

# DEPARTMENT OF HEALTH AND HUMAN SERVICES

## Food and Drug Administration

21 CFR Parts 3, 5, 10, 16, 25, 50, 56, 58, 71, 200, 201, 207, 210, 211, 310, 312, 314, 369, 429, 800, and 812

[Docket No. 98N-0210]

## Removal of Regulations Regarding Certification of Drugs Composed Wholly or Partly of Insulin

AGENCY: Food and Drug Administration, HHS.

ACTION: Direct final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is repealing its regulations governing certification of drugs containing insulin and making conforming amendments to other sections of its regulations. The agency is taking this action in accordance with provisions of the Food and Drug Administration Modernization Act of 1997 (FDAMA). FDAMA repealed the statutory provision in the Federal Food, Drug, and Cosmetic Act (the act) under which the agency certified drugs containing insulin. FDAMA also made conforming amendments to the act. FDA is using direct final rulemaking for this action because the agency expects that there will be no significant adverse comment on the rule. Most of the amendments in this rule are a direct result of the repeal of the statutory certification provision. The remainder of the amendments repeal or update out-of-date, noncontroversial regulations dealing with insulin. Elsewhere in this issue of the **Federal Register**, FDA is publishing a companion proposed rule under FDA's usual procedure for notice-and-comment rulemaking to provide a procedural framework to finalize the rule in the event the agency receives significant adverse comments and withdraws this direct final rule.

**DATES:** This regulation is effective September 25, 1998. Submit written comments on or before July 27, 1998. If no timely significant adverse comments are received, the agency will publish a document in the **Federal Register** before August 26, 1998, confirming the effective date of the direct final rule. If timely significant adverse comments are received, the agency will publish a document of significant adverse comment in the **Federal Register** withdrawing this direct final rule before August 25, 1998.

**ADDRESSES:** Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug

Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** Wayne H. Mitchell, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041.

## SUPPLEMENTARY INFORMATION:

### I. Background

On November 21, 1997, the President signed FDAMA (Pub. L. 105-115). Section 125(a) of FDAMA repealed section 506 of the act (21 U.S.C. 356). Section 506 was the section of the act under which the agency certified drugs composed wholly or partly of insulin. Section 125(a) of FDAMA also removed references to section 506 from section 301(i)(1) and (j) of the act (21 U.S.C. 331(i)(1) and (j)). Section 301(i) of the act prohibits fraudulent use of certain labeling required under various provisions of the act; while section 301(j) prohibits any person from using, or the unauthorized disclosure of, trade secret information obtained under authority of various provisions of the act.

Section 125(a) of FDAMA also repealed section 502(k) of the act (21 U.S.C. 352(k)), which provided that any drug that is, or is represented to be, composed wholly or partly of insulin is misbranded unless it has been certified or released under authority of section 506 of the act.

FDAMA also removed references to section 506 of the act in section 510(j)(1)(A) and (j)(1)(D) of the act (21 U.S.C. 360(j)(1)(A) and (j)(1)(D)), which is part of the drug listing provisions of the act, and section 125(a) of FDAMA amended a law governing procurement of drugs by certain Federal agencies (38 U.S.C. 8126(h)(2)) by removing a reference to drugs certified under authority of section 506 of the act.

FDAMA added drugs composed wholly or partly of insulin to the prohibition in section 801(d) of the act (21 U.S.C. 381(d)) against the reimportation of prescription drugs except by the original manufacturer. This amendment to section 801(d) of the act does not require implementing regulations. FDA will, however, place language reflecting this provision of FDAMA in relevant sections of a separate rule implementing the Prescription Drug Marketing Act of 1987 (Pub. L. 100-293). That rulemaking was initiated with the proposed rule published in the **Federal Register** of March 14, 1994 (59 FR 11842).

Finally, section 125(c) of FDAMA amended section 802 of the act (21

U.S.C. 382) to exempt insulin drugs from the export requirements of section 802 if the drugs meet the requirements of section 801(e)(1) of the act.

