

Food and Drug Administration
Rockville MD 20857

1774 '00 APR 14 10:03

April 12, 2000

Abu Quamruzzaman
178-10 Wexford Terr.
Apt. 5C
Jamaica, NY 11432

Re: Docket No. 93N-0462

Dear Mr. Quamruzzaman:

This is in response to your letter dated March 23, 2000, in which you seek further clarification of my letter dated April 5, 1999, regarding your debarment. That earlier letter of mine was in response to your letter of March 30, 1999, which contained questions about working for a company that makes OTC products, vitamins and herbal products, and cosmetics. You now wish to know whether you can work in a "contract laboratory that does not have any new drug applications (NDAs) or abbreviated new drug applications (ANDAs) of its own, but has pharmaceutical clients that do submit NDAs and ANDAs."

As I mentioned in my previous letter, the terms of your debarment state that you are prohibited from providing services in any capacity to a person, including a company, that has an approved or pending drug product application. I have enclosed two items that you may find useful in gaining a better understanding of the scope of your debarment. The first is a key court decision (*DiCola v. FDA*). You should note especially pages 6-7 and 9-11. The second is a draft Guidance titled *Submitting Debarment Certification Statements*. As you will see, a pharmaceutical company that uses the services of a debarred person in connection with an NDA or ANDA -- even if that debarred person worked for a contract research organization, i.e., even if the debarred person were not an employee of the pharmaceutical company -- would be in a very bad position with respect to that NDA or ANDA.

I hope this information is helpful.

Sincerely yours,

Dave Read
Supervisory Regulatory Counsel
Regulatory Policy Staff (HFD-7)
Center for Drug Evaluation and Research

Enclosures

cc: HFA-305/Docket No. 93N-0462

93N-0462

ANS 2

Notice: This opinion is subject to formal revision before publication in the Federal Reporter or U.S.App.D.C. Reports. Users are requested to notify the Clerk of any formal errors in order that corrections may be made before the bound volumes go to press.

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued October 3, 1995

Decided March 1, 1996

No. 94-1689

CHARLES G. DiCOLA
PETITIONER

v.

FOOD AND DRUG ADMINISTRATION,
RESPONDENT

On Petition for Review of an Order of the
Food and Drug Administration

Robert A. Dormer argued the cause for petitioner, with whom *Roger C. Thies* and *Alan G. Minak* were on the briefs.

Andrew E. Clark, Attorney, U.S. Department of Justice, argued the cause for respondent, with whom *Frank W. Hunger*, Assistant Attorney General, *Eugene M. Thirolf, Jr.*, Director, and *Lawrence G. McDade*, Deputy Director, Office of Consumer Litigation, U.S. Department of Justice, were on

Bills of costs must be filed within 14 days after entry of judgment. The court looks with disfavor upon motions to file bills of costs out of time.

the brief. *Gerald C. Kell*, Attorney, U.S. Department of Justice, entered an appearance.

Before: BUCKLEY, GINSBURG, and TATEL, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge GINSBURG*.

GINSBURG, Circuit Judge: Charles DiCola petitions this court for review of a final order of the Food and Drug Administration permanently debarring him from "providing services in any capacity" to the pharmaceutical industry. Finding no merit in any of the three constitutional claims he raises, we deny the petition.

I. Background

From 1980 to 1990 DiCola worked for Bolar Pharmaceutical Company, Inc. As General Manager of Production and Vice President of Operations, he was responsible for supervising the manufacture and distribution of Bolar's drug products.

In 1992 DiCola pled guilty to violations of the Food, Drug, and Cosmetic Act, as currently codified at 21 U.S.C. §§ 331(e) & (k), 333(a)(2), to wit, adulterating a drug product, within the meaning of 21 U.S.C. § 351(a)(2)(B), and failing to keep accurate batch production records, as required by 21 U.S.C. § 355(j)(1). Specifically, DiCola directed Bolar employees to manufacture a drug using ingredients and following procedures different from those that had been approved by the Food and Drug Administration and to conceal the differences from the FDA by preparing false records. DiCola paid a fine and served a prison sentence.

