

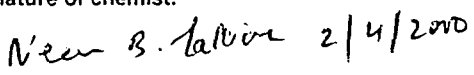
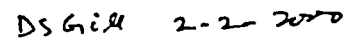
**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**75-176**

**ADMINISTRATIVE DOCUMENTS**

## ANDA APPROVAL SUMMARY

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

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**RECORD OF TELEPHONE CONVERSATION**

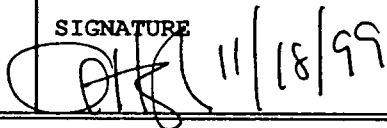
<p>Reference is made to the December 13, 1999 telecon and the firm's amendments dated December 22 and December 28, 1999. OGD's comments to the firm's response were:</p> <ol style="list-style-type: none"> <li>1. USP 24 OVI specs: the firm will provide the revised spec. sheet for the drug substance (OVI specs will be included).</li> <li>2. UNKNOWN impurities: the limit of is for total unknown impurities. The firm will provide limit for <u>individual</u> 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.</li> <li>3. Specific impurity test: the firm will provide a signed statement from the drug substance manufacturer that the impurity is not detectable.</li> <li>4. Sterilization of tweezers and stoppers: satisfactory. Dr. Andrea High of OGD was consulted and she stated that this is a cGMP issue.</li> <li>5. Nonaqueous materials/vehicles: satisfactory.</li> <li>6. Stability protocol and extension of expiration date: Satisfactory</li> </ol> <p>The firm expects to respond by 1/10/2000</p>	<p><b>DATE</b> January 3, 2000</p>
	<p><b>ANDA NUMBER</b> 75-176</p>
	<p><b>IND NUMBER</b></p>
	<p align="center"><b>TELECON</b></p>
	<p><b>INITIATED BY:</b> FDA</p>
	<p><b>PRODUCT NAME</b> Haloperidol Decanoate</p>
	<p><b>FIRM NAME</b>  King Pharmaceuticals</p>
	<p><b>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD</b>  Greg Carrier, David Tegra</p>
	<p><b>TELEPHONE NUMBER</b> 423-989-8166</p>
	<p><b>SIGNATURE</b> Dave Gill <i>DGill</i> Neeru Takiar <i>N. Takiar</i> Ruby Yu <i>Ryu</i></p>

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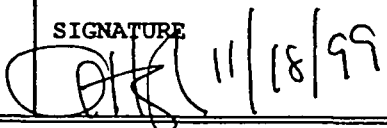
1-6-00

CC:

RECORD OF TELEPHONE CONVERSATION

<p>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 occurred 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 endotoxin limits via T. Con Fax to Ruby Yu (Project Manager).</p> <p>This was the last outstanding issue for the ANDA on the approval matrix.</p>	<b>DATE</b> 11/18/99								
	<b>ANDA NUMBER</b> 75-176								
	<b>IND NUMBER</b> n/a								
	<b>TELECON</b>								
	<table border="0"> <tr> <td><b>INITIATED BY</b></td> <td><b>MADE</b></td> </tr> <tr> <td><input type="checkbox"/> <b>APPLICANT/</b></td> <td><input checked="" type="checkbox"/> <b>BY</b></td> </tr> <tr> <td><b>SPONSOR</b></td> <td><b>TELE.</b></td> </tr> <tr> <td><input checked="" type="checkbox"/> <b>FDA</b></td> <td><input type="checkbox"/> <b>IN PERSON</b></td> </tr> </table>	<b>INITIATED BY</b>	<b>MADE</b>	<input type="checkbox"/> <b>APPLICANT/</b>	<input checked="" type="checkbox"/> <b>BY</b>	<b>SPONSOR</b>	<b>TELE.</b>	<input checked="" type="checkbox"/> <b>FDA</b>	<input type="checkbox"/> <b>IN PERSON</b>
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	<b>SPONSOR</b>	<b>TELE.</b>							
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	<b>PRODUCT NAME</b> Haloperidol Deconoate Injection								
<b>FIRM NAME</b> King Pharms									
<b>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD</b> Greg Carrier, Director of Reg. Affairs									
<b>TELEPHONE NUMBER</b> 423-989-8166									
<b>SIGNATURE</b> 									

RECORD OF TELEPHONE CONVERSATION

<p>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 occurred 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 endotoxin limits via T. Con Fax to Ruby Yu (Project Manager).</p> <p>This was the last outstanding issue for the ANDA on the approval matrix.</p>	<p><b>DATE</b> 11/18/99</p>
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	<p><b>TELEPHONE NUMBER</b> 423-989-8166</p>
	<p><b>SIGNATURE</b>  </p>

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: Jahnvi S. Kharidia

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**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 <sup>a</sup>		100 mg/mL <sup>a</sup>	
	King Pharmaceutical	R.W. Johnson	King Pharmaceutical	R.W. Johnson
Haloperidol Decanoate	70.52 <sup>1</sup>	70.52 <sup>1</sup>	141 <sup>2</sup>	141 <sup>2</sup>
Benzyl Alcohol, NF				
Sesame Oil, NF				

<sup>1</sup> equivalent to 50 mg Haloperidol

<sup>2</sup> equivalent to 100 mg Haloperidol

<sup>a</sup> 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.

*Jahnvi S. Kharidia*  
Jahnvi 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: