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May 23, 2000

## VIA FEDERAL EXPRESS

Ms. Jennie C. Butler  
Dockets Management Branch  
Food and Drug Administration  
Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Docket No. 00P-1297/CP 1

Dear Ms. Butler:

Please find enclosed four (4) copies of a revised Citizen Petition; the original was entered into Docket No. 00P-1297/CP 1. We revised the first paragraph on page 1, and we changed the format, but not substance, of Attachment B. While the rest of the document remains the same, we are submitting again the entire Citizen Petition, as amended. We ask that you replace the version that is currently in the docket with this version. We apologize for any inconvenience.

Please feel free to call me if you have any questions.

Sincerely,



Alan G. Minsk

AGM/mkm  
Enclosures

~~00P-1297/CP 1~~  
98N-0337

~~00P-1297/CP 1~~  
APP 13

# ARNALL GOLDEN & GREGORY, LLP

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Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

## CITIZEN PETITION

The undersigned, on behalf of a client, submits this petition under the Federal Food, Drug, and Cosmetic Act ("the FDC Act") and 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs amend 21 C.F.R. § 201.66 to permit an OTC drug manufacturer to include the phrase "may contain" or "may also contain" on a product label to list varying inactive ingredients when the product is sourced from multiple suppliers.

### *A. Action Requested*

This petition requests that FDA amend its regulation on the format and content requirements for OTC drug labeling, 21 C.F.R. § 201.66, to allow a manufacturer, which uses multiple suppliers to source drug products (*i.e.*, products in finished dosage form) containing different inactive ingredients, to include the phrase "may contain" or "may also contain" (for simplicity, we will refer to "may contain" in this petition to include both types of statements) on a product label to list uncommon inactive ingredients (*i.e.*, those uniquely provided by a particular supplier). The requested amendment will ensure that appropriate disclosures regarding ingredients are given, while allowing the manufacturer the flexibility to source the product from more than one supplier without incurring the expense of maintaining multiple product inventories and costly labeling changes when only the specific inactive ingredients in an OTC drug are allowed to be declared on the label. The relevant portions of the applicable statutory and regulatory provisions, as well as the amendment proposed by this petition, are included in Attachment A.

For the reasons to be discussed in section B.2., a Citizen Petition submission is proper for this request.

Dockets Management Branch  
May 23, 2000  
Page 2

**B. Statement of Grounds**

1. Introduction

Our client is a manufacturer of OTC drug products. The company also packages thousands of OTC drug products for hundreds of retail customers, typically under the distributor's name. Each product must be individually prepared to identify the particular drug product, the distributor, and any other information specific to that item. The products must be prepared for, and shipped to, distributors in a short period of time.

Our client must use multiple suppliers for some products to: (1) ensure an uninterrupted supply of product to its retail customers; (2) prevent disruption of its production schedule caused by short-term demands of its suppliers; and (3) keep its costs under control. Although the active ingredients and their respective dosages are identical and the labeling complies with all applicable OTC monograph(s), the inactive ingredients can vary slightly from supplier to supplier.

2. Regulatory Background

The Food and Drug Administration Modernization Act ("FDAMA") added a new section 502(e)(1)(A)(iii) of the FDC Act, 21 U.S.C. § 352(e)(1)(A)(iii), to require all drugs to state "the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package," and, if deemed appropriate by FDA, also on the immediate container.<sup>1</sup> FDA promulgated 21 C.F.R. § 201.66 to describe the format and content requirements for OTC product labeling. 64 Fed. Reg. 13254 (March 17, 1999). Specifically, in relevant part, the agency requires the product labeling to provide a section for "Inactive Ingredients," followed by a listing of the established name of each inactive ingredient. 21 C.F.R. § 201.66(c)(8).

According to 21 C.F.R. § 201.66(e),

FDA on its own initiative or in response to a written request from any manufacturer, packer, or distributor, may exempt or defer, based on the circumstances presented, one or more

---

<sup>1</sup> An exemption from this requirement was established for OTC drugs that are also cosmetics. Those products are already required by the cosmetic labeling regulations to list the inactive ingredients in descending order of predominance. See, e.g., 21 C.F.R. § 701.3. In addition, the alphabetical order listing requirement does not apply to OTC drugs not intended for human use. See 21 U.S.C. § 352(e)(1)(A)(iii).

Dockets Management Branch  
May 23, 2000  
Page 3

specific requirements set forth in this section on the basis that the requirement is inapplicable, impracticable, or contrary to public health or safety.

A separate request must be submitted for each OTC drug product and identified as an "Application for Exemption." Id. The exemption or deferral request must:

- (1) document why a particular requirement is inapplicable, impracticable, or is contrary to public health or safety; and
- (2) include a representation of the proposed labeling, including any outserts, panel extensions, or other graphical or packaging techniques intended to be used with the product.

Id.

Petitioner submits this Citizen Petition, instead of an Application for Exemption, for two reasons. One, this petition asks FDA to amend 21 C.F.R. § 201.66 to provide for an across-the-board variance, rather than an exemption, to permit an OTC manufacturer to include the phrase "may contain" in the "Inactive Ingredients" section of the product labeling when there are multiple sources for drug products manufactured with slightly different inactive ingredients. The manufacturer would declare on the label of the drug the inactive ingredients that are common to the multiple suppliers, as required by 21 C.F.R. § 201.66. The request in this petition is for a variance (i.e., "may contain") in the regulation and not for an exemption (which would apply if no inactives were listed).

Two, even assuming FDA treats this request as a request for an exemption and not a variance, an Application for Exemption is product-specific. This petition seeks to amend 21 C.F.R. § 201.66 to apply to all OTC drug products manufactured using slightly different inactive ingredients from multiple suppliers. Therefore, a Citizen Petition, not an Application for Exemption, is the proper administrative mechanism to effectuate the changes requested.

Nevertheless, because we expect that FDA will consider the criteria described in the Application for Exemption regulation, 21 C.F.R. § 201.66(e), when reviewing this petition, petitioner will explain why FDA should grant the request in this petition, applying the aforementioned criteria. Petitioner also wants to make clear that this petition is limited in scope and only requests a "may contain" labeling variance when multiple suppliers are used for drug products that have slightly different inactive ingredients. Manufacturers would be required to comply with all other requirements for OTC product labeling detailed in 21 C.F.R. § 201.66.

Dockets Management Branch  
May 23, 2000  
Page 4

Attachment B provides a representation of the proposed labeling intended to be used with a representative OTC drug product.

3. It is impracticable to list all inactive ingredients when an OTC drug manufacturer uses multiple suppliers.

If the declaration of inactive ingredients must list only the specific inactive ingredients actually present in the finished product, rather than provide a "may contain" statement, the manufacturer will be forced to consider one of three alternatives, all of which will cause significant reduction in the company's profitability and none of which are practical: (1) purchase the ingredients from only one supplier; (2) carry separate inventories of labeling to accommodate slight variations in inactive ingredients caused by the need to use multiple sources of supply for each supplier's ingredients; or (3) require the ingredient suppliers to manufacture the ingredients to an exact formula. Each of these alternatives is discussed below.

**Alternative 1 – Purchase drug product from only one supplier.** If a company uses only one supplier, this company runs the risk of having no product available when that single supplier is experiencing production difficulties or is otherwise unable to meet higher than forecasted retail demand.

**Alternative 2 – Carry separate inventories of packaging and labeling materials for the same product when slight differences in inactive ingredients exist.** Our client cannot reasonably carry separate inventories of multiple versions of the same carton or label for each product in its OTC product line. In addition to the substantial economic impact of maintaining adequate warehouse space to store the new materials and separate labeling and packaging, there will be increased costs relating to the establishment of new stock keeping units (SKUs) and inventory controls, as well as those relating to the revision of all supporting documentation. Moreover, the risk of labeling mixups will increase significantly. Finally, the additional personnel and resources necessary to maintain duplicate labeling and packaging inventories and to comply with the labeling requirements for each product will be cost-prohibitive and not provide any significant benefit to consumers.

**Alternative 3 – Require different suppliers to manufacture to the same formula.** Our client has explored this option with its suppliers and has determined that this option is impracticable. Each manufacturer has different equipment, different raw material sources, and different methods in compounding and processing these materials. A change to a formula with which they do not have experience would, at the very least, be time-consuming and expensive and, in many cases, not feasible. At worst, it could also lead to production problems, delays, and inferior drug product quality.

