Consistent with the terms of the Court's May 22, 2017 scheduling order, the record has been redacted for all information that plaintiff, Texas Department of Criminal Justice (Texas), has identified as confidential. In addition, Defendants have also redacted information that the drug's supplier and broker have separately advised the agency they consider confidential and private, as well as information the agency itself generally treats as confidential. This information has been redacted pending final FDA's review of confidentiality claims, and our filing of the record with these redactions does not necessarily reflect our agreement with all of the claims of confidentiality Defendants have received. Defendants explicitly reserve the right to make an independent determination regarding the proper scope of redactions at a later time. Should we identify any of Texas's redactions that are over-broad or otherwise improper, we will work with Texas's counsel to revise the redactions in the record.

MISCELLANEOUS

Sections included in this document

1. Purpose

Pending litigation, this procedure provides instructions on the handling of shipments of Sodium Thiopental by Districts and the responsibility of DIOP in the processing of Sodium Thiopental entries. Districts should disseminate this information to all pertinent staff handling these entries.

2. Scope

This procedure covers the handling of entries of Sodium Thiopental by District IB/CB staff, DIOP Operations Branch staff, and DIOP Systems Branch staff.

3. Responsibility

District: Reviews entries and associated entry documentation of Sodium Thiopental and ensures such entries are handled as per the instructions in this procedure.

Ensures appropriate staff is aware of and follows this procedure.

DIOP Operations Branch: Provides instructions to field offices. Compiles entry data and documentation, and notifies Commissioner's Office as indicated in this procedure. Reviews daily report and informs ORA management of new shipments.

DIOP Systems Branch: Maintain daily report of shipments of Sodium Thiopental offered for import. Ensure appropriate OASIS/MARCS entry screening is in place to appropriately flag subject entries.

4. Background

In the past, FDA has released shipments of sodium thiopental being imported by or on behalf of state correctional authorities. FDA did not review or approve products for the purpose of lethal injection and has not reviewed the products to determine their identity, safety, effectiveness, purity or any other characteristics. On March 27, 2012, the United States District Court for the District of Columbia has ordered FDA not to allow the entry of sodium thiopental into interstate commerce. Therefore, entries of sodium thiopental to correctional facilities shall be processed according to these procedures.

5. References

None

6. Procedure

District Staff:

When an entry of sodium thiopental is identified:

1. Request documents for the entry
2. Enter the following narrative in the entry remarks field:

   "Do not release this line or request detention of this line without direct instructions to do so from District or Headquarters management."

3. Lock the entry in MARCS Entry Review
4. Contact the CBP office covering the Port of Entry and request they do not allow the shipment to leave the port
5. Notify the DIOP contacts via email of the entry.
   - Include the entry number in the subject heading of the email.
6. Upon receipt of the entry documents:
   a. Email the entry documents to the DIOP Contacts in this assignment.

i. Include the entry number in the subject heading of the email.
ii. include the request to CBP to hold the shipment, and the CBP response (or indicate CBP did not respond)

DIOP Operations Branch:

Upon notification that an entry of sodium thiopental has been identified by a District:

1. Notify the DIOP Director's Group and the OCC contacts of all such shipments.
   a. Include the entry documents received from the District.
   .
   b. Include the following entry details:
      i. Entry number
      ii. Date of entry
      iii. Product description & quantity
      iv. Importer & consignee
      v. District and Port of Entry
      vi. Current status

Recurring Monitoring:

1. Monitor the daily report for any shipments of Sodium Thiopental offered for entry on a daily basis.

2. If a shipment is discovered on the report, but there has been no notification from the District:
   a. Contact the District Director and DIB or DIOB immediately with the entry number and request immediate status
   b. Include the DIOP Director Group and the ORO Immediate Office email lists on the "cc:" line in the email.

DIOP Systems Branch:

1. Maintain daily report of any shipments of Sodium Thiopental offered for entry at the following report page: http://oradss.fda.gov:9085/reports.jsp?sort=1&dir=%2Fcfs_bo%2Freports%2Fora%2Fdiop%2Fops_branch

7. Definitions/ Glossary None

8. Records None

9. Supporting Documents None

10. Contact Information **DIOP Contacts**: John Verbeten, 301-796-6677 and S. Max Brewster 301-796-8994

OCC Contacts: David Mednick, 301-796-8706 and Julie Dohm, 301-796-8732

11. Attachments None

Document History					
Rev #	Status (I, R, C)	Date Approved	Location of Change History	Name & Title	
				Author	Approving Official
2.00	R	4/16/2012		John Verbeten	Domenic J. Veneziano Director, DIOP

Approving Official's signature: Domenic J. Veneziano

Sections included in this document

1. Purpose

Pending litigation, this procedure provides instructions on the handling of shipments of Sodium Thiopental by Districts and the responsibility of DIOP in the processing of Sodium Thiopental entries. Districts should disseminate this information to all pertinent staff handling these entries.

2. Scope

This procedure covers the handling of entries of Sodium Thiopental by District IB/CB staff, DIOP Operations Branch staff, and DIOP Systems Branch staff.

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Ensures appropriate staff is aware of and follows this procedure.

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DIOP Systems Branch: Maintain daily report of shipments of Sodium Thiopental offered for import. Ensure appropriate OASIS/MARCS entry screening is in place to appropriately flag subject entries.

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5. References

None

6. Procedure

District Staff:

When an entry of sodium thiopental is identified:

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4. Contact the CBP office covering the Port of Entry and request they do not allow the shipment to leave the port
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   - Include the entry number in the subject heading of the email.
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   a. Email the entry documents to the DIOP Contacts in this assignment.

i. Include the entry number in the subject heading of the email.
ii. include the request to CBP to hold the shipment, and the CBP response (or indicate CBP did not respond)

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   a. Include the entry documents received from the District.

   b. Include the following entry details:
      i. Entry number
      ii. Date of entry
      iii. Product description & quantity
      iv. Importer & consignee
      v. District and Port of Entry
      vi. Current status

Recurring Monitoring:

1. Monitor the daily report for any shipments of Sodium Thiopental offered for entry on a daily basis.

2. If a shipment is discovered on the report, but there has been no notification from the District:
   a. Contact the District Director and DIB or DIOB immediately with the entry number and request immediate status
   b. Include the DIOP Director Group and the ORO Immediate Office email lists on the "cc:" line in the email.

DIOP Systems Branch:

1. Maintain daily report of any shipments of Sodium Thiopental offered for entry at the following report page: http://oradss.fda.gov:9085/reports.jsp?sort=1&dir=%2Fcfs bo%2Freports%2Fora%2Fdiop%2Fops branch

7. Definitions/ Glossary	None
8. Records	None
9. Supporting Documents	None
10. Contact Information	DIOP Contacts: John Verbeten, 301-796-6677 and S. Max Brewster 301-796-8994 OCC Contacts: David Mednick, 301-796-8706 and Julie Dohm, 301-796-8732
11. Attachments	None

Document History

Rev #	Status (1, R, C)	Date Approved	Location of Change History	Name & Title	
				Author	Approving Official
2.00	R	4/16/2012		John Verbeten	Domenic J. Veneziano Director, DIOP
3.00	R	9/05/2012	Change in numbering for SOP	William Wyeth QMS	Domenic J. Veneziano Director, DIOP

Approving Official's signature: 

United States Food and Drug Administration

Southwest Import District

Notice of FDA Action

Entry Number: [redacted]

Notice Number: 4
September 11, 2015

Filer:
[redacted]

Attention: [redacted]
Broker Box: [redacted]

>

<

Port of Entry: 5309, Houston Intercontinental Airport, Houston, TX
Carrier: [redacted]
Date Received: July 27, 2015
Arrival Date: July 24, 2015

Importer of Record: [redacted]
Consignee: [redacted]

HOLD DESIGNATED

Summary of Current Status of Individual Lines

	Line ACS/FDA	Product Description	Quantity	Current Status
*	001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	1000 PCS	Extension granted 09-10-2015

* = Status change since the previous notice. Read carefully the sections which follow for important information regarding these lines.

@ = Consignee ID

FDA will not request redelivery for examination or sampling, if the products not released by FDA are moved, following USCS conditional release to a localtion within the metropolitan area or to a location approved by the FDA office at the number below.

All products in this entry not listed above may proceed without FDA examination. This notice does not constitute assurance the products involved comply with provisions of the Food, Drug, and Cosmetic Act or other related acts, and does not preclude action should the products later be found violative.

EXTENSION REQUEST GRANTED

Line ACS/FDA	Product Description	Respond By
001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	October 23, 2015

Rosa L. Santos, Compliance Officer (Region/District) (214) 253-5269
(214) 253-5316 (FAX)

U.S. Food and Drug Administration
4040 N. Central Expressway Suite 300
Dallas, TX 75204

ROSA.SANTOS@FDA.HHS.GOV

This extension is granted until the dates shown above.

Notice Prepared For: The District Director, U.S. Food and Drug Administration
Notice Prepared By: ARM

United States Food and Drug Administration

Southwest Import District

Notice of FDA Action

Entry Number: [redacted]

Notice Number: 4
September 11, 2015

Importer:
[redacted]

[redacted]

>

<

Port of Entry: 5309, Houston Intercontinental Airport, Houston, TX
Carrier: [redacted];
Date Received: July 27, 2015
Arrival Date: July 24, 2015

Filer of Record: [redacted]
Consignee: [redacted]

HOLD DESIGNATED

Summary of Current Status of Individual Lines

	Line ACS/FDA	Product Description	Quantity	Current Status
*	001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	1000 PCS	Extension granted 09-10-2015

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All products in this entry not listed above may proceed without FDA examination. This notice does not constitute assurance the products involved comply with provisions of the Food, Drug, and Cosmetic Act or other related acts, and does not preclude action should the products later be found violative.

EXTENSION REQUEST GRANTED

Line ACS/FDA	Product Description	Respond By
001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	October 23, 2015

(214) 253-5269

Rosa L. Santos, Compliance Officer (Region/District)
U.S. Food and Drug Administration
4040 N. Central Expressway Suite 300
Dallas, TX 75204

(214) 253-5316 (FAX)
ROSA.SANTOS@FDA.HHS.GOV

This extension is granted until the dates shown above.

Notice Prepared For: The District Director, U.S. Food and Drug Administration
Notice Prepared By: ARM

From: [redacted]
To: Santos, Rosa L
Subject: Re: [redacted] Request for Release
Date: Monday, October 26, 2015 8:43:51 AM

Thanks Rosa

On Monday, October 26, 2015, Santos, Rosa L <Rosa.Santos@fda.hhs.gov> wrote:

> Good Morning,
>
> Just to let you know that I received the response.
>
> Thanks,
>
> Rosa Linda Santos
> Compliance Officer
> 4040 N. Central Expressway
> Suite 300
> Dallas, Texas 75204
> 214-253-5269 Phone
> 214-253-5316 Fax
> rosa.santos@fda.hhs.gov
>
> **From:** [redacted]
> **Sent:** Friday, October 23, 2015 4:03 PM
> **To:** Santos, Rosa L
> **Cc:** [redacted]; Veneziano, Domenic J.; Stearn, Douglas; [redacted]
> **Subject:** [redacted] Request for Release
>
> Hello Ms. Santos. I hope you are having a good Friday.
>
> Please find our request for release of the thiopental sodium detained by FDA and detained by Customs at FDA's request under the above referenced entry number. An authorization letter is included with the attached letter.

We request FDA to release the goods immediately and to instruct CBP to lift that agency's detention to permit immediate delivery to the [redacted].

Alternatively, we request FDA to grant [redacted] an in-person hearing with the appropriate FDA personnel, lift the detention, and release the goods within 30 days from receipt of this submission.

Further, I respectfully request this case be transferred to Douglas Stearn, Director, Office of Enforcement and Imports, or his designee in ORA Headquarters, who will become the Hearing Officer for this detention. Please inform me who the new Hearing Officer will be and the time and place for additional testimony to be given.

Thank you and best regards

[redacted]

--

[redacted]

is not intended for transmission to, or receipt by, any other person. If you have received this e-mail in error, please delete it without copying or forwarding it, and notify us of the error by reply e-mail so that our address records can be corrected.

IRS CIRCULAR 230 DISCLOSURE: To ensure compliance with requirements imposed by the IRS, we inform you that any U.S. tax advice contained in this communication (including any attachments) is not intended or written to be used, and cannot be used, for the purpose of (i) avoiding penalties under the Internal Revenue Code or (ii) promoting, marketing or recommending to another party any transaction or matter addressed herein. Please do not hesitate to contact me, however, if you have any questions regarding this matter.

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance
Office of Unapproved Drugs and Labeling Compliance

Memorandum

Date: April 14, 2016

From: Arthur Simone, MD, PhD
Acting Senior Medical Advisor[1]

Arthur F. Simone -S
Digitally signed by Arthur F. Simone -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300178991, cn=Arthur F. Simone -S
Date: 2016.04.14 17:07:13 -04'00'

Subject: GRASE Determination
[redacted] (Thiopental Sodium USP 1 gm Vial)

Product Information

Name: [redacted]
Alternative Name(s): none
Active Ingredient(s): Thiopental Sodium
Firm(s): [redacted]

Executive Summary

FDA has detained two shipments of [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted]. that have been offered for importation into the United States. The Office of Unapproved Drugs and Labeling Compliance (OUDLC or the Office) has been asked to review labeling and other information for [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] to determine whether the product is generally recognized as safe and effective (GRASE) under any conditions of use. We have also been asked to determine whether [redacted] (Thiopental Sodium USP 1 gm Vial) is the subject of an approved new drug application (NDA), abbreviated new drug application (ANDA), or Biologics License Application (BLA)

[1] Dr. Arthur F. Simone is Acting Senior Medical Advisor in the Office of Unapproved Drugs and Labeling Compliance in the Office of Compliance, Center for Drug Evaluation and Research (CDER), FDA. He received his medical degree (M.D.) from the Robert Wood Johnson Medical School in 1988. He is licensed to practice medicine in Pennsylvania and New Jersey. He is board certified in anesthesiology. He has been employed by the Food and Drug Administration since 2002 and has served as both a primary reviewer and team leader in the Office of New Drugs in CDER.

[redacted]. Finally, OUDLC was asked to comment on the absence of warnings in the [redacted] labeling.

A diligent search of the PubMed database, through the FDA Biosciences Library, was conducted in order to determine whether [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] is the subject of any adequate and well-controlled clinical studies of the drug under any conditions of use. The search identified no adequate and well-controlled clinical studies of that drug under any conditions of use. Therefore, I conclude that [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] is not GRASE for any indication or under any conditions of use.

A diligent search of official FDA records was conducted to determine whether [redacted] (Thiopental Sodium USP 1 gm Vial) has been approved in the United States. The search did not identify an NDA, ANDA, or BLA for [redacted] (Thiopental Sodium USP 1 gm Vial). A diligent search of official FDA records was conducted to determine whether [redacted] (Thiopental Sodium USP 1 gm Vial) is [redacted]

In summary, I conclude that [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] is not GRASE under any conditions of use and is not the subject of an approved NDA, ANDA, or BLA [redacted]

In addition, the labeling for [redacted] (Thiopental Sodium USP 1 gm Vial) did not include any warnings. Based on the mechanism of action of thiopental sodium, its pharmacokinetics, and its pharmacodynamics, the labeling for [redacted] would be expected to include warnings, such as a reference to the risks to the user if there is an absence of suitable veins for intravenous administration.

Background

OUDLC has been asked to determine whether [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] is generally recognized by qualified experts as safe and effective for any indication and whether that drug is the subject of an approved NDA, ANDA, or BLA [redacted] The Office has also been asked to provide input on the warnings associated with thiopental sodium that should be taken into consideration.

The Office of Regulatory Affairs provided images of the immediate container labels; however, package inserts that would normally accompany a drug product were not found with the product and could not be found in the public domain. The product's container label (see Appendix 1) did not include any information regarding dosing, contraindications, warnings, or precautions. Searches of the internet using Google on August 7 and 10, 2015 using the terms "[redacted]"

"[redacted]," and "[redacted]" collectively and individually did not identify a package insert for the product.

An additional search to find a package insert for [redacted] or any injectable formulation of thiopental sodium that had been approved in the United States, European Union, Australia, Japan, or Canada was conducted on August 10, 2015 (see Appendix 2). This search failed to identify any approved [redacted] product. The search identified Canadian-approved Pentothal injectable thiopental sodium products; however, I could not locate a package insert for any of those products. Using the label archives of the DailyMed database maintained by the National Library of Medicine at the National Institutes of Health, a package insert for Thiopental Sodium Injection packaged by [redacted] (Pentothal), was found. This product was marketed between May 2010 and January 2011. Its labeling had been downloaded to the database on January 19, 2011. The information contained in this labeling (Appendix 3) was reviewed regarding contraindications, warnings, and precautions associated with injectable thiopental sodium. The labeling for [redacted] Pentothal product addresses only the indications for which that drug was marketed.

GRASE Determination

A drug is a "new drug" unless it is "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof."[2] At a minimum, the contention that a drug product is GRASE must be supported by the same quantity and quality of scientific evidence that is required to obtain approval of an NDA for the product.[3]

In order to be generally recognized as safe and effective (GRASE) under particular conditions of use, a drug must satisfy three criteria:[4]

1. The particular drug product must have been subjected to adequate and well-controlled clinical investigations that establish the product as safe and effective under the proposed conditions of use.
2. Those investigations must have been published in the scientific literature available to qualified experts.
3. Qualified experts must generally agree, based on those published studies, that the product is safe and effective under its proposed conditions of use.

FDA has described the characteristics of "adequate and well-controlled" studies by regulation. These characteristics include the following[5]:

1. A clear statement of the objectives of the investigation and a summary of the proposed or actual methods of analysis in the protocol for the study and in the report of its results.

[2] See 21 U.S.C. § 321(p)(1).
[3] See 21 CFR § 314.200(e)(1).
[4] See 21 U.S.C. § 321(p)(1).
[5] See 21 CFR § 314.126(b).

The protocol should contain a description of the proposed methods of analysis, and the study report should contain a description of the methods of analysis ultimately used. If the protocol does not contain a description of the proposed methods of analysis, the study report should describe how the methods used were selected.

2. The study must use a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect. The protocol for the study and report of results should describe the study design precisely; for example, duration of treatment periods, whether treatments are parallel, sequential, or crossover, and whether the sample size is predetermined or based upon some interim analysis. Adequate and well-controlled clinical studies may be confirmatory or exploratory.
3. The method of selection of subjects provides adequate assurance that they have the disease or condition being studied, or evidence of susceptibility and exposure to the condition against which prophylaxis is directed.
4. The method of assigning patients to treatment and control groups minimizes bias and is intended to assure comparability of the groups with respect to pertinent variables such as age, sex, severity of disease, duration of disease, and use of drugs or therapy other than the test drug. The protocol for the study and the report of its results should describe how subjects were assigned to groups. Ordinarily, in a concurrently controlled study, assignment is by randomization, with or without stratification.
5. Adequate measures are taken to minimize bias on the part of the subjects, observers, and analysts of the data. The protocol and report of the study should describe the procedures used to accomplish this, such as blinding.
6. The methods of assessment of subjects' response are well-defined and reliable. The protocol for the study and the report of results should explain the variables measured, the methods of observation, and criteria used to assess response.
7. There is an analysis of the results of the study adequate to assess the effects of the drug. The report of the study should describe the results and the analytic methods used to evaluate them, including any appropriate statistical methods. The analysis should assess, among other things, the comparability of test and control groups with respect to pertinent variables, and the effects of any interim data analyses performed.

Reports of adequate and well-controlled investigations provide the primary basis for determining whether there is "substantial evidence" to support the claims of effectiveness for new drugs. Therefore, the study report should provide sufficient details of study design, conduct, and analysis to allow critical evaluation and a determination of whether the characteristics of an adequate and well-controlled study are present.[6]

For a study to be considered adequate for approval of a new drug, it is also required that the test drug be standardized as to identity, strength, quality, purity, and dosage form to give significance to the results of the investigation.[7]

[6] See 21 CFR § 314.126(a).
[7] See 21 CFR § 314.126(d).

Confirmatory studies, as a rule, are necessary to provide firm evidence of efficacy or safety. A confirmatory study is an adequately controlled trial in which the hypotheses are stated in advance and evaluated. In such studies the key hypothesis of interest follows directly from the trial's primary objective, is always predefined, and is the hypothesis that is subsequently tested when the study is complete. In a confirmatory study, it is equally important to estimate with due precision the size of the effects attributable to the treatment of interest and to relate these effects to their clinical significance.[8]

Uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness. Such studies carefully conducted and documented, may provide corroborative support of well-controlled studies regarding efficacy and may yield valuable data regarding safety of the test drug. Such studies will be considered on their merits in the light of the principles listed here, with the exception of the requirement for the comparison of the treated subjects with controls. Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered.[9]

To identify adequate and well-controlled clinical studies of safety and efficacy for [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] or [redacted], I conducted searches of the PubMed database on August 10, 2015 and again on April 1, 2016, to identify citations that referred to [redacted] (Thiopental Sodium USP 1 gm Vial) and [redacted] or [redacted]. The PubMed database was used to ensure a comprehensive search of the available literature. PubMed is produced by the U.S. National Library of Medicine and contains references to journal articles in the life sciences with a concentration on biomedicine. Subject areas also covered by PubMed include, but are not limited to, biomedical research, clinical sciences, pharmacy, pharmacology and pharmaceuticals, and toxicology. Results were evaluated to identify any articles that appeared to describe adequate and well-controlled clinical studies of [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted].

The chart below summarizes the terms used to search the literature and number of citations retrieved by each search.

Search No.	Search terms	Search limits	Search results*
Search 1	"[redacted]" AND "[redacted]"	Human; English	0 citations
Search 2	"[redacted]" AND "[redacted]"	Human; English	0 citations
Search 3	"thiopental" AND ("[redacted]" OR "[redacted]")	Human; English	0 citations
Search 4	"thiopental" AND ("[redacted]" OR "[redacted]")	Human; English	0 citations
Search 5	"[redacted]"	Human; English	0 citations

* For quoted phrases only.

