Guidance for Industry

Submitting Debarment Certification Statements

DRAFT GUIDANCE

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For questions on the content of the draft document contact Leanne Cusumano at 301-594-2041.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

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Additional copies are available from:
the Drug Information Branch (HFD-210),
Center for Drug Evaluation and Research (CDER),
5600 Fishers Lane, Rockville, MD 20857 (Tel) 301-827-4573
Internet at http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication,
Training, and Manufacturers Assistance (HFM-40)
Center for Biologics Evaluation and Research (CBER)
1401 Rockville Pike, Rockville, MD 20852-1448
Internet at http://www.fda.gov/cber/guidelines.htm
(Fax) 888-CBERFAX or 301-827-3844
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Table of Contents

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GUIDANCE FOR INDUSTRY[1]

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I. INTRODUCTION

Section 306(k) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 335a(k)), as amended by the Generic Drug Enforcement Act of 1992 (GDEA), requires that drug product applicants certify that they did not and will not use in any capacity the services of any debarred persons in connection with a drug product application. If the application is an abbreviated new drug application (ANDA), it must also include a list of all convictions described under section 306(a) and (b) of the Act (21 U.S.C. 335a(a) and (b)) that occurred within the previous 5 years and were committed by the applicant or affiliated persons responsible for the development or submission of the ANDA.

Since the passage of the GDEA, FDA has received requests for clarification of specific aspects of that part of the Act. As a result, the FDA has created this guidance to address the most common questions about the Act's certification and information requirements. The information presented here is drawn from the Act itself and from letters written by the FDA in response to specific questions.

II. 306(k)(1) CERTIFICATION REQUIREMENTS

Section 306(k)(1) of the Act states that "any application for approval of a drug product shall include a certification that the applicant did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) [section 306(a) or (b)] in connection with such application."

A. Applications Subject to the Certification Requirements of Section 306(k)(1)

The following drug product applications received by the FDA on or after June 1, 1992, should include a certification statement:

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[1] This draft guidance has been prepared by the Debarment Task Force at the Food and Drug Administration (FDA). This guidance document represents the Agency's current thinking on debarment certification statements. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

- New drug applications (NDAs)
- Abbreviated new drug applications (ANDAs)
- New animal drug applications (NADAs)
- Abbreviated new animal drug applications (ANADAs)
- Export applications for certain unapproved products
- Biological license applications (PLAs and BLAs)
- Supplements to certain drug product applications

B. Wording of the Certification Statement

The FDA regards the following wording, taken from section 306(k)(1) of the Act, as the most acceptable form of certification:

> *[Name of the applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.*

Use of conditional or qualifying language, such as *to the best of my knowledge*, is unsatisfactory.

In the case of NADAs and ANADAs, applicants may simply sign the standard certification form 356-V provided by the Agency, which contains the preferred language for certification.

C. Domestic Agents

Domestic agents should countersign the certification for foreign applicants they represent under 21 CFR 314.50(a)(5).

D. Persons Covered by the Certification

Under the Act, the term *person* includes an individual, partnership, corporation, and association. The Agency regards *services* in connection with the application to include any services related to the collection, monitoring, evaluation, analysis, or reporting of data or information that appears or is specifically incorporated by reference in the application. Persons whose services were used in any capacity in connection with the application include, but are not limited to, the following:

- Employees of the applicant

- Certain contractors and their employees (e.g., contract research organizations whose studies were used in the application)

- Certain subcontractors and their employees (e.g., consultants hired by a contract research organization)

- Clinical investigators

- Persons contributing data and information contained in a drug master file (DMF) or public master file (PMF), incorporated by reference in the application

E. Basis of Certification

To ensure the accuracy of its certification, the applicant should check its list of employees and other persons with whom it does business against the list of debarred persons. This list is available upon written request from the Division of Compliance Policy (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857 and on the Internet at http://www.fda.gov/ora/compliance_ref/debar/debar.txt.