Dockets Management Branch  
May 23, 2000  
Page 5

4. FDA should provide a general variance to minimize the potential overflow of Applications for Exemptions.

Petitioner supports the comments submitted by the Cosmetic, Toiletry, and Fragrance Association (CTFA) to FDA's Division of OTC Drugs, dated December 13, 1999. Specifically, CTFA argued for broader exemption standards, which would dramatically reduce the number of individual exemption requests filed and "substantially reduce FDA's role in reviewing confidential materials." We recognize that Dr. Charles Ganley, Director of the Division of OTC Drugs, has said that FDA will not preapprove exemptions and intends to review each request on a case-by-case basis. However, for the reasons discussed in this petition, we ask that the agency reconsider its position and grant an across-the-board variance to permit OTC manufacturers to provide "may contain" in the "Inactive ingredients" section of the product labeling when multiple sources of inactive ingredients, with identical functionality but slightly different compositions, are used. Otherwise, in these situations, companies, such as the petitioner's client, will be required to submit Applications for Exemptions for hundreds of OTC products on a case-by-case basis, which will be cumbersome, time-consuming and draining on the agency's limited personnel, time, and resources.

5. A grant of the requested variance is consistent with recent FDA action.

FDA recently reviewed a request, similar to that made in this petition. Specifically, on November 23, 1999, the agency granted Zee Medical, Inc.'s Application for Exemption regarding the listing of inactive ingredients on the company's PainAid® Pain Relief tablets. See Attachment C. Zee Medical requested that FDA allow the use of the phrase "may contain" to list inactive ingredients that may or may not be present in the product, because the company obtained bulk tablets from three different suppliers whose formulations contain different inactive ingredients and it would be impracticable for Zee Medical's manufacturing and distribution operations.

Based on this recent agency action, petitioner asks that FDA permit the inclusion of a "may contain" statement to list inactive ingredients that may or may not be in the drug product when the OTC manufacturer uses multiple suppliers. A grant of a variance in this limited case will not present a risk to the public health. The inclusion of a "may contain" statement notifies the consumer that a particular inactive ingredient may or may not be in the drug product. Based on the inactives listed, the consumer can then determine whether to purchase the drug. It is possible that the consumer is allergic to a specific inactive ingredient and will decide not to select a given product due to the possible safety considerations. At worst, because of the "may contain" statement, the consumer will not buy the drug product. Although this could have an economic effect on the manufacturer, it will not present any potential threat to the public health.

Dockets Management Branch  
May 23, 2000  
Page 6

**C. Environmental Impact**

According to 21 C.F.R. § 25.31, this petition qualifies for a categorical exclusion from the requirement for submission of an environmental assessment.

**D. Economic Impact**

According to 21 C.F.R. § 10.30(b), petitioner will, upon request by the Commissioner, submit economic impact information.

**E. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,



Alan G. Minsk  
Arnall Golden & Gregory, LLP  
2800 One Atlantic Center  
1201 West Peachtree Street  
Atlanta, GA 30309-3450  
404-873-8690 (phone)  
404-873-8691 (fax)

Attachments

ATTACHMENT A

- Proposed amendment to current 21 C.F.R. § 201.66 would read:

...  
(c)(8) “Inactive ingredients”, followed by a listing of the established name of each inactive ingredient. If the product is an OTC drug product that is not also a cosmetic product, then the inactive ingredients shall be listed in alphabetical order. **However, for an OTC drug product that is sourced from more than one supplier with differing inactive ingredients, the product labeling may state: “May [or may also] contain [name of the uncommon inactive ingredients]” (i.e., that inactive ingredient which is uniquely provided by a particular supplier) after the listing of common inactive ingredients. . . .**

(Emphasis added.)

...  
(e) *Exemptions and deferrals.* FDA on its own initiative or in response to a written request from any manufacturer, packer, or distributor, may exempt or defer, based on the circumstances presented, one or more specific requirements set forth in this section on the basis that the requirement is inapplicable, impracticable, or contrary to public health or safety. **However, for an OTC drug product that is comprised of inactive ingredients manufactured from different suppliers, the product label may contain the statement described in paragraph (c)(8) of this section. . . .**

(Emphasis added.)

## ATTACHMENT B

***Inactive ingredients*** FD&C blue no. 1, FD&C red no. 40, gelatin, glycerin, methylparaben, polyethylene glycol, propylparaben, propylene glycol, sorbitol, titanium dioxide. May also contain D&C red no. 33, ethyl vanillin, purified water.

ATTACHMENT C



DEPARTMENT OF HEALTH & HUMAN SERVICES

Zee Medical, Inc.  
Attn: Kevin Lloyd  
Manager, Quality and Regulatory Affairs  
22 Corporate Park  
Irvine, California 92606

Food and Drug Administration  
Rockville MD 20857

NOV 23 1999

Re: Docket No. 98N-0337  
Comment No. APP6

Dear Mr. Lloyd:

Please refer to your Application for Exemption dated September 15, 1999, and the facsimile dated October 22, 1999, submitted under 21 CFR 201.66(e) for Zee Medical, Inc. PainAid <sup>®</sup> Pain Relief tablets.

Your application requested an exemption from the labeling requirements for OTC drugs set forth in § 201.66 (c)(8) regarding the listing of inactive ingredients on the OTC drug label. You stated that, because your company obtained bulk tablets from three different suppliers whose formulations contain different inactive ingredients, this requirement is impracticable for your method of manufacturing and distribution. Therefore, you requested to be allowed to use the phrase "may contain" to list inactive ingredients that may or may not be present in the product.

We have completed our review of your request and it is granted for this specific product. Accordingly, you are authorized to present the required information set forth in 21 CFR 201.66 (c)(8) for labeling of Zee Medical, Inc. PainAid <sup>®</sup> Pain Relief tablets in the following manner:

- The inactive ingredients common to all three formulas (cellulose, FD&C Yellow #6, and starch) should follow the words "Inactive ingredients" as provided for in § 201.66 (c)(8).
- The list of inactive ingredients should then state "may contain" and should only list the following ingredients:  
croscarmellose sodium, D&C yellow #10, magnesium stearate,  
polyvinylpyrrolidone, silicon dioxide, sodium meta bisulfate, sodium starch glycolate, stearic acid.

This granting of your exemption request does not constitute a full labeling review of this product. The labeling for this product continues to be subject to all other applicable labeling requirements in 21 CFR 201.66, and to any future applicable regulations.

98N-0337

ANS6

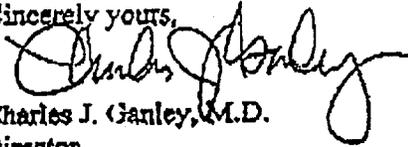
The labeling for this product should contain the information listed in § 201.66(c)(9) so that any consumer who has questions about the inactive ingredient information has a telephone number to call for information. You also need to follow all applicable current good manufacturing practice for finished pharmaceuticals regulations in 21 CFR Part 211 so that you have appropriate records of which lot numbers of the product contain which inactive ingredients. You should be able to provide this information readily in response to telephone inquiries.

Please be advised that this approved modification could be suspended if the agency issues specific regulations for the listing of inactive ingredients in OTC drug product labeling. You should also notify the agency if your suppliers' formulations change and, thus, you may need to modify this exemption accordingly.

For a copy of 21 CFR 201.66, please refer to the Dockets Management Branch website located at <http://fdas.gov/cder/otc/label/label-fr-wr2.htm>

If you have any questions, please contact Elizabeth F. Yuan, R.Ph., Regulatory Health Project Manager, at 301-827-2222.

Sincerely yours,



Charles J. Janley, M.D.

Director

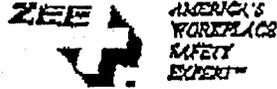
Division of Over-the-Counter Drug Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

10/22/99 FRI 09:41 PAX

*copy - 10/22*



Zee Medical, Inc.

**FAX TRANSMISSION**

To: Ms. Babette Merritt  
Of: FDA, Center for Drugs  
Fax No: 301-827-2315

From: Kevin Lloyd  
Company: Zee Medical, Inc.  
Address: 22 Corporate Park  
Irvine, CA 92606

Date: October 22, 1999  
Pages: 1

Fax No: 949-252-9527  
Phone No: 949-252-9530

This is in response to our phone conversation earlier today concerning our application for exemption from the requirements for listing of inactive ingredients. Shown below are the inactive ingredients for three different formulas for Zee PainAid tablets, which we procure from three different suppliers.

The inactive ingredients common to all three formulas are: cellulose, starch and FD&C Yellow #6.

Supplier 1 Formula (inactives only)

cellulose, croscarmellose sodium, D&C yellow #10, FD&C yellow #6, starch

Supplier 2 Formula (inactives only)

cellulose, croscarmellose sodium, FD&C yellow #6, magnesium stearate, polyvinylpyrrolidone, silicon dioxide, sodium meta bisulfate, sodium starch glycolate, starch, stearic acid

Supplier 3 Formula (inactives only)

cellulose, D&C Yellow #10, FD&C Yellow #6, silicon dioxide, starch, stearic acid

Please call me at 949-252-9530 if you need additional information.