[8] Guidance for Industry: E9 Statistical Principles for Clinical Trials; September 1998, pp. 4-5.
[9] See 21 CFR § 314.126(e).

These searches identified no adequate and well-controlled clinical studies of [redacted] (Thiopental Sodium USP 1 gm Vial), manufactured and/or distributed by [redacted], for any indication. Therefore, I conclude that [redacted] (Thiopental Sodium USP 1 gm Vial), manufactured and/or distributed by [redacted] is not GRASE under any conditions of use.

There Are No NDAs, ANDAs, BLAs [redacted] for the Detained Drugs

When an applicant submits to FDA an NDA, ANDA, BLA [redacted] for any intended use of a new drug, the existence of that submission is reflected in various records that FDA regularly makes and preserves in the normal course of its regulatory affairs. On April 1, 2016, I conducted diligent searches of the FDA's Orange Book: Approved Drug Products With Therapeutic Equivalence Evaluations (Orange Book), Document Archiving, Reporting, and Regulatory Tracking System (DARRTS), and Drugs@FDA databases to determine whether [redacted] has sought approval for [redacted] (Thiopental Sodium USP 1 gm Vial) and to determine whether the product has been approved by FDA [redacted] A record of the searches is appended to this document (see Appendix 4).

The searches identified no NDA, ANDA, BLA [redacted] for [redacted] (Thiopental Sodium USP 1 gm Vial) manufactured and/or distributed by [redacted] (Thiopental Sodium USP 1 gm Vial), and the product has not been approved by FDA. [redacted]

Information Necessary for Use

The labeling, and in particular the package insert, for prescription drugs contains the information needed to use the product effectively while minimizing the risks associated with its use. The labeling typically includes sections on "Dosing and Administration," "Contraindications," and "Warnings and Precautions," among other things. As discussed above, however, the detained [redacted] bears no labeling containing information regarding dosing, methods of administration, contraindications, warnings, precautions, or adverse reactions.

In determining what contraindications, warnings, and precautions are necessary for a particular drug product, the Agency considers a number of sources, some of which include safety data from adequate and well-controlled studies, information reported in peer-reviewed biomedical literature, and post-marketing reports of adverse events. As part of this process, the Agency also considers safety issues that have been identified for similar products, i.e., those with the same active ingredient(s), and other products in the same class of drugs.

As indicated above, there are no published studies regarding the use of [redacted] and I am not aware of any unpublished studies regarding use of the product. However, there are a number of reports in the biomedical literature of safety issues related to the use of thiopental sodium products. Some of this information would need to be considered for the appropriate labeling of [redacted] to assure that it meets the statutory requirement that its labeling bears adequate warnings

against "unsafe... methods... of administration... as are necessary for the protection of users..."[10] One example of this use of the available safety information from various sources involves the risks associated with inadvertent intra-arterial administration of thiopental.

Case reports of intra-arterial injections of thiopental sodium products (referred to as thiopentone sodium products in British literature) can be found in the biomedical literature as far back as the 1940's. The adverse effects of these inadvertent injections have been well documented and included similar signs and symptoms[11] and in some cases, serious sequelae.[12] Animal studies reported in the biomedical literature also describe deleterious effects of intra-arterial injections of thiopental sodium that were consistent with findings in humans.[13][14]

These risks, and suggestions for managing an inadvertent intra-arterial injection of thiopental sodium, were incorporated into the labeling for [redacted] Pentothal (thiopental sodium injection), a product that has not been approved by FDA (see Appendix 3). For example, the Pentothal labeling states in its Warnings section: "Avoid extravasation or intra-arterial injection."

The biomedical literature also provides information on the possible etiology of the reactions observed with intra-arterial injections of thiopental sodium.[15]

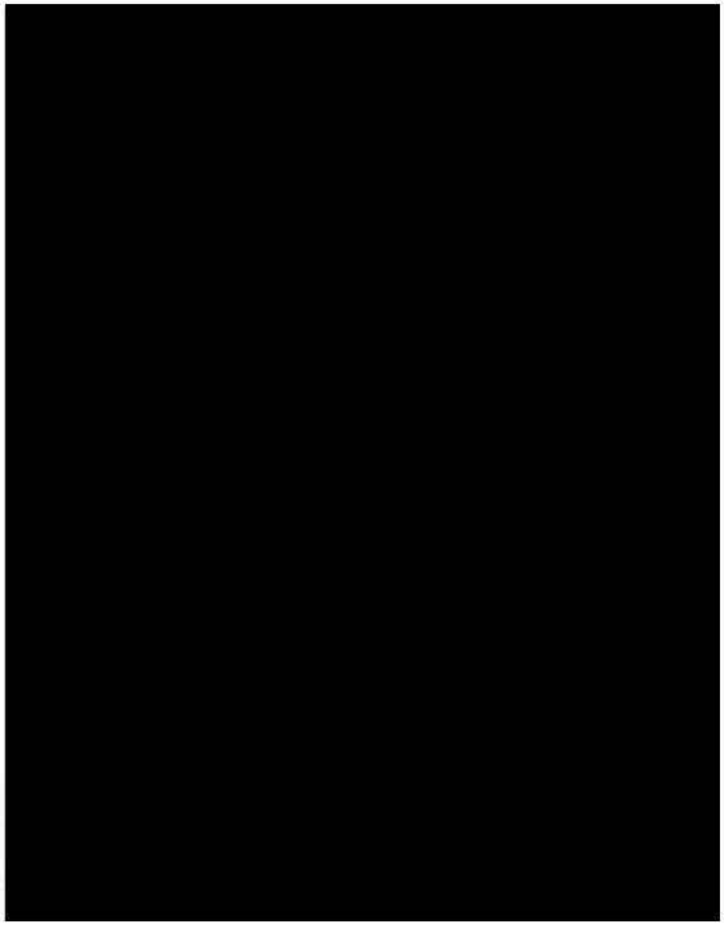
Thiopental sodium is the only active ingredient in both [redacted] and Pentothal, and the two products both have a high alkaline pH of 10-11 (see Pentothal label in Appendix 3 and the Certificate of Analysis for [redacted] in Appendix 5), which has been considered one of the factors triggering injury following intra-arterial injection.[16] Given the in vitro, animal and clinical safety data available and the chemical similarity of the two products, it would be expected that both products would pose the same risks with intra-arterial injections. Based on the information I have reviewed, absent scientific information demonstrating that the risks associated with intra-arterial administration of thiopental are not applicable to [redacted] I would expect a statement warning about the risks of intra-arterial administration of [redacted] to be necessary for the protection of users.

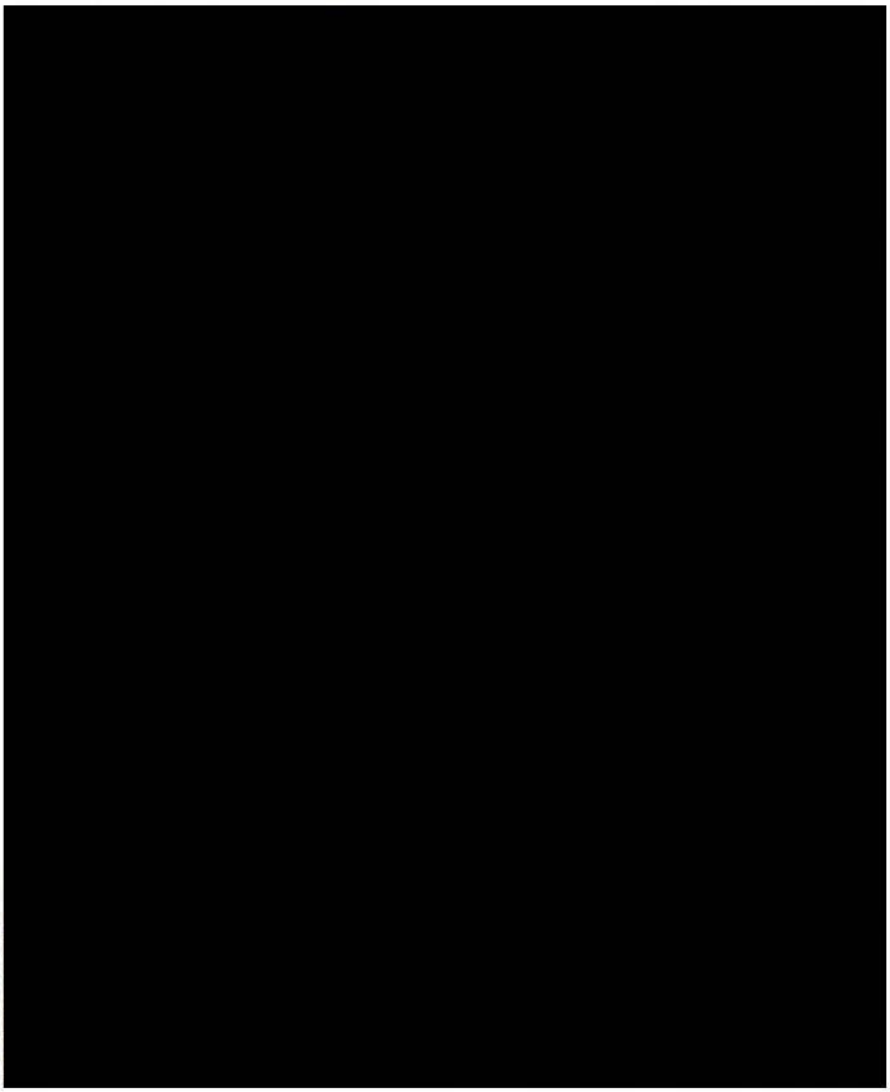
As noted, the risks associated with intra-arterial injection of thiopental sodium are just one example of warnings that would be expected to appear on [redacted] labeling. Although particular

[10] See 21 U.S.C. § 352(f)(2).
[11] The accidental intraarterial injection of thiopental. Stone HH and Donnelly CC. Anesthesiology. 1961 Nov-Dec; 22:995-1006.
[12] Intraarterial injection of 2.5% thiamylal does cause gangrene. Dohi S, Naito H. Anesthesiology. 1983 Aug; 59(2):154.
[13] Intraarterial drug injury: studies of etiology and potential treatment. Buckspan GS, Franklin JD, Novak GR, Bennett BD, Lynch JB, Dean RH. J Surg Res. 1978 Apr; 24(4):294-301;
[14] The role of intraarterial vasodilators in the treatment of inadvertent intraarterial injection injuries. Crawford CR, Terranova WA. Ann Plast Surg. 1990 Oct; 25(4):279-82.
[15] Complications after unintentional intra-arterial injection of drugs; risks, outcomes and management strategies. Sen S, Chini EN, Brown MJ. Mayo Clin Proc 2005; 80:783-95.
[16] Intra-arterial thiopentone: A physico-chemical phenomenon. Water DJ. Anaesthesia 1966 July; 21(3):346-356.

formulations and uses of drug products may make certain safety and efficacy information more or less relevant, it is likely that additional labeling information for Pentothal would apply to all such drug products, including [redacted] particularly that information related to the molecular properties, mechanism of action, pharmacodynamics, and pharmacokinetics of injected thiopental sodium. Based on the product similarities, the Pentothal labeling appears to be illustrative of some of the other important information that is missing from [redacted] labeling but would nonetheless be critical to take into consideration before administering either product.

Appendix 1: [redacted] Container Labeling





7/28/2015 RES 24

Appendix 2: Search for [redacted] and other Injectable Thiopental Sodium Package Inserts
The searches were conducted on August 10, 2015.

European Medicines Agency, Human Medicines
[http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d124]

1. Active substance or common name: Thiopental
    a. Authorized medicine: no records
    b. Withdrawn post-approval: no records
    c. Suspended: no records
    d. Refused: no records
2. Name: [redacted]
    a. Authorized medicine: no records
    b. Withdrawn post-approval: no records
    c. Suspended: no records
    d. Refused: no records

Australian Department of Health, Therapeutic Goods Administration, Australian Public Assessment Report for prescription medicines (AusPAR)
[https://www.tga.gov.au/australian-public-assessment-reports-prescription-medicines-auspars]

1. Active ingredient: Thiopental
    a. Thiopental: no records
    b. Sodium Thiopental: no records
2. Product name:
    a. [redacted] no records
    b. Pentothal: no records
3. Sponsor:
    a. [redacted]: no records
    b. [redacted].: no records
    c. Search of all Sponsors for product containing the active ingredient thiopental: no records

Japan's Pharmaceuticals and Medical Devices Agency
List of Approved Products; New Drugs
[http://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0002.html]

1. Search of active ingredient "thiopental:" no records for 2004-September 2014

Health Canada; Drug Product Database
[http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp]

1. Search Criteria:
    - Status: Marketed
    - Active Ingredient(s): thiopental
    - Class(es): Human
    - Route(s) of Administration: Select All
    - Dosage Form(s): Select All
    - Schedule(s): Select All

    Results: Five products listed in the table below.

Active ingredient "thiopental" in "human" class: 5 records

Status	DIN	Company	Product	Class	PM[1]	Schedule	#[2]	A.I. Name[3]	Strength
Marketed	00695017	[redacted] Healthcare Corporation	Pentothal Inj 25mg/Ml	Human	No	Schedule G (CDSA IV)	1	Thiopental Sodium	25 mg/ml
Marketed	00038393	[redacted] Healthcare Corporation	Pentothal Inj 500mg/Syr	Human	No	Schedule G (CDSA IV)	1	Thiopental Sodium	500 mg
Marketed	00372536	[redacted] Healthcare Corporation	Pentothal Ready To Mix Syringe 250mg	Human	No	Schedule G (CDSA IV)	1	Thiopental Sodium	250 mg/syr
Marketed	00038407	[redacted] Healthcare Corporation	Pentothal Sodium Inj 1gm Sterile	Human	No	Schedule G (CDSA IV)	1	Thiopental Sodium	1 g/vial
Marketed	00038415	[redacted] Healthcare Corporation	Pentothal Sodium PWS 5gm	Human	No	Schedule G (CDSA IV)	1	Thiopental Sodium	5 g/bottle

[1] Product Monograph Availability
[2] Number of Active Ingredients
[3] Only one active ingredient is displayed per DIN.

2. Search Criteria:
    - Status: Approved
    - Active Ingredient(s): thiopental
    - Class(es): Human
    - Route(s) of Administration: Select All
    - Dosage Form(s): Select All
    - Schedule(s): Select All

    Search Results: No records were found.

3. Search Criteria:
    - Status: Cancelled Post Market
    - Active Ingredient(s): thiopental
    - Class(es): Human
    - Route(s) of Administration: Select All
    - Dosage Form(s): Select All
    - Schedule(s): Select All

    Search Results: No records were found.

4. Search Criteria:
    - Status: Cancelled Pre Market
    - Active Ingredient(s): thiopental
    - Class(es): Human
    - Route(s) of Administration: Select All
    - Dosage Form(s): Select All
    - Schedule(s): Select All

    Search Results: No records were found.

Appendix 3: Thiopental Sodium Labeling

Archived drug label on DailyMed website, at link below, accessed on 8/10/15.

https://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=48745

THIOPENTAL SODIUM - thiopental sodium injection, powder, for solution
[redacted]

PENTOTHAL™

THIOPENTAL SODIUM FOR INJECTION

CIII

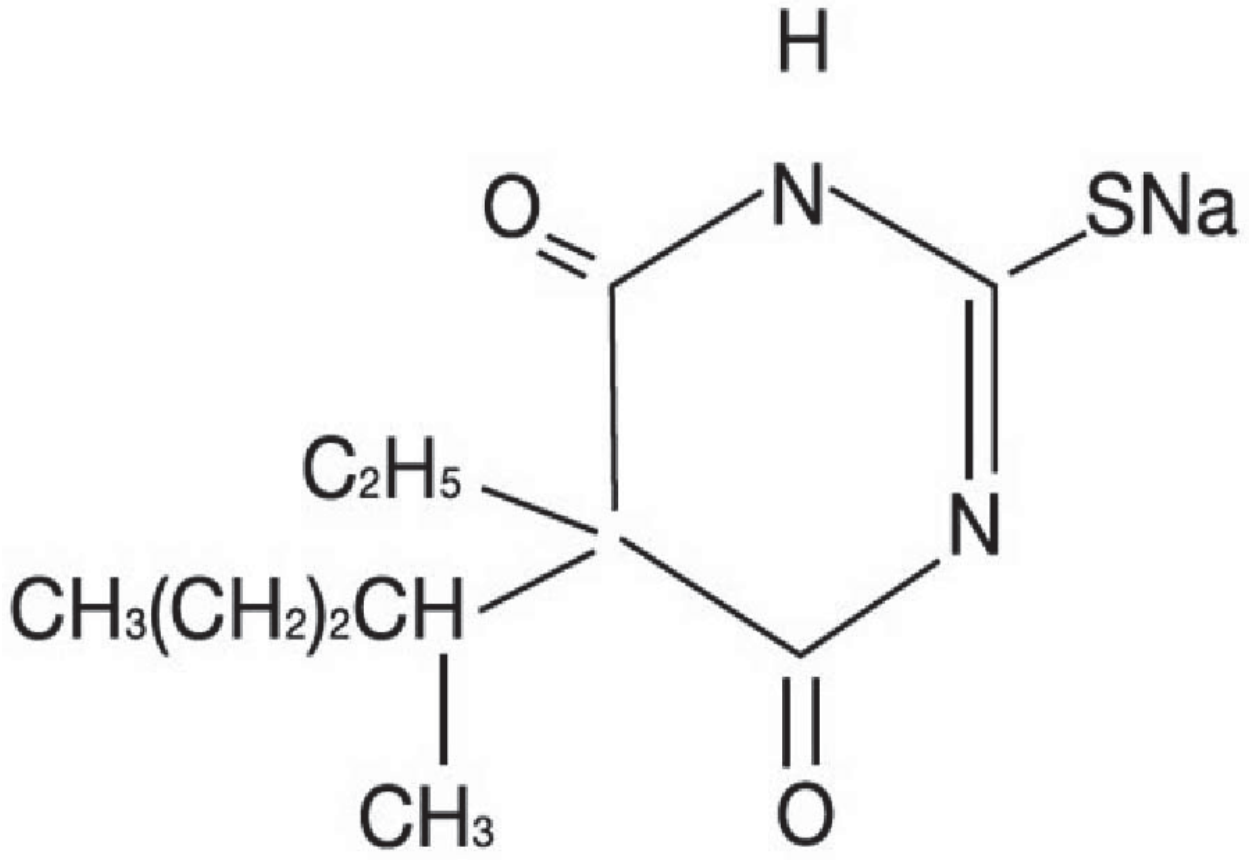
Rx only

DESCRIPTION

Pentothal (Thiopental Sodium for Injection) is a thiobarbiturate, the sulfur analogue of sodium pentobarbital.

The drug is prepared as a sterile powder and after reconstitution with an appropriate diluent is administered by the intravenous route.

Pentothal is chemically designated sodium 5-ethyl-5-(1-methylbutyl)-2-thiobarbiturate and has the following structural formula:



The drug is a yellowish, hygroscopic powder, stabilized with anhydrous sodium carbonate as a buffer (60 mg/g of thiopental sodium).

CLINICAL PHARMACOLOGY

Pentothal (Thiopental Sodium for Injection) is an ultrashort-acting depressant of the central nervous system which induces hypnosis and anesthesia, but not analgesia. It produces hypnosis within 30 to 40 seconds of intravenous injection. Recovery after a small dose is rapid, with some somnolence and retrograde amnesia. Repeated intravenous doses lead to prolonged anesthesia because fatty tissues act as a reservoir; they accumulate Pentothal in concentrations 6 to 12 times greater than the plasma concentration, and then release the drug slowly to cause prolonged anesthesia.

The half-life of the elimination phase after a single intravenous dose is three to eight hours.

The distribution and fate of Pentothal (as with other barbiturates) is influenced chiefly by its lipid solubility (partition coefficient), protein binding and extent of ionization. Pentothal has a partition coefficient of 580.

Approximately 80% of the drug in the blood is bound to plasma protein. Pentothal is largely degraded in the liver and to a smaller extent in other tissues, especially the kidney and brain. It has a pKa of 7.4.

Concentration in spinal fluid is slightly less than in the plasma.

Biotransformation products of thiopental are pharmacologically inactive and mostly excreted in the urine.

INDICATIONS AND USAGE

Pentothal (Thiopental Sodium for Injection) is indicated (1) as the sole anesthetic agent for brief (15 minute) procedures, (2) for induction of anesthesia prior to administration of other anesthetic agents, (3) to supplement regional anesthesia, (4) to provide hypnosis during balanced anesthesia with other agents for analgesia or muscle relaxation, (5) for the control of convulsive states during or following inhalation anesthesia, local anesthesia, or other causes, (6) in neurosurgical patients with increased intracranial pressure, if adequate ventilation is provided, and (7) for narcoanalysis and narcosynthesis in psychiatric disorders.

CONTRAINDICATIONS

Absolute Contraindications:

(1) Absence of suitable veins for intravenous administration, (2) hypersensitivity (allergy) to barbiturates and (3) variegate porphyria (South African) or acute intermittent porphyria.

Relative Contraindications:

(1) Severe cardiovascular disease, (2) hypotension or shock, (3) conditions in which the hypnotic effect may be prolonged or potentiated — excessive premedication, Addison’s disease, hepatic or renal dysfunction, myxedema, increased blood urea, severe anemia, asthma, myasthenia gravis, and (4) status asthmaticus.

WARNINGS

KEEP RESUSCITATIVE AND ENDOTRACHEAL INTUBATION EQUIPMENT AND OXYGEN READILY AVAILABLE. MAINTAIN PATENCY OF THE AIRWAY AT ALL TIMES.

This drug should be administered only by persons qualified in the use of intravenous anesthetics.

Avoid extravasation or intra-arterial injection.