Prior to DiCola's guilty plea but still several years after the conduct to which he confessed, the Congress passed the Generic Drug Enforcement Act of 1992, an amendment to the FDCA. 21 U.S.C. §§ 335a-385c. In the 1992 Act, the Congress reported having found "substantial evidence [of] significant corruption" in the drug approval process, and the need for measures "designed to restore and to ensure the integrity of the . . . process and to protect the public health." 21

U.S.C. § 335a note (quoting Pub. L. No. 102-282, § 1(c)). To that end, the Congress required the Secretary of Health and Human Services to debar anyone convicted of a felony related to the federal regulation of drug products from thereafter "providing services in any capacity to a person that has an approved or pending drug product application." 21 U.S.C. § 335a(a)(2).

In February 1993 the Secretary, proposing to debar DiCola, notified him of his right to a hearing if he could establish a genuine issue of fact relevant to the proposed debarment. See 21 U.S.C. § 335a(i). DiCola requested the hearing but raised no issue of fact. Instead, he objected to his proposed debarment on the ground that it would violate the Ex Post Facto and Double Jeopardy Clauses of the United States Constitution (Article I, § 9 and Amendment V, respectively). In addition, DiCola claimed that the vagueness of the proposed order of debarment—which reiterated the terms of § 335a(a)(2) without further specification—would prevent him from engaging in "activities [that] could not adversely affect the regulatory process or public health and safety" and thus impose upon him a penalty "unrelated to any valid regulatory purpose." Specifically, DiCola informed the FDA that prior to his conviction he had been "employed as a salesman of printing materials including labels and labeling used with drug products" and that he feared "such activities might be debarred because of the vagueness of [§ 335a(a)(2)] combined with the FDA's lack of interpretation." In a follow-up letter, DiCola asked the FDA to define the phrase "service in any capacity" and to indicate whether DiCola's renewed employment as a salesman of drug labels and labeling would indeed be precluded by his debarment.

In November 1993 the Secretary denied DiCola's request for a hearing, rejected DiCola's constitutional claims, and permanently debarred him. 58 Fed. Reg. 59,044. As for DiCola's request for clarification, the Secretary concluded that the statutory phrase "provide services in any capacity" is "clear on its face." To wit: "A debarred individual cannot provide any type of service to a person that has an approved or pending drug product application." *Id.* at 59,045/2. To

DiCola's objection that the phrase, read literally, describes conduct unrelated to any valid regulatory purpose, the Secretary responded that the

Congress can legitimately achieve [its] purpose [of protecting the public health] by prescribing "all services" due to the serious administrative difficulties involved in distinguishing between those positions clearly related to drug regulation from those clearly not regulated. These difficulties would include the problem of ascertaining the exact nature of the employee's relationship with the employer as well as defining what constitutes a sufficient nexus with the regulatory scheme under all circumstances.

Id. at 59,045/2-3.

When the Secretary denied his petition for reconsideration, DiCola petitioned this court for review of the final debarment order. Here he renews his claims that the order violates the double jeopardy and *ex post facto* clauses of the Constitution and reasserts as a deprivation of due process his claim that the order does not give him adequate notice of what conduct it prohibits. The parties agree that DiCola raised these issues before the agency, that no material facts are in dispute, and that this court should review DiCola's legal arguments *de novo*.^{*}

^{*} In a footnote to his opening brief, DiCola suggests that, properly interpreted, § 335a does not apply retroactively. The FDA answers, also in a footnote, that DiCola has waived the issue because he failed to raise it before the agency. In his reply brief DiCola, who again relegates the matter to a footnote, does not claim that he did raise the issue before the FDA. As the parties have argued the issue in the margins, so too do we dispose of it.

Because DiCola apparently concedes his failure to raise the issue of statutory construction before the agency, we hold that this circuit's waiver doctrine precludes him from raising the issue in his petition for review. See *State of Ohio v. U.S.E.P.A.*, 997 F.2d 1520, 1528-29 (D.C. Cir. 1993) (interests in agency autonomy and judicial efficiency both served by extending waiver doctrine to "purely legal" statutory interpretation claim not raised during rulemaking).

II. Analysis

The validity of DiCola's debarment under the double jeopardy and ex post facto clauses of the Constitution depends upon whether it is a wholly remedial or in part a punitive measure. *DeVeau v. Braisted*, 363 U.S. 144, 160 (1960) ("The mark of an ex post facto law is the imposition of what can fairly be designated punishment for past acts [or] ... whether the restriction of the individual comes about as a relevant incident to a regulation of a present situation"); *United States v. Halper*, 490 U.S. 435, 446-451 (1989) (discussing "whether and under what circumstances a civil penalty may constitute punishment for the purpose of the Double Jeopardy Clause"). The Supreme Court's decision in *United States v. Halper*, *supra*, governs that question. DiCola's due process claim turns upon whether the terms of the debarment order, which are prescribed by the statute itself, provide him with fair notice of the conduct they forbid.

A. The Double Jeopardy and Ex Post Facto Claims: Punishment vs. Remediation

In *Halper*, *supra*, the Supreme Court gave us what the Second Circuit has aptly dubbed a "rule of reason," *see United States v. Certain Real Property and Premises*, 954 F.2d 29, 34 (1992), for the resolution of disputes such as this:

[T]he determination whether a given civil sanction constitutes punishment in the relevant sense requires a particularized assessment of the penalty imposed and the purposes that the penalty may fairly be said to serve.

[A] civil sanction that cannot fairly be said solely to serve a remedial purpose, but rather can only be explained as also serving either retributive or deterrent purposes, is punishment, as we have come to understand this term. [A] defendant who already has been punished

As DiCola notes, we recognize an exception to the waiver doctrine where "a matter of great public importance" is at stake. *Id.* DiCola's waiver is not likely, however, to have an adverse impact upon anyone but himself.

in a criminal prosecution may not be subjected to an additional civil sanction to the extent that the second sanction may not fairly be characterized as remedial, but only as a deterrent or retribution.

Halper, 490 U.S. at 448-49. DiCola argues that a debarment imposed pursuant to § 335a(a) must be regarded as punitive because of its (1) broad sweep, (2) unlimited duration, and (3) origin in the purpose of the Congress (as reflected in legislative history) to punish. The Seventh Circuit recently rejected the same arguments and endorsed the agency's view of the matter, holding that a debarment under § 335a(a) is "solely remedial." See *Bae v. Shalala*, 44 F.3d 489, 497 (7th Cir. 1995). For the reasons set forth below, so do we.

1. *Breadth.* DiCola argues that the statutory terms, which the agency incorporated into the order, describe "more than those activities that are rationally related to the drug approval process"; as a result, he urges, the debarment is "so broad as to be excessive and serves no valid [i.e., remedial] regulatory purpose." For example, says DiCola, under the order he cannot be employed by "a construction company that builds a drug manufacturing facility," "a telephone company that provides service to a drug company," or "a company that prints labels approved by FDA for a drug company."

The FDA concedes that in some applications the literal terms of the statute (and hence of the order) would be "absurd." We take this as an acknowledgment that the FDA must construe and apply those terms with an eye to the remedial purpose of the statute and that this remedial purpose does not justify a literal reading of those terms. If the FDA had not wisely conceded the point, we would have insisted upon it in order to save the statute from constitutional infirmity under the double jeopardy clause. See *DeBartolo Corp. v. Florida Gulf Coast Building and Construction Trades Council*, 485 U.S. 562, 573 (1988).

Having conceded that the statute and the debarment order cannot mean quite what they say, the FDA nevertheless defends the terms of both as necessary in order to avoid two

administrative difficulties. The first is the problem of "ascertaining the exact nature of [an] employee's relationship with [his] employer," and the second is the difficulty of "defining what constitutes a sufficient nexus with the regulatory scheme under all circumstances." 58 Fed. Reg. 59,045/2-3. The latter problem explains the agency's unwillingness to write its debarment order in terms more specific than those of the statute. We will focus upon that problem when we take up DiCola's due process claim. For the moment, we confine our attention to the first problem identified by the FDA; it is the one that explains why the agency believes that the remedial purpose of the statute justifies a broader scope of debarment than DiCola believes it does.

DiCola does not dispute that in some cases the agency may encounter genuine difficulty in "ascertaining the exact nature of [his] relationship with [an] employer." Indeed, we think it quite reasonable for the FDA to be concerned about any employment that might create an opportunity for regular and frequent contact between DiCola and the management of a drug company. The agency would find it very difficult, if not impossible, to assure itself and the public that DiCola is not, through that contact, actually selling advice or other services related to the circumvention of federal regulation. This is reason enough for making the debarment sufficiently broad to cover DiCola's employment as a salesman of labels and printing services to the pharmaceutical industry, to take his example. See *Siegel v. Lyng*, 851 F.2d 412, 416, 417-18 (D.C. Cir. 1988). We remind the agency, however, that even its legitimate concern with prophylaxis has its limits, and the debarment order must not be applied beyond them.

2. *Duration.* With exceptions not relevant here, debarment under 21 U.S.C. § 335a(a)(2) is permanent. § 335a(c)(2)(ii), (d)(3)(B) and (4)(D). The permanence of the debarment can be understood, without reference to punitive intent, as reflecting a congressional judgment that the integrity of the drug industry, and with it public confidence in that industry, will suffer if those who manufacture drugs use the services of someone who has committed a felony subversive of FDA regulation. See 21 U.S.C. § 355a note. That judgment

may proceed from a skeptical view of the malleability of individual men and women, see *Harcker v. New York*, 170 U.S. 189, 196 (1898) ("It is not open to doubt that the commission of crime . . . has some relation to the question of character. It is not, as a rule, the good people who commit crime"); or from a greater concern with the cost of an error visited upon the public than with the cost of an error felt only by the excluded felon, see *id.* at 197 ("Doubtless, one who has violated the criminal law may thereafter reform, and become in fact possessed of a good moral character. But the legislature has power in cases of this kind to make rule of universal application"); or more likely from the cumulative force of both sentiments.

DiCola urges us to distinguish the many cases construing various employment restrictions as remedial on the ground that none involved a debarment of breadth and duration comparable to the debarment imposed upon him by the FDA, yet he offers no reason to suppose that the agency's legitimate enforcement concerns, which account for the breadth, will fade over time. For the present purpose, therefore, the remedial understanding of the congressional judgment that the debarment should be permanent is not unreasonable.

3. *Purpose.* The legislative history that DiCola cites indicates that the legislators who spoke to the 1992 Act appreciated and approved its deterrent (*i.e.*, punitive) as well as its remedial effects. That history does not indicate that they regarded either the scope or the duration of the debarment required by § 335a(a) as punitive, however. The remarks upon which DiCola relies were addressed to the 1992 Act as a whole, rather than to the mandatory debarment provision specifically. Because the Act also provided for civil penalties, 21 U.S.C. § 335b, which obviously are punitive, we cannot say with the needed confidence that the legislature intended debarment to be at all punitive. The legislative history, therefore, hardly offers the "unmistakable evidence of punitive intent." *Flemming v. Nestor*, 363 U.S. 603, 619 (1960), that would impel a court to hold that § 335a(a) violates the double jeopardy clause or that its application in this case violates the *ex post facto* clause. *Id.* at 617 ("Judicial Inqui-

ries into Congressional motives are at best a hazardous matter, and when that inquiry seeks to go behind objective manifestations it becomes a dubious affair indeed").

B. The Due Process Claim: Herein of Vagueness

"Two principal concerns undergird the requirement that governmental enactments be sufficiently precise: *first*, that notice be given to those who may run afoul of the enactment and, *second*, that the enactment channel the discretion of those who enforce it." *United States v. Thomas*, 864 F.2d 188, 194 (D.C. Cir. 1989); see *Connally v. General Construction Co.*, 269 U.S. 385, 391 (1926). Of these, the second is the greater, *id.* (citing *Kolender v. Lawson*, 461 U.S. 352, 358 (1983)), yet DiCola focuses upon the first. He argues that the debarment order requires him to guess, at his peril, what employment it prohibits.

The precision required by due process varies, of course, with "the nature of the enactment." *Village of Hoffman Estates v. Flipside, Hoffman Estates, Inc.*, 455 U.S. 489, 498 (1982). The Constitution is most demanding of a criminal statute that limits First Amendment rights; yet even there it requires only a "reasonable specificity to provide fair notice," and not "that a person contemplating a course of behavior know with certainty whether his or her act will be found to violate the proscription." *Thomas*, 864 F.2d at 195. Still "greater leeway" is permissible in a statute regulating business activities: "[N]o more than a reasonable degree of certainty can be demanded and it is not unfair to require that one who deliberately goes perilously close to an area of proscribed conduct shall take the risk that he may cross the line." *Throckmorton v. Nat'l Transportation Safety Board*, 963 F.2d 441, 444-45 (D.C. Cir. 1992) (citing *Boycie Motor Lines v. United States*, 342 U.S. 337, 340 (1952)).

Literally construed, the order debaring DiCola establishes a fairly simple rule of conduct: Do not provide any service to a drug manufacturer, either directly as an employee or indirectly as the employee of a company that provides such a

service. As noted earlier, however, literal application of the order would also be excessive when measured by the remedial purpose of the statute that it implements. The FDA chose, nonetheless, not to write the debarment order in terms more specific than those in the statute because of the difficulty inherent in "defining what constitutes a sufficient nexus with the regulatory scheme under all circumstances." 58 Fed. Reg. 59,045/2-3. DiCola does not deny that this is a problem, but he does not even try to show that there might be a standard that would provide better notice to persons debarred without unduly restricting the agency's ability to take appropriate action in the unanticipated case sure to arise.

Moreover, that the statute and the order must be construed not literally but with reference to their remedial purpose does not render them unconstitutionally vague. As we have said, the remedial purpose of the statute constrains the FDA's discretion to sanction DiCola for a violation, and DiCola is on notice that, without prior approval from the FDA, he gets close to the pharmaceutical industry at his peril. Cf. *Throckmorton*, 663 F.2d at 443, 444 (sustaining prohibition against flying an aircraft "so close to another as to create a collision hazard").

For the most part, DiCola should have little or no trouble determining whether his debarment precludes his availing himself of a particular opportunity. He professes not to know whether he may work as a cook in the cafeteria of a drug company or even whether he may sell goods to a food service contractor that operates a drug company's cafeteria. We think it quite clear, however, that all direct employment by a drug company, whether in the board room or the cafeteria or somewhere in between, comes within the remedial scope of the debarment order; such employment would raise the risk to which we have alluded and concomitantly increase the supervisory burden upon the FDA. Just as clearly, DiCola's selling provisions to a food service contractor that in turn operates a drug company's cafeteria is not even within the literal scope of the debarment order.

The hard cases involve DiCola's employment by an enterprise that provides goods or services to a drug manufacturer—which is not to say that all such cases are hard. Indeed, the FDA concedes that it would be "ludicrous" to apply the debarment so as to sanction DiCola for "doing janitorial work at a telephone company" that provides service to a drug manufacturer. The agency does not say why it would be ludicrous, but surely the answer is that the position in question would not put DiCola into regular contact with the management of a drug company. Other types of employment by a supplier of goods or services to a drug company might do just that.