September 15, 1999



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Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

## APPLICATION FOR EXEMPTION

Re: Request for Exemption from 21 CFR 201.66 (OTC Labeling Format)  
Docket Number 98N-0337

Subject: Zee Medical, Inc.  
PainAid® Pain Relief Tablets (#1417, 1418, 1419)

This is a request for exemption from 21 CFR 201.66(c)(8), the requirement for listing the inactive ingredients on the OTC drug label, for Zee Medical, Inc. PainAid® Pain Relief tablets. We believe this requirement is impracticable for our method of manufacturing and distribution due to the factors outlined below. We are requesting to be allowed to use the phrase "may contain" to list inactive ingredients that may or may not be present in the product.

### Confidentiality

We request that the information in this document be kept confidential to the fullest extent possible, particularly information concerning the financial impact of this request on our company.

### Overview of Zee Medical, Inc.

Zee Medical, Inc. is a wholesale distributor of first aid and safety products. We provide these products to independent distributors and company-owned distributors who in turn sell them to employers for use in the employers' workplace first aid cabinets. These products are delivered to the employer by means of a van-based delivery system.

### Description of Product

PainAid® Pain Relief tablets are OTC pain reliever/fever reducer tablets packaged in sealed unit dose packets (2 tablets per packet). The packets are then packaged into dispenser boxes of 100, 250 or 1000 tablets each. The product is sold by our distributors to employers for use in workplace first aid cabinets, also supplied by Zee Medical. This product and other products of our OTC tablet line comprise the largest and most important segment of our business.

98N-0337

A1226

### Manufacturing/Distribution Process

Our company purchases the finished tablets in bulk form, then repackages the tablets into the unit dose packets and dispenser boxes bearing our label. In order to (1) ensure an uninterrupted supply of bulk tablets, (2) prevent short term emergencies at our suppliers from affecting our production schedule and (3) keep our costs under control, it is essential that we have multiple suppliers for the bulk tablets. We currently have three suppliers for the bulk PainAid® Tablets. Although the active ingredients are identical, the inactive ingredients vary from supplier to supplier. Due to this variation, we have not listed any inactive ingredients on the label in the past.

### Reasons for Exemption Request

As indicated above, PainAid® tablets together with the other products of our OTC tablet line comprise the largest and most important segment of our business. Any significant reduction in the profitability of these products would cause serious consequences for our company. If we are required to list the inactive ingredients on the dispenser box, we will be forced into one of three alternatives: (1) purchase the bulk tablets from only one supplier, (2) carry separate inventories of dispenser boxes for each supplier's tablets, or (3) require our bulk tablet suppliers to manufacture the tablets to our exact formula. Each of these alternatives is discussed below.

**Alternative 1 - Purchase tablets from only one supplier.** This is a practice that we have strictly forbidden for many years. With only one supplier, we would run the risk of having no product available during situations where the supplier is experiencing production difficulties. In fact, this very thing happened to us several years ago, which led to a disastrous situation where we were unable to obtain the product for a period of 8 months. As a result, we have established a firm policy that we will always have more than one approved supplier for our bulk tablets.

**Alternative 2 - Carry separate inventories of packaging and labeling materials for multiple suppliers of the same product.** We have evaluated this from an operations standpoint and have determined that we do not have the capability to carry separate and distinct inventories of two or three versions of the same box or label for each product in our tablet line. Aside from the logistics of the increased warehouse space required to store the new materials, the establishment of new SKU's and inventory controls, and the revision of all supporting documentation (batch records product specifications, bill of materials), there would be the increased threat of labeling mixups and the increased burden of having to triple our efforts for every new FDA labeling requirement. The burden of this would cripple our operation.

**Alternative 3 - Require different tablet suppliers to manufacture to the same formula.** We have explored this option with our suppliers and have determined that this is impracticable. Each manufacturer has different blending, granulating and tablet compressing equipment; different raw material sources; and different expertise in compounding and processing these materials. A change to a formula with which they do not have experience would, at the very least, be time consuming and expensive. At worst, it could also lead to production problems, delays, and inferior tablet quality.

FDA Exemption Request  
September 15, 1999

Page 3

Exemption Request

We are requesting exemption for this product from 21 CFR 201.66(c)(8), which requires listing the inactive ingredients on the OTC drug label. We note that many OTC drug labels currently use the phrase "May also contain [list of ingredients]" to describe ingredients that may or may not be present in the formula. We request that we be allowed to make the following statement to convey inactive ingredients that may be present in PainAid® Tablets:

Inactive ingredients may contain cellulose, corn starch, croscarmellose sodium, D&C yellow #10, FD&C yellow #6, magnesium stearate, polyvinylpyrrolidone, silicon dioxide, sodium meta bisulfate, sodium starch glycolate, starch, stearic acid.

The label for this product will meet all other requirements of 21 CFR 201.66.

We appreciate your consideration of this request and look forward to receiving your response as soon as possible. If you need additional information or would like to discuss this matter in person, please call me directly at (949) 252-9530.

Very truly yours,



Kevin Lloyd  
Manager, Quality and Regulatory Affairs  
Zee Medical, Inc.



Zee Medical, Inc.

**FAX TRANSMISSION**

To: Ms. Jenny Butler  
Of: Food and Drug Administration  
Fax No: 301-827-6870

From: Kevin Lloyd  
Company: Zee Medical, Inc.  
Address: 22 Corporate Park  
Irvine, CA 92606

Date: October 14, 1988  
Pages: 1

Fax No: 949-252-9527  
Phone No: 949-252-9530

This is in reference to our Application for Exemption from certain requirements of 21 CFR 201.66 (OTC Labeling Format), Docket Number 98N-037, for Zee Medical PainAid Pain Relief Tablets. The Application for Exemption is dated September 15, 1988.

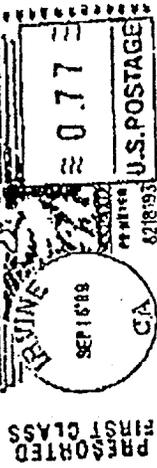
As you indicated during our telephone conversation today, the application includes a section requesting that the submitted information be kept confidential to the extent possible, however, in order for FDA to consider the application, Zee Medical must allow the information to be released publicly.

Please accept this as authorization for FDA to publicly release the information contained in the Application for Exemption referenced above.

If you need additional information, please contact me 949-252-9530.

Sincerely,

Kevin Lloyd  
Manager, Regulatory Affairs  
Zee Medical, Inc.



**ZEE** AMERICA'S **ZEE SERVICE, INC.**  
**WORKPLACE A MAXIMUS COMPANY**  
**SAFETY P.O. BOX 18827, IRVINE, CA 92713 (714) 252-9800**  
**EXPERTS™ 22 CORPORATE PARK, IRVINE, CA 92714-3105**

Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
- Rockville, MD 20852

Attn: Request for Exemption from  
21 CFR 201.66 (OTC Labeling Format)  
Docket Number 98N-0337



## 35. — Weight and sufficiency of evidence

Evidence permitted finding that defendant pharmacist received adulterated drugs with intent to defraud or mislead, where defendant purchased sample prescription drugs and sold samples to customers; drug manufacturer's quality control director testified that jugs defendant used to store samples of cough syrup were intended only for short-term contact and doubted purity if cough syrup stored in jugs, which appeared to have collapsed inward during period before trial, as material used to construct jugs might have leaked into cough syrup and caused its adulteration. *U.S. v. Dino*, C.A.8 (Mo.) 1990, 919 F.2d 72, certiorari denied 112 S.Ct. 50, 502 U.S. 808, 116 L.Ed.2d 28.

Evidence established that Government water test was not arbitrary or irrelevant in that test itself allegedly created holes in prophylactics but rather that prophylactics in violation of prohibition of this chapter against interstate shipment of defective devices contained holes when shipped in interstate commerce. *Dean Rubber Mfg. Co. v. U.S.*, C.A.8 (Mo.) 1966, 356 F.2d 161.

In prosecution for violation of this chapter, by interstate shipment of drugs, whose strength was below that declared on labels, testimony by Food and Drug Administration chemists as to assays conducted on the drugs was substantial, and even if such testimony were regarded as circumstantial evidence, it was not as consistent with a reasonable hypothesis of innocence as with guilt, and it did not, therefore, justify reversal of conviction. *Woodard Laboratories v. U.S.*, C.A.9 (Cal.) 1952, 198 F.2d 995.

In prosecution for violation of former § 8 of this title, evidence that samples of the drug were taken in the ordinary course of business for the purpose of being retained as samples, were put in the usual place where samples were kept to remove them from accident or meddling and there remained undisturbed until seized three years later, was sufficient to justify admission of samples in evidence and it was for jury to decide how likely it was that some other substance had been substituted for what was originally put in bottles. *U.S. v. S B Penick & Co.*, C.C.A.2 (N.Y.) 1943, 136 F.2d 413.

Evidence justified conviction of corporation for shipping in interstate com-

merce adulterated cold tablets represented to contain one grain of acetanilid and .625 grains of quinine sulphate, whereas each tablet contained not more than .83 grains of acetanilid and not more than .56 grains of quinine sulphate. *Strong, Cobb & Co. v. U.S.*, C.C.A.6 (Ohio) 1939, 103 F.2d 671.

Storing latex surgical gloves were held in warehouse and manufacturing facility which harbored rodents violated Federal Food, Drug, and Cosmetic Act, even in absence of showing of actual product contamination. *U.S. v. 789 Cases, More or Less, of Latex Surgeons' Gloves, an Article of Device*, D.Puerto Rico 1992, 799 F.Supp. 1275.

Articles containing amygdalin and hydrogen cyanide, intended for use in treatment and prevention of cancer, were adulterated and misbranded. *U.S. v. General Research Laboratories*, C.D.Cal. 1975, 397 F.Supp. 197.

Evidence established that manufacturer of Vitamin K for injection, otherwise known as Menadione Sodium Bisulfite Injection, maintained no system of label accountability. *U.S. v. Dianovin Pharmaceuticals, Inc.*, D.C.Puerto Rico 1972, 342 F.Supp. 724, affirmed 475 F.2d 100, certiorari denied 94 S.Ct. 60, 414 U.S. 830, 38 L.Ed.2d 65.

Ampules of Vitamin K, Menadione Sodium Bisulfite Injection, which were not completely sealed were not manufactured in conformity with current good manufacturing practice and were "adulterated" within meaning of this section. *U.S. v. Dianovin Pharmaceuticals, Inc.*, D.C.Puerto Rico 1972, 342 F.Supp. 724, affirmed 475 F.2d 100, certiorari denied 94 S.Ct. 60, 414 U.S. 830, 38 L.Ed.2d 65.

Failure of manufacturer of Vitamin K for injection to make any comparison between theoretic and actual batch yield established that the manufacturer did not conform to the requirement of provisions of this subchapter of good manufacturing practices. *U.S. v. Dianovin Pharmaceuticals, Inc.*, D.C.Puerto Rico 1972, 342 F.Supp. 724, affirmed 475 F.2d 100, certiorari denied 94 S.Ct. 60, 414 U.S. 830, 38 L.Ed.2d 65.

Evidence established that drug company's products were deficient as to contents declared on its labels, that basic criteria employed in establishing control methods was economic, with changes in-

fluenced entirely by cost to company rather than desire to make certain that actual strength and quality of drug ingredients was as label declared them to be, and that failure to eliminate inadequacy in manufacturing processes was deliberate, wilful and intentional. *U.S. v. Schlicksup Drug Co.*, S.D.Ill.1962, 206 F.Supp. 801.

## 36. Instructions

In proceeding for forfeiture of allegedly "adulterated" new animal drugs, proposed instructions that would have advised jury to take into consideration intended use and characteristics of drug under investigation, i.e., that drugs were intended for use in immobilizing or destroying feral dogs, was properly refused. *U.S. v. An Article of Drug*, C.A.9 (Cal.) 1981, 661 F.2d 742.

It was not error to refuse to give an instruction, in action against manufacturer of polio vaccine by plaintiff who took the drug and contracted polio as a result, that under Montana law the manufacturer was held to an implied warranty that there was no impurity in the vaccine, where record showed scrupulous attention in the matter of preparation and testing, so that the resulting product was precisely what was intended. *Davis v. Wyeth Laboratories, Inc.*, C.A.9 (Idaho) 1968, 399 F.2d 121.

Assuming that coupled counts of information, the first charging defendants with having introduced adulterated drug into interstate commerce, and the second charging them with having introduced misbranded drug into interstate commerce, rested upon a single shipment, defendants' potential criminal liabilities were restricted to one count in each of the allegedly duplicitous pairings, and accordingly, defendants could either demand that the government elect, or request court to charge jury that it could find defendants guilty of one of the counts, but not both. *U.S. v. Bel-Mar Laboratories, Inc.*, E.D.N.Y.1968, 284 F.Supp. 875.

## 37. Injunctions

Government was entitled to preliminary injunction directing drug manufacturer to comply with Federal Food, Drug and Cosmetic Act, requiring it to cease distribution of certain drugs until concurrent or prospective validation studies for each were completed, and requiring recall of batches released on basis of successful resample alone, and those which had content uniformity and assay difficulties; manufacturer had introduced adulterated drugs into commerce, and there was threat of future violations. *U.S. v. Barr Laboratories, Inc.*, D.N.J.1993, 812 F.Supp. 458.

## § 352. Misbranded drugs and devices

A drug or device shall be deemed to be misbranded—

## (a) False or misleading label

If its labeling is false or misleading in any particular. Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 290aa-4 or under section 262(a) of Title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 290aa-4(a) or in section 262(a) of Title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic infor-

mation presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term "health care economic information" means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.

**(b) Package form; contents of label**

If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count: *Provided*, That under clause (2) of this paragraph reasonable variations shall be permitted, and exemptions as to small packages shall be established, by regulations prescribed by the Secretary.

**(c) Prominence of information on label**

If any word, statement, or other information required by or under authority of this chapter to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

**(d) Repealed.** Pub.L. 105-115, Title I, § 126(b), Nov. 21, 1997, 111 Stat. 2327

**(e) Designation of drugs or devices by established names**

(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

(ii) the established name and quantity or, if determined to be appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if determined to be appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscyne, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such sub-

stances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if determined to be appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, except that nothing in this subclause shall be deemed to require that any trade secret be divulged, and except that the requirements of this subclause with respect to alphabetical order shall apply only to nonprescription drugs that are not also cosmetics and that this subclause shall not apply to nonprescription drugs not intended for human use.

(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of subclause (ii) or (iii) of clause (A) or this clause is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(2) If it is a device and it has an established name, unless its label bears, to the exclusion of any other nonproprietary name, its established name (as defined in subparagraph (4)) prominently printed in type at least half as large as that used thereon for any proprietary name or designation for such device, except that to the extent compliance with the requirements of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(3) As used in subparagraph (1), the term "established name", with respect to a drug or ingredient thereof, means (A) the applicable official name designated pursuant to section 358 of this title, or (B), if there is no such name and such drug, or such ingredient, is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug or of such ingredient, except that where clause (B) of this subparagraph applies to an article recognized in the United States Pharmacop-

eia and in the Homeopathic Pharmacopoeia under different official titles, the official title used in the United States Pharmacopoeia shall apply unless it is labeled and offered for sale as a homeopathic drug, in which case the official title used in the Homeopathic Pharmacopoeia shall apply.

(4) As used in paragraph (2), the term "established name" with respect to a device means (A) the applicable official name of the device designated pursuant to section 358 of this title, (B) if there is no such name and such device is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this paragraph applies, then any common or usual name of such device.

**(f) Directions for use and warnings on label**

Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users, except that where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement.

**(g) Representations as recognized drug; packing and labeling; inconsistent requirements for designation of drug**

If it purports to be a drug the name of which is recognized in an official compendium, unless it is packaged and labeled as prescribed therein. The method of packing may be modified with the consent of the Secretary. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homeopathic Pharmacopoeia of the United States, it shall be subject to the requirements of the United States Pharmacopoeia with respect to packaging and labeling unless it is labeled and offered for sale as a homeopathic drug, in which case it shall be subject to the provisions of the Homeopathic Pharmacopoeia of the United States, and not to those of the United States Pharmacopoeia, except that in the event of inconsistency between the requirements of this paragraph and those of paragraph (c) as to name by which the drug or its ingredients shall be designated, the requirements of paragraph (c) shall prevail.

**(h) Deteriorative drugs; packing and labeling**

If it has been found by the Secretary to be a drug liable to deterioration, unless it is packaged in such form and manner, and its label bears a statement of such precautions, as the Secretary shall by regulations require as necessary for the protection of the public health. No such regulation shall be established for any drug recognized in an official compendium until the Secretary shall have informed the appropriate body charged with the revision of such compendium of the need for such packaging or labeling requirements and such body shall have failed within a reasonable time to prescribe such requirements.

**(i) Drug; misleading container; imitation; offer for sale under another name**

(1) If it is a drug and its container is so made, formed, or filled as to be misleading; or (2) if it is an imitation of another drug; or (3) if it is offered for sale under the name of another drug.

**(j) Health-endangering when used as prescribed**

If it is dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.

**(k) Repealed.** Pub.L. 105-115, Title I, § 125(a)(2)(B), Nov. 21, 1997, 111 Stat. 2325

**(l) Repealed.** Pub.L. 105-115, Title I, § 125(b)(2)(D), Nov. 21, 1997, 111 Stat. 2325

**(m) Color additives; packing and labeling**

If it is a color additive the intended use of which is for the purpose of coloring only, unless its packaging and labeling are in conformity with such packaging and labeling requirements applicable to such color additive, as may be contained in regulations issued under section 379e of this title.