PRECAUTIONS

Observe aseptic precautions at all times in preparation and handling of Pentothal (Thiopental Sodium for Injection) solutions.

If used in conditions involving relative contraindications, reduce dosage and administer slowly.

Care should be taken in administering the drug to patients with advanced cardiac disease, increased intracranial pressure, ophthalmoplegia plus, asthma, myasthenia gravis and endocrine insufficiency (pituitary, thyroid, adrenal, pancreas).

Drug interactions: The following drug interactions have been reported with thiopental.

Drug	Effect
Probenecid	Prolonged action of thiopental
Diazoxide	Hypotension
Zimelidine	Thiopental antagonism
Opioid analgesics	Decreased antinociceptive action
Aminophylline	Thiopental antagonism
Midazolam	Synergism

Nursing Mothers: Thiopental sodium readily crosses the placental barrier and small amounts may appear in the milk of nursing mothers following administration of large doses.

Pregnancy Category C. Animal reproduction studies have not been conducted with Pentothal. It is also not known whether Pentothal can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Pentothal should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS

Adverse reactions include respiratory depression, myocardial depression, cardiac arrhythmias, prolonged somnolence and recovery, sneezing, coughing, bronchospasm, laryngospasm and shivering. Anaphylactic and anaphylactoid reactions to Pentothal (Thiopental Sodium for Injection) have been reported. Symptoms, e.g., urticaria, bronchospasm, vasodilation and edema should be managed by conventional means.

Rarely, immune hemolytic anemia with renal failure and radial nerve palsy have been reported.

DRUG ABUSE AND DEPENDENCE

Thiopental sodium is classified as a Schedule III controlled substance.

OVERDOSAGE

Overdosage may occur from too rapid or repeated injections. Too rapid injection may be followed by an alarming fall in blood pressure even to shock levels. Apnea, occasional laryngospasm, coughing and other respiratory difficulties with excessive or too rapid injections may occur. In the event of suspected or apparent overdosage, the drug should be discontinued, a patent airway established (intubate if necessary) or maintained, and oxygen should be administered, with assisted ventilation if necessary. The lethal dose of barbiturates varies and cannot be stated with certainty. Lethal blood levels may be as low as 1 mg/100 mL for short-acting barbiturates; less if other depressant drugs or alcohol are also present.

MANAGEMENT OF OVERDOSAGE

It is generally agreed that respiratory depression or arrest due to unusual sensitivity to thiopental sodium or overdosage is easily managed if there is no concomitant respiratory obstruction. If the airway is patent, any method of ventilating the lungs (that prevents hypoxia) should be successful in maintaining other vital functions. Since depression of respiratory activity is one of the characteristic actions of the drug, it is important to observe respiration closely.

Should laryngeal spasm occur, it may be relieved by one of the usual methods, such as the use of a relaxant drug or positive pressure oxygen. Endotracheal intubation may be indicated in difficult cases.

DOSAGE AND ADMINISTRATION

Pentothal is administered by the intravenous route only. Individual response to the drug is so varied that there can be no fixed dosage. The drug should be titrated against patient requirements as governed by age, sex and body weight. Younger patients require relatively larger doses than middle-aged and elderly persons; the latter metabolize the drug more slowly. Pre-puberty requirements are the same for both sexes, but adult females require less than adult males. Dose is usually proportional to body weight and obese patients require a larger dose than relatively lean persons of the same weight.

Premedication

Premedication usually consists of atropine or scopolamine to suppress vagal reflexes and inhibit secretions. In addition, a barbiturate or an opiate is often given. Sodium pentobarbital injection (Nembutal®) is suggested because it provides a preliminary indication of how the patient will react to barbiturate anesthesia. Ideally, the peak effect of these medications should be reached shortly before the time of induction.

Test Dose

It is advisable to inject a small “test” dose of 25 to 75 mg (1 to 3 mL of a 2.5% solution) of Pentothal (Thiopental Sodium for Injection) to assess tolerance or unusual sensitivity to Pentothal, and pausing to observe patient reaction for at least 60 seconds. If unexpectedly deep anesthesia develops or if respiratory depression occurs, consider these possibilities: (1) the

patient may be unusually sensitive to Pentothal, (2) the solution may be more concentrated than had been assumed, or (3) the patient may have received too much premedication.

Use in Anesthesia

Moderately slow induction can usually be accomplished in the “average” adult by injection of 50 to 75 mg (2 to 3 mL of a 2.5% solution) at intervals of 20 to 40 seconds, depending on the reaction of the patient. Once anesthesia is established, additional injections of 25 to 50 mg can be given whenever the patient moves.

Slow injection is recommended to minimize respiratory depression and the possibility of overdosage. The smallest dose consistent with attaining the surgical objective is the desired goal. Momentary apnea following each injection is typical, and progressive decrease in the amplitude of respiration appears with increasing dosage. Pulse remains normal or increases slightly and returns to normal. Blood pressure usually falls slightly but returns toward normal. Muscles usually relax about 30 seconds after unconsciousness is attained, but this may be masked if a skeletal muscle relaxant is used. The tone of jaw muscles is a fairly reliable index. The pupils may dilate but later contract; sensitivity to light is not usually lost until a level of anesthesia deep enough to permit surgery is attained. Nystagmus and divergent strabismus are characteristic during early stages, but at the level of surgical anesthesia, the eyes are central and fixed. Corneal and conjunctival reflexes disappear during surgical anesthesia.

When Pentothal (Thiopental Sodium for Injection) is used for induction in balanced anesthesia with a skeletal muscle relaxant and an inhalation agent, the total dose of Pentothal can be estimated and then injected in two to four fractional doses. With this technique, brief periods of apnea may occur which may require assisted or controlled pulmonary ventilation. As an initial dose, 210 to 280 mg (3 to 4 mg/kg) of Pentothal is usually required for rapid induction in the average adult (70 kg).

When Pentothal (Thiopental Sodium for Injection) is used as the sole anesthetic agent, the desired level of anesthesia can be maintained by injection of small repeated doses as needed or by using a continuous intravenous drip in a 0.2% or 0.4% concentration. (Sterile water should not be used as the diluent in these concentrations, since hemolysis will occur.) With continuous drip, the depth of anesthesia is controlled by adjusting the rate of infusion.

Use in Convulsive States

For the control of convulsive states following anesthesia (inhalation or local) or other causes, 75 to 125 mg (3 to 5 mL of a 2.5% solution) should be given as soon as possible after the convulsion begins. Convulsions following the use of a local anesthetic may require 125 to 250 mg of Pentothal given over a ten minute period. If the convulsion is caused by a local anesthetic, the required dose of Pentothal will depend upon the amount of local anesthetic given and its convulsant properties.

Use in Neurosurgical Patients with Increased Intracranial Pressure

In neurosurgical patients, intermittent bolus injections of 1.5 to 3.5 mg/kg of body weight may be given to reduce intraoperative elevations of intracranial pressure, if adequate ventilation is provided.

Use in Psychiatric Disorders

For narcoanalysis and narcosynthesis in psychiatric disorders, premedication with an anticholinergic agent may precede administration of Pentothal. After a test dose, Pentothal (Thiopental Sodium for Injection) is injected at a slow rate of 100 mg/min (4 mL/min of a 2.5% solution) with the patient counting backwards from 100. Shortly after counting becomes confused but before actual sleep is produced, the injection is discontinued. Allow the patient to return to a semidrowsy state where conversation is coherent. Alternatively, Pentothal may be administered by rapid I.V. drip using a 0.2% concentration in 5% dextrose and water. At this concentration, the rate of administration should not exceed 50 mL/min.

MANAGEMENT OF SOME COMPLICATIONS

Respiratory depression (hypoventilation, apnea), which may result from either unusual responsiveness to Pentothal or overdosage, is managed as stated above. Pentothal should be considered to have the same potential for producing respiratory depression as an inhalation agent, and patency of the airway must be protected at all times.

Laryngospasm may occur with light Pentothal narcosis at intubation, or in the absence of intubation if foreign matter or secretions in the respiratory tract create irritation. Laryngeal and bronchial vagal reflexes can be suppressed, and secretions minimized by giving atropine or scopolamine premedication and a barbiturate or opiate. Use of a skeletal muscle relaxant or positive pressure oxygen will usually relieve laryngospasm. Tracheostomy may be indicated in difficult cases.

Myocardial depression, proportional to the amount of drug in direct contact with the heart, can occur and may cause hypotension, particularly in patients with an unhealthy myocardium. Arrhythmias may appear if PCO2 is elevated, but they are uncommon with adequate ventilation. Management of myocardial depression is the same as for overdosage. Pentothal (Thiopental Sodium for Injection) does not sensitize the heart to epinephrine or other sympathomimetic amines.

Extravascular infiltration should be avoided. Care should be taken to insure that the needle is within the lumen of the vein before injection of Pentothal. Extravascular injection may cause chemical irritation of the tissues varying from slight tenderness to venospasm, extensive necrosis and sloughing. This is due primarily to the high alkaline pH (10 to 11) of clinical concentrations of the drug. If extravasation occurs, the local irritant effects can be reduced by injection of 1% procaine locally to relieve pain and enhance vasodilatation. Local application of heat also may help to increase local circulation and removal of the infiltrate.

Intra-arterial injection can occur inadvertently, especially if an aberrant superficial artery is present at the medial aspect of the antecubital fossa. The area selected for intravenous injection

of the drug should be palpated for detection of an underlying pulsating vessel. Accidental intra-arterial injection can cause arteriospasm and severe pain along the course of the artery with blanching of the arm and fingers. Appropriate corrective measures should be instituted promptly to avoid possible development of gangrene. Any patient complaint of pain warrants stopping the injection. Methods suggested for dealing with this complication vary with the severity of symptoms. The following have been suggested:

1. Dilute the injected Pentothal (Thiopental Sodium for Injection) by removing the tourniquet and any restrictive garments.

2. Leave the needle in place, if possible.

3. Inject the artery with a dilute solution of papaverine, 40 to 80 mg, or 10 mL of 1% procaine, to inhibit smooth muscle spasm.

4. If necessary, perform sympathetic block of the brachial plexus and/or stellate ganglion to relieve pain and assist in opening collateral circulation. Papaverine can be injected into the subclavian artery, if desired.

5. Unless otherwise contraindicated, institute immediate heparinization to prevent thrombus formation.

6. Consider local infiltration of an alpha-adrenergic blocking agent such as phentolamine into the vasospastic area.

7. Provide additional symptomatic treatment as required.

Shivering after Pentothal anesthesia, manifested by twitching face muscles and occasional progression to tremors of the arms, head, shoulder and body, is a thermal reaction due to increased sensitivity to cold. Shivering appears if the room environment is cold and if a large ventilatory heat loss has been sustained with balanced inhalation anesthesia employing nitrous oxide. Treatment consists of warming the patient with blankets, maintaining room temperature near 22° C (72° F), and administration of chlorpromazine or methylphenidate.

PREPARATION OF SOLUTIONS

Pentothal (Thiopental Sodium for Injection) is supplied as a yellowish, hygroscopic powder. Solutions should be prepared aseptically with the following diluent: Sterile Water for Injection, USP. Reconstitute 500 mg Pentothal with 20 mL Sterile Water for Injection, USP. Reconstitute 1 g Pentothal with 20 mL Sterile Water for Injection, USP. Clinical concentrations used for intermittent intravenous administration vary between 2.0% and 5.0%. A 2.0% or 2.5% solution is most commonly used. A 3.4% concentration in sterile water for injection is isotonic; concentrations less than 2.0% in this diluent are not used because they cause hemolysis. For continuous intravenous drip administration, concentrations of 0.2% or 0.4% are used. Solutions may be prepared by adding Pentothal to 5% Dextrose Injection, USP, 0.9% Sodium Chloride Injection, USP or Normosol®-R pH 7.4.

Since Pentothal contains no added bacteriostatic agent, extreme care in preparation and handling should be exercised at all times to prevent the introduction of microbial contaminants. Solutions should be freshly prepared and used promptly. Sterilization by heating should not be attempted.

COMPATIBILITY

Any solution of Pentothal (Thiopental Sodium for Injection) with a visible precipitate should not be administered. The stability of Pentothal solutions depends upon several factors, including the diluent, temperature of storage and the amount of carbon dioxide from room air that gains access to the solution. Any factor or condition which tends to lower pH (increase acidity) of Pentothal solutions will increase the likelihood of precipitation of thiopental acid. Such factors include the use of diluents which are too acidic and the absorption of carbon dioxide which can combine with water to form carbonic acid.

Solutions of succinylcholine, tubocurarine or other drugs which have an acid pH should not be mixed with Pentothal solutions. The most stable solutions are those reconstituted in water or isotonic saline, kept under refrigeration and tightly stoppered. The presence or absence of a visible precipitate offers a practical guide to the physical compatibility of prepared solutions of Pentothal.

CALCULATIONS FOR VARIOUS CONCENTRATIONS				
Concentration Desired			Amounts to Use	
Percent	mg/mL		Pentothal g	Diluent mL
0.2	2		1	500
0.4	4	{	1	250
			2	500
2.0	20	{	5	250
			10	500
2.5	25	{	1	40
			5	200
5	50	{	1	20
			5	100

Reconstituted solutions of Pentothal (Thiopental Sodium for Injection) should be inspected visually for particulate matter and discoloration, whenever solution and container permit.

HOW SUPPLIED

Pentothal is available as shown.

WARNINGS

Intravenous administration of Sterile Water for Injection, USP without a solute may result in hemolysis.

Use aseptic technique for preparing Pentothal solutions during withdrawal from reconstituted single -use containers.

Administer only clear reconstituted solutions.

Use within 24 hours after reconstitution. Discard unused portions.

PRECAUTIONS

Do not use unless solution is clear and container is undamaged.

Inspect reconstituted (mixed) solutions of Pentothal (Thiopental Sodium for Injection) for clarity and freedom from precipitation or discoloration prior to administration. Use reconstituted solution only if it is clear, free from precipitate and not discolored.

Pregnancy Category C. Animal reproduction studies have not been conducted with sterile water for injection or sodium chloride injection. It is also not known whether sterile water or sodium chloride injection containing additives can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Sterile water for injection or sodium chloride injection with additives should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS

Reactions which may occur because of the diluent, technique of preparation or mixing, or administration of reconstituted solutions of Pentothal include febrile response or infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection and extravasation.

If an adverse reaction does occur, discontinue the injection, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of unused solution (or the used container or syringe) for examination if deemed necessary.

DRUG ABUSE AND DEPENDENCE

None known.

DOSAGE AND ADMINISTRATION

Pentothal solutions should be administered only by intravenous injection and by individuals experienced in the conduct of intravenous anesthesia.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. See PRECAUTIONS.

Store at 20 to 25°C (68 to 77°F) [See USP Controlled Room Temperature.]

Keep reconstituted solution in a cool place.

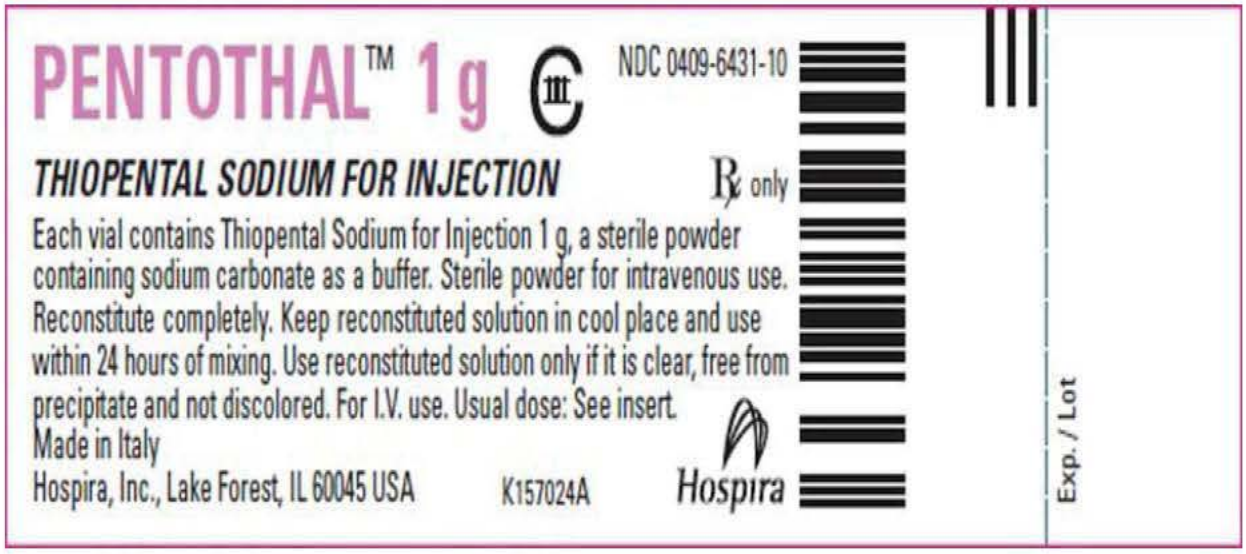
NDC No.	Pentothal	Pentothal Container	Diluent (mL)*	Theoretical Reconstituted Conc.
0409-3158-10	500 mg	Vial	W (20)	2.5% (25 mg/mL)
0409-6431-10	1 g	Vial	W (20)	5% (50 mg/mL)

Revised: April, 2010

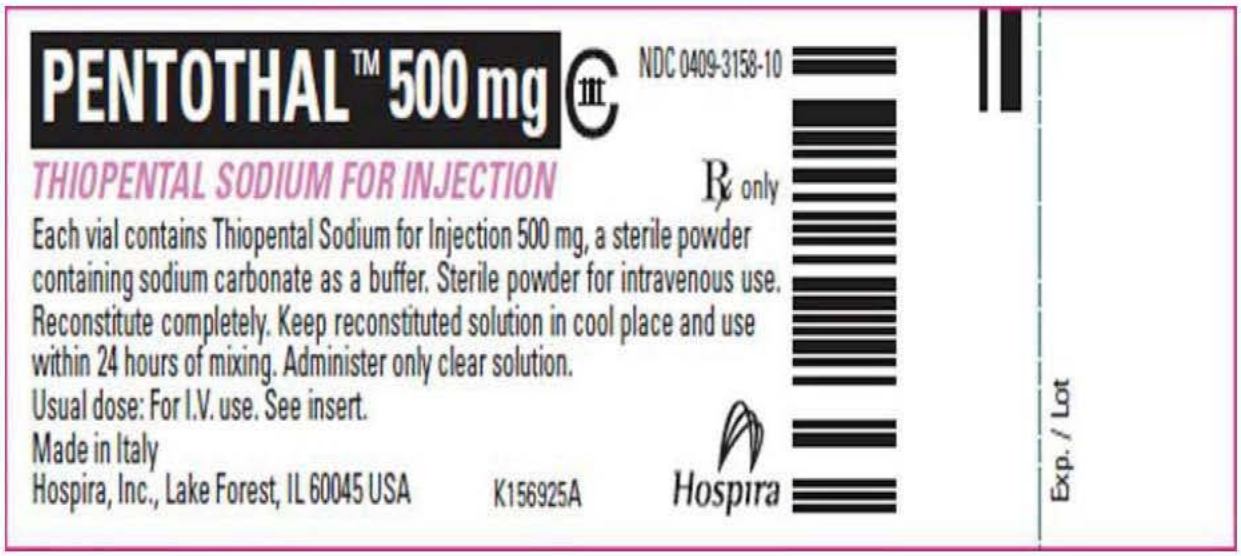
Made in [redacted] K156946A

[redacted]

K157024A



K156925A



THIOPENTAL SODIUM
thiopental sodium injection, powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	NDC Product Code (Source)	[redacted]
Route of Administration	INTRAVENOUS	DEA Schedule	CIII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
THIOPENTAL SODIUM (THIOPENTAL)	THIOPENTAL SODIUM	25 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CARBONATE	

Product Characteristics

Color	Score
Shape	Size
Flavor	Imprint Code
Contains	

Packaging

# NDC	Package Description	Multilevel Packaging
1 [redacted]	1 VIAL In 1 CARTON	contains a VIAL
1	20 mL In 1 VIAL	This package is contained within the CARTON ([redacted])

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug other		05/25/2010	01/21/2011

THIOPENTAL SODIUM
thiopental sodium injection, powder, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	NDC Product Code (Source)	[redacted]
Route of Administration	INTRAVENOUS	DEA Schedule	CIII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
THIOPENTAL SODIUM (THIOPENTAL)	THIOPENTAL SODIUM	50 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CARBONATE	

Product Characteristics

Color	Score
Shape	Size
Flavor	Imprint Code
Contains	

Packaging

#	NDC	Package Description	Multilevel Packaging
1	[redacted]	1 VIAL In 1 CARTON	contains a VIAL
1		20 mL In 1 VIAL	This package is contained within the CARTON [redacted]

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug other		05/25/2010	01/21/2011

Labeler - [redacted] (141588017)
Revised: 02/2011 [redacted]

Appendix 4: Search of FDA Records
Product: [redacted] (Thiopental Sodium USP 1 gm Vial)
Firms: [redacted]
Dates of Search: April 1, 2015

1. **Database: FDA Orange Book**
   (http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm)

   Active Ingredient Search
   Search term: thiopental
   - Rx products: No records were found.
   - OTC products: No records were found.
   - Discontinued products: NDA 011679 for Abbott's Pentothal (thiopental sodium rectal suspension) was found. No records related to [redacted] were found.

   Proprietary Name Searches
   Search terms: [redacted]
   - Rx products: No records were found.
   - OTC products: No records were found.
   - Discontinued products: No records were found.

   Applicant Holder Search
   Search term: [redacted]
   - Rx products: Five records were found. No record for [redacted] or thiopental sodium was found
   - OTC products: No records were found.
   - Discontinued products: No records were found.

   Search term: [redacted]
   - Rx products: 38 records were found. No records related to [redacted] were found.
   - OTC products: 27 records were found. No records related to [redacted] were found.
   - Discontinued products: 65 records were found. No records related to [redacted] were found.

2. **Database: Drugs@FDA**
(http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Active Ingredient Searches
Search term: thiopental
Results: One record was found: NDA 011679 for Abbott's Pentothal (thiopental sodium rectal suspension) was found. No records related to [redacted] were found.

Proprietary Name Searches
Search term: [redacted]
Results: No Records were found.

3. **Database: DARRTS (an internal FDA database):**

a. Application type: NDA, ANDA, BLA[redacted]
Center: CDER
Product name: [redacted]
Results: [redacted]

b. Application type: NDA, ANDA, BLA[redacted]
Center: CDER
Product Name: thiopental
Results: [redacted]

[redacted], ANDA, BLA[redacted]

d. Application type: NDA, ANDA, BLA[redacted]
Center: CDER
Submitter: [redacted]

e. Application [redacted]NDA, ANDA, BLA[redacted]

Center: CDER
Submitter: [redacted]

f. Application type: NDA, ANDA, BLA [redacted]
Center: CDER
Submitter: [redacted]

Appendix 5: Certificate of Analysis for [redacted]

[redacted]

QUALITY CONTROL DEPARTMENT

CERTIFICATE OF ANALYSIS-FINISHED PRODUCT

Product Name [redacted] **Generic Name**	Thiopental Sodium for injection USP		
Manufactured by: [redacted]		**Mfg. Date.**	06/15
		Exp. Date.	05/17
Batch No. [redacted]		**Date Sampled.**	10/06/15
Batch Size. [redacted]		**Qty Sampled.**	40 Units
Sampled by. [redacted]		**Release Date.**	24/06/15
Specification	USP specification	**A.R. No**	[redacted]

S.No	TEST	SPECIFICATION	RESULT
1.	Description	Yellowish to white powder filled in colorless glass vials.	Yellowish to white powder filled in colorless glass vials.
2.	Identification	Should be positive for Thiopentone Sodium	Complies
3.	Average filled wt.	1.095 g ± 10 %	1.0210 g
4.	Reconstituted Solution	When reconstituted with SWFI solution is clear & free from Suspended matter.	Complies
5.	pH	10.2-11.2	10.6
6.	Particulate Matter	Should be free from particulate matter when examined visually	Complies
7.	Residual solvent s	Meets the requirements	Complies
8.	Appearance of Solution	10 .0 % w/v Test solutions in carbon dioxide free water is clear than reference standard solution.	Complies
9.	Bacterial Endotoxin	Not more than 1.0 EU/ mg	Less than 1.0 EU/mg
10.	Sterility Test	Should be sterile	sterile
11.	Assay: Each vial contains :	Result	Limit
	Thiopentone Sodium USP	989.1 mg	930 mg to 1070 mg

Remarks: The above Sample Complies as per USP Specification.

	Analyzed by	Checked by	Ap[redacted]C Manager)
Sign	[redacted]	[redacted]	
Date	8.9.15	24/9/15	

From: [redacted]
To: Santos, Rosa L
Cc: [redacted]
Subject: Extension Request re Entry [redacted]
Date: Thursday, April 28, 2016 1:13:08 PM

Hi Rosa Linda

The [redacted] is requesting a short extension of time, to and including May 20, 2016, to respond in writing to the tentative determination attached to your April 18, 2016 email. I would appreciate it if you would please let me know via return email if a deadline of May 20 is acceptable.

Thanks and best regards.

[redacted]

On Monday, April 18, 2016, Santos, Rosa L <Rosa.Santos@fda.hhs.gov> wrote:

> Good Morning,
>
> Please see attached letter.
>
> Thanks,

Rosa Linda Santos
Compliance Officer
4040 N. Central Expressway
Suite 300
Dallas, Texas 75204
214-253-5269 Phone
214-253-5316 Fax
rosa.santos@fda.hhs.gov

--

[redacted]

From: [redacted]
To: Santos, Rosa L
Subject: Re: Extension Request re Entry [redacted]
Date: Thursday, April 28, 2016 3:36:40 PM

Thanks Ms. Santos

On Thursday, April 28, 2016, Santos, Rosa L <Rosa.Santos@fda.hhs.gov> wrote:

> Good Afternoon [redacted];
>
> The extension was granted until May 20, 2016.
>
> Thanks,
>
> Rosa Linda Santos
> Compliance Officer
> 4040 N. Central Expressway
> Suite 300
> Dallas, Texas 75204
> 214-253-5269 Phone
> 214-253-5316 Fax
> rosa.santos@fda.hhs.gov
>
> **From:** [redacted]
> **Sent:** Thursday, April 28, 2016 1:13 PM
> **To:** Santos, Rosa L
> **Cc:** [redacted]
> **Subject:** Extension Request re Entry [redacted]
>
> Hi Rosa Linda
>
> The [redacted] is requesting a short extension of time, to and including May 20, 2016, to respond in writing to the tentative determination attached to your April 18, 2016 email. I would appreciate it if you would please let me know via return email if a deadline of May 20 is acceptable.

Thanks and best regards.

[redacted]

On Monday, April 18, 2016, Santos, Rosa L <Rosa.Santos@fda.hhs.gov> wrote:

Good Morning,

Please see attached letter.

Thanks,

Rosa Linda Santos
Compliance Officer
4040 N. Central Expressway

Suite 300
Dallas, Texas 75204
214-253-5269 Phone
214-253-5316 Fax
rosa.santos@fda.hhs.gov

--

[redacted]

--

[redacted]

United States Food and Drug Administration

Southwest Import District

Notice of FDA Action

Entry Number: [redacted]

Notice Number: 5
April 29, 2016

Filer:
[redacted]

Attention: [redacted]
Broker Box: [redacted]

>

<

Port of Entry: 5309, Houston Intercontinental Airport, Houston, TX
Carrier: [redacted];
Date Received: July 27, 2015
Arrival Date: July 24, 2015

Importer of Record: [redacted]
Consignee: [redacted]

HOLD DESIGNATED

Summary of Current Status of Individual Lines

	Line ACS/FDA	Product Description	Quantity	Current Status
*	001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	1000 PCS	Extension granted 04-28-2016

* = Status change since the previous notice. Read carefully the sections which follow for important information regarding these lines.

@ = Consignee ID

FDA will not request redelivery for examination or sampling, if the products not released by FDA are moved, following USCS conditional release to a localtion within the metropolitan area or to a location approved by the FDA office at the number below.

All products in this entry not listed above may proceed without FDA examination. This notice does not constitute assurance the products involved comply with provisions of the Food, Drug, and Cosmetic Act or other related acts, and does not preclude action should the products later be found violative.

EXTENSION REQUEST GRANTED

Line ACS/FDA	Product Description	Respond By
001/001	THIOPENTAL-NA STERILE PWDR (LAW ENFORCEMENT ONLY)	May 20, 2016

Rosa L. Santos, Compliance Officer (Region/District) (214) 253-5269
(214) 253-5316 (FAX)

U.S. Food and Drug Administration
4040 N. Central Expressway Suite 300
Dallas, TX 75204

ROSA.SANTOS@FDA.HHS.GOV

This extension is granted until the dates shown above.

Notice Prepared For: The District Director, U.S. Food and Drug Administration
Notice Prepared By: ARM

From: [redacted]
To: Santos, Rosa L
Cc: [redacted]; Veneziano, Domenic J.; Stearn, Douglas; [redacted].
Subject: Re: [redacted] Request for Release (3 Missing Exhibits)
Date: Friday, May 13, 2016 10:24:23 AM
Attachments: Ex.7 TX Texas DEA 236.pdf
Ex.14 TX FDA Policy Statement re Sodium Thiopental.pdf
Ex.17 TX Physicians Desk Reference.pdf

Good morning Ms. Santos

In preparing our responses to the government we discovered the three attached exhibits were inadvertently omitted from our request for release submission to you on October 23, 2015.

We ask that these three exhibits be included as part of the record.

Thanks and best regards

[redacted]

On Fri, Oct 23, 2015 at 5:02 PM, [redacted] wrote:

> Hello Ms. Santos. I hope you are having a good Friday.
>
> Please find our request for release of the thiopental sodium detained by FDA and detained by Customs at FDA's request under the above referenced entry number. An authorization letter is included with the attached letter.
>
> We request FDA to release the goods immediately and to instruct CBP to lift that agency's detention to permit immediate delivery to the [redacted].
>
> Alternatively, we request FDA to grant [redacted] an in-person hearing with the appropriate FDA personnel, lift the detention, and release the goods within 30 days from receipt of this submission.

Further, I respectfully request this case be transferred to Douglas Stearn, Director, Office of Enforcement and Imports, or his designee in ORA Headquarters, who will become the Hearing Officer for this detention. Please inform me who the new Hearing Officer will be and the time and place for additional testimony to be given.

Thank you and best regards

[redacted]

From: Santos, Rosa L
To: [redacted]
Cc: Veneziano, Domenic J.; Stearn, Douglas; [redacted]
Subject: RE: Detained Thiopental Sodium/Entry No. [redacted]
Date: Monday, May 23, 2016 10:18:00 AM

Thanks for the letter and attachments.

Rosa Linda Santos
Compliance Officer
4040 N. Central Expressway
Suite 300
Dallas, Texas 75204
214-253-5269 Phone
214-253-5316 Fax
rosa.santos@fda.hhs.gov

From: [redacted]
Sent: Friday, May 20, 2016 3:50 PM
To: Santos, Rosa L
Cc: Veneziano, Domenic J.; Stearn, Douglas; [redacted]
Subject: Detained Thiopental Sodium/Entry No. [redacted]

Hello Ms. Santos

I am writing as counsel for the [redacted] providing the attached submission (with five attachments) in response to the Tentative Decision that you sent to me on April 15, 2016.

I would appreciate it if you would confirm receipt via return email.

Best regards

[redacted]

purpose of (i) avoiding penalties under the Internal Revenue Code or (ii) promoting, marketing or recommending to another party any transaction or matter addressed herein. Please do not hesitate to contact me, however, if you have any questions regarding this matter.

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance
Office of Unapproved Drugs and Labeling Compliance

Memorandum

Date: November 15, 2016

From: Arthur Simone, MD, PhD
Senior Medical Advisor

Arthur F. Simone -S
Digitally signed by Arthur F Simone S
DN: c=US, o=U S Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300178991, cn=Arthur F Simone S
Date: 2016.11.15 12:41:16 05'00'

Subject: Products Containing Sodium Thiopental

Product Information

Name: sodium thiopental
Alternative Names: thiopental sodium, pentothal, and thiopentone

Executive Summary

Beyond my previous assessment (dated April 14, 2016) as to whether [redacted] (thiopental sodium) was generally recognized as safe and effective, I have been asked to evaluate, separately, whether there are published reports of any adequate and well-controlled studies of any sodium thiopental-containing product associated with lethal injection. Specifically, it was requested that the search include the following terms:

- Sodium thiopental
- Thiopental sodium
- Pentothal
- Thiopentone

In combination with each of the following terms:

- Lethal injection
- Capital punishment
- Execution
- Euthanasia
- Death Penalty

A diligent search of the PubMed database, through the FDA Biosciences Library, was conducted to this end. Search results were evaluated to identify citations that appeared to describe adequate and well-controlled clinical studies of any sodium thiopental-containing product associated with lethal injection. The search identified no adequate and well-controlled clinical studies.[1]

Literature Search

FDA has described the characteristics of "adequate and well-controlled" studies by regulation.[2] To identify adequate and well-controlled clinical studies of safety and efficacy for any sodium thiopental-containing product associated with lethal injection, I conducted searches of the PubMed database on November 4, 2016, to identify citations that referred to thiopental, pentothal, or thiopentone in combination with lethal injection, capital punishment, execution, euthanasia or death penalty. The PubMed database was used to ensure a comprehensive search of the available literature. Results were evaluated to identify any articles that appeared to describe adequate and well-controlled clinical studies of any sodium thiopental-containing product associated with lethal injection.

The chart below summarizes the terms used to search the literature and the number of citations retrieved by each search. The abstract for the citation found is provided in the Appendix.

Search Number	Search terms	Search limits	Search Results*
1	"thiopental" AND "lethal injection"	Clinical Trials, Human, and English	0 citations
2	"thiopental" AND "capital punishment"	Clinical Trials, Human, and English	0 citations
3	"thiopental" AND "execution"	Clinical Trials, Human, and English	0 citations
4	"thiopental" AND "euthanasia"	Clinical Trials, Human, and English	1 citations
5	"thiopental" AND "death penalty"	Clinical Trials, Human, and English	0 citations
6	"pentothal" AND "lethal injection"	Clinical Trials, Human, and English	0 citations
7	"pentothal" AND "capital punishment"	Clinical Trials, Human, and English	0 citations
8	"pentothal" AND "execution"	Clinical Trials, Human, and English	0 citations
9	"pentothal" AND "euthanasia"	Clinical Trials, Human, and English	0 citations
10	"pentothal" AND "death penalty"	Clinical Trials, Human, and English	0 citations
11	"thiopentone" AND "lethal injection"	Clinical Trials, Human, and English	0 citations
12	"thiopentone" AND "capital punishment"	Clinical Trials, Human, and English	0 citations

[1] Dr. Arthur F. Simone is the Senior Medical Advisor in the Office of Unapproved Drugs and Labeling Compliance in the Office of Compliance, Center for Drug Evaluation and Research (CDER), FDA. He received his medical degree (M.D.) from the Robert Wood Johnson Medical School in 1988. He is licensed to practice medicine in Pennsylvania and New Jersey. He is board certified in anesthesiology. He has been employed by the Food and Drug Administration since 2002 and has served as both a primary reviewer and team leader in the Office of New Drugs in CDER.

[2] See 21 CFR § 314.126(b).

Search Number	Search terms	Search limits	Search Results*
13	“thiopentone” AND “execution”	Clinical Trials, Human, and English	0 citations
14	“thiopentone” AND “euthanasia”	Clinical Trials, Human, and English	1 citations
15	“thiopentone” AND “death penalty”	Clinical Trials, Human, and English	0 citations

* For quoted phrases only.

Search 4

The PubMed database was searched with search terms “thiopental” AND “euthanasia.” The search limits imposed were Clinical Trials, Human, and English. This search identified one citation.

The citation[3] referenced prospective, randomized, open-label, study of the potential of thiopentone to prevent brain damage in patients with cardiac arrest who were comatose and had no purposeful motor response to painful stimuli 10 minutes after restoration of spontaneous circulation with systolic blood pressure > 90 mm Hg. Patients were randomized to either receive or not receive 30 mg/kg of thiopentone over the course of not more than one hour. This was an open-label study that was not designed to assess the use of thiopentone administered for lethal injection.

Therefore, this search did not identify any clinical studies of any sodium thiopental-containing product associated with lethal injection.

Search 14

The PubMed database was searched with search terms “thiopentone” AND “euthanasia.” The search limits imposed were Clinical Trials, Human, and English. This search identified a single citation, which was the same citation identified in Search 4.

Therefore, this search did not identify any clinical studies of any sodium thiopental-containing product associated with lethal injection.

Conclusion

In summary, these searches identified no clinical studies of any sodium thiopental-containing product associated with lethal injection.

[3] Assessment of neurological prognosis in comatose survivors of cardiac arrest. BRCT I Study Group. Edgren E, Hedstrand U, Kelsey S, Sutton-Tyrrell K, Safar P. Lancet. 1994 Apr 30; 343(8905):1055-9.

Appendix

Lancet. 1994 Apr 30; 343(8905):1055-9.
Assessment of neurological prognosis in comatose survivors of cardiac arrest. BRCT I Study Group.
Edgren E, Hedstrand U, Kelsey S, Sutton-Tyrrell K, Safar P.
Abstract
When a patient resuscitated from cardiac arrest remains unconscious the clinician would like to have a reliable early method for predicting the outcome. The objective of our study was to predict cerebral outcome after cardiac arrest by clinical neurological examination. The data were drawn from an international multicentre controlled clinical trial of thiopentone. Twelve hospitals in nine countries took part. 262 comatose cardiac arrest survivors were followed up for one year. These patients were given advanced life support (American Heart Association guidelines) followed by intensive care to a standardised protocol. Glasgow and Glasgow-Pittsburgh coma scores and their constituent signs were recorded at fixed times. Outcome was taken to be the best cerebral performance at any time during follow-up, and for that purpose we used cerebral performance categories (CPC 1-5) of the Glasgow outcome categories. A poor outcome (CPC 3-5) could be predicted immediately after reperfusion (at entry into the study) with an accuracy ranging from 52% to 84% for various signs and scores. On the third day it was possible to identify severely disabled or permanently comatose survivors without false predictions using both coma scores and several of their constituent variables. The best predictor was absence of motor response to pain. This modelling exercise now needs to be repeated on a new series of patients but the results do suggest that, after 3 days, stringent ethical criteria can be met and used in decision-making about termination of care in comatose cardiac arrest survivors.
Comment in Coma after cardiac arrest: will he recover all right? [Lancet. 1994]
PMID: 7909098

From: Santos, Rosa L
To: [redacted]
Subject: Ref Entry: [redacted]
Date: Thursday, April 20, 2017 3:59:00 PM
Attachments: FDA Determination on [redacted] Shipment 20 Apr 2017x.pdf
image001.png

Good Afternoon,

Please see attached.

Regards,

Rosa Linda Santos
Compliance Officer

Office of Regulatory Affairs
Southwest Import District
U.S. Food and Drug Administration
Tel: 214-253-5269
rosa.santos@fda.hhs.gov

as provided for in Rule XXII, nor any other action taken as thereby provided to prevent said initial decision becoming the decision of the Commission thirty days from service thereof upon the parties, said initial decision, including said order to cease and desist, accordingly, under the provisions of said Rule XXII became the decision of the Commission on April 21, 1952.

The said order to cease and desist is as follows:

It is ordered, That the respondents, National Coaching Service Institute, Inc., a corporation, and its officers, and Archie K. Babson, individually and as an officer of said corporation and also doing business under the names National Service Institute and Career Institute, and respondents' agents, representatives and employees, directly or through any corporate or other device, in connection with the offering for sale, sale and distribution in commerce, as "commerce" is defined in the Federal Trade Commission Act, of respondents' courses of study and instruction, do forthwith cease and desist from:

1. Using the word "Institute" or any simulation thereof as a part of respondents' corporate or trade names; or otherwise representing, directly or by implication, that respondents' school is a resident institution of higher learning.

2. Representing, directly or by implication:

(a) That respondents' school has any connection with the United States Civil Service or any other agency of the United States Government.

(b) That respondents' sales agents are representatives or employees of the United States Civil Service or have any connection therewith.

(c) That the completion of respondents' courses of study assures students of positions in the United States Civil Service or makes them eligible for appointment to such positions.

(d) That respondents have any power or authority to hold open for any person any position in the United States Civil Service.

(e) That it is necessary that persons seeking Civil Service positions take respondents' courses of study in order to qualify for or obtain such positions.

(f) That the examinations given by respondents are examinations for specific positions in the Civil Service.

(g) That all persons completing respondents' courses and passing Civil Service examinations will obtain positions immediately or within a short time.

(h) That positions obtained in the United States Civil Service will be at or near the place of residence of the employee.

(i) That Civil Service positions requiring certain physical, mental or educational qualifications or veterans' status may be obtained by persons not meeting such requirements.

(j) That the United States Civil Service Commission is looking to or relying upon respondents to locate persons to fill positions in the Civil Service.

By "Decision of the Commission and order to file report of compliance", Docket 5876, April 21, 1952, which announced and decreed fruition of said initial decision, report of compliance with the said order was required as follows:

It is ordered, That the respondents herein shall, within sixty (60) days after service upon them of this order, file with the Commission a report in writing setting forth in detail the manner and form in which they have complied with the order to cease and desist.

Issued: April 21, 1952.

By the Commission.

[SEAL] D. C. DANIEL, *Secretary.*

[F. R. Doc. 52-8170; Filed, July 24, 1952; 8:57 a. m.]

TITLE 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Federal Security Agency

PART 1—REGULATIONS FOR THE ENFORCEMENT OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

DRUGS AND DEVICES; DIRECTIONS FOR USE; EXEMPTION FROM PRESCRIPTION REQUIREMENTS; FINAL ORDER

By virtue of the authority vested in the Federal Security Administrator by the provisions of sections 502 (f), 503 (b), and 701 (a) of the Federal Food, Drug, and Cosmetic Act (52 Stat. 1051, 1055; 65 Stat. 648; 21 U. S. C. 352 (f), 353 (b), 371 (a)), and after having considered all written comments filed with respect to the notice of proposed rule making published in the FEDERAL REGISTER on February 5, 1952 (17 F. R. 1130), the following regulations are promulgated.

1. Section 1.106 is revoked and a new § 1.106 is added to read as follows:

§ 1.106 *Drugs and devices; directions for use*—(a) *Adequate directions for use.* "Adequate directions for use" means directions under which the layman can use a drug or device safely and for the purposes for which it is intended. Directions for use may be inadequate because (among other reasons) of omission, in whole or in part, or incorrect specification of:

(1) Statements of all conditions, purposes, or uses for which such drug or device is intended, including conditions, purposes, or uses for which it is prescribed, recommended, or suggested in its oral, written, printed, or graphic advertising, and conditions, purposes, or uses for which the drug or device is commonly used; except that such statements shall not refer to conditions, uses, or purposes for which the drug or device can be safely used only under the supervision of a practitioner licensed by law and for which it is advertised solely to such practitioner.

(2) Quantity of dose (including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages and different physical conditions).

(3) Frequency of administration or application.

(4) Duration of administration or application.

(5) Time of administration or application (in relation to time of meals, time of onset of symptoms, or other time factors).

(6) Route or method of administration or application.

(7) Preparation for use (shaking, dilution, adjustment of temperature, or other manipulation or process).