### II. Direct Final Rulemaking

FDA has determined that the subjects of this rulemaking are suitable for a direct final rule. The actions taken should be noncontroversial, and the agency does not anticipate receiving any significant adverse comments.

The repeal of section 506 of the act eliminated the statutory provision on which the agency relied to certify drugs composed wholly or partly of insulin. FDA will, therefore, remove all provisions of title 21 of the Code of Federal Regulations (CFR) relating to the certification of insulin products. FDA will also make various ministerial changes to title 21, such as removing references to section 506 of the act in authority sections and regulations whose subjects are not certification of insulin.

FDA has also determined that it is appropriate to use direct final rulemaking to update the definition of insulin in § 200.15 (21 CFR 200.15). The statutory references in the definition are being changed to reflect changes in the law and the scope of the definition is being clarified to reflect the existence of new forms of insulin that have been introduced since the definition was originally issued.

If FDA does not receive significant adverse comment on or before July 27, 1998, the agency will publish a document in the **Federal Register** before August 25, 1998, confirming the effective date of the direct final rule. A significant adverse comment is one that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without a change. A comment recommending a rule change in addition to this rule will not be considered a significant adverse comment, unless the comment states why this rule would be ineffective without the additional change. If timely significant adverse comments are received, the agency will publish a document of significant adverse comment in the **Federal Register** withdrawing this direct final rule before August 26, 1998.

The companion proposed rule, which is identical to the direct final rule, provides a procedural framework within which the rule may be finalized in the event the direct final rule is withdrawn because of significant adverse comment. The comment period for the direct final rule runs concurrently with that of the

companion proposed rule. Any comments received under the companion proposed rule will be treated as comments regarding the direct final rule. Likewise, significant adverse comments submitted to the direct final rule will be considered comments to the companion proposed rule, and the agency will consider such comments in developing a final rule. FDA will not provide additional opportunity for comment on the companion proposed rule.

If a significant adverse comment applies to part of this rule and that part may be severed from the remainder of the rule, FDA may adopt as final those parts of the rule that are not the subject of a significant adverse comment. A full description of FDA's policy on direct final rule procedures may be found in a guidance document published in the **Federal Register** of November 21, 1997 (62 FR 62466).

### III. Description of the Rule

The rule eliminates references to section 506 of the act in all authority citations in 21 CFR, chapter I.

The rule amends the delegation of authority provisions in 21 CFR part 5 to eliminate provisions dealing with the authority to sign citizen petitions regarding the certification of insulin, the authority to certify batches of insulin, and the authority to issue regulations under section 506 of the act pertaining to drugs containing insulin.

The rule eliminates a reference to section 506(c) of the act in 21 CFR 10.50, which deals with issuance of regulations and orders after an opportunity for a formal evidentiary public hearing. Former section 506(c) of the act dealt with the issuance of insulin regulations prescribing tests or methods of assay for batch certification that differed from those specified in an official compendium.

The rule removes a reference to 21 CFR 429.50, which relates to suspension of certification services for certain persons, in 21 CFR 16.1, which defines the scope of 21 CFR part 16.

The regulations in 21 CFR 25.31 (see 62 FR 40570 at 40595, July 29, 1997) are amended to eliminate testing and certification of batches of insulin under section 506 of the act from a list of actions that are categorically excluded from the requirement to prepare an environmental assessment or an environmental impact statement.

The rule removes a reference to section 506 of the act in 21 CFR 50.1, which defines the scope of 21 CFR part 50.

This rule amends the statutory references in the definition of insulin

found in § 200.15 to reflect the repeal of sections 502(k) and 506 of the act; the addition of insulin drug products to the reimportation provision of section 801(d) of the act by FDAMA; the use of the term "insulin" in the export labeling provisions of section 801(f) of the act, which was added by the Technical Amendments to the FDA Export Reform and Enhancement Act of August 6, 1996 (Pub. L. 104-180); and FDAMA's addition of section 802(i) to the act, which exempts insulin drugs from the export requirements of section 802 of the act. The new definition also clarifies the scope of the term "insulin" to reflect the existence of synthetic and biotechnologically derived human insulin. The definition is designed to encompass chemical analogs of insulin, the first of which, insulin lispro (an Eli Lilly & Co. product), was recently approved.

The labeling requirements found in part 201 (21 CFR part 201) are being amended by this rule. Section 201.50(b) is amended to remove a sentence that refers to labeling requirements contained in part 429 (21 CFR part 429), which is also being eliminated by this rule. A reference to section 506 of the act is being removed from § 201.100(c)(2).

Several references to section 506 of the act are being removed from 21 CFR parts 207 and 314.

FDA is repealing all of part 429 and those portions of part 369 (21 CFR part 369) that deal with insulin drug products.

Part 429 contains the primary provisions the agency has relied on to carry out the batch certification of drugs composed wholly or partly of insulin. Subpart A of part 429 defines key terms used in the insulin certification regulations; subpart B of part 429 contains packaging and labeling requirements for products subject to batch certification; subparts C and D of part 429 contain applicable standards and tests and methods of assay for determining whether batches of insulin may be certified; subpart E of part 429 contains the requirements for submitting a request for certification; subpart F of part 429 contains the administrative procedures and fees applicable to insulin certification; and subpart G of part 429 imposes additional recordkeeping requirements applicable to batch certified insulin products. With the repeal of section 506 of the act, and the elimination of the insulin batch certification program, the agency is eliminating these subparts.

The agency notes that several of the provisions in part 429, such as those covering packaging and labeling and

tests and methods of assay, could be retained under provisions of the act other than section 506 of the act. However, the agency has determined, as explained in this section of this document, that it would not be appropriate or necessary to do so at this time.

The current regulations in § 429.10 require insulin drug products to be packaged in sterile immediate containers with closures through which the insulin may be withdrawn with a conventional hypodermic syringe and needle. Section 429.10 also provides for distinctive containers for certain insulin drug products, none of which is currently marketed. Although all insulin drug products are currently marketed in immediate containers that meet the requirements contained in § 429.10, there is no assurance that a new, safe, and effective container/closure system would conform to the regulation. To avoid having to amend the regulation each time a new, acceptable container/closure system is developed, the agency is removing § 429.10 and, instead, will rely on the new drug approval process to approve appropriate container/closure systems for drug products containing insulin. Applicants for drug products containing insulin submit descriptions of the container/closure system with the new drug application (NDA); FDA reviews the container/closure system for use with the drug product and, if appropriate, approves its use with the drug product as part of the NDA approval. This system is used to approve container/closure systems for most new drug products on the market today, and it provides the flexibility necessary to provide for approval of new, safe, and effective container/closure systems.

The current regulations in §§ 369.21, 429.11, and by cross reference § 369.5, set out detailed requirements for the labeling of insulin drug products. The current regulations require, among other information and warnings, information on potency of the drug product, expiration date of the lot, storage instructions, instructions on injecting insulin, and descriptions of how the type of insulin-containing drug product differs from other types of insulin drug products.

FDA is removing §§ 369.5 and 429.11 and those portions of § 369.21 that apply to insulin drug products, and will rely on the new drug approval process, in conjunction with the general drug labeling requirements found in part 201, to establish appropriate labeling requirements for each drug product containing insulin. Applicants submit copies of proposed labeling with the

marketing applications for all new drug products, including those containing insulin; FDA then reviews the application and, if appropriate, approves it, after the applicant has made necessary changes. This system is used to establish labeling for most new drug products and provides the flexibility necessary to provide adequate labeling for new types of insulin drug products. Because all currently marketed insulin drug products are the subject of effective NDA's under section 505(b) of the act, the labeling of these products is not expected to change as a result of the removal of these rules.

The current regulations in § 429.12 contain a distinguishing color scheme, which is outdated. The current system includes distinguishing colors for 40 units per milliliter strengths of insulin drug products, which are no longer being marketed. It also provides an identifying color scheme for insulin zinc globin, which is also not marketed. Under § 429.12, most of the currently marketed insulin drug products are identified by the color combination of black and white, which provides limited usefulness. No provisions are made for either of the two types of mixtures of human insulin and insulin suspension isophane currently being marketed or insulin lispro, a human insulin analogue. Accordingly, FDA is removing § 429.12.

Major insulin manufacturers, working with the International Diabetes Federation (IDF), have developed a new color coding system in which each type of insulin would be identified with a distinctive color. FDA has been favorably impressed with the IDF system. However, the agency believes that it is administratively more efficient to remove part 429 in its entirety at this time, and implement the IDF system in a separate rulemaking proceeding or incorporate it into a guidance issued under FDA's "Good Guidance Practices" published in the **Federal Register** of February 27, 1997 (62 FR 8961).

FDA is also removing § 429.25, which establishes standards of quality and purity for protamine, and § 429.26, which establishes standards of quality and purity for globin hydrochloride. (No insulin products using globin hydrochloride are currently being marketed.) FDA does not, at this time, intend to issue regulations directly establishing other product standards relating to drugs composed wholly or partly of insulin. Insulin manufacturers and FDA laboratories use the requirements set out in the approved NDA for analyzing an insulin drug product and, where appropriate, the

standards set out in the United States Pharmacopeia (USP).

FDA is also removing § 429.30, which sets out testing and assay methods. Section 429.30 provides, generally, that insulin injection, insulin suspension protamine zinc, insulin zinc globin, insulin suspension isophane, insulin zinc suspension, insulin zinc suspension prompt, and insulin zinc suspension extended be tested and assayed according to methods set out in the USP. Section 429.30 also provides tests for isophane ratio, chloride in globin hydrochloride, sulfate in protamine, nitrogen, and zinc. At least one of these products (insulin zinc globin) is no longer marketed. The tests and methods of assay for the remaining products are either outdated or if still in use, have been incorporated into the applicable NDA.

FDA intends to avoid the potential for this type of outdated, codified specification by not proposing at this time regulations specifying testing or assay methods. Instead, insulin will be required to conform to all applicable USP monographs and the approved NDA for each product. This will mean that insulin drug products will be regulated just as other new drugs are regulated by FDA.

#### IV. Environmental Impact

The agency has determined under 21 CFR 25.24(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

#### V. Analysis of Impacts

FDA has examined the impacts of the direct final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 12866 classifies a rule as significant if it meets any one of a number of specified conditions, including having an annual effect on the economy of \$100 million or adversely affecting in a material way a sector of the economy, competition, or jobs, or if it raises novel legal or policy issues. As discussed below, the agency believes that this final rule is consistent with the

regulatory philosophy and principles identified in the Executive Order. In addition, the direct final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options to minimize any significant impact on small entities. The only two manufacturers currently marketing insulin drug products in the United States are not small entities. Furthermore, by eliminating the certification process, this direct final rule would lower market entry barriers for small entities. The agency certifies that the direct final rule will not have a significant impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

The Unfunded Mandates Reform Act requires an agency to prepare a budgetary impact statement before issuing any rule likely to result in a Federal mandate that may result in expenditures by State, local, and tribal governments or the private sector of \$100 million (adjusted annually for inflation) in any 1 year. The elimination of the insulin certification program will lower the costs of marketing insulin drug products, by eliminating both the direct cost of applying for certification and the cost of holding batches of insulin while awaiting certification. Because this rule will not result in an expenditure of \$100 million or more on any governmental entity or the private sector, no budgetary impact statement is required.

#### VI. Paperwork Reduction Act of 1995

This direct final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

#### VII. Request for Comments

Interested persons may, on or before July 27, 1998, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

**List of Subjects****21 CFR Part 3**

Administrative practice and procedure, Biologics, Drugs, Medical devices.

**21 CFR Part 5**

Authority delegations (Government agencies), Imports, Organization and functions (Government agencies).

**21 CFR Part 10**

Administrative practice and procedure, News media.

**21 CFR Part 16**

Administrative practice and procedure.

**21 CFR Part 25**

Environmental impact statements, Foreign relations, Reporting and recordkeeping requirements.

**21 CFR Part 50**

Human research subjects, Prisoners, Reporting and recordkeeping requirements, Safety.

**21 CFR Part 56**

Human research subjects, Reporting and recordkeeping requirements, Safety.

**21 CFR Part 58**

Laboratories, Reporting and recordkeeping requirements.

**21 CFR Part 71**

Administrative practice and procedure, Color additives, Confidential business information, Cosmetics, Drugs, Reporting and recordkeeping requirements.

**21 CFR Part 200**

Drugs, Prescription drugs.

**21 CFR Part 201**

Drugs, Labeling, Reporting and recordkeeping requirements.

**21 CFR 207**

Drugs, Reporting and recordkeeping requirements.

**21 CFR 210**

Drugs, Packaging and containers.

**21 CFR Part 211**

Drugs, Labeling, Laboratories, Packaging and containers, Prescription drugs, Reporting and recordkeeping requirements, Warehouses.

**21 CFR Part 310**

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

**21 CFR Part 312**

Drugs, Exports, Imports, Investigations, Labeling, Medical research, Reporting and recordkeeping requirements, Safety.

**21 CFR Part 314**

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

**21 CFR Part 369**

Labeling, Medical devices, Over-the-counter drugs.

**21 CFR Part 429**

Administrative practice and procedure, Drugs, Labeling, Packaging and containers, Reporting and recordkeeping requirements.

**21 CFR Part 800**

Administrative practice and procedure, Medical devices, Ophthalmic goods and services, Packaging and containers, Reporting and recordkeeping requirements.

**21 CFR Part 812**

Health records, Medical devices, Medical research, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 3, 5, 10, 16, 25, 50, 56, 58, 71, 200, 201, 207, 210, 211, 310, 312, 314, 369, 429, 800, and 812 are amended as follows:

**PART 3—PRODUCT JURISDICTION**

1. The authority citation for 21 CFR part 3 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 353, 355, 357, 360, 360c–360f, 360h–360j, 360gg–360ss, 371(a), 379e, 381, 394; 42 U.S.C. 216, 262.

**PART 5—DELEGATIONS OF AUTHORITY AND ORGANIZATION**

2. The authority citation for 21 CFR part 5 continues to read as follows:

**Authority:** 5 U.S.C. 504, 552, App. 2; 7 U.S.C. 138a, 2271; 15 U.S.C. 638, 1261–1282, 3701–3711a; 15 U.S.C. 1451–1461; 21 U.S.C. 41–50, 61–63, 141–149, 321–394, 467f, 679(b), 801–886, 1031–1309; 35 U.S.C. 156; 42 U.S.C. 241, 242, 242a, 242l, 242n, 243, 262, 263, 264, 265, 300u–300u–5, 300aa–1; 1395y, 3246b, 4332, 4831(a), 10007–10008; E.O. 11921, 41 FR 24294, 3 CFR, 1977 Comp., p. 124–131; E.O. 12591, 52 FR 13414, 3 CFR, 1988 Comp., p. 220–223.

**§ 5.31 [Amended]**

3. Section 5.31 *Petitions under part 10* is amended by removing and reserving paragraphs (f)(2)(iii) and (f)(2)(iv).

**§ 5.73 [Removed]**

4. Section 5.73 *Certification of insulin* is removed.

**§ 5.74 [Removed]**

5. Section 5.74 *Issuance, amendment, or repeal of regulations pertaining to drugs containing insulin* is removed.

**PART 10—ADMINISTRATIVE PRACTICES AND PROCEDURES**

6. The authority citation for 21 CFR part 10 continues to read as follows:

**Authority:** 21 U.S.C. 41–50, 141–149, 321–394, 467f, 679, 821, 1034; 42 U.S.C. 201, 262, 263b, 264; 15 U.S.C. 1451–1461; 5 U.S.C. 551–558, 701–721; 28 U.S.C. 2112.