**(n) Prescription drug advertisements: established name; quantitative formula; side effects, contraindications, and effectiveness; prior approval; false advertising; labeling; construction of the Convention on Psychotropic Substances**

In the case of any prescription drug distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug a true statement of (1) the established name as defined in paragraph (e) of this section, printed prominently and in type at least half as large

as that used for any trade or brand name thereof, (2) the formula showing quantitatively each ingredient of such drug to the extent required for labels under paragraph (e) of this section, and (3) such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with the procedure specified in section 371(e) of this title, except that (A) except in extraordinary circumstances, no regulation issued under this subsection shall require prior approval by the Secretary of the content of any advertisement, and (B) no advertisement of a prescription drug, published after the effective date of regulations issued under this subsection applicable to advertisements of prescription drugs, shall with respect to the matters specified in this subsection or covered by such regulations, be subject to the provisions of sections 52 to 57 of Title 15. This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title. Nothing in the Convention on Psychotropic Substances, signed at Vienna, Austria, on February 21, 1971, shall be construed to prevent drug price communications to consumers.

**(o) Drugs or devices from nonregistered establishments**

If it was manufactured, prepared, propagated, compounded, or processed in an establishment in any State not duly registered under section 360 of this title, if it was not included in a list required by section 360(j) of this title, if a notice or other information respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires.

**(p) Packaging or labeling of drugs in violation of regulations**

If it is a drug and its packaging or labeling is in violation of an applicable regulation issued pursuant to section 1472 or 1473 of Title 15.

**(q) Restricted devices using false or misleading advertising or used in violation of regulations**

In the case of any restricted device distributed or offered for sale in any State, if (1) its advertising is false or misleading in any particular, or (2) it is sold, distributed, or used in violation of regulations prescribed under section 360j(e) of this title.

**(r) Restricted devices not carrying requisite accompanying statements in advertisements and other descriptive printed matter**

In the case of any restricted device distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that device (1) a true statement of the device's established name as defined in paragraph (e), printed prominently and in type at least half as large as that used for any trade or brand name thereof, and (2) a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications and, in the case of specific devices made subject to a finding by the Secretary after notice and opportunity for comment that such action is necessary to protect the public health, a full description of the components of such device or the formula showing quantitatively each ingredient of such device to the extent required in regulations which shall be issued by the Secretary after an opportunity for a hearing. Except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement and no advertisement of a restricted device, published after the effective date of this paragraph shall, with respect to the matters specified in this paragraph or covered by regulations issued hereunder, be subject to the provisions of sections 52 through 55 of Title 15. This paragraph shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title.

**(s) Devices subject to performance standards not bearing requisite labeling**

If it is a device subject to a performance standard established under section 360d of this title, unless it bears such labeling as may be prescribed in such performance standard.

**(t) Devices for which there has been a failure or refusal to give required notification or to furnish required material or information**

If it is a device and there was a failure or refusal (1) to comply with any requirement prescribed under section 360h of this title respecting the device, (2) to furnish any material or information required by or under section 360i of this title respecting the

device, or (3) to comply with a requirement under section 360l of this title.

(June 25, 1938, c. 675, § 502, 52 Stat. 1050; June 23, 1939, c. 242, § 3, 53 Stat. 854; 1940 Reorg. Plan No. IV, §§ 12, 13, eff. June 30, 1940, 5 F.R. 2422, 54 Stat. 1237; Dec. 22, 1941, c. 613, § 2, 55 Stat. 851; July 6, 1945, c. 281, § 2, 59 Stat. 463; Mar. 10, 1947, c. 16, § 2, 61 Stat. 11; July 13, 1949, c. 305, § 1, 63 Stat. 409; 1953 Reorg. Plan No. 1, § 5, eff. Apr. 11, 1953, 18 F.R. 2053, 67 Stat. 631; Aug. 5, 1953, c. 334, § 1, 67 Stat. 389; July 12, 1960, Pub.L. 86-618, Title I, § 102(b)(2), 74 Stat. 398; Oct. 10, 1962, Pub.L. 87-781, Title I, §§ 105(c), 112(a), (b), 131(a), Title III, § 305, 76 Stat. 785, 790, 791, 795; July 13, 1968, Pub.L. 90-399, § 105(a), 82 Stat. 352; Dec. 30, 1970, Pub.L. 91-601, § 7(d), 84 Stat. 1673; Dec. 30, 1970, Pub.L. 91-601, § 6(d), formerly § 7(d), 84 Stat. 1673; renumbered § 6(d), Aug. 13, 1981, Pub.L. 97-35, Title XII, § 1205(c), 95 Stat. 716, and amended May 28, 1976, Pub.L. 94-295, §§ 3(e), 4(b)(2), 5(a), 9(b)(2), 90 Stat. 577, 580, 583; Nov. 10, 1978, Pub.L. 95-633, Title I, § 111, 92 Stat. 3773; June 16, 1992, Pub.L. 102-300, § 3(a)(2), 106 Stat. 239; Oct. 29, 1992, Pub.L. 102-571, Title I, § 107(9), 106 Stat. 4499; Aug. 13, 1993, Pub.L. 103-80, § 3(m), 107 Stat. 777; Nov. 21, 1997, Pub.L. 105-115, Title I, §§ 114(a), 125(a)(2)(B), (b)(2)(D), 126(b), Title IV, § 412(c), 111 Stat. 2312, 2325, 2327, 2375.)

#### HISTORICAL AND STATUTORY NOTES

##### Revision Notes and Legislative Reports

1941 Acts. House Committee Report No. 1542, see 1941 U.S. Code Cong. Service, p. 1036.

1949 Acts. Senate Report No. 600, see 1949 U.S. Code Cong. Service, p. 1530.

1953 Acts. House Report No. 706, see 1953 U.S. Code Cong. and Adm. News, p. 2086.

1960 Acts. House Report No. 1761, see 1960 U.S. Code Cong. and Adm. News, p. 2887.

1962 Acts. Senate Report No. 1744 and Conference Report No. 2526, see 1962 U.S. Code Cong. and Adm. News, p. 2884.

1968 Acts. Senate Report No. 1308, see 1968 U.S. Code Cong. and Adm. News, p. 2607.

1970 Acts. House Report No. 91-1642 and Conference Report No. 91-1755, see 1970 U.S. Code Cong. and Adm. News, p. 5326.

1976 Acts. Senate Report No. 94-33 and House Conference Report No. 94-1090, see 1976 U.S. Code Cong. and Adm. News, p. 1070.

1978 Acts. House Report No. 95-1193, see 1978 U.S. Code Cong. and Adm. News, p. 9496.

1997 Acts. House Conference Report No. 105-399, see 1997 U.S. Code Cong. and Adm. News, p. 2881.

##### Amendments

1997 Amendments. Subsec. (a). Pub.L. 105-115, § 114(a), added, "Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 290aa-4 or under section 262(a) of Title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 290aa-4(a) or in section 262(a) of Title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term 'health care economic information' means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes,

of the use of a drug to the use of another drug, to another health care intervention, or to no intervention."

Subsec. (d). Pub.L. 105-115, § 126(b), repealed subsec. (d), which read:

##### "(d) Habit forming substances"

"If it is for use by man and contains any quantity of the narcotic or hypnotic substance alpha eucaine, barbituric acid, betaeucaine, bromal, cannabis, carbomal, chloral, coca, cocaine, codeine, heroin, marihuana, morphine, opium, paraldehyde, peyote, or sulphonmethane; or any chemical derivative of such substance, which derivative has been by the Secretary, after investigation, found to be, and by regulations designated as, habit forming; unless its label bears the name and quantity or proportion of such substance or derivative and in juxtaposition therewith the statement 'Warning—May be habit forming.'"

Subsec. (e)(1). Pub.L. 105-115, § 412(c), rewrote par. (1), which read:

"(1) If it is a drug, unless (A) its label bears, to the exclusion of any other non-proprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (3)) of the drug, if such there be, and (ii), in case it is fabricated from two or more ingredients, the established name and quantity of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including, whether active or not, the established name and quantity or proportion of any bromides, ether, chloroform, acetanilid, acetphenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury ouabain strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein; *Provided*, That the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this paragraph, shall apply only to prescription drugs; and (B) for any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) is printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or

ingredient; *Provided*, That to the extent that compliance with the requirements of clause (A)(ii) or clause (B) of this paragraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary."

Subsec. (k). Pub.L. 105-115, § 125(a)(2)(B), struck out subsec. (k), which read:

##### "(k) Insulin not properly certified"

"If it is, or purports to be, or is represented as a drug composed wholly or partly of insulin, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 356 of this title, and (2) such certificate or release is in effect with respect to such drug."

Subsec. (l). Pub.L. 105-115, § 125(b)(2)(D), struck out subsec. (l), which read:

##### "(l) Antibiotic drugs improperly certified"

"If it is, or purports to be, or is represented as a drug (except a drug for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 357 of this title, and (2) such certificate or release is in effect with respect to such drug; *Provided*, That this subsection shall not apply to any drug or class of drugs exempted by regulations promulgated under section 357(c) or (d) of this title."

1993 Amendments. Par. (e)(3). Pub.L. 103-80, § 3(m)(1), substituted ", except that" for ": Provided further, That".

Par. (f). Pub.L. 103-80, § 3(m)(2), substituted ", except that" for ": Provided, That".

Par. (g). Pub.L. 103-80, § 3(m)(3), substituted "The method" for ": Provided, That the method" and substituted ", except that" for ": Provided further, That".

Par. (n). Pub.L. 103-80, § 3(m)(4), substituted ", except that" for ": Provided, That".

1992 Amendments. Par. (m). Pub.L. 102-571, § 107(9), substituted "379e" for "376".

EFFECTIVE DATE NOTE 1: At 62 FR 19925, Apr. 24, 1997, the effective date for § 201.64 (a) through (h) was delayed until further notice.

EFFECTIVE DATE NOTE 2: At 64 FR 13286, Mar. 17, 1999, § 201.64 was amended by revising the last sentence in paragraph (b), effective Apr. 16, 1999. For the convenience of the user the superseded text is set forth as follows:

§ 201.64 Sodium labeling.

(b) \* \* \* The sodium content per dosage unit shall be listed on a separate line after the heading "Sodium Content" as the last statement in the ingredients section.

§ 201.66 Format and content requirements for over-the-counter (OTC) drug product labeling.

(a) *Scope.* This section sets forth the content and format requirements for the labeling of all OTC drug products. Where an OTC drug product is the subject of an applicable monograph or regulation that contains content and format requirements that conflict with this section, the content and format requirements in this section must be followed unless otherwise specifically provided in the applicable monograph or regulation.

(b) *Definitions.* The following definitions apply to this section:

(1) *Act* means the Federal Food, Drug, and Cosmetic Act (secs. 201 *et seq.* (21 U.S.C. 321 *et seq.*)).

(2) *Active ingredient* means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of humans. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

(3) *Approved drug application* means a new drug (NDA) or abbreviated new drug (ANDA) application approved under section 505 of the act (21 U.S.C. 355).

(4) *Bullet* means a geometric symbol that precedes each statement in a list of statements. For purposes of this sec-

tion, the bullet style is limited to solid squares or solid circles, in the format set forth in paragraph (d)(4) of this section.

(5) *Established name* of a drug or ingredient thereof means the applicable official name designated under section 508 of the act (21 U.S.C. 358), or, if there is no designated official name and the drug or ingredient is recognized in an official compendium, the official title of the drug or ingredient in such compendium, or, if there is no designated official name and the drug or ingredient is not recognized in an official compendium, the common or usual name of the drug or ingredient.

(6) *FDA* means the Food and Drug Administration.

(7) *Heading* means the required statements in quotation marks listed in paragraphs (c)(2) through (c)(9) of this section, excluding subheadings (as defined in paragraph (a)(9) of this section).

(8) *Inactive ingredient* means any component other than an active ingredient.

(9) *Subheading* means the required statements in quotation marks listed in paragraphs (c)(5)(ii) through (c)(5)(vii) of this section.

(10) *Drug facts labeling* means the title, headings, subheadings, and information required under or otherwise described in paragraph (c) of this section.

(11) *Title* means the heading listed at the top of the required OTC drug product labeling, as set forth in paragraph (c)(1) of this section.

(12) *Total surface area available to bear labeling* means all surfaces of the outside container of the retail package or, if there is no such outside container, all surfaces of the immediate container or container wrapper except for the flanges at the tops and bottoms of cans and the shoulders and necks of bottles and jars.

(c) *Content requirements.* The outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper, shall contain the title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(8) of this section, and may contain the information under the heading in paragraph (c)(9) of this section, in the order listed.

(1) (Title) "Drug Facts". If the drug facts labeling appears on more than one panel, the title "Drug Facts (continued)" shall appear at the top of each subsequent panel containing such information.

(2) "Active ingredient" or "Active ingredients" "(in each [insert the dosage unit stated in the directions for use (e.g., tablet, 5 mL teaspoonful) or in each gram as stated in §§ 333.110 and 333.120 of this chapter])", followed by the established name of each active ingredient and the quantity of each active ingredient per dosage unit. Unless otherwise provided in an applicable OTC drug monograph or approved drug application, products marketed without discrete dosage units (e.g., topicals) shall state the proportion (rather than the quantity) of each active ingredient.

(3) "Purpose" or "Purposes", followed by the general pharmacological category(ies) or the principal intended action(s) of the drug or, where the drug consists of more than one ingredient, the general pharmacological categories or the principal intended actions of each active ingredient. When an OTC drug monograph contains a statement of identity, the pharmacological action described in the statement of identity shall also be stated as the purpose of the active ingredient.

(4) "Use" or "Uses", followed by the indication(s) for the specific drug product.

(5) "Warning" or "Warnings", followed by one or more of the following, if applicable:

(i) "For external use only" [in bold type] for topical drug products not intended for ingestion, or "For" (select one of the following, as appropriate: "rectal" or "vaginal") "use only" [in bold type].

(ii) All applicable warnings listed in paragraphs (c)(5)(ii)(A) through (c)(5)(ii)(G) of this section with the appropriate subheadings highlighted in bold type:

(A) Allergic reaction warnings set forth in any applicable OTC drug monograph or approved drug application for any product that requires a separate allergy warning. This warning shall follow the subheading "Allergy alert:"

(B) Reye's syndrome warning for drug products containing salicylates set forth in § 201.314(h)(1). This warning shall follow the subheading "Reye's syndrome."

(C) Flammability warning, with appropriate flammability signal word (e.g., §§ 358.150(c) and 358.550(c) of this chapter). This warning shall follow a subheading containing the appropriate flammability signal word described in an applicable OTC drug monograph or approved drug application.

(D) Water soluble gums warning set forth in § 201.319. This warning shall follow the subheading "Choking:"

(E) Alcohol warning set forth in § 201.322. This warning shall follow the subheading "Alcohol warning:"

(F) Sore throat warning set forth in § 201.315. This warning shall follow the subheading "Sore throat warning:"

(G) Warning for drug products containing sodium phosphates set forth in § 201.307(b)(2)(i) or (b)(2)(ii). This warning shall follow the subheading "Dosage warning:"

(iii) "Do not use" [in bold type], followed by all contraindications for use with the product. These contraindications are absolute and are intended for situations in which consumers should not use the product unless a prior diagnosis has been established by a doctor or for situations in which certain consumers should not use the product under any circumstances regardless of whether a doctor or health professional is consulted.

(iv) "Ask a doctor before use if you have" [in bold type] or, for products labeled only for use in children under 12 years of age, "Ask a doctor before use if the child has" [in bold type], followed by all warnings for persons with certain preexisting conditions (excluding pregnancy) and all warnings for persons experiencing certain symptoms. The warnings under this heading are those intended only for situations in which consumers should not use the product until a doctor is consulted.

(v) "Ask a doctor or pharmacist before use if you are" [in bold type] or, for products labeled only for use in children under 12 years of age, "Ask a doctor or pharmacist before use if the child is" [in bold type], followed by all

drug-drug and drug-food interaction warnings.

(vi) "When using this product" [in bold type], followed by the side effects that the consumer may experience, and the substances (e.g., alcohol) or activities (e.g., operating machinery, driving a car, warnings set forth in § 369.21 of this chapter for drugs in dispensers pressurized by gaseous propellants) to avoid while using the product.

(vii) "Stop use and ask a doctor if" [in bold type], followed by any signs of toxicity or other reactions that would necessitate immediately discontinuing use of the product.

(viii) Any required warnings in an applicable OTC drug monograph, other OTC drug regulations, or approved drug application that do not fit within one of the categories listed in paragraphs (c)(5)(i) through (c)(5)(vii), (c)(5)(ix), and (c)(5)(x) of this section.

(ix) The pregnancy/breast-feeding warning set forth in § 201.63(a); the third trimester warning set forth in § 201.63(e) for products containing aspirin or carbaspirin calcium; the third trimester warning set forth in approved drug applications for products containing ketoprofen, naproxen sodium, and ibuprofen (not intended exclusively for use in children).

(x) The "Keep out of reach of children" warning and the accidental overdose/ingestion warning set forth in § 330.1(g) of this chapter.

(6) "Directions", followed by the directions for use described in an applicable OTC drug monograph or approved drug application.

(7) "Other information", followed by additional information that is not included under paragraphs (c)(2) through (c)(6), (c)(8), and (c)(9) of this section, but which is required by or is made optional under an applicable OTC drug monograph, other OTC drug regulation, or is included in the labeling of an approved drug application.

(i) Required information about certain ingredients in OTC drug products (e.g., sodium in § 201.64(c)) shall appear as follows: "each (insert appropriate dosage unit) contains:" [in bold type] (insert name(s) of ingredient(s) and the quantity of each ingredient). This information shall be the first statement under this heading.

(ii) The phenylalanine/aspartame content required by § 201.21(b), if applicable, shall appear as the next item of information.

(iii) Additional information that is authorized to appear under this heading shall appear as the next item(s) of information. There is no required order for this subsequent information.

(8) "Inactive ingredients", followed by a listing of the established name of each inactive ingredient. If the product is an OTC drug product that is not also a cosmetic product, then the inactive ingredients shall be listed in alphabetical order. If the product is an OTC drug product that is also a cosmetic product, then the inactive ingredients shall be listed as set forth in § 701.3(a) or (f) of this chapter, the names of cosmetic ingredients shall be determined in accordance with § 701.3(c) of this chapter, and the provisions in § 701.3(e), (g), (h), (l), (m), (n), and (o) of this chapter and § 720.8 of this chapter may also apply, as appropriate. If there is a difference in the labeling provisions in this § 201.66 and §§ 701.3 and 720.8 of this chapter, the labeling provisions in this § 201.66 shall be used.

(9) "Questions?" or "Questions or comments?", followed by the telephone number of a source to answer questions about the product. It is recommended that the days of the week and times of the day when a person is available to respond to questions also be included. A graphic of a telephone or telephone receiver may appear before the heading. The telephone number must appear in a minimum 6-point bold type.

(d) *Format requirements.* The title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(9) of this section shall be presented on OTC drug products in accordance with the following specifications. In the interest of uniformity of presentation, FDA strongly recommends that the Drug Facts labeling be presented using the graphic specifications set forth in appendix A to part 201.

(1) The title "Drug Facts" or "Drug Facts (continued)" shall use uppercase letters for the first letter of the words "Drug" and "Facts." All headings and subheadings in paragraphs (c)(2) through (c)(9) of this section shall use an uppercase letter for the first letter

in the first word and lowercase letters for all other words. The title, headings, and subheadings in paragraphs (c)(1), (c)(2), and (c)(4) through (c)(9) of this section shall be left justified.

(2) The letter height or type size for the title "Drug Facts" shall appear in a type size larger than the largest type size used in the Drug Facts labeling. The letter height or type size for the title "Drug Facts (continued)" shall be no smaller than 8-point type. The letter height or type size for the headings in paragraphs (c)(2) through (c)(9) of this section shall be the larger of either 8-point or greater type, or 2-point sizes greater than the point size of the text. The letter height or type size for the subheadings and all other information described in paragraphs (c)(2) through (c)(9) of this section shall be no smaller than 6-point type.

(3) The title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section shall be legible and clearly presented, shall not appear in reverse type, shall have at least 0.5-point leading (i.e., space between two lines of text), and shall not have letters that touch. The type style for the title, headings, subheadings, and all other required information described in paragraphs (c)(2) through (c)(9) of this section shall be any single, clear, easy-to-read type style, with no more than 39 characters per inch. The title and headings shall be in bold italic, and the subheadings shall be in bold type, except that the word "(continued)" in the title "Drug Facts (continued)" shall be regular type. The type shall be all black or one dark color, printed on a white or other light, neutral color, contrasting background, except that the title and the headings may be presented in a single, alternative, contrasting dark color unless otherwise provided in an approved drug application, OTC drug monograph (e.g., current requirements for bold print in §§ 341.76 and 341.80 of this chapter), or other OTC drug regulation (e.g., the requirement for a box and red letters in § 201.308(c)(1)).

(4) When there is more than one statement, each individual statement listed under the headings and subheadings in paragraphs (c)(4) through (c)(7) of this section shall be preceded

by a solid square or solid circle bullet of 5-point type size. Bullets shall be presented in the same shape and color throughout the labeling. The first bulleted statement on each horizontal line of text shall be either left justified or separated from an appropriate heading or subheading by at least two square "ems" (i.e., two squares of the size of the letter "M"). If more than one bulleted statement is placed on the same horizontal line, the end of one bulleted statement shall be separated from the beginning of the next bulleted statement by at least two square "ems" and the complete additional bulleted statement(s) shall not continue to the next line of text. Additional bulleted statements appearing on each subsequent horizontal line of text under a heading or subheading shall be vertically aligned with the bulleted statements appearing on the previous line.

(5) The title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(9) of this section may appear on more than one panel on the outside container of the retail package, or the immediate container label if there is no outside container or wrapper. The continuation of the required content and format onto multiple panels must retain the required order and flow of headings, subheadings, and information. A visual graphic (e.g., an arrow) shall be used to signal the continuation of the Drug Facts labeling to the next adjacent panel.

(6) The heading and information required under paragraph (c)(2) of this section shall appear immediately adjacent and to the left of the heading and information required under paragraph (c)(3) of this section. The active ingredients and purposes shall be aligned under the appropriate headings such that the heading and information required under paragraph (c)(2) of this section shall be left justified and the heading and information required under paragraph (c)(3) of this section shall be right justified. If the OTC drug product contains more than one active ingredient, the active ingredients shall be listed in alphabetical order. If more than one active ingredient has the same purpose, the purpose need not be

repeated for each active ingredient, provided the information is presented in a manner that readily associates each active ingredient with its purpose (i.e., through the use of brackets, dot leaders, or other graphical features). The information described in paragraphs (c)(4) and (c)(6) through (c)(9) of this section may start on the same line as the required headings. None of the information described in paragraph (c)(5) of this section shall appear on the same line as the "Warning" or "Warnings" heading.

(7) Graphical images (e.g., the UPC symbol) and information not described in paragraphs (c)(1) through (c)(9) of this section shall not appear in or in any way interrupt the required title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section. Hyphens shall not be used except to punctuate compound words.

(8) The information described in paragraphs (c)(1) through (c)(9) of this section shall be set off in a box or similar enclosure by the use of a barline. A distinctive horizontal barline extending to each end of the "Drug Facts" box or similar enclosure shall provide separation between each of the headings listed in paragraphs (c)(2) through (c)(9) of this section. When a heading listed in paragraphs (c)(2) through (c)(9) of this section appears on a subsequent panel immediately after the "Drug Facts (continued)" title, a horizontal hairline shall follow the title and immediately precede the heading. A horizontal hairline extending within two spaces on either side of the "Drug Facts" box or similar enclosure shall immediately follow the title and shall immediately precede each of the subheadings set forth in paragraph (c)(5) of this section, except the subheadings in paragraphs (c)(5)(ii)(A) through (c)(5)(ii)(G) of this section.

(9) The information set forth in paragraph (c)(6) of this section under the heading "Directions" shall appear in a table format when dosage directions are provided for three or more age groups or populations. The last line of the table may be the horizontal barline immediately preceding the heading of the next section of the labeling.

(10) If the title, headings, subheadings, and information in para-

graphs (c)(1) through (c)(9) of this section, printed in accordance with the specifications in paragraphs (d)(1) through (d)(9) of this section, and any other FDA required information for drug products, and, as appropriate, cosmetic products, other than information required to appear on a principle display panel, requires more than 60 percent of the total surface area available to bear labeling, then the Drug Facts labeling shall be printed in accordance with the specifications set forth in paragraphs (d)(10)(i) through (d)(10)(v) of this section. In determining whether more than 60 percent of the total surface area available to bear labeling is required, the indications for use listed under the "Use(s)" heading, as set forth in paragraph (c)(4) of this section, shall be limited to the minimum required uses reflected in the applicable monograph, as provided in §330.1(c)(2) of this chapter.

(i) Paragraphs (d)(1), (d)(5), (d)(6), and (d)(7) of this section shall apply.

(ii) Paragraph (d)(2) of this section shall apply except that the letter height or type size for the title "Drug Facts (continued)" shall be no smaller than 7-point type and the headings in paragraphs (c)(2) through (c)(9) of this section shall be the larger of either 7-point or greater type, or 1-point size greater than the point size of the text.

(iii) Paragraph (d)(3) of this section shall apply except that less than 0.5-point leading may be used, provided the ascenders and descenders do not touch.

(iv) Paragraph (d)(4) of this section shall apply except that if more than one bulleted statement is placed on the same horizontal line, the additional bulleted statements may continue to the next line of text, and except that the bullets under each heading or subheading need not be vertically aligned.

(v) Paragraph (d)(8) of this section shall apply except that the box or similar enclosure required in paragraph (d)(8) of this section may be omitted if the Drug Facts labeling is set off from the rest of the labeling by use of color contrast.

(11)(i) The following labeling outlines the various provisions in paragraphs (c) and (d) of this section:

OTC Drug Product Labeling Outline

Drug Facts	
Active Ingredient (In each dosage unit)	Purpose
XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXX
<b>Uses</b>	
XXXXXXXXXXXXXXXXXXXX	
<b>Warnings</b>	
Do not use XXXXXXXXXXXXXXXXXXXXXXX	
Ask a doctor before use if you have	
XXXXXXXXXXXXXXXXXXXX	
XXXXXXXXXXXXXXXXXXXX	
Ask a doctor or pharmacist before use if you are XXXXXXXXXXXXXXX	
<b>When using this product</b>	
XXXXXXXXXXXXXXXXXXXX	
XXXXXXXXXXXXXXXXXXXX	
<b>Stop use and ask a doctor if</b>	
XXXXXXXXXXXXXXXXXXXX	
XXXXXXXXXXXXXXXXXXXX	
If pregnant or breast-feeding, ask a health professional before use. Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.	