The applicant also may request certification statements from employees, contractors, subcontractors, clinical investigators, DMF or PMF holders, and the employees of such persons. The DMF or PMF holder may include a certification in the DMF or PMF, thereby allowing all referencing applicants to rely on that one certification, or the DMF or PMF holder may provide a separate certification to each applicant. The applicant's certification should pertain to all persons who have contributed data or information related to the collection, monitoring, evaluation, analysis, or reporting of data or information that appears or is specifically incorporated by reference in the application, regardless of whether such persons submit certifications directly to the FDA or to the applicant.

Because the statutory language of the certification statement is both retrospective and prospective (i.e., the applicant *did not* and *will not* use in any capacity the services of any person debarred in connection with the application), the applicant need not later obtain updated written statements from employees, contractors, and others, unless there is reason to believe that the original certification statement is incorrect or that the applicant has used, in connection with the application, amendment, or supplement, the services of a person not used in the previous submission. In such instances, the applicant has an ongoing duty to ensure the continued correctness of the certification.

F. Supplements

Supplements to ANDAs that provide for a *different or additional* use of the drug are the only kind of supplement that should contain a certification.

For the purpose of this Guidance, supplements providing for a *different or additional use* of the drug are those that provide for a new use (1) not covered by the application approved for the listed drug and (2) supported by clinical data (i.e., a supplement providing for a new indication, dosage form, or strength that requires supporting clinical data). ANDA requests for approval of a new use not approved for the listed drug and supported by clinical data submitted under section 505(b)(2) of the Act (21 U.S.C. 355(b)(2)) are deemed *applications,* rather than *supplements,* and should include a certification.

For example, a supplement to an ANDA that improves the formulation or manufacturing process, changes ingredient suppliers, or proposes other production changes not requiring clinical data, does not require certification. A supplement to an ANDA that adds an indication to the labeling of the generic drug because exclusivity has expired for that indication need not contain a certification.

G. Scope of Debarment

The Act prohibits a debarred individual from providing services in any capacity to a person that has an approved or pending drug product application (section 306(a)(2) and (b)(1) of the Act). The Agency has interpreted "services in any capacity" to mean any service provided to the drug applicant, regardless of whether related to drug regulation. That means a debarred individual may not provide non-drug-related services to a drug product applicant (e.g., as a landscaper, a computer software supplier, an accountant, a telephone repair person, a janitor, an interior decorator, a landlord) without violating debarment. Both the firm and individual are subject to substantial civil penalties for violation of this provision.

H. Scope of Certification

The scope of certification under section 306(k) of the Act is narrower than the scope of debarment under section 306(a)(2) and (b)(1). Section 306(k) of the Act states that an applicant should certify that it did not and will not use in any capacity the services of a debarred person *in connection with such application*. Thus, the applicant should certify only with regard to any services received in connection with the application. FDA considers such services to include but not be limited to services related to the collection, monitoring, evaluation, analysis, or reporting of data or information that appears or is

specifically incorporated by reference in the application.

Persons included in the certification include but are not limited to the applicant's own employees, contractors (e.g., a contract research organization used to run a study), subcontractors (e.g., a special consultant hired by a contract research organization), clinical investigators, DMF or PMF holders, and employees of such persons, regardless of whether foreign or domestic.

An applicant using the services of a debarred person may certify that they have not used the services of a debarred person as long as the services provided by the debarred person were not provided in connection with the application. However, under section 307(a) of the Act (21 U.S.C. 335b(a)), both the applicant using the services of a debarred person in any capacity and the debarred person may be subject to substantial civil money penalties.

I. Limitations on Stock Ownership of Debarred Persons

A debarred person may own stock in a firm that has an approved or pending drug product application, but may not participate in any capacity in business decisions or operations of such a firm (e.g., participating in shareholder voting) without violating debarment.

In addition, if a debarred person exercises any control over business decisions or operations of a firm that has an approved or pending drug product application, for example, via shares owned by someone other than the debarred person (i.e., any member of the debarred person's family, or any other individual, partnership, corporation, or association), the FDA will regard the debarred person as providing services to a drug product applicant in violation of debarment. In such instances, both the firm and the debarred person would be subject to substantial civil money penalties for violation of debarment.