**§ 10.50 [Amended]**

7. Section 10.50 *Promulgation of regulations and orders after an opportunity for a formal evidentiary public hearing* is amended by removing and reserving paragraph (c)(10).

**PART 16—REGULATORY HEARING BEFORE THE FOOD AND DRUG ADMINISTRATION**

8. The authority citation for 21 CFR part 16 continues to read as follows:

**Authority:** 21 U.S.C. 41–50, 141–149, 321–394, 467f, 679, 821, 1034; 42 U.S.C. 201, 262, 264; 15 U.S.C. 1451–1461; 28 U.S.C. 2112.

**§ 16.1 [Amended]**

9. Section 16.1 *Scope* is amended in paragraph (b)(2) by removing the entry for “§ 429.50.”

**PART 25—ENVIRONMENTAL IMPACT CONSIDERATIONS**

10. The authority citation for 21 CFR part 25 continues to read as follows:

**Authority:** 21 U.S.C. 321–393; 42 U.S.C. 262, 263b–264; 42 U.S.C. 4321, 4332; 40 CFR parts 1500–1508; E.O. 11514, 35 FR 4247, 3 CFR, 1971 Comp., p. 531–533 as amended by E.O. 11991, 42 FR 26967, 3 CFR, 1978 Comp., p. 123–124 and E.O. 12114, 44 FR 1957, 3 CFR, 1980 Comp., p. 356–360.

**§ 25.31 [Amended]**

11. Section 25.31 *Human drugs and biologics* is amended in paragraph (f) by removing the words “or insulin.”

**PART 50—PROTECTION OF HUMAN SUBJECTS**

12. The authority citation for 21 CFR part 50 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 346, 346a, 348, 352, 353, 355, 357, 360, 360c–360f, 360h–360j, 371, 379e, 381; 42 U.S.C. 216, 241, 262, 263b–263n.

**§ 50.1 [Amended]**

13. Section 50.1 *Scope* is amended in the last sentence of paragraph (a) by removing the number “506.”

**PART 56—INSTITUTIONAL REVIEW BOARDS**

14. The authority citation for 21 CFR part 56 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 346, 346a, 348, 351, 352, 353, 355, 357, 360, 360c–360f, 360h–360j, 371, 379e, 381; 42 U.S.C. 216, 241, 262, 263b–263n.

**PART 58—GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES**

15. The authority citation for 21 CFR part 58 is revised to read as follows:

**Authority:** 21 U.S.C. 342, 346, 346a, 348, 351, 352, 353, 355, 357, 360, 360b–360f, 360h–360j, 371, 379e, 381; 42 U.S.C. 216, 262, 263b–263n.

**PART 71—COLOR ADDITIVE PETITIONS**

16. The authority citation for 21 CFR part 71 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 342, 348, 351, 355, 357, 360, 360b–360f, 360h–360j, 361, 371, 379e, 381; 42 U.S.C. 216, 262.

**PART 200—GENERAL**

17. The authority citation for 21 CFR part 200 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 358, 360e, 371, 374, 375.

18. Section 200.15 is revised to read as follows:

**§ 200.15 Definition of term “insulin.”**

For purposes of sections 801 and 802 of the act and this title, the term insulin means the active principle of the pancreas that affects the metabolism of carbohydrates in the animal body and which is of value in the treatment of diabetes mellitus. The term includes synthetic and biotechnologically derived products that are the same as, or similar to, naturally occurring insulins in structure, use, and intended effect and are of value in the treatment of diabetes mellitus.