Drug Facts (continued)
<b>Directions</b>
XXXXXXXXXXXXXXXXXXXX
XXXXXXXXXXXXXXXXXXXX
<b>Other Information</b>
XXXXXXXXXXXXXXXXXXXX
XXXXXXXXXXXXXXXXXXXX
<b>Inactive Ingredients</b> XXXXXXXXXXXXXXX
<b>Questions?</b> 1-800-555-1234

(11) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section:

<b>Drug Facts</b>	
<b>Active Ingredient (in each tablet)</b> Chlorpheniramine maleate 2 mg.....	<b>Purpose</b> .....Antihistamine
<b>Uses</b> temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat	
<b>Warnings</b> Ask a doctor before use if you have ■ glaucoma ■ a breathing problem such as emphysema or chronic bronchitis ■ trouble urinating due to an enlarged prostate gland Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives When using this product ■ you may get drowsy ■ avoid alcoholic drinks ■ alcohol, sedatives, and tranquilizers may increase drowsiness ■ be careful when driving a motor vehicle or operating machinery ■ excitability may occur, especially in children If pregnant or breast-feeding, ask a health professional before use. Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.	
<b>Directions</b>	
adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years	ask a doctor

<b>Drug Facts (continued)</b>	
<b>Other information</b> ■ store at 20-25°C (68-77°F) ■ protect from excessive moisture	
<b>Inactive Ingredients</b> D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch	

(iii) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section, including para-

<b>Drug Facts</b>	
<b>Active Ingredients (in each tablet)</b> Aluminum hydroxide gel 200 mg..... Magnesium hydroxide 200 mg..... Simethicone 25 mg.....	<b>Purpose</b> .....Antacid .....Antacid .....Antigas
<b>Uses</b> ■ relieves symptoms referred to as gas ■ relieves: ■ heartburn ■ acid indigestion ■ sour stomach ■ upset stomach due to these symptoms	
<b>Warnings</b> Ask a doctor before use if you have kidney disease Ask a doctor or pharmacist before use if you are taking a prescription drug. Antacids may interact with certain prescription drugs. Stop use and ask a doctor if symptoms last for more than 2 weeks Keep out of reach of children.	
<b>Directions</b> ■ chew 1 to 4 tablets 4 times daily ■ do not take more than 16 tablets in 24 hours or use the maximum dosage for more than 2 weeks	
<b>Inactive Ingredients</b> D&C red no. 30, D&C yellow no. 10, dextrose, FD&C blue no. 1, glycerin, magnesium stearate, mannitol, saccharin sodium, sorbitol, starch, sugar, talc	

(iv) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section for a drug product marketed with cosmetic claims:

Drug Facts	
<b>Active Ingredient</b>	<b>Purpose</b>
Selenium sulfide 1%	Antidandruff
<b>Use</b> controls scalp itching and flaking due to dandruff	
<b>Warnings</b>	
For external use only	
Ask a doctor before use if you have ■ seborrheic dermatitis that covers a large area of the body	
When using this product ■ do not get into eyes. If contact occurs, rinse eyes thoroughly with water.	
Stop use and ask a doctor if ■ condition worsens or does not improve after regular use	
Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.	
<b>Directions</b>	
■ shake well ■ for best results, use at least 2 times a week	
<b>Inactive Ingredients</b> water, ammonium lauryl sulfate, ammonium lauryl sulfate, cocamide MEA, glycol distearate, ammonium xylenesulfonate, dimethicone, incetylmonium chloride, cetyl alcohol, DMDM hydantoin, sodium chloride, stearyl alcohol, hydroxypropyl methylcellulose, FD&C red no. 4	

(e) *Exemptions and deferrals.* FDA on its own initiative or in response to a written request from any manufacturer, packer, or distributor, may exempt or defer, based on the circumstances presented, one or more specific requirements set forth in this section on the basis that the requirement is inapplicable, impracticable, or contrary to public health or safety. Requests for exemptions shall be submitted in three copies in the form of an "Application for Exemption" to the Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. The request shall be clearly identified on the envelope as a "Request for Exemption from 21 CFR 201.66 (OTC Labeling Format)" and shall be directed to Docket No. 98N-0337. A separate request shall be submitted for each OTC

drug product. Sponsors of a product marketed under an approved drug application shall also submit a single copy of the exemption request to their application. Decisions on exemptions and deferrals will be maintained in a permanent file in this docket for public review. Exemption and deferral requests shall:

(1) Document why a particular requirement is inapplicable, impracticable, or is contrary to public health or safety; and

(2) Include a representation of the proposed labeling, including any outserts, panel extensions, or other graphical or packaging techniques intended to be used with the product.

(f) *Interchangeable terms and connecting terms.* The terms listed in §330.1(i) of this chapter may be used

interchangeably in the labeling of OTC drug products, provided such use does not alter the meaning of the labeling that has been established and identified in an applicable OTC drug monograph or by regulation. The terms listed in §330.1(j) of this chapter may be deleted from the labeling of OTC drug products when the labeling is revised to comply with this section, provided such deletion does not alter the meaning of the labeling that has been established and identified in an applicable OTC drug monograph or by regulation. The terms listed in §330.1(i) and (j) of this chapter shall not be used to change in any way the specific title, headings, and subheadings required under paragraphs (c)(1) through (c)(9) of this section.

(g) *Regulatory action.* An OTC drug product that is not in compliance with the format and content requirements in this section is subject to regulatory action.

[64 FR 13286, Mar. 17, 1999]

EFFECTIVE DATE NOTE: At 64 FR 13286, Mar. 17, 1999, §201.66 was added, effective Apr. 16, 1999.

### Subpart D—Exemptions From Adequate Directions for Use

#### §201.100 Prescription drugs for human use.

A drug subject to the requirements of section 503(b)(1) of the act shall be exempt from section 502(f)(1) if all the following conditions are met:

(a) The drug is:

(1)(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; or

(iii) In the possession of a practitioner licensed by law to administer or prescribe such drugs; and

(2) It is to be dispensed in accordance with section 503(b)

(b) The label of the drug bears:

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

(2) The recommended or usual dosage and

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

(4) The quantity or proportion of each active ingredient, as well as the information required by section 502 (d) and (e); and

(5) If it is for other than oral use, the names of all inactive ingredients, except that:

(i) Flavorings and perfumes may be designated as such without naming their components.

(ii) Color additives may be designated as coloring without naming specific color components unless the naming of such components is required by a color additive regulation prescribed in subchapter A of this chapter.

(iii) Trace amounts of harmless substances added solely for individual product identification need not be named. If it is intended for administration by parenteral injection, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust the pH or to make the drug isotonic may be declared by name and a statement of their effect; and if the vehicle is water for injection it need not be named.

(6) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug.

(7) A statement directed to the pharmacist specifying the type of container to be used in dispensing the drug product to maintain its identity, strength, quality, and purity. Where there are standards and test procedures for determining that the container meets the requirements for specified types of containers as defined in an official compendium, such terms may be used. For example, "Dispense in tight, light-resistant container as defined in the National Formulary". Where standards and test procedures for determining the types of containers to be used in dispensing the drug product are not included in an official compendium, the specific container or types of containers known to be adequate to maintain the identity, strength, quality,



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Company: **RM 1061**

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 30TH FLR  
 ATLANTA  
 (404)873-8160

GA 30309

SHIP DATE: 23MAY00  
 ACCOUNT #: 030013034  
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TO: MS. JENNIE C. BUTLER  
 FOOD AND DRUG ADMIN.  
 12420 PARKLAWN DRIVE  
 ROOM 1-23  
 ROCKVILLE

MD 20857

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REF: 9440/1 PERRIGO COMPANY/FDA

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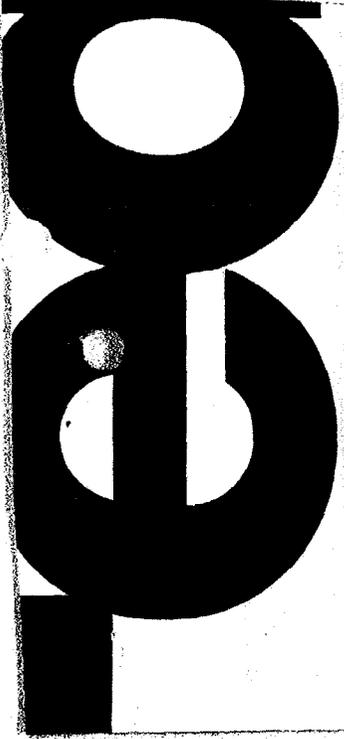
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