J. Investigational Drugs

Applications for investigational drugs described under 21 CFR 312.40 (INDs), 21 CFR 312.110(a) (import INDs), 21 CFR 312.110(b) (export INDs), or 21 CFR 511.1 (INADs) do not require a certification statement because INDs and INADs are not considered drug product applications under the GDEA. INDs and INADs are submitted for the purpose of clinical research. However, it should be noted that the certification required in a drug application for approval (e.g., an NDA) precludes the use of a debarred person in connection with any IND associated with that application.

K. Over-the-Counter (OTC) Monograph Drugs

The certification requirement applies to any application for approval of a drug product. A monograph is *not* an application; thus, drugs marketed under the conditions of an OTC monograph are not subject to the certification requirement.

L. Biologics License Applications

Upon submission of an application for approval of a biological drug product by the single biologics license application (BLA) (§ 351(a) of the Public Health Service Act), an applicant would be asked to certify that no debarred person was used in connection with the application. This certification, if truthful, would preclude the use of a debarred person in connection with both the establishment and the application.

M. Debarment Status

If the services of a debarred person were used in connection with the application prior to that person's debarment or after termination of debarment, a firm could still properly certify because the person was not debarred at the time his or her services were rendered. However, data generated by a person prior to the person's debarment, or data generated after termination by a formerly debarred person, may be subject to closer examination by the Agency. Therefore, the applicant should inspect and ensure the integirty of such data.

III. 306(k)(2) CONVICTION INFORMATION REQUIREMENTS

Section 306(k)(2) of the Act states that "any application for approval of a drug product shall include . . . if such application is an abbreviated drug application, a list of all convictions, described in subsections (a) and (b) [section 306(a) and (b)] which occurred within the previous 5 years, of the applicant and affiliated persons responsible for the development or submission of such application."

A. Applications Subject to the Conviction Information Requirement

The Act requires that ANDAs and supplements to ANDAs providing for a *different or additional use* and submitted on or after June 1, 1992, contain a list of all convictions

within the previous 5 years[2] committed by the applicant and affiliated persons responsible for the development or submission of such application.

The section 306(k)(2) requirement for conviction information in ANDA supplements for a *different or additional* use is limited to those supplements that provide for a new use (1) not covered by the application approved for the listed drug and (2) supported by clinical data (i.e., supplements providing for a new indication, dosage form, or strength that requires supporting clinical data). ANDA requests for approval of a new use, not approved for the listed drug and not supported by clinical data, submitted under section 505(b)(2) of the Act are deemed *applications*, rather than *supplements*, and should include conviction information.

Note that a supplement to an ANDA that adds an indication to the labeling of the generic drug because exclusivity has expired for that indication need not contain conviction information. A supplement to an ANDA that improves the formulation or manufacturing process, changes ingredient suppliers, or proposes other production changes does not require conviction information, unless the supplement contains clinical data.

B. Definition of an Affiliated Person

An *affiliated person* for whom an applicant for approval of an ANDA should provide conviction information includes any individual, partnership, corporation, or association, including employees thereof, involved with development or submission of data that (1) are used to obtain approval of an application and (2) relate to the manufacturing, processing, or testing of the active ingredient(s) or the finished dosage form(s).

The ANDA applicant should provide conviction information for persons falling within the scope of this definition. Generally, the conviction information provided by an applicant for approval of an ANDA pertains to employees of the applicant, contractors, subcontractors, and so on, responsible for the development or submission of the abbreviated application because such persons are within the meaning of *affiliated person*. Some examples follow.

1. Clinical investigators, nurses, technicians, and other parties involved with the development or submission of data related to clinical studies: These are *affiliated persons*.

[2] Section 306(a) and (b) describes *types* of convictions that fall under the scope of the debarment provisions in very broad terms. Therefore, the FDA cannot provide a definitive list of such offenses or a list of all individuals and businesses with convictions for such offenses.

2. CGMP record keepers: Because the FDA reviews CGMP records when determining whether to grant or continue approval of a drug product, persons who develop and record CGMP data related to the manufacturing, processing, or testing of the active ingredient(s) or the finished dosage form(s) are *affiliated persons*.