It is therefore fanciful for DiCola to say that he can only "guess" at the meaning of the debarment order; he will usually have a pretty good idea whether a position with a firm that is not itself a drug manufacturer runs afoul of the remedial purpose for which he has been debarred from providing services to a drug house. As we have said before, it is often sufficient, so far as due process is concerned, "that the proscription mark out the rough area of prohibited conduct, allowing law-abiding individuals to conform their conduct by steering clear of the prohibition." *Thomas*, 864 F.2d at 194.

Finally, DiCola is not utterly without relief from such real uncertainty, if any, as he may face. At oral argument counsel for the FDA represented that DiCola may seek a prospective ruling about a specific employment opportunity by filing a "citizen's petition" with the agency. DiCola conceded this and that the FDA has said it will endeavor to respond to such petitions within 60 days, but claims that the agency has, in fact, kept some citizens' petitions pending for years. Given the nature of DiCola's interest, the opportunity to obtain a prospective ruling would be worthless if the agency unreasonably delayed its response to his inquiry. If DiCola in fact encounters unreasonable delay, however, he may petition this court for a writ of mandamus, see *Telecommunications Research & Action v. F.C.C.*, 750 F.2d 70, 79 (D.C. Cir. 1984); in such an action the court will consider that DiCola's livelihood may be at stake, *id.* at 80, and "need not find any impropriety

12

lurking behind agency lassitude in order to hold that agency action is unreasonably delayed," *id.*

III. Conclusion

For the foregoing reasons, DiCola's petition for review of the FDA's order debarring him from providing services in any capacity to the pharmaceutical industry is

Denied.

Guidance for Industry

Submitting Debarment Certification Statements

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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)**

**September 1998
Procedural #**

Draft - Not for Implementation

Table of Contents

I.	INTRODUCTION	1
II.	306(k)(1) CERTIFICATION REQUIREMENTS	1
A.	Applications Subject to the Certification Requirements of Section 306(k)(1)	1
B.	Wording of the Certification Statement	2
C.	Domestic Agents	2
D.	Persons Covered by the Certification	2
E.	Basis of Certification	3
F.	Supplements	3
G.	Scope of Debarment	3
H.	Scope of Certification	3
I.	Limitations on Stock Ownership of Debarred Persons	5
J.	Investigational Drugs	5
K.	Over-the-Counter (OTC) Monograph Drugs	6
L.	Biologics License Applications	5
M.	Debarment Status	6
III.	306(k)(2) CONVICTION INFORMATION REQUIREMENTS	6
A.	Applications Subject to the Conviction Information Requirement	6
B.	Definition of an Affiliated Person	7
C.	Contents of Conviction Information	8
D.	Basis of Conviction Information	9
E.	Effect on Review Process	9
IV.	MISCELLANEOUS 306(k) CERTIFICATION AND CONVICTION INFORMATION REQUIREMENTS	9
A.	Amendments to Pending Drug Product Applications	9
B.	Effective Date of Certification and Conviction Information Requirements	10
C.	Placement in the Application	10
D.	Missing or Incorrect Information	10
E.	Signature	10
V.	REFERENCES	10

Draft - Not for Implementation

GUIDANCE FOR INDUSTRY¹

Submitting Debarment Certification Statements

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:

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.

Draft - Not for Implementation

- 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

Draft - Not for Implementation

- 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.

Draft - Not for Implementation

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

Draft - Not for Implementation

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.

Draft - Not for Implementation

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 integrity 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

Draft - Not for Implementation

within the previous 5 years² 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.

Draft - Not for Implementation

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

Draft - Not for Implementation

- 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

Draft - Not for Implementation

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.

Draft - Not for Implementation

January 15, 1993, letter from FDA's Director for the Office of Generic Drugs, CDER.