limits posted in the LAL Guideline; however, those limits do not reflect the current dose as labeled. I explained to GC that the Guideline may not reflect changes in the human dosage amount if labeling/indication changes have occured since the LAL Guideline in 1987. These changes may not be reflected the Guideline draft in 1994. He agreed to provide a commitment to change the endotxin limits via T. Con Fax to Ruby Yu (Project Manager).

This was the last outstanding issue for the ANDA on the approval matrix.

DATE
11/18/99

ANDA NUMBER
75-176

IND NUMBER
n/a

TELECON

INITIATED BY **MADE**
_ **APPLICANT/ SPONSOR** _X **BY TELE.**
_X **FDA** _ **IN PERSON**

PRODUCT NAME
Haloperidol Deconoate Injection

FIRM NAME
King Pharms

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Greg Carrier, Director of Reg. Affairs

TELEPHONE NUMBER
423-989-8166

SIGNATURE
11/18/99

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TELECON

INITIATED BY **MADE**
_ APPLICANT/ SPONSOR _X BY TELE.
_X FDA _ IN PERSON

PRODUCT NAME
Haloperidol Deconoate Injection

FIRM NAME
King Pharms

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Greg Carrier, Director of Reg. Affairs

TELEPHONE NUMBER
423-989-8166

SIGNATURE
11/18/99

DEC 12 1997

Haloperidol Decanoate Injection
50 mg/mL in 1 mL & 5 mL vials
100 mg/mL in 1 mL & 5 mL vials
ANDA #75-176
Reviewer: Jahnavi S. Kharidia
X:\NEW\FIRMSAM\KING\LTRS&REV\75176W.797

King Pharmaceuticals, Inc.
501 Fifth Street
Bristol, Tennessee
Submission Date:
30 July, 1997

Review of a Waiver Request

Haloperidol decanoate is a long-acting parenteral antipsychotic drug intended for use in the management of patients requiring prolonged parenteral antipsychotic therapy. It is supplied in two dosage strengths: 50 mg haloperidol as 70.5 mg per mL haloperidol decanoate and 100 mg haloperidol as 141.04 mg per mL haloperidol decanoate. Innovator products are Haldol® Decanoate 50 and Haldol® Decanoate 100 manufactured by R.W. Johnson Company.

The firm has submitted the application for haloperidol decanoate injection 50 mg/mL and 100 mg/mL and is requesting a waiver of *in vivo* bioavailability requirements based on 21 CFR 320.22 (b)(1).

Formulation:

Ingredient (mg/mL)	Haloperidol Decanoate Injection 50 mg/mL[a]		100 mg/mL[a]	
	King Pharmaceutical	R.W. Johnson	King Pharmaceutical	R.W. Johnson
Haloperidol Decanoate	70.52[1]	70.52[1]	141[2]	141[2]
Benzyl Alcohol, NF				
Sesame Oil, NF				

[1] equivalent to 50 mg Haloperidol
[2] equivalent to 100 mg Haloperidol
[a] target fill volume 1.15 mL for 1 mL ampule and 5.5 mL for 5 mL vial

Comments:

1. The test product is in a sesame oil vehicle intended solely for intramuscular administration.

2. The active ingredient, route of administration, dosage form and strengths of the test drug products are the same as those of the reference listed drug.

3. All ingredients in test and reference products are qualitatively and quantitatively the same.

Recommendations:

The Division of Bioequivalence agrees that the information submitted by King Pharmaceuticals, Inc. demonstrates that haloperidol decanoate injections 50 mg/mL and 100 mg/mL fall under the criteria set forth in 21 CFR 320.22(b)(1) of the Bioavailability/ Bioequivalence Regulations. The waivers of the *in vivo* bioequivalence study requirements for 50 mg/mL and 100 mg/mL haloperidol decanoate injections are granted. From the bioequivalence point of view the Division of Bioequivalence deems the test products to be bioequivalent to Haldol® decanoate 50 and Haldol® decanoate 100 manufactured by R. W. Johnson Company, respectively.

Jahnavi S. Kharidia

Jahnavi S. Kharidia, Ph.D.
Review Branch II
Division of Bioequivalence

RD INITIALED RMHATRE
FT INITIALED RMHATRE Ramakant M. Mhatre Date 12/12/97
Ramakant M. Mhatre, Ph.D.
Team Leader, Branch III
Division of Bioequivalence

Concur: Dale P. Conner Date 12/12/97
Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence

cc: