

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: September 28, 1999
To: Dockets Management Branch (HFA-305)
From: Melissa Lamb
Office of Generic Drugs

Subject: What Challenges OGD Faces and How The Industry Can Help

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

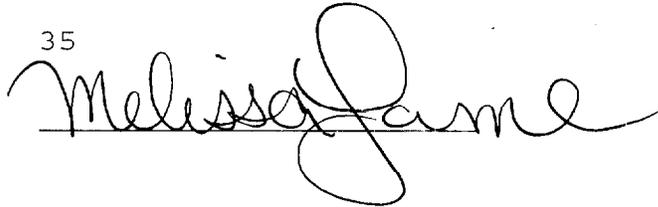
Title of Presentation: What Challenges OGD Faces and How The Industry Can Help

Presented for: NPA 1999 Fall Meeting

Date Presented: 9/28/1999

Presented by: Douglas L. Sporn

Number of Pages: 35



Attachment

5 4 9 4 '00 MAR 22 10:12

90S-0308

M670

NPA 1999 Fall Meeting

What Challenges OGD Faces
and How The Industry Can
Help

Douglas L. Sporn

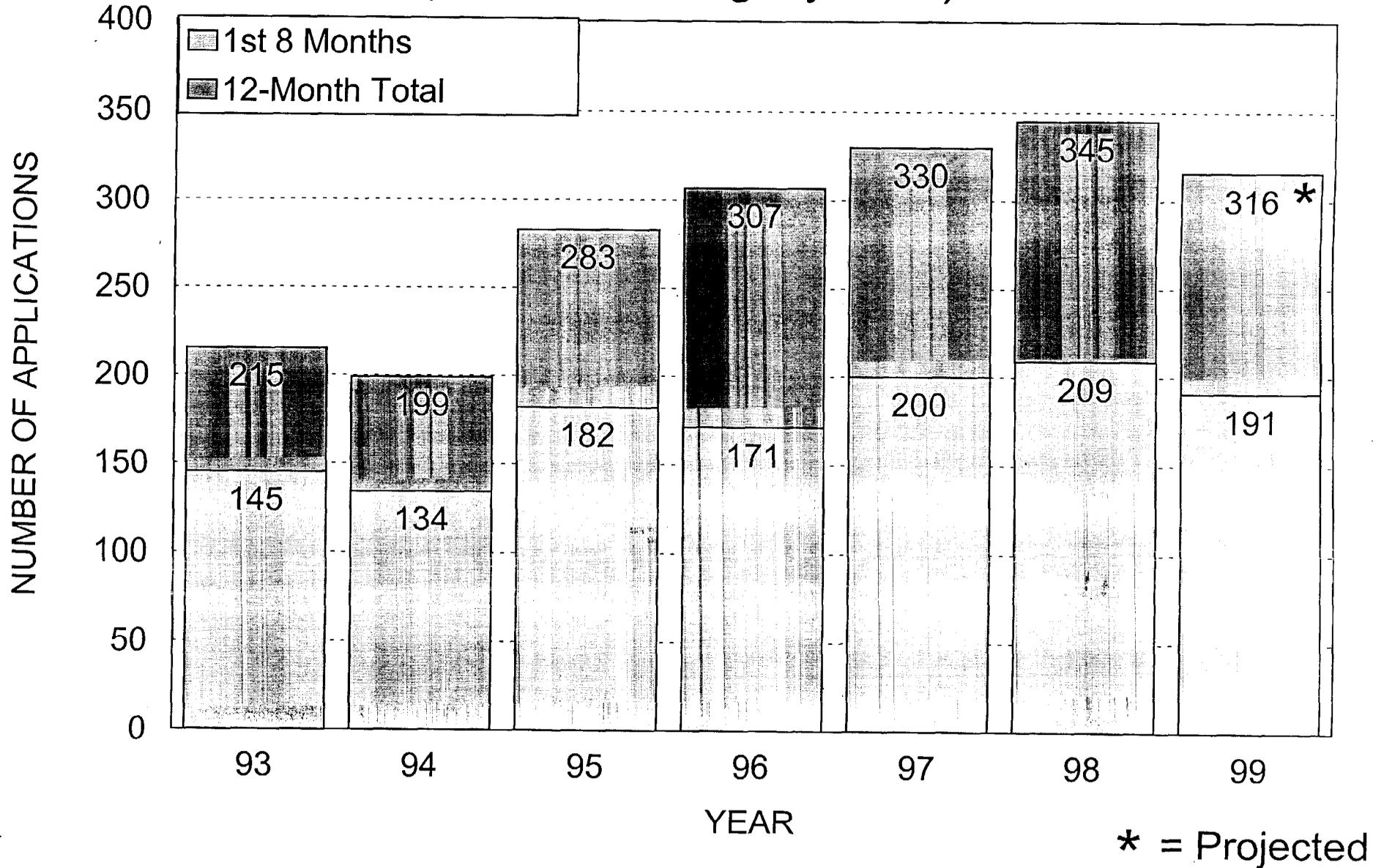
Director

Office of Generic Drugs

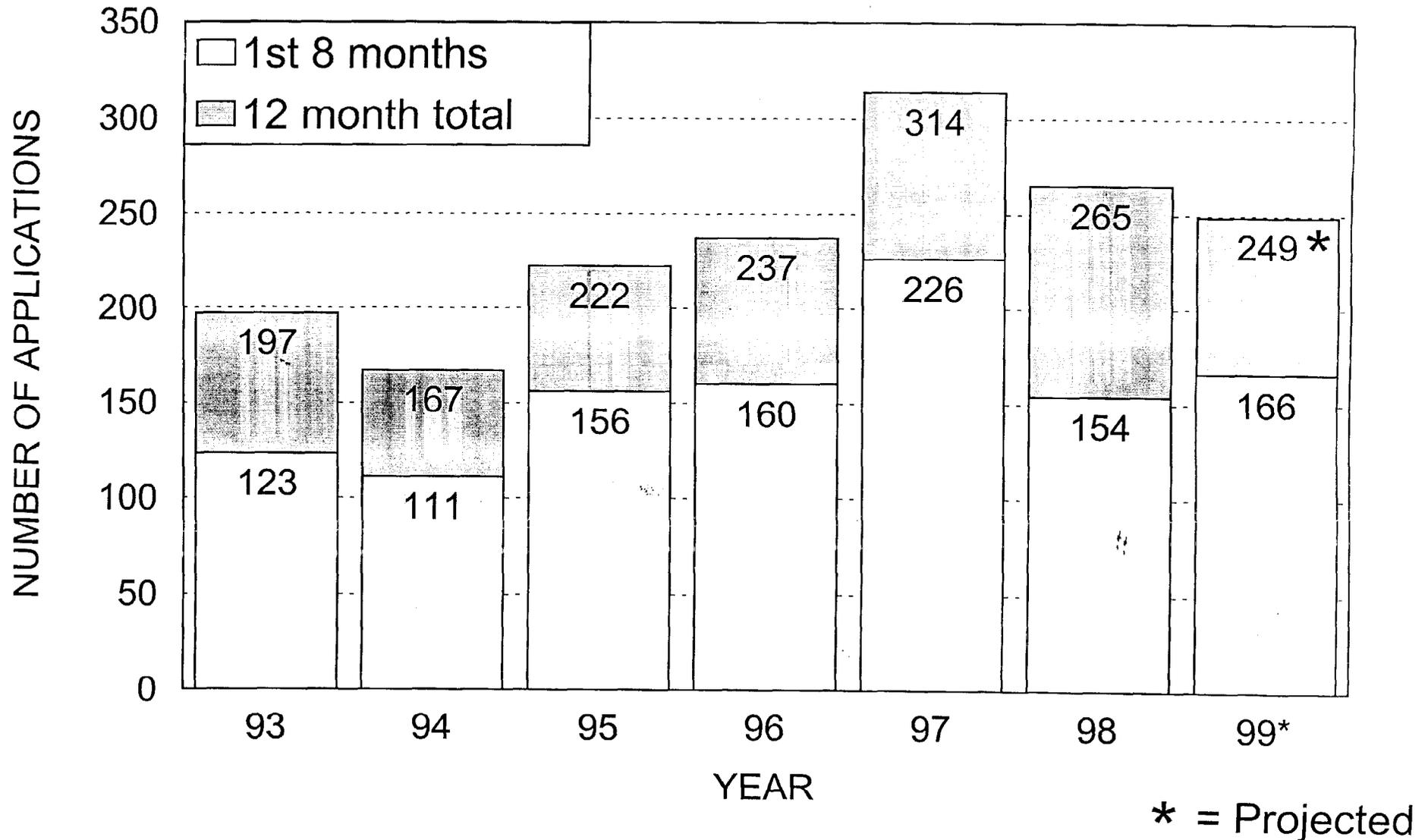
September 28, 1999

Las Vegas, Nevada

Calendar Year Receipts (New Counting System)

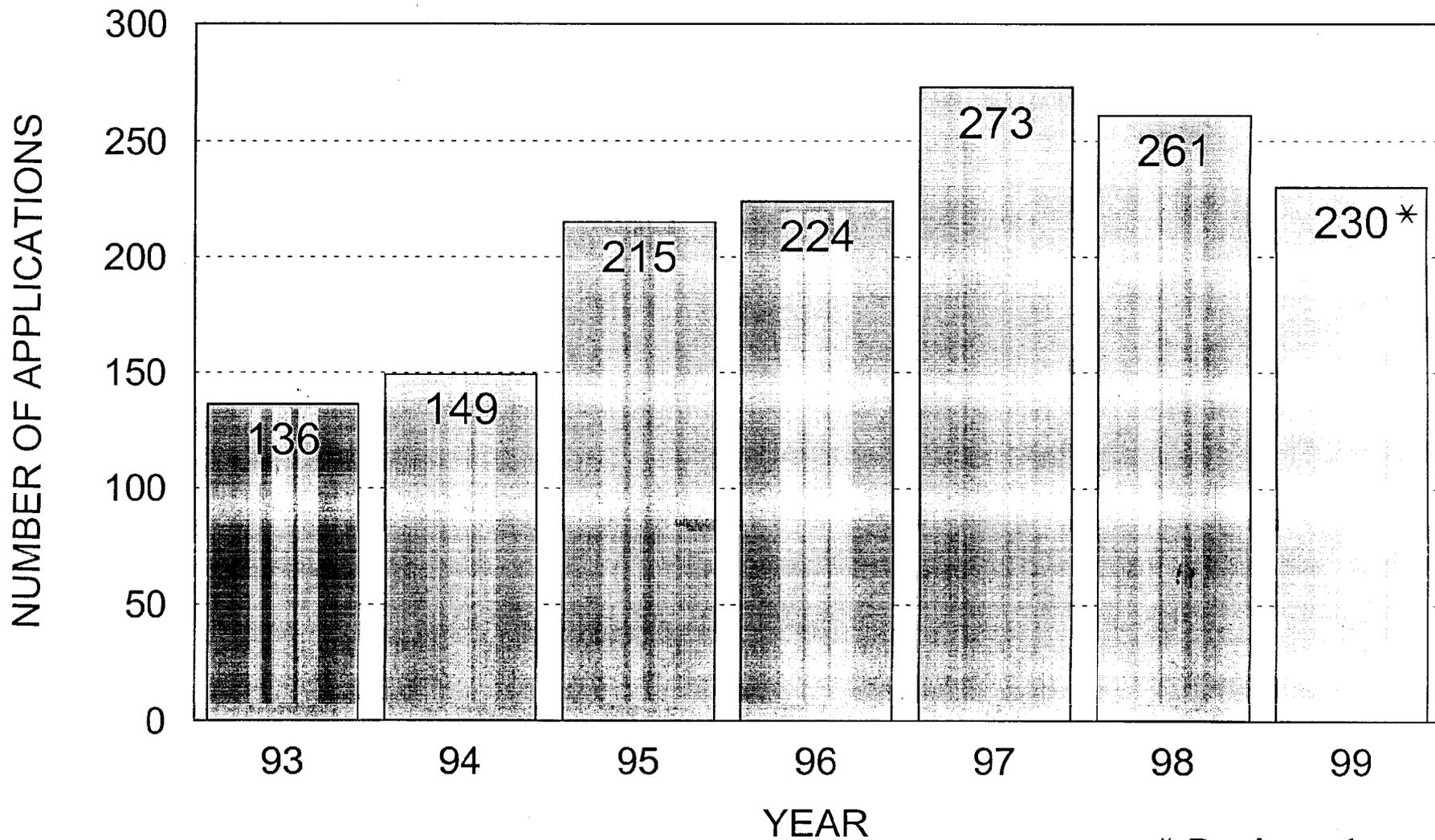


Calendar Year Approvals & Tentative Approvals (New Counting System)



Calendar Year Tentative or Actual Approvals

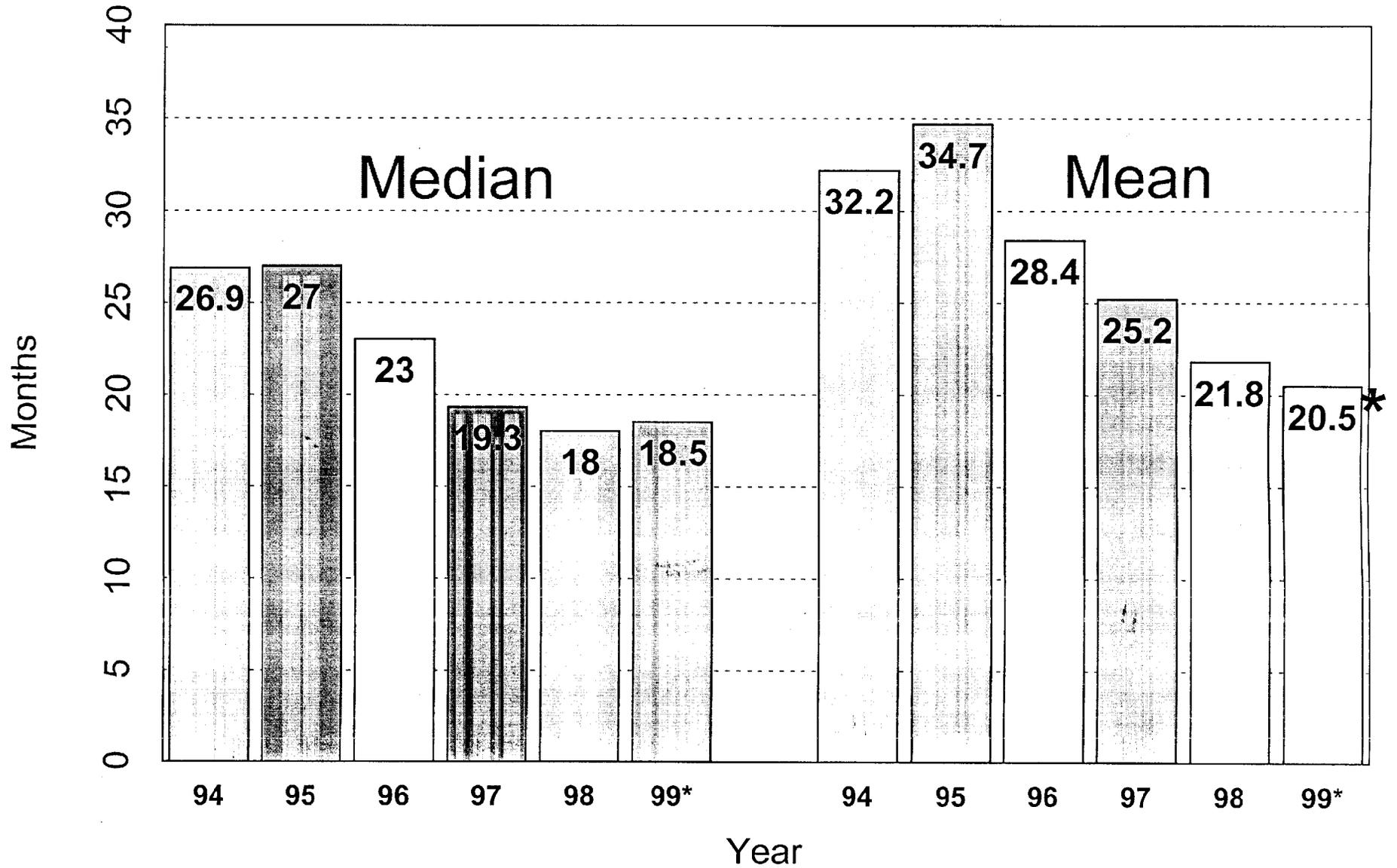
(Subsequent approvals of TAs not counted again)



(New Counting System)

* Projected

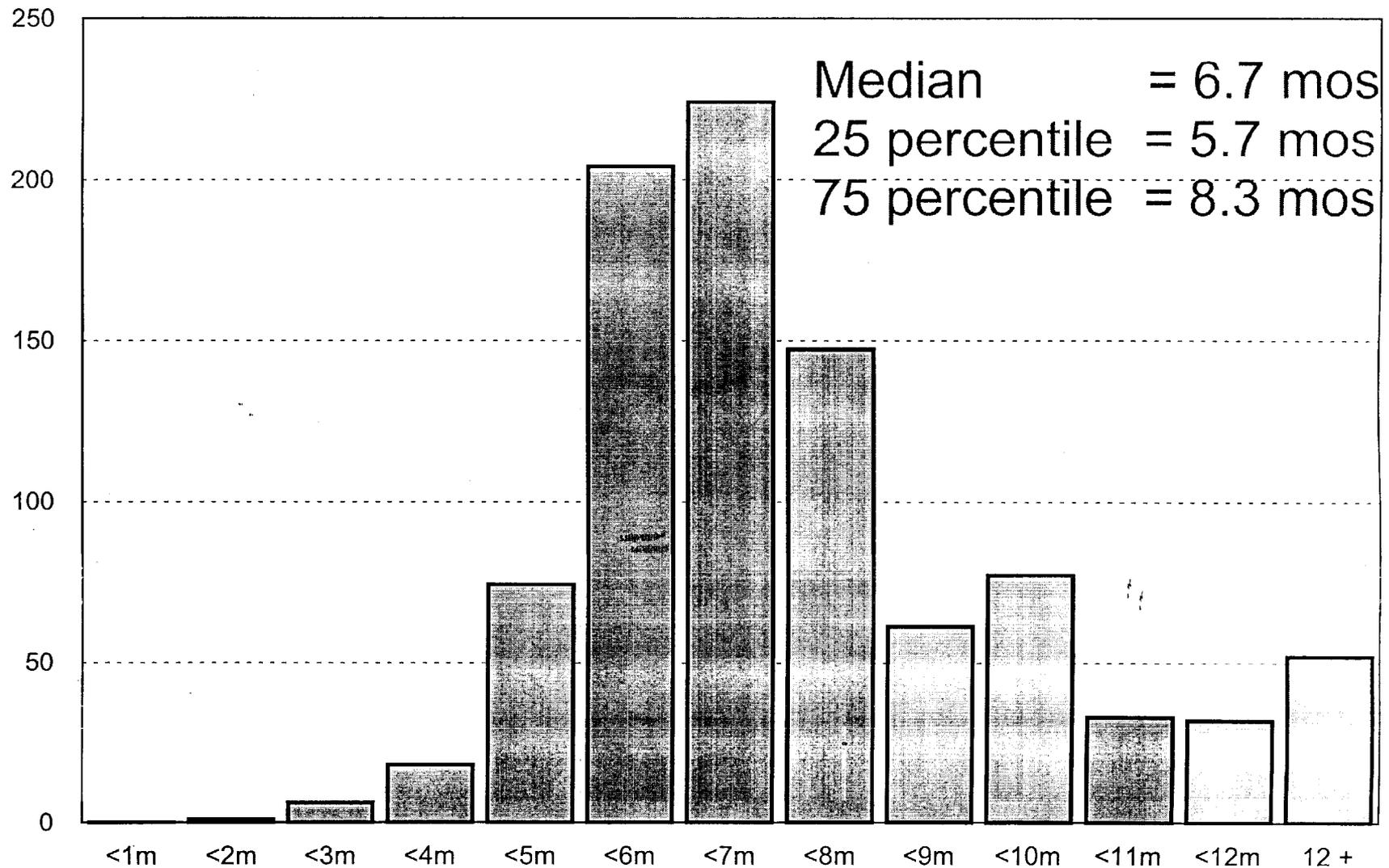
Calendar Year Approval Times



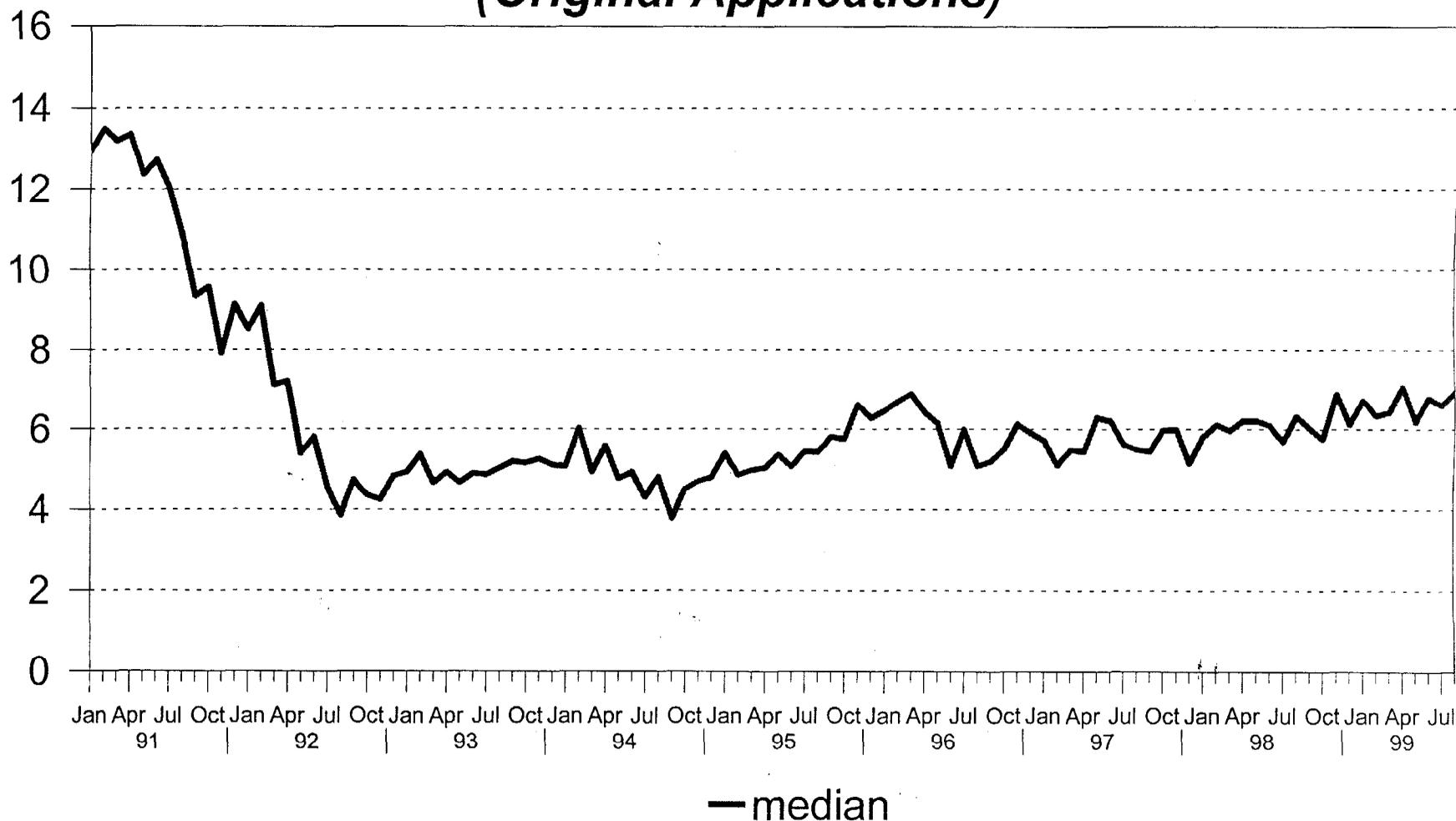
* = Through August 31, 1998

Distribution of Review Times for Original ANDAs

Major Cycles Only--1/1/98--8/31/99



Median ANDA Review Cycle (Months) ***(Original Applications)***

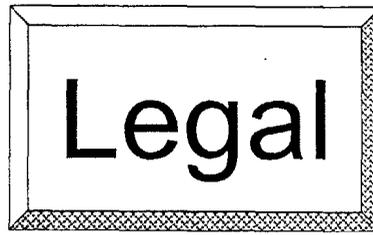


1-Times correspond to actual applications received . The new ANDA/AADA submission policy that went into effect 1/1/91 allows certain variations in a drug product to be included in a single application.

2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.

Challenges - Four Areas

- ◆ Legal
- ◆ Regulatory/Legislative
- ◆ Scientific/Pharmaceutical Use Issues
- ◆ Submission/Review Related



- ◆ Lawsuits
- ◆ Petitions

Pending Petitions & Lawsuits

Number of Pending Petitions Needing OGD Input	22	(13)
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Number of Lawsuits Involving OGD	7	(4)
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Active Citizen Petitions and Lawsuits

<u>Topic</u>	<u>Petitions</u>	<u>Lawsuit</u>
Amiodarone	✓	
Clozapine	✓	
Cyclosporine		✓
Diltiazem	✓ ✓ ✓	
Gabapentin	✓	
Estradiol	✓	
Naproxen	✓	

Active Citizen Petitions and Lawsuits

<u>Topic</u>	<u>Petitions</u>	<u>Lawsuit</u>
Phenytoin		✓
Propafenone	✓	
Propofol	✓ ✓ ✓	✓
Ticlopidine		✓
Ursodiol	✓	

Regulatory/Legislative

- ◆ Proposed 180-Day Exclusivity Regulation
- ◆ State Legislature Efforts for NTI & Critical Care Drugs Continue
- ◆ Continue FDAMA Mandates

Scientific/Pharmaceutical Use Issues

- ◆ Post-Marketing Strategies
- ◆ New Methodologies - Need to Validate
- ◆ Variations in Reference Listed Drugs

Submission/Review Related

- ◆ Industry Training and Education
- ◆ Better Approach to Inactive Ingredients Questions
- ◆ Submit a Quality ANDA
 - ✓ Cover letters
 - ✓ Complete submissions
 - ✓ Call to clarify deficiencies
 - ✓ In house quality control
 - ✓ Sterility assurance--separate section

HIGH QUALITY PHARMACEUTICALS

September 1, 1999

THE OFFICE OF GENERIC DRUGS, HFD-600

ATTN: Douglas L. Sporn

7500 Standish Place

MPN2, Room 286

Rockville, Maryland 20855

RE: ANDA 12-345 0.9% Sodium Chloride Injection

High Quality Pharmaceuticals hereby submits a supplemental application to the above referenced ANDA to provide for a new partial fill presentation, 50 mL fill in a 100 mL container for 0.9% Sodium Chloride Injection, USP. High Quality Pharmaceuticals is filing this supplement in accordance with 21 CFR 314.70(b)(viii). The new partial fill presentation utilizes the same manufacturing process, terminal sterilization, release testing, container/closure system and stability protocol as the approved 100 mL full fill container. Provided herein are the chemistry, manufacturing and controls information and terminal sterilization validation data to support the new partial fill presentation.

High Quality Pharmaceuticals requests approval for parametric release and a twenty-four month expiration date based on sterility validation and accelerated stability data enclosed herein. High Quality Pharmaceuticals respectfully requests an expedited review of this supplemental application.

Thank you for your prompt handling....

HIGH QUALITY PHARMACEUTICALS

September 1, 1999

THE OFFICE OF GENERIC DRUGS, HFD-600

ATTN: Douglas L. Sporn

7500 Standish Place

MPN2, Room 286

Rockville, Maryland 20855

**EXPEDITED REVIEW REQUESTED
CONTAINS STERILITY DATA**

RE: ANDA 12-345 0.9% Sodium Chloride Injection

High Quality Pharmaceuticals hereby submits a supplemental application to the above referenced ANDA to provide for a new partial fill presentation, 50 mL fill in a 100 mL container for 0.9% Sodium Chloride Injection, USP. High Quality Pharmaceuticals is filing this supplemental application in accordance with 21 CFR 314.70(b)(viii). The new partial fill presentation utilizes the same manufacturing process, terminal sterilization, release testing, container/closure system and stability protocol as the approved 100 mL full fill container. Provided herein are the chemistry, manufacturing and controls information and terminal sterilization validation data to support the new partial fill presentation.

High Quality Pharmaceuticals requests approval for parametric release and a twenty-four month expiration date based on sterility validation and accelerated stability data enclosed herein. High Quality Pharmaceuticals respectfully requests an expedited review of this supplemental application.

Thank you for prompt handling of this submission....

LOW QUALITY PHARMACEUTICALS

September 1, 1999

THE OFFICE OF GENERIC DRUGS, HFD-600

ATT: Douglas L. Sporn

7500 Standish Place

MPN2, Room 286

Rockville, Maryland 20855

RE: ANDA 12-345 0.9% Sodium Chloride Injection

Low Quality Pharmaceuticals hereby submits an amendment to the above referenced ANDA to provide for a new partial fill presentation, 50 mL fill in a 100 mL container for 0.9% Sodium Chloride Injection, USP. Low Quality Pharmaceuticals is filing this amendment in accordance with 21 CFR 314.96 and 314.120. The new partial fill presentation utilizes the same manufacturing process, terminal sterilization, release testing, container/closure system and stability protocol as the approved 100 mL full fill container. Provide herein is the chemistry, manufacturing and controls information and terminal sterilization validation data to support the new partial fill presentation.

Low Quality Pharmaceuticals requests approval for parametric release and a twenty-four month expiration date based on sterility validation and accelerated stability data enclosed herein. This amendment also contains a revised patent certification per 21 CFR 314.95.

Thank you for your prompt handling of this submission....

September 1, 1999

HIGH QUALITY PHARMACEUTICALS

MAJOR AMENDMENT
CONTAINS MICRO DATA
AND PATENT INFORMATION

THE OFFICE OF GENERIC DRUGS, HFD-600

ATT: Douglas L. Sporn

7500 Standish Place

MPN2, Room 286

Rockville, Maryland 20855

RE: ANDA 12-345 0.9% Sodium Chloride Injection

High Quality Pharmaceuticals hereby submits an amendment to the above referenced ANDA to provide for a new partial fill presentation, 50 mL fill in a 100 mL container for 0.9% Sodium Chloride Injection, USP. High Quality Pharmaceuticals is filing this amendment in accordance with 21 CFR 314.96 and 314.120. The new partial fill presentation utilizes the same manufacturing process, terminal sterilization, release testing, container/closure system and stability protocol as the approved 100 mL full fill container. Provide herein is the chemistry, manufacturing and controls information and terminal sterilization validation data to support the new partial fill presentation.

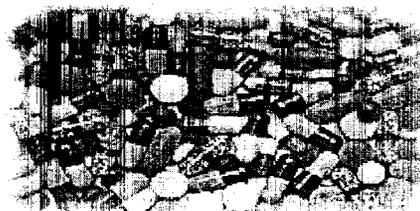
High Quality Pharmaceuticals request approval for parametric release and a twenty-four month expiration date based on sterility validation and accelerated stability data enclosed herein. This amendment also contains a revised patent certification per 21 CFR 314.95.

Thank you for your prompt handling of this submission....

Submission/Review Related (continued)

- ◆ Check DMF Status
- ◆ Submit Electronic ANDAs
- ◆ QC Electronic Submissions
- ◆ Fatally Flawed Applications
- ◆ Phone Inquiries
- ◆ Use the Internet
- ◆ "Chain of Command"

U.S. Food and Drug Administration
Center for Drug Evaluation and Research



OFFICE OF GENERIC DRUGS (OGD)

Office of Generic Drugs
Division of Labeling and
Program Support
Labeling Review Branch
HFD-613

John F. Grace, R.Ph. - Labeling Review Team Leader for Division of Chemistry I
Charles V. Hoppes, R.Ph. - Labeling Review Team Leader for Division of Chemistry II

Phone - (301) 827-5846
Fax - (301) 443-3847

Click on links

The purpose of this page is to provide information on recently approved labeling changes for **Reference Listed Drug (RLD)** products. The supplements are grouped by month and year of approval. Some are linked to the approved labeling and/or the supplemental approval letter in Adobe Acrobat format. Click on a month and year below to view the list for that month:

1999	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug				
1998						Jun	Jul	Aug	Sep	Oct	Nov	Dec

In addition, a comprehensive list of the most recently approved labeling supplements for all RLD products is available in Adobe Acrobat Format. The list is in order of NDA number.

CDER Home Page Search Comment What's New

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Reference Listed Drug Labeling Approved in August 1999

Some of the product names below contain links to the approved labeling or the supplemental approval letter describing the specific changes. Click on the product name to view the approved labeling changes in Adobe Acrobat format.

Product Name	Drug Name	NDA No	Supp.No	Firm	Date
LARIAM	Mefloquine HCl Tablets	19-591	S-012	Roche	02-Aug-1999
PROSCAR	Finasteride Tablets	20-180	S-018	Merck	02-Aug-1999
CEFOTAN	Cefatetan Disodium	50-588	S-026	Zeneca	05-Aug-1999
MARINOL	Dronabinol Capsules	18-651	S-011	Unimed	05-Aug-1999
ZOCOR	Simvastatin Tablets	19-766	S-032	Merck	05-Aug-1999
GLUCOTROL	Glipizide Tablets	17-783	S-015	Pfizer	06-Aug-1999
PROLOPRIM	Trimethoprim Tablets	17-943	S-015	Monarch Pharms	06-Aug-1999
PRANDIN	Repaglinide Tablets	20-741	S-001	Novo Nordisk Pharm	10-Aug-1999
DROXIA	Hydroxyurea Capsules	16-295	S-026	Bristol Myers Squibb	11-Aug-1999
HYDREA	Hydroxyurea Capsules	16-295	S-026	Bristol Myers Squibb	11-Aug-1999
IDAMYCIN PFS	Idarubicin HCl Injection	50-734	S-004	Pharmacia & Upjohn	12-Aug-1999
AZULFIDINE	Sulfasalazine Tablets	07-073	S-110	Pharmacia & Upjohn	13-Aug-1999
AZULFIDINE EN-TABS	Sulfasalazine Tablets	07-073	S-110	Pharmacia & Upjohn	13-Aug-1999
PREPIDIL	Dinoprostone Gel	19-617	S-002	Pharmacia & Upjohn	13-Aug-1999
ZAROXOLYN	Metolazone Tablets	17-386	S-030	Medeva Pharms	13-Aug-1999
RESCRIPTOR	Delavirdine Mesylate Tablets	20-705	S-004	Pharmacia & Upjohn	16-Aug-1999
BENTYL	Dicyclomine HCl Injection	08-370	S-028	Hoechst Marion Rssl	17-Aug-1999
BENTYL	Dicyclomine HCl Syrup	07-961	S-025	Hoechst Marion Rssl	17-Aug-1999
BENTYL	Dicyclomine HCl Tablets	07-409	S-039	Hoechst Marion Rssl	17-Aug-1999
DERMA-SMOOTHIE/FS	Fluocinolone Acetonide Sol.	19-452	S-015	Hill Derm	18-Aug-1999
EULEXIN	Flutamide Capsules	18-554	S-015	Schering	19-Aug-1999
MEPERGAN	Meperidine HCl/Promethazine HCl	11-730	S-023	Wyeth Ayerst Labs	19-Aug-1999
ALDOCLOR-250	Methyldopa/Chlorthiazide Tablets	16-016	S-070	Merck	22-Aug-1999

Click on links



NDA 7-409/S-039
NDA 8-370/S-028
NDA 7-961/S-025

AUG 17 1999

Hoechst Marion Roussel
Attention: Kim Leitzke
10236 Marion Park Drive, P.O. Box 9627
Kansas City, MO 64134

Dear Ms. Leitzke:

Please refer to your supplemental new drug applications dated April 2, 1999, received April 5, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bentlyl (dicyclomine hydrochloride USP) Tablets/Capsules, Injection, and Syrup.

We note that these supplements were submitted as 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

These supplemental new drug applications provide for the revision of the **OVERDOSAGE** section of the package insert to include a description of a 15 Day adverse event report in which a 37 year old female reported numbness, cold fingertips, abdominal pain, decreased appetite, dry mouth, and nervousness following the ingestion of 320 mg daily for several days. Your submission stated March 18, 1999 as the implementation date for the change.

We have completed the review of these supplemental applications, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling submitted April 2, 1999. Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about these drug products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

Page thru document
or
Click on links

OVERDOSAGE

Proposed Electronic Labeling Requirement

- ◆ Require the Submission of Electronic Package Insert Text
- ◆ NDAs, ANDAs, Supplements, Annual Reports
- ◆ Portable Document Format (PDF) - in 8.5 x 11 text

Proposed Electronic Labeling Requirement

- ◆ **Benefits:**
 - **Enables Posting of Reference Listed Drug on Web**
 - **Faster, More Efficient Review**

SPEAK

WITH

ONE

VOICE

NPA 1999 Fall Meeting

Update from the
Office of Generic Drugs

Douglas L. Sporn

Director

Office of Generic Drugs

September 28, 1999

Las Vegas, Nevada

OGD Initiatives

- ◆ 180 Day Exclusivity
- ◆ Electronic Labeling

OGD Guidances

- ◆ Major/Minor/FAX/Telephone
- ◆ Skin Irritation Study Guidance
- ◆ Inactive Ingredients
- ◆ Electronic Submission Guidance
- ◆ Section 119 MAPP - Field Recommendations

Chemistry Manufacturing & Controls

- ◆ Blend Uniformity
- ◆ Impurities in Drug Substances
- ◆ Impurities in Drug Products
- ◆ DMF's for Bulk Antibiotic Drug Substances
- ◆ Stability Guidance
 - Site Specific Stability

Post-Approval Changes

- ◆ FDAMA 116 - 314.70
Rewrite/Guidance
- ◆ BAC PAC I
- ◆ BAC PAC II
- ◆ SUPAC-IR Rewrite
- ◆ PAC SAS

BA/BE Guidances

- ◆ General BA/BE Guidance
- ◆ Food Effect Studies
- ◆ Biopharmaceutics Classification System
- ◆ Individual Bioequivalence
- ◆ Topical Dermatological Drug Products

Orally Inhaled & Nasal Drug Products

◆ CMC

- Nasal Spray and Inhalation Solutions - Comment Period closed 8/31/99
- MDI & Dry Powder Inhaler Products - Comment period closed early this year - Comments under review

◆ BA/BE

- Nasal Inhalation Drug Products - Comment period closed 9/22/99
- Oral Inhalation Drug Products - Under development