(b) *Exemption for prescription drugs.* A drug subject to the requirements of section 503 (b) (1) of the act, as amended by 65 Stat. 648, shall be exempt from section 502 (f) (1) if all the following conditions are met:

(1) The drug is:

(i) In the possession of a person (or his agents or employees) regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale distribution of prescription drugs; or

(ii) In the possession of a retail, hospital, or clinic pharmacy, or a public health agency, regularly and lawfully engaged in dispensing prescription drugs;

and is to be dispensed in accordance with section 503 (b), as amended.

(2) The label of the drug bears:

(i) The statement "Caution: Federal law prohibits dispensing without prescription"; and

(ii) The recommended or usual dosage; and

(iii) The route of administration, if it is not for oral use; and

(iv) If it is fabricated from two or more ingredients and is not designated conspicuously by a name recognized in an official compendium, the quantity or proportion of each active ingredient, and if it is not for oral use the names of all other ingredients.

Provided, however, That the information referred to in subdivisions (ii), (iii), and (iv) of this subparagraph may be contained in the labeling on or within the package from which it is to be dispensed, and, in the case of ampuls too small or otherwise unable to accommodate a label but which are packaged in a container from which they are withdrawn for dispensing or use, the information referred to in subdivision (i) of this subparagraph may be placed on the outside container only.

(3) The labeling of the drug (which may include brochures readily available to licensed practitioners) bears information as to the use of the drug by practitioners licensed by law to administer it: *Provided, however,* That such information may be omitted from the labeling if it is contained in scientific literature widely disseminated among practitioners licensed by law to administer the drug.

(c) *Exemption for veterinary drugs.* A drug intended solely for veterinary use which, because of toxicity or other potentiality for harmful effect, or the method of its use, is not safe for animal use except under the supervision of a licensed veterinarian, and hence for which "adequate directions for use" cannot be prepared, shall be exempt from section 502 (f) (1) of the act if all the following conditions are met:

(1) The drug is in the possession of a person (or his agents or employees) regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale or retail distribution of veterinary drugs and is to be sold only to or on the prescription or other order of a licensed veterinarian for use in the course of his professional practice.

(2) The label of a drug bears:

(i) The statement "Caution: Federal law restricts this drug to sale by or on the order of a licensed veterinarian"; and

(ii) The recommended or usual dosage; and

(iii) The route of administration, if it is not for oral use; and

(iv) The quantity or proportion of each active ingredient if it is fabricated from two or more ingredients and is not designated conspicuously by a name recognized in an official compendium.

Provided, however, That the information referred to in subdivisions (ii), (iii), and (iv) of this subparagraph may be contained in the labeling on or within the package from which it is to be dispensed.

(3) The labeling of the drug (which may include brochures readily available to licensed veterinarians) bears information as to use of the drug by licensed veterinarians: *Provided, however,* That such information may be omitted from the labeling if it is contained in scientific literature widely disseminated among veterinarians licensed by law to administer such drug.

(d) *Exemption for prescription devices.* A device which, because of any potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe except under the supervision of a practitioner licensed by law to direct the use of such device, and hence for which "adequate directions for use" cannot be prepared, shall be exempt from section 502 (f) (1) of the act if all the following conditions are met:

(1) The device is in the possession of a person (or his agents or employees) regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale or retail distribution of such device and is to be sold only to or on the prescription or other order of such practitioner for use in the course of his professional practice.

(2) The label of the device (other than surgical instruments) bears:

(i) The statement "Caution: Federal law restricts this device to sale by or on the order of a _____," the blank to be filled with the word "physician," "dentist," "veterinarian," or with the descriptive designation of any other practitioner licensed by the law of the State in which he practices to use or order the use of the device; and

(ii) The method of its application or use.

(3) The labeling of the device (which may include brochures readily available to licensed practitioners) bears information as to the use of the device by practitioners licensed by law to use it or direct its use: *Provided, however,* That such information may be omitted from the labeling if it is contained in scientific literature widely disseminated among practitioners licensed by law to use or order the use of such device.

(e) *Exemptions for drugs and devices shipped directly to licensed practitioners, hospitals, clinics, or public-health agencies for professional use.* Except as provided in paragraph (g) of this section, a drug or device shipped directly to or in the possession of a practitioner licensed by law to administer the drug or to use or direct the use of the device, or shipped directly to or in the possession of a hospital, clinic, or public-health agency, for use in the course of the professional practice of such a licensed practitioner, shall be exempt from section 502 (f) (1) of the act if it meets the conditions of paragraphs (b) (2) and (3), (c) (2) and (3), or (d) (2) and (3) of this section.

(f) *Retail exemption for veterinary drugs and prescription devices.* A drug or device subject to paragraph (c) or (d) of this section shall be exempt at the time of delivery to the ultimate purchaser or user from section 502 (f) (1) of the act if it is delivered by a licensed practitioner in the course of his professional practice or upon a prescription or other order lawfully issued in the course of his professional practice, with labeling bearing the name and address of such licensed practitioner and the directions for use and cautionary statements, if any, contained in such order.

(g) *Exemption for new drugs.* A new drug shall be exempt from section 502 (f) (1) of the act:

(1) To the extent to which such exemption is claimed in an effective application with respect to such drug under section 505 of the act; or

(2) If no application under section 505 of the act is effective with respect to such drug but it complies with section 505 (i) and regulations thereunder.

No exemption shall apply to any other drug which would be a new drug if its labeling bore representations for its intended uses.

(h) *Exemption for drugs or devices when directions are commonly known.* A drug or device shall be exempt from section 502 (f) (1) of the act insofar as adequate directions for common uses thereof are known to the ordinary individual.

(i) *Exemptions for inactive ingredients.* A harmless drug that is ordinarily used as an inactive ingredient, such as a coloring, emulsifier, excipient, flavoring, lubricant, preservative, or solvent, in the preparation of other drugs shall be exempt from section 502 (f) (1) of the act. This exemption shall not apply to any substance intended for a use which results in the preparation of a new drug, unless an effective new-drug application provides for such use.

(j) *Exemption for diagnostic reagents.* A drug intended solely for use in the professional diagnosis of disease and which is generally recognized by qualified experts as useful for that purpose shall be exempt from section 502 (f) (1) of the act if its label bears the statement "Diagnostic reagent—For professional use only."

(k) *Exemption for prescription chemicals and other prescription components.* A drug prepared, packaged, and primarily sold as a prescription chemical or other component for use by registered pharmacists in compounding prescriptions or for dispensing in dosage unit form upon prescriptions shall be exempt from section 502 (f) (1) of the act if all the following conditions are met:

(1) The drug is an official liquid acid or official liquid alkali, or is not a liquid solution, emulsion, suspension, tablet, capsule, or other dosage unit form; and

(2) The label of the drug bears:

(i) The statement "For prescription compounding"; and

(ii) If in substantially all dosage forms in which it may be dispensed it is subject to section 503 (b) (1) of the act, the statement "Caution: Federal law prohibits dispensing without prescription"; or

(iii) If it is not subject to section 503 (b) (1) of the act and is by custom among retail pharmacists sold in or from the interstate package for use by consumers, "adequate directions for use" in the conditions for which it is so sold.

Provided, however, That the information referred to in subdivision (iii) of this subparagraph may be contained in the labeling on or within the package from which it is to be dispensed.

(3) This exemption shall not apply to any substance intended for use in compounding which results in a new drug, unless an effective new-drug application covers such use of the drug in compounding prescriptions.

(l) *Exemption for processing, repacking, or manufacture.* A drug in a bulk package (except tablets, capsules, or other dosage unit forms) or a device intended for processing, repacking, or use in the manufacture of another drug or device shall be exempt from section 502 (f) (1) of the act if its label bears the statement "Caution: For manufacturing, processing, or repacking"; and, if in substantially all dosage forms in which it may be dispensed it is subject to section 503 (b) (1), the statement "Caution: Federal law prohibits dispensing without prescription." This exemption and the exemption under paragraph (k) of this section may be claimed for the same article. But the exemption shall not apply to a substance intended for a use in manufacture, processing, or repacking which causes the finished article to be a new drug, unless:

(1) An effective new-drug application held by the person preparing the dosage form or drug for dispensing covers the production and delivery to him of such substance; or

(2) If no application is effective with respect to such new drug, the label statement "Caution: For manufacturing, processing, or repacking" is immediately supplemented by the words "in the preparation of a new drug limited by Federal law to investigational use," and the delivery is made for use only in the manufacture of such new drug limited to investigational use as provided in § 1.114.

(m) *Exemption for drugs and devices for use in teaching, research, and analysis.* A drug or device subject to paragraph (b), (c), or (d) of this section shall be exempt from section 502 (f) (1) of the act if shipped or sold to, or in the

possession of, persons regularly and lawfully engaged in instruction in pharmacy, chemistry, or medicine not involving clinical use, or engaged in research not involving clinical use, or in chemical analysis, or physical testing, and is to be used only for such instruction, research, analysis, or testing.

(n) *Expiration of exemptions.* (1) If a shipment or delivery, or any part thereof, of a drug or device which is exempt under the regulations in this section is made to a person in whose possession the article is not exempt, or is made for any purpose other than those specified, such exemption shall expire, with respect to such shipment or delivery or part thereof, at the beginning of that shipment or delivery. The causing of an exemption to expire shall be considered an act which results in such drug or device being misbranded unless it is disposed of under circumstances in which it ceases to be a drug or device.

(2) The exemptions conferred by paragraphs (i), (j), (k), (l), and (m) of this section shall continue until the drugs or devices are used for the purposes for which they are exempted, or until they are relabeled to comply with section 502 (f) (1) of the act. If, however, the drug is converted, compounded, or manufactured into a dosage form limited to prescription dispensing, no exemption shall thereafter apply to the article unless the dosage form is labeled as required by section 503 (b) and paragraph (b), (c), or (d) of this section.

(o) *Intended uses.* The words "intended uses" or words of similar import in paragraphs (a), (g), (i), (j), (k), and (l) of this section refer to the objective intent of the persons legally responsible for the labeling of drugs and devices. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. The intended uses of an article may change after it has been introduced into interstate commerce by its manufacturer. If, for example, a packer, distributor, or seller intends an article for different uses than those intended by the person from whom he received the drug, such packer, distributor, or seller is required to supply adequate labeling in accordance with the new intended uses. But if a manufacturer knows, or has knowledge of facts that would give him notice, that a drug or device introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put.

2. A new § 1.108 is added, to read as follows:

§ 1.108 *Exemption from prescription requirements.* The prescription-dispensing requirements of section 503 (b) (1) (A) of the act are not necessary for the protection of the public health with respect to the following drugs subject to section 502 (d):

(a) Exempt narcotic preparations described in 26 CFR 151.2 and sold as required by 26 CFR 151.180 through 151.185a.

(b) Drugs containing chlorobutanol, intended for external use only.

(c) Epinephrine solution, 1 percent, preserved with chlorobutanol and intended for use solely as a spray.

(d) Drugs containing one or more of the derivatives of barbituric acid and in addition a sufficient quantity or proportion of another drug or drugs to prevent the ingestion of a sufficient amount of barbiturate derivative to cause a hypnotic or somnifacient effect.

Effective date. These regulations shall be effective upon the date of publication of this final order in the FEDERAL REGISTER except the requirements of § 1.106 (b) (2) (ii), (iii), and (iv), (c) (2), and (k) (2) (iii), which shall be effective on August 1, 1953. Action taken in reliance upon the tentative regulations after April 26, 1952, and before this final order issued will be regarded as in compliance with the law.

(Sec. 701, 52 Stat. 1055; 21 U. S. C. 371. Interpret or apply secs. 502, 503, 52 Stat. 1050, 1051; 21 U. S. C. 352, 353)

Dated: July 22, 1952.

[SEAL] JOHN L. THURSTON,
Acting Administrator.

[F. R. Doc. 52-8156; Filed, July 24, 1952; 8:51 a. m.]

TITLE 26—INTERNAL REVENUE

Chapter I—Bureau of Internal Revenue, Department of the Treasury

Subchapter A—Income and Excess Profits Taxes

[T. D. 5921; Regs. 111]

PART 29—INCOME TAX; TAXABLE YEARS BEGINNING AFTER DECEMBER 31, 1941

DEFINITION OF PERSONNEL HOLDING COMPANY; PERSONAL HOLDING COMPANY INCOME

On March 14, 1952, notice of proposed rule making with respect to amendments to conform Regulations 111 to Public Law 680 (81st Cong., 2d Sess.), approved August 9, 1950, relating to definition of personal holding company, and to section 223 of the Revenue Act of 1950 (81st Cong., 2d Sess.), approved September 23, 1950, relating to personal holding company income, was published in the FEDERAL REGISTER (17 F. R. 2231). No objection to the rules proposed having been received, the amendments of Regulations 111 set forth below are hereby adopted.

PARAGRAPH 1. There is inserted immediately preceding § 29.501–1 the following:

PUBLIC LAW 680 (EIGHTY-FIRST CONGRESS, SECOND SESSION), APPROVED AUGUST 9, 1950

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That section 501 (b) (6) of the Internal Revenue Code is amended to read as follows:

(6) (A) A licensed personal finance company under State supervision, 80 per centum or more of the gross income of which is lawful interest received from loans made to individuals in accordance with the provisions of applicable State law if at least 60 per centum of such gross income is lawful interest (i) received from individuals each of whose indebtedness to such company did not at any time during the taxable year exceed in principal amount the limit prescribed for small loans by such law (or, if there is no such limit, $500), and (ii) not payable in advance or compounded and computed only on unpaid balances, and if the loans to a person, who is a shareholder in such company during the taxable year by or for whom 10 per centum or more in value of its outstanding stock is owned directly or indirectly (including in the case of an individual, stock owned by the members of his family as defined in section 503 (a) (2)), outstanding at any time during such year do not exceed $5,000 in principal amount; and

(B) A lending company, not otherwise excepted by section 501 (b), authorized to engage in the small loan business under one or more State statutes providing for the direct regulation of such business, 80 per centum or more of the gross income of which is lawful interest, discount or other authorized charges (i) received from loans maturing in not more than thirty-six months made to individuals in accordance with the provisions of applicable State law, and (ii) which do not, in the case of any individual loan, exceed in the aggregate an amount equal to simple interest at the rate of 3 per centum per month not payable in advance and computed only on unpaid balances, if at least 60 per centum of the gross income is lawful interest, discount or other authorized charges received from individuals each of whose indebtedness to such company did not at any time during the taxable year exceed in principal amount the limit prescribed for small loans by such law (or, if there is no such limit, $500), and if the deductions allowed to such company under section 23 (a) (relating to expenses), other than for compensation for personal services rendered by shareholders (including members of the shareholder's family as described in section 503 (a) (2)) constitute 15 per centum or more of its gross income, and the loans to a person, who is a shareholder in such company during the taxable year by or for whom 10 per centum or more in value of its outstanding stock is owned directly or indirectly (including in the case of an individual, stock owned by the members of his family as defined in section 503 (a) (2)), outstanding at any time during such year do not exceed $5,000 in principal amount.

SEC. 2. That section 501 (b) of the Internal Revenue Code is amended by adding at the end thereof the following new paragraph:

(8) A finance company, actively and regularly engaged in the business of purchasing or discounting accounts or notes receivable or installment obligations, or making loans secured by any of the foregoing or by tangible personal property, at least 80 per centum of the gross income of which is derived from such business in accordance with the provisions of applicable State law or does not constitute personal holding company income as defined in section 502, if 60 per centum of the gross income is derived from one or more of the following classes of transactions:

(A) Purchasing or discounting accounts or notes receivable, or installment obligations evidenced or secured by contracts of conditional sale, chattel mortgages, or chattel lease agreements, arising out of the sale of goods or services in the course of the transferor's trade or business;

(B) Making loans, maturing in not more than thirty-six months, to, and for the busi-

(a) That the initial period of admission shall be for not less than four weeks and not more than six months. The initial period of admission or any extension thereof shall not extend beyond June 30, 1959;

* * * * *

(c) That the period of temporary admission shall be subject to immediate revocation, without notice, by the district director of the district having jurisdiction over the place of the alien's employment upon—

* * * * *

(4) Termination of the Migrant Labor Agreement of 1951, as amended.

2. Paragraph (c) of § 214k.4 *Compliance by employer* is amended to read as follows:

(c) If a Mexican agricultural worker leaves his employment without proper authorization, the employer shall report such departure immediately or within five days thereof to the reception center where the worker was admitted. Such notification shall contain the individual worker's name, as shown in the employer's copy of the contract; the worker's Form I–100C number; the date the worker left the employer, and the present whereabouts of the worker, if known.

3. Paragraph (a) of § 214k.6 *Readmission after temporary visits to Mexico* is amended to read as follows:

(a) An agricultural worker who has been admitted to the United States under the provisions of this part or of prior regulations pertaining to Title V of the Agricultural Act of 1949, as amended, may be readmitted after temporary visits to Mexico on presentation of Form I–100C, Alien Laborer's Permit, if he is still maintaining the status of an agricultural worker in the United States.

4. Section 214k.21 *Recruitment centers; preliminary inspection* is amended by deleting the words "Form I–100a" and "Form I–100" and by substituting therefor the words "Form I–100C".

5. Sections 214k.22, 214k.23, and 214k.24 are amended to read as follows:

§ 214k.22 *Immigration inspection at reception centers*—(a) *Authority to admit.* An alien who presents a conditional permit, as described in § 214k.21, duly noted by an immigration officer at a recruitment center, may be admitted at the reception center if he is found admissible by the examining immigration officer. The examining officer shall fingerprint each alien admitted. The alien shall be given the Form I–100C bearing his photograph and stating his name and place of birth. Such form shall be duly noted by an immigration officer to show the date, place, and period of the alien's admission to the United States and shall be signed by such officer across the photograph. Such noted card shall be the sole document required for admission to the United States as an agricultural worker under this part.

(b) *Hearing before special inquiry officer.* If the examining immigration officer is not satisfied that an alien seeking admission under this part is admissible, the alien shall be held for hearing before a special inquiry officer, and the hearing procedure applicable generally to aliens seeking admission to the United States under the immigration laws shall be followed: *Provided, however,* That the case of an alien believed to be inadmissible to the United States under the provisions of paragraph (27), (28), or (29) of section 212 (a) of the Immigration and Nationality Act shall be handled in accordance with the provisions of section 235 (c) of that act and § 235.15 of this chapter.

§ 214k.23 *Recontracting in the United States.* During the period for which he is admitted, or any authorized extension thereof, an agricultural worker may be recontracted by another employer. When an agricultural worker is recontracted, his Form I–100C shall be appropriately noted and the admitting reception center notified.

§ 214k.24 *Duplicate identification cards.* A duplicate Form I–100C may be issued by the admitting reception center when the original has been lost, mutilated, or destroyed. An application for such a card shall be made on Form I–102.

PART 243—DEPORTATION OF ALIENS IN THE UNITED STATES

The first sentence of subparagraph (2) of paragraph (b) *Stay of deportation* of § 243.3 *Execution of warrants of deportation* is amended to read as follows: "If the request for a stay of deportation is predicated upon a claim by the alien that he would be subject to physical persecution if deported to the country designated by the Service, he shall be requested, upon notice, to appear before a special inquiry officer for interrogation under oath."

PART 299—IMMIGRATION FORMS

The list of forms in § 299.1 *Prescribed forms* is amended by adding the following in numerical sequence:

I–100C—Alien Laborer's Permit.
I–102—Application for copy of Alien Laborer's Permit in lieu of one lost, mutilated, or destroyed.

PART 316a—RESIDENCE, PHYSICAL PRESENCE, AND ABSENCE

Paragraph (b) of § 316a.21 *Application for benefits with respect to absences: appeal* is amended by deleting the last sentence thereof.

PART 341—CERTIFICATES OF CITIZENSHIP

Part 341 is amended to read as follows:

SUBPART A—SUBSTANTIVE PROVISIONS

§ 341.1 *Application.* A person who claims to have derived United States citizenship through the naturalization of a parent or parents or through the naturalization or citizenship of a husband, or who claims to be a citizen at birth outside the United States under the provisions of any of the statutes or acts specified in section 341 of the act, or who claims to be a citizen at birth outside the United States under the provisions of section 309 (c) of the act, may apply for a certificate of citizenship on Form N–600. The applicant shall be notified of the decision and, if the application is denied, of the reasons therefor and of his right to appeal within 10 days from the receipt of such notification in accordance with Part 7 of this chapter. If the application is granted, the certificate shall be issued on Form N–560 or N–562, as appropriate. The applicant shall, unless he is too young to understand the meaning thereof, take and subscribe to, before an officer or employee of the Service authorized to administer oaths, the oath of renunciation and allegiance prescribed by Part 337 of this chapter. Thereafter, personal delivery of the original of the certificate shall be made to the applicant, or to his parent or guardian, who shall sign a receipt therefor.

SUBPART B—PROCEDURAL AND OTHER NONSUBSTANTIVE PROVISIONS [RESERVED]

(Sec. 103, 66 Stat. 173; 8 U. S. C. 1103. Interpret or apply secs. 287, 309, 332, 333, 337, 341, 344; 66 Stat. 233, 238, 252, 254, 258, 263, 264; 8 U. S. C. 1357, 1409, 1443, 1444, 1448, 1452, 1455)

PART 499—NATIONALITY FORMS

The list of forms in § 499.1 *Prescribed forms* is amended by adding the following in numerical sequence:

N–562—Certificate of Citizenship.

(Sec. 103, 66 Stat. 173; 8 U. S. C. 1103)

This order shall become effective on the date of its publication in the FEDERAL REGISTER. Compliance with the provisions of section 4 of the Administrative Procedure Act (60 Stat. 238; 5 U. S. C. 1003) as to notice of proposed rule making and delayed effective date is unnecessary in this instance because the rules prescribed by the order, other than those which relieve restrictions and are clearly advantageous to persons affected thereby and those which relate to interpretative rules, relate to matters of agency procedure.

Dated: April 6, 1956.

J. M. SWING,
Commissioner of Immigration and Naturalization.

[F. R. Doc. 56–2747; Filed, Apr. 10, 1956; 8:54 a. m.]

TITLE 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare

Subchapter A—General

PART 1—REGULATIONS FOR THE ENFORCEMENT OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT

EXEMPTION OF CERTAIN DRUGS AND DEVICES FROM LABELING REQUIREMENTS

Pursuant to the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (sec. 502 (f) (1), 52 Stat. 1051; 21 U. S. C. 352 (f) (1)) and delegated to the Commissioner of Food and Drugs by the Secretary (21 F. R. 1996),

Part 1 of the regulations for the enforcement of the act (21 CFR 1.106) is amended as follows:

Section 1.106 *Drugs and devices; directions for use* is amended by changing paragraph (m) to read as follows:

(m) *Exemption for drugs and devices for use in teaching, law enforcement, research, and analysis.* A drug or device subject to paragraph (b), (c), or (d) of this section shall be exempt from section 502 (f) (1) of the act if shipped or sold to, or in the possession of, persons regularly and lawfully engaged in instruction in pharmacy, chemistry, or medicine not involving clinical use, or engaged in law enforcement, or in research not involving clinical use, or in chemical analysis, or physical testing, and is to be used only for such instruction, law enforcement, research, analysis, or testing.

Notice and public procedure are not necessary prerequisites to the promulgation of this order, and I so find, since the exemption granted applies only to drugs and devices shipped, sold, or in the possession of persons engaged in law-enforcement and in such cases the labeling requirements are not necessary for the protection of the public health; since the amendment relaxes existing requirements; and since it would be against public interest to delay providing for the amendment.

This order shall become effective upon publication in the FEDERAL REGISTER.

(Secs. 502 (f) (1), 701, 52 Stat. 1051, 1055, as amended; 21 U. S. C. 352 (f) (1), 371)

Dated: April 5, 1956.

[SEAL] GEO. P. LARRICK,
Commissioner of Food and Drugs.

[F. R. Doc. 56-2709; Filed, Apr. 10, 1956; 8:46 a. m.]

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

PESTICIDE CHEMICALS; FURTHER EXTENDED DATES ON WHICH STATUTE SHALL BECOME FULLY EFFECTIVE

Requests have been received for further extensions of the date when the amendment to section 402 (a) of the Federal Food, Drug, and Cosmetic Act (68 Stat. 511 et seq.; 21 U. S. C. 342, 346a) shall become effective for certain pesticide chemicals. Extensions requested involve nonseasonal uses and in some instances involve petitions that have recently been submitted but not yet processed by the agencies of the Government. Extensions are necessary for the uses of the pesticide chemicals listed below.

Now, therefore, in exercise of the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (secs. 402 (a) (2), 408, 68 Stat. 511, 517 (Ch. 559, Secs. 2, 5); 21 U. S. C. 342 (a) (2) and note 1 under section 342; 346a) and delegated to the Commissioner of Food and Drugs by the Secretary (20 F. R. 1996), the following order is promulgated:

Section 3.44 *Pesticide chemicals; further extended dates on which statute shall become fully effective,* published in the FEDERAL REGISTER December 20, 1955 (21 CFR 3.44; 20 F. R. 9553) as amended (20 F. R. 9884; 21 F. R. 445, 1172, 1463) is further amended by rearranging and adding to the list of pesticide chemicals in paragraph (a) (6), so that as changed this paragraph reads as follows:

(6) Effective date July 22, 1956:

Carbon bisulfide: As a grain fumigant. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

Carbon tetrachloride: As a grain fumigant. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

Chloropicrin: As a grain fumigant. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

DDT: In or on meat, sweetpotatoes. (Extended, as to meat, from March 1, 1956. See subparagraph (2) of this paragraph.)

Ethylene dibromide: As a fumigant. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

Ethylene dichloride: As a grain fumigant. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

Malathion: On citrus. (Extended from March 1, 1956. See subparagraph (2) of this paragraph.)

MGK 264: In fly sprays. (Extended from March 1, 1956. See subparagraph (2) of this paragraph, as amended 20 F. R. 9884.)

(Sec. 701, 52 Stat. 1055, as amended; 21 U. S. C. 371. Interprets or applies secs. 402, 52 Stat. 1046, as amended, secs. 408, 68 Stat. 511; 21 U. S. C. 342, 346a)

Dated: April 5, 1956.

[SEAL] GEO. P. LARRICK,
Commissioner of Food and Drugs.

[F. R. Doc. 56-2707; Filed, Apr. 10, 1956; 8:46 a. m.]

TITLE 25—INDIANS

Chapter I—Bureau of Indian Affairs, Department of the Interior

Subchapter L—Irrigation Projects; Operation and Maintenance

PART 130—OPERATION AND MAINTENANCE CHARGES

FLATHEAD INDIAN IRRIGATION PROJECT, MONTANA

Pursuant to section 4 (a) of the Administrative Procedure Act of June 11, 1946 (60 Stat. 238), and authority contained in the acts of Congress approved August 1, 1914, May 18, 1916, and March 7, 1928 (38 Stat. 583; 39 Stat. 142), and by virtue of authority delegated by the Secretary of the Interior to the Commissioner of Indian Affairs (Order No. 2508; 14 F. R. 258), and by virtue of the authority delegated by the Commissioner of Indian Affairs to the Area Director (Bureau Order No. 551, Amendment No. 1; 16 F. R. 5454-7), notice is hereby given of the intention to modify §§ 130.16 and 130.17 of Title 25, Code of Federal Regulations, dealing with the irrigable lands of the Flathead Indian Irrigation Project, Montana, that are subject to the jurisdiction of the several irrigation districts. There was published on March 1, 1956, in the daily issue of the FEDERAL REGISTER, notice of intention to modify §§ 130.16 and 130.17 of Title 25, Code of Federal Regulations, as follows:

Interested persons were thereby given opportunity to participate in preparing the modification by submitting data or written arguments within 30 days from the publication of the notice. No objections were submitted. Accordingly, §§ 130.16 and 130.17 are modified as follows:

§ 130.16 *Charges, Jocko Division.* (a) An annual minimum charge of $2.97 per acre, for the season of 1956 and thereafter until further notice, shall be made against all assessable irrigable land in the Jocko Division that is not included in an Irrigation District organization, regardless of whether water is used.

(b) The minimum charge when paid shall be credited on the delivery of the pro rata per acre share of the available water up to one and one-half acre feet per acre for the entire assessable area of the farm unit, allotment or tract. Additional water, if available will be delivered at the rate of one dollar and ninety-seven cents ($1.97) per acre foot or fraction thereof.

§ 130.17 *Charges, Mission Valley and Camas Divisions.* (a) (1) An annual minimum charge of $3.38 per acre, for the season of 1956 and thereafter until further notice, shall be made against all assessable irrigable land in the Mission Valley Division that is not included in an Irrigation District organization regardless of whether water is used.

(2) The minimum charge when paid shall be credited on the delivery of the pro rata per acre share of the available water up to one and one-half acre feet per acre for the entire assessable area of the farm unit, allotment or tract. Additional water, if available, will be delivered at the rate of two dollars and twenty-six cents ($2.26) per acre foot or fraction thereof.

(b) (1) An annual minimum charge of $3.18 per acre, for the season of 1956 and thereafter until further notice, shall be made against all assessable irrigable land in the Camas Division that is not included in an irrigation district organization regardless of whether water is used.

(2) The minimum charge when paid shall be credited on the delivery of the pro rata per acre share of the available water up to one and one-half acre feet per acre for the entire assessable area of the farm unit, allotment or tract. Additional water, if available, will be delivered at the rate of two dollars and twelve cents per acre foot ($2.12) or fraction thereof.

(Sec. 1, 3, 33 Stat. 270, 272, as amended; 25 U. S. C. 385)

M. A. JOHNSON,
Acting Area Director.

[F. R. Doc. 56-2710; Filed, Apr. 10, 1956; 8:46 a. m.]

TITLE 26—INTERNAL REVENUE

Chapter I—Internal Revenue Service, Department of the Treasury

Subchapter D—Employment Taxes

[Regs. 114; T. D. 6168]

PART 411—EMPLOYERS' TAX, EMPLOYEES' TAX, AND EMPLOYEE REPRESENTATIVES' TAX UNDER THE RAILROAD RETIREMENT TAX ACT

MISCELLANEOUS AMENDMENTS

In order to conform Regulations 114 (26 CFR (1939) Part 411), relating to

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 01N–0336]

Schering Corp. et al.; Withdrawal of Approval of 51 New Drug Applications and 25 Abbreviated New Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of 51 new drug applications (NDAs) and 25 abbreviated new drug applications (ANDAs). The holders of the applications notified the agency in writing that the drug products were no longer marketed and requested that the approval of the applications be withdrawn.

DATES: Effective September 17, 2001.

FOR FURTHER INFORMATION CONTACT: Florine P. Purdie, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

SUPPLEMENTARY INFORMATION: The holders of the applications listed in the table in this document have informed FDA that these drug products are no longer marketed and have requested that FDA withdraw approval of the applications. The applicants have also, by their requests, waived their opportunity for a hearing.

Application No.	Drug	Applicant
NDA 3–158	Oreton Methyl (methyltestosterone) Tablets, 10 milligrams (mg) and 25 mg.	Schering Corp., 2000 Galloping Hill Rd., Kenilworth, NJ 07033.
NDA 5–963	Sodium Sulamyd (sulfacetamide sodium) Ophthalmic Solution and Ointment.	Do.
NDA 6–325	Tubocurarine Chloride Injection.	Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285.
NDA 6–632	Metubine Iodide (metocurine iodide) Injection.	Do.
NDA 6–772	Vasoxyl (methoxamine hydrochloride (HCl)) Injection.	GlaxoSmithKline (GSK), P.O. Box 13398, Five Moore Dr., Research Triangle Park, NC 27709.
NDA 6–925	Nisentil (alphaprodine HCl) Injection.	Hoffman-LaRoche, Inc., 340 Kingsland St., Nutley, NJ 07110–1199.
NDA 7–600	Surital (thiamylal sodium).	Parkdale Pharmaceuticals, 2800 Plymouth Rd., Ann Arbor, MI 48105.
NDA 8–200	Sodium Iodide I-131 Capsules, Solution, and Injection.	Syncor International Corp., 6464 Canoga Ave., Woodland Hills, CA 91367.
NDA 8–592	Ravocaine HCl (propoxycaine HCl and procaine HCl, with nordefrin or norepinephrine bitartrate).	Eastman Kodak Co., Health Imaging, 343 State St., Rochester, NY 14612–1122.
NDA 9–127	Cortril (hydrocortisone) Tablets.	Pfizer, Inc., 235 East 42d St., New York, NY 10017.
NDA 9–130	Cortril (hydrocortisone acetate) Ophthalmic Ointment.	Do.
NDA 9–238	Progesterone Injection.	Eli Lilly and Co., Lilly Corporate Center, Indianapolis, IN 46285.
NDA 9–458	Cortisone Acetate Tablets, 25 mg.	Impax Laboratories, Inc., 30831 Huntwood Ave., Hayward, CA 94544.
NDA 9–996	Sterane (prednisolone) Tablets.	Pfizer, Inc.
NDA 10–423	Lorfan (levallorphan tartrate) Injection.	Hoffman-LaRoche, Inc.
NDA 10–554	Magnacort (hydrocortamate HCl) Topical Ointment.	Pfizer Pharmaceuticals, 235 East 42d St., New York, NY 10017.
NDA 11–539	Ultra-Feminine (Topical Liquid).	Coscelebre, Inc., 415 Madison Ave., New York, NY 10017.
NDA 11–557	Trilafon (perphenazine) Concentrate, 16 mg/5 mL (milliliters).	Schering Corp.
NDA 11–679	Pentothal Sodium (thiopental sodium) Suspension.	Abbott Laboratories, D–389, Bldg. AP30, 200 Abbott Park Rd., Abbott Park, IL 60064–6157.
NDA 12–148	Oreticyl Tablets and Oreticyle Forte (hydrochlorothiazide and deserpidine) Tablets.	Do.
NDA 12–715	Gantanol (sulfamethoxazole) Tablets.	Hoffman-LaRoche, Inc.

Application No.	Drug	Applicant
NDA 13–056	Penthrane (methoxyflurane) Inhalation Liquid.	Abbott Laboratories.
NDA 13–934	Stoxil (idoxuridine) Ophthalmic Solution, 0.1%.	SmithKline Beecham Pharmaceuticals, One Franklin Plaza, P.O. Box 7929, Philadelphia, PA 19101.
NDA 14–083	Apodol (anileridine HCl) Tablets.	Bristol-Myers Squibb, P.O. Box 4000, Princeton, NJ 08543–4000.
NDA 14–087	Apodol (anileridine) Injection.	Do.
NDA 15–868	Stoxil (idoxuridine) Ophthalmic Ointment, 0.5%.	SmithKline Beecham Pharmaceuticals.
NDA 17–255	DTPA (chelate) Multidose (kit for the preparation of Tc-99m pentetate injection).	Nycomed Amersham Imaging, 101 Carnegie Center, Princeton, NJ 08540.
NDA 17–256	Xenon Xe-133.	Do.
NDA 17–257	Selenomethionine Se-75 Injection.	Do.
NDA 17–266	Technetium Tc-99m Sulfur Colloid Injection.	Do.
NDA 17–267	Sodium Pertechnetate Tc-99m Injection.	Do.
NDA 17–383	Methosarb (calusterone) Tablets.	The Upjohn Co., 7000 Portage Rd., Kalamazoo, MI 49001.
NDA 17–456	Technetium Tc–99m Sulfur Colloid.	Do.
NDA 17–483	Methadone HCl Bulk (methadone HCl).	Penick Corp., 158 Mount Olivet Ave., Newark, NJ 07114.
NDA 17–562	Technetium Tc-99m Diphosphonate Injection (Tin Kit).	Nycomed Amersham Imaging.
NDA 17–664	Sodium Polyphosphate Injection (Tin Kit).	Do.
NDA 17–667	Stannous Diphosphonate Injection.	Do.
NDA 18–228	Hypnomidate (etomidate) Injection.	Janssen Research Foundation, 1125 Trenton-Harbourton Rd., P.O. Box 200, Titusville, NJ 08560.
NDA 18–289	Iodohippurate Sodium I-123.	Nycomed Amersham Imaging.
NDA 18–871	Protostat (metronidazole) Tablets.	R. W. Johnson Pharmaceutical Research Institute, Route 202 South, P.O. Box 300, Raritan, NJ 08869–0602.
NDA 19–450	Velosulin BR Human (semisynthetic purified human insulin) Injection.	Novo Nordisk Pharmaceuticals, Inc., 100 College Rd. West, Princeton, NJ 08540.
NDA 20–420	GenESA (arbutamine HCl) Injection.	Gensia Automedics, Inc., 9360 Towne Centre Dr., San Diego, CA 92121.
NDA 20–689	Posicor (miobefradil dihydrochloride) Oral Tablets, 50 mg and 100 mg.	Hoffmann-LaRoche, Inc.
ANDA 40–059	Fluocinolone Acetonide Topical Solution USP, 0.01%.	Bausch & Lomb Pharmaceuticals, Inc., 8500 Hidden River Pkwy., Tampa, FL 33637.
NDA 50–311	Rondomycin (methacycline HCl) Capsules.	Pfizer, Inc.
NDA 50–448	Grifulvin (griseofulvin) Oral Suspension.	Johnson & Johnson Consumer Products Co., 199 Grandview Rd., Skillman, NJ 8558–9418.
NDA 50–637	Zefazone (cefmetazole sodium) Sterile Powder.	Pharmacia & Upjohn Co., 7000 Portage Rd., Kalamazoo, MI 49001.
NDA 50–683	Zefazone (cefmetazole sodium) Intraveous Solution.	Do.
ANDA 60–760	Oxytetracycline HCl Capsules, 250 mg.	Impax Laboratories, Inc.
ANDA 62–223	Totacillin (Ampicillin Trihydrate for Oral Suspension USP).	SmithKline Beecham Pharmaceuticals.
ANDA 62–736	Bactocill (oxacillin sodium) Injection.	GlaxoSmithKline (GSK).
ANDA 64–055	Neomycin Sulfate and Dexamethosone Sodium Phosphate Ophthalmic Solution	Bausch & Lomb Pharmaceuticals, Inc.

Application No.	Drug	Applicant
ANDA 74–813	Etoposide Injection 20 mg/mL.	Pierre Fabre Medicament, c/o Guidelines Integrated Service, 10320 USA Today Way, Miramar, FL 33062.
ANDA 80–079	Trisulfapyrimidines Tablets USP.	Impax Laboratories, Inc.
ANDA 80–151	Thyroglobulin Tablets USP.	Do.
ANDA 80–153	Isoniazid Tablets USP.	Do.
ANDA 80–281	Oreton Methyl Buccal Tablets (Methyltestosterone Tablets USP).	Schering Corp.
ANDA 80–780	Prednisolone Tablets USP, 5 mg.	Impax Laboratories, Inc.
ANDA 80–807	Diphenhydramine HCl Capsules USP, 25 mg and 50 mg.	Do.
ANDA 80–951	Ergocalciferol Capsules USP.	Do.
ANDA 80–952	Vitamin A Capsules USP.	Do.
ANDA 80–953	Vitamin A Capsules USP.	Do.
ANDA 80–955	Vitamin A Capsules USP.	Do.
ANDA 83–011	Hydrocortisone Cream USP, 1%.	Solvay Pharmaceuticals, Inc., 901 Sawyer Rd., Marietta, GA 30062.
ANDA 83–347	Quinidine Sulfate Tablets USP, 200 mg.	Impax Laboratories, Inc.
ANDA 84–214	Promethazine HCl Tablets USP, 25 mg.	Do.
ANDA 84–340	Triamcinolone Tablets USP, 4 mg.	Do.
ANDA 84–575	Aminophylline Tablets USP, 200 mg.	Do.
ANDA 84–577	Aminophylline Tablets USP, 100 mg.	Do.
ANDA 85–098	Hydrocholorothiazide Tablets USP, 100 mg.	Do.
ANDA 85–563	Glycopyrrolate Tablets, 2 mg.	Circa, 130 Lincoln St., Copiague, NY 11726.
ANDA 86–639	Levsin PB (hyoscyamine sulfate and phenobarbital) Oral Solution.	Schwarz Pharma, Inc., P.O. Box 2038, Milwaukee, WI 53201.

Therefore, under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) and under authority delegated to the Director, Center for Drug Evaluation and Research (21 CFR 5.82), approval of the applications listed in the table in this document, and all amendments and supplements thereto, is hereby withdrawn, effective September 17, 2001.

Dated: August 1, 2001.

Janet Woodcock,

Director, Center for Drug Evaluation and Research.

[FR Doc. 01–20605 Filed 8–15–01; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Center for Research Resources; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Center for Research Resources Special Emphasis Panel, Biomedical Research Technology.

Date: October 22–23, 2001.

Time: October 22, 2001, 8:00 am to adjournment.

Agenda: To review and evaluate grant applications.

Place: Gaithersburg Marriott, Washingtonian Center, 9751 Washingtonian Boulevard, Gaithersburg, MD 20878.

Contact Person: Mohan Viswanathan, Phd, Scientific Review Administrator, National Center for Research Resources, National Institutes of Health, Office of Review, 6705 Rockledge Drive, MSC 7965, One Rockledge Centre, Room 6018, Bethesda, MD 20892, (301) 435–0829, viswanathanm@ncrr.nih.gov

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine, 93.306; 93.333, Clinical Research, 93.333; 93.371, Biomedical Technology; 93.389, Research Infrastructure, National Institutes of Health, HHS)

TRAFFIC IN, AND CONTROL OF, NARCOTICS, BARBITURATES, AND AMPHETAMINES

WEDNESDAY, DECEMBER 14, 1955

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON NARCOTICS OF THE
COMMITTEE ON WAYS AND MEANS,
Washington, D. C.

The committee met at 10 a. m., Hon. Hale Boggs (chairman of the subcommittee) presiding.

Mr. BOGGS. The committee will come to order.

Since the subcommittee last met at Washington in October we have conducted hearings in some of the principal cities of the United States, including New York, Chicago, San Francisco, and others.

At the conclusion of our Washington hearing it was agreed that the agencies in the Government—Health, Education, and Welfare, the Narcotics Bureau and others—would submit recommendations to the committee when we reconvened here this morning.

However, we at no time have heard from the Army. The committee has repeated complaints from parents about the alleged problem of addiction in the Army, so we are very pleased this morning to have as our first witness Maj. Gen. William H. Maglin, Provost Marshal General of the Army.

STATEMENT OF MAJ. GEN. WILLIAM H. MAGLIN, PROVOST MARSHAL GENERAL OF THE ARMY, ACCOMPANIED BY LT. COL. GEORGE C. WILLIAMS, OFFICE OF THE PROVOST MARSHAL GENERAL; FRED M. COUGHLIN, OFFICE OF THE GENERAL COUNSEL, DEPARTMENT OF THE ARMY; AND CAPT. ROBERT M. LATHROP, CHIEF OF LEGISLATIVE LIAISON, DEPARTMENT OF THE ARMY

General MAGLIN. I have a prepared statement, Mr. Chairman, that I am ready to read, if the committe desires.

Mr. BOGGS. You may proceed, General.

General MAGLIN. To aid the armed services in its constant effort to reduce narcotic usage among service personnel, two important surveys have been conducted. In October of 1954 the publication of the Army Forces Far East Supplement to the Far East Command Narcotic Study of 1953 completed a survey of conditions in Okinawa, Japan, and Korea. A more recent survey directed by the Department of Defense and conducted by the Armed Forces on a worldwide basis was completed in September of 1955. This latter survey provided material for the Interdepartmental Narcotics Committee and forms a basis for the armed services' continuing suppression effort.

Mr. BOGGS. The total decrease is equally significant, reflecting a decrease from 4,937 cases to 2,489 cases.

Mr. ANSLINGER. Yes, sir.

Mr. BOGGS. Mr. Commissioner, thank you very much for your testimony. You have been very helpful to the committee.

The committee will now recess until 2 o'clock.

AFTER RECESS

The subcommittee met at 2 p. m., pursuant to the taking of a recess, Hon. Hale Boggs (subcommittee chairman) presiding.

Mr. BOGGS. The committee will come to order. Our first witness this afternoon is Dr. John L. Harvey, Deputy Commissioner of the Food and Drug Administration.

Commissioner Larrick will you come up too, please, sir?

Mr. LARRICK. Yes, sir.

STATEMENT OF JOHN L. HARVEY, DEPUTY COMMISSIONER, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY G. P. LARRICK, COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Mr. BOGGS. Mr. Harvey, do you have a prepared statement?

Mr. HARVEY. Yes, Mr. Chairman, I do. I have a brief prepared statement which I would like to read to the committee.

Mr. BOGGS. You may proceed, sir.

Mr. HARVEY. Mr. Chairman and members of the committee, my name is John L. Harvey, Deputy Commissioner of Food and Drugs.

I am here, Mr. Chairman, at your request, as I understand it, not to repeat my testimony previously given before this committee in October of this year, but to give you anything new that I may have that touches on the extent of the problem you are considering, and to offer for your consideration any suggestions that I may have for a procedure for additional regluation of amphetamine and barbiturate production and distribution from a Federal level—that is, if it is concluded that additional Federal control is needed.

Mr. Chairman, I would like to make it abundantly clear that we do not have good quantitative data by which to measure the total extent of nonmedical use of these drugs. So far as I can ascertain no one has such quantitative estimates. This is not too surprising since we are rarely able to get good quantitative data about human behavior of a kind that people try to keep secret. Your committee has heard many witnesses in a number of localities and I am sure you have formed some views as to the prevalence of misuse of these drugs from the people close to such matters in the various cities. There are, I know, some wide differences of opinion among people concerned with the distribution and use of these drugs, as to the overall extent of social evil involved as well as the best way to improve the situation. These differences of opinion are honest differences. While none of us knows accurately the extent of the problem, each of us has opinions according to his actual experience. For a period of more than 15 years the Food and Drug Administration has been working with the problem of the sale of these drugs other than on prescription and has encountered

many complaints from people who have blamed these drugs for many different kinds of misconduct and misfortune. Their judgment as to what is cause and what is effect may be faulty, but the misuse of these drugs appears, in our experience, to be associated with hundreds of cases bound up with much unhappiness and antisocial behavior. The complaints are not so much of addiction but of misbehavior and neglect of obligations.

Mr. Chairman, as to the barbiturate-amphetamine situation, speaking from my standpoint as a food and drug law enforcement officer, I know there is a problem, but I do not pretend to know how big it is.

A number of States have enacted a uniform barbiturate act which is a good piece of legislation for the control of those drugs and which makes unauthorized possession an offense. Other States have laws which are reasonably effective in reaching most of the aspects of the problem. Philosophically, we believe that the primary responsibility for enforcement should rest with the States. If we had good reason to hope that all the States would and could effectively control this entire problem, we would prefer to see the job done by them. Unfortunately, such a hope at the present time is unrealistic. I speak, not from surmise, but from survey. We have learned from the State enforcement officers themselves what the outlook is, and we must say that their manpower and facilities, and in many instances, their laws as well, are woefully inadequate. Several States have enough resources to be active on the problems and a few of them are doing good work, but the opposite is true in most States. I do not say this to be critical of State officials. I was one, once. They are capable officials, but they cannot get results without the men, and funds and facilities. I am sure that there will be much improvement in State and local enforcement in this field as the years go by and whenever they can and will do the whole job, I for one, would want the Federal Government to let them do it. It is a hope for the future, but no promise for the present.

As suggested by the chairman at an earlier session of this hearing, we have given thought to legislation. Both the need for legislation at the Federal level and the nature of such legislation, if it is needed, are worthy of much study and consideration, not only by people in Government but by the different parts of the drug producing and distributing industry, and the medical profession. We know the committee will always give paramount consideration to the public interest. We are sure you will agree that ideal legislation is that which will prevent misuse of these drugs, but preserve them for every use that may be directed by physicians in healing the sick and alleviating suffering, and at the same time add to the burdens of manufacturers and distributors as little as possible. Now this principle, Mr. Chairman, has controlled our thinking on possible legislation. Barbiturates and amphetamines are now restricted by law to sale on prescription only. Let us keep them so, and consider only restrictions designed to prevent their sale otherwise than on prescription.

The Congress has already provided, under the Durham-Humphrey amendment to the Food, Drug, and Cosmetic Act, certain controls over prescription drugs in interstate channels. The Food and Drug Administration is the agency charged with the enforcement of that law. As such, we are in a position to see in what respects enforcement at the Federal level could be made more effective. However, further exten-

sion of the Federal laws into areas of intrastate commerce involves basic policy questions. On these questions, which this committee will undoubtedly consider, we are not attempting to speak for the administration.

As an enforcement agency, we can point out the elements of legislation which would be helpful if the scope of Federal responsibility is to be extended. The essential features would be (1) recordkeeping throughout distribution channels to show stocks received and stocks sold with right of inspection by Government inspectors; (2) listing of manufacturers for identification so that clandestine and unauthorized producers may be more easily identified; and (3) prohibition of possession except by listed manufacturers, authorized dealers, licensed physicians, and users who receive on prescription or from a physician. These provisions would apply whether in intrastate or interstate commerce. Exemptions for use in scientific or research work would be provided.

We understand the Department of Justice has expressed the view that where a burden upon interstate commerce occurs from the indistinguishably commingled intrastate commerce so that regulation of intrastate commerce is incident to the interstate regulation, such can be done under the Constitution. This principle, Mr. Chairman, is employed in the legislation which amended the Food, Drug, and Cosmetic Act for a coverage of oleomargarine. The reason for raising the intrastate commerce issue is that a real enforcement obstacle has been the difficulty of proving interstate shipment.

Legislation such as I have described would add no additional burdens by way of recordkeeping because it would use the records that are already kept, would subject no one to special license, and would affect legitimate dealers not at all. So far as physicians are concerned they would be unaffected by this proposal and could continue to prescribe and dispense these drugs as they do without being circumscribed in any way.

I hope I have made it clear that these suggestions concerning possible legislation are being put forth only as a basis for study and further discussion. Even if the committee should conclude that there is a need for further Federal legislation, we feel that all those who are concerned with possible legislation should have ample opportunity to study and understand anything that is proposed—including particularly the drug and medical groups. I am sure it is understood that we offer these suggestions as only one approach.

Aside from any question of legislation it seems to us that there is need for an educational program designed to accurately acquaint the public with the hazards involved in misusing drugs of this nature. Such a program might well at the same time be designed to reassure the public with regard to the use of such drugs when prescribed by physicians. The public is already receiving considerable information about the misuse of these drugs and much of it is on a basis perhaps more calculated to produce hysteria than the exercise of sound judgment. Within the Department of Health, Education, and Welfare we are actively considering how we can improve our educational program.

Mr. BOGGS. Thank you very much, Mr. Harvey.

Mr. Karsten, do you have any questions?

Mr. KARSTEN. Yes, Mr. Chairman, I do have a few questions to ask.

On page 4 where you start to outline this program you suggest—

(1) recordkeeping throughout distribution channels to show stocks received and stocks sold with right of inspection by Government inspectors.

Now, wherein is that different from the present situation?

Mr. HARVEY. So far as recordkeeping is concerned, Mr. Karsten, it would not be different at all. All manufacturers keep a record of production and keep invoices on what they ship, all the way down the line. What they get and what they ship is covered by invoices.

Mr. KARSTEN. The record is already there in that case?

Mr. HARVEY. Yes, the record is already there. This would make that a mandatory requirement because at the present time if a person chose to cover up a little bit it would be very convenient to skip a few.

Mr. KARSTEN. Thus far have you found manufacturers who would do such a thing, that is, cover up?

Mr. HARVEY. Manufacturers of these products?

Mr. KARSTEN. Yes.

Mr. HARVEY. So far we have had no instances of covering up, no, sir.

Mr. KARSTEN. Evidently the problem is not on the manufacturing level, then.

Mr. HARVEY. Not so far.

Mr. KARSTEN. Then we get down to the corner drugstore where the prescription record is kept.

Mr. HARVEY. Yes, that is right.

Mr. KARSTEN. So, actually, your first recommendation is already being done or carried out. It is not mandatory, but it is being done.

Mr. HARVEY. It is being done so far as I know, yes, sir.

Mr. KARSTEN. In point No. 2 you say—

listing of manufacturers for identification so that clandestine and unauthorized producers may be more easily identified.

Today you do know the names of drug manufacturers who process and put up barbituric acid preparations? Do you not have that information already, sir?

Mr. HARVEY. Only partially, Mr. Karsten. Both groups of these drugs are relatively easy to manufacture, and as we go into the investigation of the clandestine sale of these things like we have had, for instance, in some of our recently publicized investigations among truckdrivers we find that very few of the samples that we got from the vendors in that investigation traced back to the leading manufacturers.

Mr. KARSTEN. Whom do you classify as a manufacturer? You say here, "listing of manufacturers for identification." Whom do you classify as manufacturers? Would it be a corner drugstore, for instance?

Mr. HARVEY. No, my thought would be, Mr. Karsten, that a manufacturer would be one who takes a chemical into his plant and converts it into dosage form.

Mr. KARSTEN. There are only a relatively few big firms who would be equipped to do that on a wholesale basis, is not that true?

Mr. HARVEY. No, sir; Mr. Karsten. It is a simple thing in the case of these products.

Mr. KARSTEN. How many of them would you estimate?

Mr. HARVEY. My information is that there are probably 1,300 at it now.

Mr. KARSTEN. 1,300?

Mr. HARVEY. Yes, and there could be many more of them.

Mr. KARSTEN. Is it possible also to prepare these barbituric acid preparations and other sleeping-pill concoctions in the back room of a corner drugstore; is that possible?

Mr. HARVEY. It is possible; yes.

Mr. KARSTEN. How would you list those manufacturers, or how could you list them?

Mr. HARVEY. They could file their names under the act and they would be manufacturers, and they would be subject to the same accountability for keeping records as any other manufacturer.

Mr. KARSTEN. This would apply strictly to barbiturates as we know them today. Suppose you listed the phenobarbital manufacturers and all of the rest of them in that category, could they then turn to preparations like chloral hydrate and other chemicals and get around the law that way?

Mr. HARVEY. Yes, that would be possible.

Mr. KARSTEN. You cannot get a registration that would cover everything; can you?

Mr. HARVEY. You cannot unless you could see a way to extend or supplement the law as I have suggested——

Mr. KARSTEN. Then under No. 3 you say—

prohibition of possession except by listed manufacturers, authorized dealers, licensed physicians—

and so forth. Is not that pretty much the existing situation, that its possession is prohibited unless you have a prescription, and you are not supposed to dispense it or have it unless you have a prescription?

Mr. HARVEY. The statute at the present time makes it an offense to dispense these drugs other than on prescription. It does not make it an offense to manufacture the article, nor does it make it an offense to possess the article, nor does it make it an offense to bring the articles in from Mexico.

Mr. KARSTEN. That is, provided it is properly labeled and meets the other requiremnets.

Mr. HARVEY. Yes.

Mr. KARSTEN. On that point do you have any problem with the smuggling of things of this sort from Mexico?

Mr. HARVEY. We have some information and a great deal of rumor, frankly, sir. We know that some of the products are brought in from Mexico, that people make trips into Mexico for that purpose.

Mr. KARSTEN. But actually under existing law the ordinary person is not authorized to possess it, yet there is no penalty for possession. If it can be dispensed only by a physician a layman could not get it unless he had a prescription for it.

Mr. HARVEY. There is no prohibition against the possession of it.

Mr. KARSTEN. Could you be a little bit more specific about what you recommend in reference to a person who may be found with an unauthorized bottle of sleeping pills or something of that kind? What would you recommend in the way of penalty in such a case?

Mr. HARVEY. Assuming it may come under the Food, Drug, and Cosmetic Act I would recommend that the sanctions and penalties attaching to any violation of that act attach to these offenses. That is, there would be power for the seizure of contraband goods outside

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of the legitimate channels of trade. Where they are illegally possessed there should be power to punish them for misdemeanor with second-offense provisions for 3 years in prison and 1 year for the first offense. Also there may be cases where there would be statutory injunctions where you might want to restrain a manufacturer.

Mr. KARSTEN. What about the States? Do some of them have prohibitions on the possession of these barbiturates?

Mr. HARVEY. Yes.

Mr. KARSTEN. How many of them have such prohibitions?

Mr. HARVEY. There is a uniform barbiturate law which is proposed by the Council on State Governments. There are a number of States—I hesitate to say exactly how many, possibly about eight—that have enacted that legislation which prohibits possession except from any authorized channels. There are other States, as I indicated in the text of my remarks, and nearly all States have some law that gets at a part of this.

Mr. KARSTEN. Against the dispensing of these barbiturates without a prescription from a physician?

Mr. HARVEY. Yes, sir; that is right.

Mr. KARSTEN. What is the difference between these ordinary sleeping pills that you can buy at the corner drugstore and a barbiturate? Can you tell me that, or would that be out of your department?

Mr. HARVEY. I can try; I am not sure that I can. What is the ordinary sleeping pill you have in mind?

Mr. KARSTEN. I mean the sleeping pills that you can buy without a prescription.

Mr. HARVEY. There are certain products on the market that are offered to aid in producing sleep that are in the classification of antihistamines, and I suspect that is what you have in mind. There has been quite a string of them in the last year under various brand names. Originally antihistamines were offered for the treatment of symptoms of colds and they had a warning on them not to take them and drive an automobile and a few other things, because you get drowsy after taking them. They have such an effect as the doctors advise me.

Mr. KARSTEN. Can you buy antihistamines without a prescription?

Mr. HARVEY. Yes.

Mr. KARSTEN. What about methapyrilene? Is that an antihistamine?

Mr. HARVEY. I will have to have that checked.

Mr. KARSTEN. What about scopolamine; is that an antihistamine?

Mr. HARVEY. I do not believe that it is.

Mr. KARSTEN. I went down to the corner drugstore and asked them what they had in the way of sleeping pills the other day, and the druggist opened a drawer in which there must have been 150 to 200 different kinds, everything from "Sleeping Shut-Eye" to "Forty Winks," everything you wanted. They seemed to have two main ingredients. One of them is, I think, scopolamine.

Here is a box of methapyrilene. There were 150 of these preparations down in the druggist's drawer. What about the effect of these pills? Have you made any inspection of them to find out how they actually work? Is the public being defrauded or are they really a barbiturate preparation? Here is one of them here.

Mr. HARVEY. From your description I am satisfied they are not a barbiturate preparation.

Mr. KARSTEN. Do they induce sleep, or have the same effect as a barbiturate?

Mr. HARVEY. No, I do not think this has quite the same effect.

Mr. KARSTEN. What is the effect, and what is the difference? I guess you have made some study of them, have you not?

Mr. HARVEY. We have made some studies of some of them in which the results are inconclusive. It is very different in testing products of this kind. We have made studies of them and the results so far are not very conclusive. We do know that some people do become sleepy from taking these antihistamines.

Mr. KARSTEN. Is it not true, Mr. Harvey, that scopolamine itself is more of a heavy sleep producing agent?

Mr. HARVEY. Scopolamine itself is an older drug that has been used in connection with or it has some association with the so-called truth serum, and with twilight sleep in childbirth.

Mr. KARSTEN. Would you recommend any controls for things of this sort?

Mr. HARVEY. Well, the need for control from the standpoint of misuse is not at present apparent.

Mr. KARSTEN. Well, they say plainly on the directions here:

Take 1 or 2 capsules 20 minutes before retiring. For continuous use of dosage in excess of the recommended, consult a physician.

Would you classify it as a dangerous drug or not?

Mr. HARVEY. I think any drug can be taken to excess. We would classify that as a drug, as far as the information we have now is concerned, as suitable for over-the-counter use.

Mr. KARSTEN. Suppose I took 12 of these, would I get the same kind of effect that I would get out of a barbiturate?

Mr. HARVEY. I think you would not get the same effect.

Mr. KARSTEN. Would it put me to sleep or what?

Mr. HARVEY. I think no matter how much you take of a different drug you will not get the same effect.

Mr. KARSTEN. Well, would this put you to sleep?

Mr. HARVEY. If you are one of those who get drowsy from antihistamines, yes. I am sorry that I cannot give you a better answer than that, but the studies which we have made indicate that they work on some people.

Mr. KARSTEN. I believe this is of the antihistamine variety, and this other one, scopolamine, is more of a heavier sleep-producing agent.

Mr. HARVEY. Yes, that has a very low dosage, scopolamine.

Mr. KARSTEN. Even a very low dosage of barbiturates or morphine would be extremely questionable, I would think, unless given under the direction of a physician——

Mr. HARVEY. But I do not know that it necessarily follows with these preparations.

Mr. KARSTEN. That is all I have, Mr. Chairman.

Mr. BOGGS. Mr. Byrnes.

Mr. BYRNES. Did I understand you to say that at the present time you do or do not have a complete list of all manufacturers of barbiturates?

Mr. HARVEY. I am not at all sure that we have.

Mr. BYRNES. You say that in checking on these purchases by truck-drivers or somebody you discovered that the source of the barbiturates in the first instance was not from the chief manufacturers?

Mr. HARVEY. We were unable to recognize them as coming from the manufacturers we were familiar with.

Mr. BYRNES. In other words you had no list of those manufacturers as manufacturers of barbiturates?

Mr. HARVEY. That is right.

Mr. BYRNES. What is the situation today? Could I print a letterhead having on it what may look like I was a retail druggist and write to one of these manufacturers and put in an order for barbiturates and automatically receive them back, receive the order?

Mr. HARVEY. On a druggist's letterhead?

Mr. BYRNES. Yes.

Mr. HARVEY. It is possible, Mr. Byrnes. I do know that many, if not all, of the drug manufacturers have taken great pains to try to prevent their sales forces from being hoodwinked in such ways, so that they are trying to identify definitely their customers so that they do not sell these drugs in what would be unauthorized channels. It is difficult to answer your question. Ordinarily drugs are bought by druggists through jobbers, and unknown druggists with no credit rating do not write to a manufacturer for drugs.

Mr. BYRNES. Well, but other than the factor which any manufacturer would be concerned with—namely, whether he was going to be paid—there is not any restriction today upon a manufacturer, for instance, selling barbiturates direct to anybody who buys in a quantity which would be comparable to a retail outfit?

Mr. HARVEY. Well, the statute is not precise on that question. In the sale of a drug, such as a barbiturate, by a manufacturer that is sold under a legend on the label reserving it for use only on prescription, I am well satisfied that if a manufacturer knowingly and deliberately sells a drug so labeled for another purpose, not intending it to be sold on prescription, he can be reached under existing law.

If you put the question as to what happens if he is fooled by this fake letterhead, that is a pretty involved question that the courts would have to answer before we had a good answer.

Mr. BYRNES. There is no legal obligation on him, is there, to make sure that the druggist—I mean the potential purchaser—is a licensed druggist or pharmacist?

Mr. HARVEY. It depends on how careless a man can be without reaching the point of wanton indifference.

Mr. BYRNES. You think that there might be a chance of prosecuting a manufacturer for, let us say, shipping to a person who was not a licensed druggist?

Mr. HARVEY. I do, sir; yes, sir.

Mr. BYRNES. And there you might carry that one step further and say there was negligence on his part if he did not at least take some steps to verify that the person writing on this letterhead was in truth and in fact a druggist.

Mr. HARVEY. That is right. He is dealing with a restricted article. The matter of how far his duty goes is a case of law for each case.

Mr. BYRNES. There is one thing that seems rather peculiar to me, or that disturbs me, in this barbiturate picture and that is the amount of increase in the manufacture of the barbituric acid derivatives. The information which I have, which apparently is furnished from your office, is that in 1954 there were produced 798,000 pounds. A

witness in Chicago, I believe it was, calculated that was equal to about 3 billion capsules of 1½ grains each which, according to this witness, is the usual sized dose. That would mean about 18 doses for every man, woman, and child in the United States during the year.

Mr. HARVEY. Yes, sir.

Mr. BYRNES. That figure to me seems to raise a warning flag that something has gone amiss because manufacturers generally try to estimate their market. They are not going to get the place flooded, so they must assume there is going to be some consumption.

Mr. HARVEY. I also have difficulty in coming to the belief that normal consumption in the United States of these kinds of drugs would be 18 doses for every man, woman, and child. I do not want to argue either side, or both sides, but I think it is fair to say there is a tremendous medical usage of these drugs. They are used by almost every doctor every day and for many, many patients. These drugs have some uses in producing anesthesia as well as the more common uses, so there are great quantities used by the doctors. I am not trying to justify the quantities. I think in fairness we do not know.

Mr. BYRNES. I do not want to draw some conclusions from these figures that are not warranted, and that is why I asked the question whether or not that is alarming. I have a family of seven and we have not used any. There is 18 doses times 7 that we are entitled to.

Mr. HARVEY. Someone else is getting your share.

We regard those figures as very intriguing. We are, with the limited facilities that we have, trying to find out more about them. We do not have all the answers as yet.

Mr. KARSTEN. With regard to the 78,000 pounds, does that include the antihistamines?

Mr. HARVEY. It does not include antihistamines. Those figures are barbiturates. Those are the products of barbituric acid.

Mr. BYRNES. My understanding is there is also some problem of a person who becomes addicted to these barbiturates going to 2 or 3 doctors and getting a prescription from each of them. I suppose there is not anything you can do to control that except to depend upon the medical profession itself to use proper diligence—knowing that they are handling a drug that can be misused.

Mr. HARVEY. Let me put it the other way. I think that it would be unwise to undertake to invade the regulation, the legitimate practice of medicine with a Federal statute like the Food, Drug, and Cosmetic Act. Basically medical practice laws are State laws, and I think that it would be mad to try to tie the two together. If there needs to be those kinds of laws, I think that they should come from somewhere else. There is a vast difference in my mind between a physician practicing medicine and using his best judgment—even though his judgment might be a little more liberal with these things than his brother's—and one who dispenses them willfully for their nonmedical effects. I do not think the Federal Bureau should go too far in telling the doctor how to practice medicine, but if he is not practicing medicine, but is hiding behind a license, that is a different thing.

Mr. BYRNES. I was not criticizing the doctors because my understanding of what happens is that the patient goes to Dr. A and exhibits certain symptoms which under good medical practice would entitle the patient to a prescription for some of these drugs, but then the

patient goes to Dr. B and that doctor also is a good doctor, so he prescribes, and so on down the line, and finally the individual has 5 or 6 prescriptions.

Mr. HARVEY. Yes, and in our investigation of cases of injury, suicide, and accidental deaths, and so forth, we have encountered that—the indications in the deceased person that they had received prescriptions from a number of physicians. How common it is I do not know.

Mr. BYRNES. There would not be any way to get into that?

Mr. HARVEY. I do not think it can be reached by any Federal legislation that I envision.

Mr. BOGGS. Mr. Harvey, as I understand your proposal, you would have recordkeeping?

Mr. HARVEY. Yes.

Mr. BOGGS. You would have a listing?

Mr. HARVEY. Of the manufacturer.

Mr. BOGGS. And you would provide certain penalties for illegal possession; is that correct?

Mr. HARVEY. Yes.

Mr. BOGGS. Now, what would the listing consist of? How would your listing differ from licensing?

Mr. HARVEY. In this respect: Listing would be mandatory. If a manufacturer furnished his name and address to the Food and Drug Administration with a statement that he did manufacture, or proposed to manufacture these articles, we would accept it and file it. We would have no power to direct him in any way as a result of that listing. We would have identification of him, and when we at any time encountered an unlisted manufacturer, or the stocks of an unlisted manufacturer, without further ado those stocks are contraband and would be subject to seizure. So, with means of that kind we would get at the clandestine operator.

Mr. BOGGS. Suppose that a manufacturer listed himself under the act.

Mr. HARVEY. Yes.

Mr. BOGGS. But then he sent drugs to distributors who were not legally entitled to receive drugs, or suppose that he sent them to individuals, would you have any authority under this proposal to get at him?

Mr. HARVEY. It is my intention that the language make it a specific offense for that dealer to supply a person not in channels, or not a legitimate dealer.

Mr. BOGGS. Your act would go a little further than listing?

Mr. HARVEY. Oh, yes.

Listing is 1 provision—listing of the manufacturer is merely 1 provision.

Mr. BOGGS. So you would also recommend certain provisions having to do with distribution?

Mr. HARVEY. That is right.

Mr. BOGGS. That is not included in the three provisions I read in your paper.

Mr. HARVEY. It is perhaps not as clear as I would like to have it there, as I noticed myself in going over it. The causing of the illegal possession as well as the illegal possession are intended to be covered.

Mr. BOGGS. Now, assuming this manufacturer committed this offense, what penalties would you recommend?

Mr. HARVEY. My recommendation would be that the penalties that now attach to violations of the Food, Drug, and Cosmetic Act would apply to these offenses.

Mr. BOGGS. What are those?

Mr. HARVEY. For the first offense the law provides not to exceed 1 year in prison and a fine of not to exceed $1,000.

In a second, or subsequent offense, or a willful offense, the penalties are raised to 3 years and $10,000.

Mr. BOGGS. You consider those penalties adequate?

Mr. HARVEY. For the violations that we have dealt with on the improper sale of these types of drugs which has been adjudicated, those penalties seemed reasonably effective.

In many instances there are terms of probation and it tends to stop the practice pretty well.

Mr. BOGGS. Have you consulted with the drug manufacturers with respect to this problem?

Mr. HARVEY. We have, yes.

Mr. BOGGS. Is it their feeling your proposal is adequate and reasonable?

Mr. HARVEY. With those that I have consulted, with the reservation they necessarily have made, it would have to be individually considered by the board of directors of each firm, and so forth. The drug manufacturers have looked at these proposals in a most favorable light.

They have said that they would give a better answer if I would give them a draft to work from, and I agree they could.

Mr. BOGGS. Have you had any consultations with representatives of the retail drug trade?

Mr. HARVEY. A brief consultation with the Washington representatives of the two largest retail drug associations; yes.

Mr. BOGGS. Have they offered any objection?

Mr. HARVEY. Yes.

Mr. BOGGS. What has been the nature of their objection?

Mr. HARVEY. So far as I can speak for them, I think their principal objection as expressed is based upon a feeling they do not want our inspectors, Federal Food and Drug inspectors, looking at their prescriptions.

Mr. BOGGS. This does not have any effect on that, does it? That is taken care of in another act.

Mr. HARVEY. No. I think this would. If you recall the Durham-Humphrey provisions, and more particularly the statements made from the floor and the committee, there is a doubt, or a mixture of views on the question of whether that provision for inspection does permit the examination of prescription files.

Mr. BOGGS. You do not examine prescription files now.

Mr. HARVEY. We do in most of them. While the association objects, the individual druggist rarely does.

Mr. BOGGS. Do you have any question in your mind as to whether or not you have the authority to do it?

Mr. HARVEY. I do, yes. Let me put it this way: I have a question as to where we would come out in court because of the legislative history.

Mr. BOGGS. As I understand it, you propose recordkeeping on the part of the manufacturer; is that right?

Mr. HARVEY. Yes.

Mr. BOGGS. Those records would include what?

Mr. HARVEY. His production records and his invoices of shipments made.

Mr. BOGGS. Then you would list the manufacturers?

Mr. HARVEY. That is right.

Mr. BOGGS. Then you yould have some control over his distribution. You would want to know where he distributes the drugs.

Mr. HARVEY. Have an opportunity to examine his records and see where he had shipped.

Mr. BOGGS. Then you would provide penalties for illegal possession?

Mr. HARVEY. Yes.

Mr. BOGGS. What would constitute illegal possession?

Mr. HARVEY. Possession by an individual of drugs other than when he received them on a prescription of a physician or from a physician in the course of a physician's practice.

Mr. BOGGS. Or in the case of a druggist.

Mr. HARVEY. In the case of any dealer in the retail trade who was not in a position to fill prescriptions.

Mr. BOGGS. Suppose that he obtained the drugs from an unlicensed manufacturer.

Mr. HARVEY. The product would be subject to seizure. I would have to think a minute as to whether the dealer would be subject to action for buying from an illicit source or not.

Mr. BOGGS. What would the illicit manufacturer be subject to?

Mr. HARVEY. He would be subject to criminal punishment for the offense of having produced and distributed drugs without being listed.

Mr. BOGGS. So that failure to list would carry a criminal penalty?

Mr. HARVEY. That is right.

Mr. BOGGS. Would there be any provision for unlisting someone?

Mr. HARVEY. No, sir.

Mr. BOGGS. Suppose that someone violated the act.

Mr. HARVEY. If you establish that violation you have penalties, you have injunction powers and you have seizure powers. I have not contemplated we would make this listing a registration or a license. As soon as you place power to revoke that listing it does become a license.

Mr. BOGGS. What I am trying to determine in my own mind is what the practical difference between listing and licensing would be.

Mr. HARVEY. I think that is the practical difficulty. Listing would be supplying us with a tool to reach the unlisted who presumably want to operate on the quiet, whereas licensing would give us a power over the manufacturer who listed himself.

Mr. BOGGS. Yet the purchaser who acquired from an unlisted manufacturer would be subject to a penalty and the unlisted manufacturer who delivered to the purchaser would be subject to a penalty.

Mr. HARVEY. The latter, Mr. Chairman, I agree to. I expressed some uncertainty, I believe, as to what the status of the retailer, for example, who bought from an unlicensed manufacturer might be. I would want to think about that. I do not think if he operated in complete good faith that perhaps he, himself, would have committed a crime against the peace and dignity. His product might be contraband.

Mr. BOGGS. Would a listing last forever, or would you have a relisting?

Mr. HARVEY. I think that perhaps it should be renewed from time to time.

Mr. BOGGS. Would there be any qualifications established for listing? Suppose that a criminal wanted to make barbiturates. I understand that you can make them in your kitchen if you have the basic ingredients.

Mr. HARVEY. It is similar to buying a gambling stamp. You can buy one but other things might follow afterward.

Mr. BOGGS. Your analogy is not exactly right. You would not charge a thief with a listing; would you?

Mr. HARVEY. That is right. I think that as soon as we make this listing a thing that can be withheld, denied or revoked, that we are into a licensing provision.

Mr. BOGGS. Do you not really get into a practical problem right off the bat? Assume for the moment that you had a criminal who wanted to be listed, would you list him? Suppose that he had been convicted of violating a State barbiturate act; would you list him?

Mr. HARVEY. I think that you would list him, the idea being here that the judgment of crime and the punishment thereof would still be left to the courts. There would be no administrative decision as to whether this or that person is entitled to engage in the business.

Mr. BOGGS. Some years ago the Justice Department recommended a system of licensing, as you will recall.

Mr. HARVEY. Yes.

Mr. BOGGS. Do you object to that system? Why have you recommended listing rather than licensing?

Mr. HARVEY. I proceeded on the theory we ought to impose the minimum of burden upon legitimate industry that seemed necessary—no more. I have tried to deal with this thing in the light of the experience that we have had rather than the conjectures we might think up.

Mr. BOGGS. Would it be any more burdensome upon a legitimate manufacturer to license him rather than list him?

Mr. HARVEY. Well, he would be placed at the mercy, so to speak, of an administrative body as to whether he got a license or not.

Mr. BOGGS. If you are going to follow up on where he ships all his drugs, and if you are going to have a penalty attached to the unlicensed manufacturer who ships, where is the burden any different? If a man is legitimate, and 99 percent of them are, why should be object?

Mr. HARVEY. Object to the Bureau licensing him?

Mr. BOGGS. Yes.

Mr. HARVEY. I assure you he does object.

Mr. BOGGS. But he does not object to being listed.

Mr. HARVEY. So far as he has had an opportunity to consider this, I think that his answer would be he does not object to being listed, so long as——

Mr. BOGGS. I do not quite understand your answer. He objects to the licensing?

Mr. HARVEY. That is right.

Mr. BOGGS. But he does not object to the listing proposal?

Mr. HARVEY. As a generalization. There may be many manufacturers that will object to the whole thing, but with those that I have

discussed it, the consensus is they see no harm and possibly a great enforcement convenience in their listing their names, addresses, and the product they manufacture, but they would have to give much consideration before they could agree to any proposition of licensing.

Mr. BOGGS. Let me ask you this question. From the point of view of enforcement—and it is your business to enforce the law?

Mr. HARVEY. Yes.

Mr. BOGGS. What would be the best plan for you, licensing or listing?

Mr. HARVEY. So far as I have been able to visualize it in line with the type of enforcement that my more than 30 years of experience encompasses, I think the listing would be a satisfactory procedure to get at what we are trying to get at.

Mr. BOGGS. The only difference would be, as I see it, you would not have the power to revoke a license. Is there any difference other than that?

Mr. HARVEY. That is the principal difference, but it is a great difference.

Mr. BOGGS. But you would have the power of fine and imprisonment?

Mr. HARVEY. No. That power rests with the United States courts after we have proven our case.

Mr. BOGGS. I know that you would not have it, but the law would grant that power.

Mr. HARVEY. But that is a big difference.

Mr. BOGGS. You do not have that power now? No one but the United States courts has the power to fine or imprison.

Mr. HARVEY. But who is going to have the power to decide who is going to be licensed?

Mr. BOGGS. The same people who decide who were going to be listed.

Mr. HARVEY. Of course, the Congress is going to decide about the listing.

Mr. BOGGS. Congress would decide about the licensing, too.

Mr. HARVEY. I yield on that point, Mr. Chairman.

Mr. KARSTEN. Suppose this unauthorized manufacturer is not engaged in interstate commerce, could you get at him?

Mr. HARVEY. Under the description that I have offered here, yes.

Mr. KARSTEN. If the druggist were a manufacturer in a back room where no interstate commerce is involved?

Mr. HARVEY. Yes.

Mr. KARSTEN. In your statement about the antihistamines did you say that you could buy them without prescription? Did I understand you correctly?

Mr. HARVEY. Yes.

Mr. KARSTEN. I have some here that read, "Caution. Federal law prohibits distribution without prescription."

Mr. HARVEY. There are some both ways.

Mr. KARSTEN. Are there two kinds of antihistamines?

Mr. HARVEY. There are a number of different chemical compounds that fall within the classification of antihistamines. There are certain antihistamines that have been reserved for prescription use. They are usually in doses twice as great as the dosage that you have there.

Mr. KARSTEN. Fifty milligrams on this one.

Mr. HARVEY. And 25 milligrams for the other.

Mr. KARSTEN. I can take a double dose from the 25 milligram bottle and get the same effect?

Mr. HARVEY. That is true. It may be a different antihistamine.

Mr. KARSTEN. Antihistimine is spelled the same way on both bottles.

Mr. HARVEY. I agree, Mr. Karsten, but antihistimine is a generic term, just as barbiturate is. One may have a potency that may differ from another.

Mr. KARSTEN. Antihistamines may not be purchased indiscriminately without prescription?

Mr. HARVEY. Not all of them.

Mr. KARSTEN. It is the volume that you are talking about? These are 50 milligrams in this bottle here.

Mr. HARVEY. Yes.

Mr. KARSTEN. And I could get two 25-milligram bottles without the prescription?

Mr. HARVEY. It would be the same quantity but perhaps a different antihistamine.

Mr. KARSTEN. Would you recommend any changes in that law?

Mr. HARVEY. Your question is, do I recommend any changes in that law?

Mr. KARSTEN. There is a Federal law that prohibits me from getting 50 milligrams of this particular preparation.

Mr. HARVEY. I do not recommend any legislative action to change that.

Mr. KARSTEN. You are going to go ahead and enforce that law and I can get around it by taking two doses from this other bottle if I am so inclined?

Mr. HARVEY. I do not think that you will get the same product.

Mr. KARSTEN. I will get 50 milligrams.

Mr. HARVEY. You will get 50 milligrams by taking the 2 doses, but whether you would get 50 milligrams of precisely the same product that you got from the prescription would be outside of my information.

Mr. KARSTEN. One difference is that one bottle has a yellow label and one a blue label.

Mr. HARVEY. They are different chemicals.

Mr. BOGGS. Thank you very much. I have one final question. I presume that your statement has cleared channels, has it not?

Mr. HARVEY. Yes; it has.

Mr. BOGGS. I wonder if you would be good enough to submit to me in legislation the recommendations that you have made here.

Mr. HARVEY. In the form of a draft?

Mr. BOGGS. Yes.

Mr. HARVEY. I would be very happy to do so.

(The proposed draft is as follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
FOOD AND DRUG ADMINISTRATION,
Washington 25, D. C., January 31, 1956.

HON. HALE BOGGS,
House of Representatives.

DEAR CONGRESSMAN BOGGS: In response to the request that you made of me when I testified before the Subcommittee on Narcotics on December 14, 1955,

there is enclosed a draft bill. This is being sent to you on a technical service basis and does not constitute any recommendation of this Department.

Sincerely yours,

JOHN L. HARVEY,
Deputy Commissioner of Food and Drugs.

A BILL To protect the public health by regulating the manufacture, compounding, processing, distribution, and possession of habit-forming barbiturate and amphetamine drugs

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That the Congress hereby finds and declares that regulation of intrastate commerce in barbiturates and amphetamines is essential to the effective regulation of interstate commerce in such drugs, because in the form in which they are consumed their place of origin ordinarly cannot be determined; and that the regulation of interstate commerce without the regulaiton of intrastate commerce in such drugs, as provided in this bill, would discriminate against and depress interstate commerce.

SEC. 2. Section 201 of the Federal Food, Drug, and Cosmetic Act, as amended, is amended by adding at the end thereof:

"(s) The term "barbiturate" means any drug consisting in whole or in part of any of the salts of barbituric acid, or any derivative of barbituric acid, or any of the salts of such derivative, which has been designated by the Secretary, under section 502(d), as habit forming.

"(t) The term "amphetamine" means any drug consisting in whole or in part of racemic amphetamine sulfate or dextro amphetamine sulfate."

SEC. 3. Section 301 of such Act is amended by adding at the end thereof:

"(o) (1) The manufacture, compounding, processing, or possession of any barbiturate or amphetamine in violation of section 508 (a); (2) the sale, delivery, or other disposition of any barbiturate or amphetamine in violation of section 508 (b); or (3) (A) the failure to prepare or keep, or (B) the refusal to permit access to or copying of, any record with respect to any barbiturate or amphetamine as required by section 508 (c)."

SEC. 4. Section 302 (a) of such Act is amended by inserting after "(j)", and before the period, a comma and the following: "and clause (3) (B) of paragraph (o)".

SEC. 5. The first sentence of section 304 (a) of such Act is amended by inserting before ": *Provided, however,*" the following: "; and any barbiturate or amphetamine manufactured, compounded, processed, possessed, sold, delivered, or disposed of in violation of section 508 shall be liable to be proceeded against at any time on libel of information and condemned in any United States district court within the jurisdiction of which the article is found".

SEC. 6. Chapter V of such Act is amended by adding at the end thereof a new section as follows:

BARBITURATES AND AMPHETAMINES

"SEC. 508. (a) No person shall manufacture, compound, process, or possess any barbiturate or amphetamine except the following:

"(1) Manufacturers, compounders, and processors who have listed their names and places of business with the Secretary and who are regularly engaged in preparing pharmaceutical chemicals or prescription drugs for distribution through branch outlets, wholesale druggists, or by direct shipment to retail pharmacies or to hospitals, clinics, public health agencies, or physicians for dispensing by registered pharmacists upon prescriptions or for use by or under the supervision of practitioners licensed by law to administer such drugs in the course of their professional practice.

"(2) Branch outlets established by listed manufacturers, compounders, or processors described in paragraph (1), and wholesale druggists who maintain establishments in conformance with local laws and are regularly engaged in supplying prescription drugs to retail pharmacies, or to hospitals, clinics, public health agencies, or physicians, for dispensing by registered pharmacists upon prescriptions or for use by or under the supervision of practitioners licensed by law to administer such drugs in the course of their professional practice.

"(3) Retail pharmacies, hospitals, clinics, and public health agencies which maintain establishments, in conformance with local laws regulating the practice of pharmacy and medicine, regularly engaged in dispensing prescription drugs upon prescriptions of practitioners licensed to administer such drugs for patients under the care of such practitioners in the course of their professional practice.

"(4) Practitioners licensed by law to prescribe or administer barbiturates or amphetamines who have such drugs in their possession for use in the course of their professional practice.

"(5) Carriers and warehousemen who possess barbiturates or amphetamines in the ordinary course of their business of transporting and storing such drugs.

"(6) Persons who possess barbiturates or amphetamines for use in research, teaching, or chemical analysis and not for sale.

"(7) Officers and employees of Federal, State, Territorial, or local governments whose possession of such drugs is in the course of their official duties.

"(8) Persons to whom barbiturates or amphetamines have been dispensed, or for whom such drugs have been prescribed in conformance with section 503 (b), by practitioners licensed by law to prescribe and administer such drugs in the course of such practitioner's professional practice.

"(9) An employee of any person described in paragraph (1) through paragraph (7), and a nurse or other medical technician under the supervision of a practitioner licensed by law to administer such drugs, having possession of such drugs by reason of his employment or occupation and not on his own account.

"(b) No person shall sell, deliver, or otherwise dispose of any barbiturate or amphetamine to a person not authorized by subsection (a) to possess such drugs.

"(c) Every person engaged in manufacturing, compounding, processing, selling, delivering. or otherwise disposing of any barbiturate or amphetamine shall, upon the effective date of this section, prepare a complete record of all stocks of barbiturates and amphetamines on hand and shall keep such record for 3 years. Thereafter, every such person manufacturing, compounding, or processing any birbiturate or amphetamine shall prepare and keep, for not less than 3 years, a record of the kind and quantity of barbiturates and amphetamines manufactured, compounded, or processed and the date of such manufacture, compounding, or processing; and every such person selling, delivering, or otherwise disposing of any barbiturate or amphetamine shall prepare or obtain, and keep for not less than 3 years, a record of the kind and quantity of such barbiturate or amphetamine received, sold, delivered, or otherwise disposed of, the name and address of the person from whom it was received and to whom it was sold, delivered, or otherwise disposed of, and the date of such transaction: *Provided, however,* That the provisions of the subsection shall not apply to practitioners licensed by law to prescribe or administer barbiturates or amphetamines who dispense such drugs in the course of their professional practice. Every person required by this subsection to prepare, or obtain and keep, records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at reasonable times to have access to and copy such records.

"(d) The Secretary may by regulations remove any barbiturate or amphetamine from the operation of this section when such regulation of its manufacture, compounding, processing, possession, and disposition is not necessary for the protection of the public health.

SEC. 7. Nothing in this act shall be construed as authorizing the manufacture, compounding, processing, possession, sale, delivery, or other disposal of any barbiturate or amphetamine in any State or territory in contravention of the laws of such State or territory.

SEC. 8. This act shall take effect 180 days after its enactment.

Mr. BOGGS. Thank you very much. You have been very helpful. Our next witness is Dr. Kenneth Chapman. Will you identify yourself, please?

STATEMENT OF DR. KENNETH CHAPMAN, CONSULTANT, NARCOTIC DRUG ADDICTION, NATIONAL INSTITUTE OF MENTAL HEALTH, PUBLIC HEALTH SERVICE

Dr. CHAPMAN. I am Dr. Kenneth Chapman, consultant on narcotic addiction for the Public Health Service. I have no prepared statement, but I am free to answer questions such as I may for your information.

Mr. IKARD. Dr. Chapman, what is your opinion, and what has been your experience with the rehabilitation of addicts?