3. Commercial manufacturing facility workers: Such persons are *affiliated persons* if they are involved in the development or submission of records or data that are used to obtain and maintain approval of an application or relate to the manufacturing, processing, or testing of the active ingredient(s) or the finished dosage form(s). For example, persons recording and generating data solely for the approved commercial product are *affiliated persons* because FDA reviews such records in determining whether to grant or continue approval of a drug product.

4. Persons working on drug master files (DMFs) or public master files (PMFs): Persons recording and generating data for DMFs or PMFs that are relied on to support approval and that relate to, for example, the manufacturing, processing, or testing of the active ingredient(s) or finished dosage form(s), come within the definition of *affiliated person*.

5. Secretaries: If the secretary merely transcribes data, the secretary is not regarded as an *affiliated person* within the intended definition of the Act. In the rare instances that the secretary may develop data used to obtain approval, that secretary is an *affiliated person.*

6. Janitors, packers, production crew, and assembly persons: As long as these persons do not develop or submit data, they are not *affiliated persons.*

C. Contents of Conviction Information

The list of convictions should include the following information:

- The name(s) of the convicted persons(s)
- The title and section of the Federal or State statute involved
- The date of the conviction (for which a person can be debarred, as described in section 306(a) and (b), that occurred within 5 years before the date of the application)
- The date of sentencing

- The court entering judgment
- The case number, if known
- A brief description of the offense
- The role of the person in the development or submission of the application
- The time period of the person's involvement in the development of the application

D. Basis of Conviction Information

Background checks are not necessary. The applicant may request conviction information received from the applicant's affiliated persons.

Under the Act (section 306(k)(2)), conviction information is required for persons no longer working for the firm, but who were affiliated persons involved with the development or submission of the application. However, if the applicant cannot ascertain conviction information for all affiliated persons because of unavailability of the person(s), the FDA may accept the names and job titles of such people (including a description of the responsibilities that person had concerning the application) together with an explanation of why the person is unavailable (e.g., the person died or the person no longer works for the firm and reasonable efforts to locate the person have proven unsuccessful) and a statement that the applicant has no knowledge that the person has been convicted of any offense(s) for which a person can be debarred.

E. Effect on Review Process

If the conviction information provided raises a question concerning the integrity of the data or information contained in the application for which the certification is submitted, or in any other application, the application(s) may be subject to closer Agency scrutiny.

IV. MISCELLANEOUS 306(k) CERTIFICATION AND CONVICTION INFORMATION REQUIREMENTS

A. Amendments to Pending Drug Product Applications

As long as the original application contains the required statement of certification and/or conviction information, there is no need to resubmit such statements in amendments described under 21 CFR 314.60(a). However, the applicant has an ongoing duty to ensure

the continued correctness of the certification and conviction information. Therefore, if the original statement becomes incorrect (i.e., the applicant has used the services of a debarred or convicted person not used in the previous submission), the applicant has a responsibility to correct the certification and/or conviction information in the amendment as soon as possible.

B. Effective Date of Certification and Conviction Information Requirements

Drug product applications, including certain supplements submitted on or after June 1, 1992, are subject to the certification and/or conviction information requirements.

C. Placement in the Application

The certification and/or conviction information should appear at the beginning of the application and be clearly identified. The applicant may indicate the placement of the information in the table of contents. In the case of an NADA or ANADA, a standard certification form 356-V is provided by the Agency; thus the placement of the certification statement in such applications is already established.

D. Missing or Incorrect Information

If a drug product application, amendment, or supplement submitted on or after June 1, 1992, lacks or contains incorrect certification or conviction information, the applicant should amend the application, amendment, or supplement to include or correct the certification or conviction information as soon as possible. Since February 25, 1993, the FDA has not accepted for filing ANDAs that do not contain certification and conviction information. The applicant has an ongoing duty to ensure that the certification or conviction information is correct.

E. Signature

The certification and/or conviction information should be signed by a responsible officer of the applicant or by the individual responsible for signing the application.

V. REFERENCES

The Generic Drug Enforcement Act of 1992, section 306 (21 U.S.C. 335a).

July 27, 1992, guidance letter from FDA's Deputy Commissioner for Operations.

April 8, 1994, letter from FDA's Acting Director for the Office of Generic Drugs, CDER.