**PART 201—LABELING**

19. The authority citation for 21 CFR part 201 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 358, 360, 360b, 360gg–360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

**§ 201.50 [Amended]**

20. Section 201.50 *Statement of identity* is amended in paragraph (b) by removing the second sentence.

**§ 201.100 [Amended]**

21. Section 201.100 *Prescription drugs for human use* is amended in paragraph (c)(2) by removing the number “, 506,”.

**PART 207—REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION**

22. The authority citation for 21 CFR part 207 is revised to read as follows:

**Authority:** 21 U.S.C. 331, 351, 352, 355, 357, 360, 360b, 371, 374; 42 U.S.C. 262.

**§ 207.25 [Amended]**

23. Section 207.25 *Information required in registration and drug listing* is amended in paragraphs (b)(2), (b)(5), and (b)(6) by removing the number “506,” and in paragraph (b)(4) by removing the number “, 506,”.

**§ 207.31 [Amended]**

24. Section 207.31 *Additional drug listing information* is amended in paragraph (a)(1) by removing the number “, 506,” and in paragraphs (a)(2), (a)(3), and (c) by removing the number “506,”.

**§ 207.37 [Amended]**

25. Section 207.37 *Inspection of registrations and drug listings* is amended in paragraph (a)(2)(i) by removing the number “506,”.

**PART 210—CURRENT GOOD MANUFACTURING PRACTICE IN MANUFACTURING, PROCESSING, PACKING, OR HOLDING OF DRUGS; GENERAL**

26. The authority citation for 21 CFR part 210 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 355, 357, 360b, 371, 374.

**PART 211—CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS**

27. The authority citation for 21 CFR part 211 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 355, 357, 360b, 371, 374.

**PART 310—NEW DRUGS**

28. The authority citation for 21 CFR part 310 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 360b–360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b–263n.

**PART 312—INVESTIGATIONAL NEW DRUG APPLICATION**

29. The authority citation for 21 CFR part 312 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 371; 42 U.S.C. 262.

30. The authority citation for 21 CFR part 312, subpart E is revised to read as follows:

**Authority:** 21 U.S.C. 351, 352, 353, 355, 357, 371; 42 U.S.C. 262.

**PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG OR AN ANTIBIOTIC DRUG**

31. The authority citation for 21 CFR part 314 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 371, 374, 379e.

**§ 314.170 [Amended]**

32. Section 314.170 *Adulteration and misbranding of an approved drug* is amended in the first sentence by removing the phrase “under sections 505, 506, and 507” and adding in its place the phrase “under sections 505(j) and 507”.

**§ 314.430 [Amended]**

33. Section 314.430 *Availability for public disclosure of data and information in an application or abbreviated application* is amended in paragraph (f)(6) by removing the phrase “under sections 505(j), 506, and 507” and adding in its place the phrase “under sections 505(j) and 507”.

**PART 369—INTERPRETATIVE STATEMENTS RE WARNINGS ON DRUGS AND DEVICES FOR OVER-THE-COUNTER SALE**

34. The authority citation for 21 CFR part 369 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 371.

**§ 369.5 [Removed]**

35. Section 369.5 *Warning required on insulin intended for over-the-counter sale* is removed.

**§ 369.21 [Amended]**

36. Section 369.21 *Drugs; warning and caution statements required by regulations* is amended by removing the entry for “INSULIN”.

**PART 429—DRUGS COMPOSED WHOLLY OR PARTLY OF INSULIN****Part 429 [Removed]**

37. Under authority of section 701(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371(a)) and section 125(a) of the Food and Drug Modernization Act (Pub. L. 105–115), amend Title 21 of the Code of Federal Regulations by removing part 429.

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**PART 800—GENERAL**

38. The authority citation for 21 CFR part 800 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 334, 351, 352, 355, 357, 360e, 360i, 360k, 361, 362, 371.

**PART 812—INVESTIGATIONAL  
DEVICE EXEMPTIONS**

39. The authority citation for 21 CFR part 812 is revised to read as follows:

**Authority:** 21 U.S.C. 331, 351, 352, 353, 355, 357, 360, 360c–360f, 360h–360j, 371, 372, 374, 379e, 381, 382, 383; 42 U.S.C. 216, 241, 262, 263b–263n.

Dated: April 17, 1998.

**William B. Schultz,**

*Deputy Commissioner for Policy.*

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