many cancer studies of industrial cohorts have excluded women. This study will provide information concerning: (1) the incidence of breast cancer in a cohort of women exposed to ethylene oxide (ETO), and (2) the incidence of breast cancer in a cohort of women exposed to polychlorinated biphenyls (PCBs). Both compounds are suspected breast carcinogens. These two cohorts have been previously assembled by NIOSH, and each represents the largest and best defined female study cohort in the U.S. for the respective exposure.

All women in the existing NIOSH ethylene oxide cohort (n=9,929) and PCB cohort (13,736) will be enrolled in the study. For both cohorts, data from personnel records has been coded into a computer file containing demographic, and work history information. This information will be used to estimate workplace exposures. Vital status has been determined through automated data sources. Questionnaires are currently being mailed to each living cohort member to obtain information on breast cancer incidence and risk factors for breast cancer. For deceased cohort members, next-of-kin will be asked to provide this information. Other record sources such as death certificates and population-based cancer incidence registries will also be used to identify cancer cases. The diagnosis will be confirmed by medical records. Each questionnaire will take approximately 30 minutes to complete. Total annual burden hours are 12,500.

Respondents	Number of respondents	Number of responses/ respondent	Avg. burden/response (in hours)	Total burden (in hours)
Workers	23,000	1	.50	11,500
Medical providers	2,000	1	.50	1,000

2. Tests and Requirements for Certification and Approval of Respiratory Protective Devices—42 CFR 84—Regulation—(0920–0109)—Extension—The regulatory authority for the National Institute for Occupational Safety and Health (NIOSH) certification program for respiratory protective devices is found in the Mine Safety and Health Amendments Act of 1977 (30 U.S.C. 577a, 651 et seq., and 657(g)) and the Occupational Safety and Health Act of 1970 (30 U.S.C. 3, 5, 7, 811, 842(h), 844). These regulations have, as their basis, the performance tests and criteria for approval of respirators used by millions of American construction workers, miners, painters, asbestos removal workers, fabric mill workers, and fire fighters. In addition to benefitting industrial workers, the improved testing requirements also benefit health care workers implementing the current CDC Guidelines for Preventing the Transmission of Tuberculosis. Regulations of the Environmental Protection Agency (EPA) and the Nuclear Regulatory Commission (NRC) also require the use of NIOSH-approved respirators.

NIOSH, in accordance with implementing regulations 42 CFR 84: (1) Issues certificates of approval for respirators which have met improved construction, performance, and protection requirements; (2) establishes procedures and requirements to be met in filing applications for approval; (3) specifies minimum requirements and methods to be employed by NIOSH and by applicants in conducting inspections, examinations, and tests to determine effectiveness of respirators; (4) establishes a schedule of fees to be charged applicants for testing and certification, and (5) establishes approval labeling requirements. Total annual burden hours are 177,968.

Respondents (section/data type)	Number of respondents	Number of responses/ respondent	Average burden/response (in hours)	Total burden (in hours)
84.11/Applications	56	14.0	63.56	49,831
84.33/Labeling	56	14.0	1.54	1,207
84.35/Modifications	56	14.0	79.45	62,289
84.41/Reporting	56	14.0	22.70	17,797
84.43/Record keeping	56	14.0	56.75	44,492
84.257/Labeling	56	14.0	1.50	1,176
84.1103/Labeling	56	14.0	1.50	1,176

Dated: June 18, 1998.

Charles W. Gollmar,

Acting Associate Director for Policy Planning and Evaluation, Centers for Disease Control and Prevention (CDC).

[FR Doc. 98–16752 Filed 6–24–98; 8:45 am]

BILLING CODE 4163–18–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 92N–0429]

Constantine I. Kostas; Denial of Hearing; Final Debarment Order

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) denies a request for a hearing and issues a final order under the Federal Food, Drug, and Cosmetic Act (the act) permanently debarring Constantine I. Kostas, Nine Cedar Mill Rd., Lynnfield, MA 01940, from providing services in any capacity to a person that has an approved or pending drug product application. FDA bases this order on its finding that Dr. Kostas was convicted of felonies under Federal law for conduct relating to the development or approval, including the process for development or approval, of a drug product, and conduct relating to

the regulation of a drug product under the act.

EFFECTIVE DATE: June 25, 1998.

ADDRESSES: Application for termination of debarment to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Leanne Cusumano, 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

Constantine I. Kostas, a former clinical investigator retained by a pharmaceutical drug manufacturer to conduct two investigational drug studies, pled guilty and was sentenced on October 13, 1988, to one count of mail fraud and one count of making false statements to a governmental agency. These are Federal felony offenses under 18 U.S.C. 1341 and 1001, respectively. These convictions were based upon Dr. Kostas' submission of fabricated patient case report forms to the sponsor of investigational drug studies from whom Dr. Kostas received, via the U.S. Postal Service, payments for conducting the clinical studies.

On December 14, 1992, Dr. Kostas received a certified letter from FDA offering Dr. Kostas an opportunity for a hearing on the agency's proposal to issue an order under the Generic Drug Enforcement Act (GDEA), section 306(a)(2) of the act (21 U.S.C. 335a(a)(2)). Under section 306(a)(2) of the act, an individual who has been convicted of a felony under Federal law for conduct relating to the development or approval, including the process for development or approval, of a drug product, or conduct relating to the regulation of a drug product, shall be debarred from providing services in any capacity to a person that has an approved or pending drug product application. FDA found that Dr. Kostas was subject to debarment under section 306(a)(2) of the act because he had been convicted of Federal felony offenses for conduct related to drug product development, approval, and regulation.

The certified letter informed Dr. Kostas that his request for a hearing could not rest upon mere allegations or denials, but must present specific facts showing that there was a genuine and substantial issue of fact requiring a hearing. The certified letter further notified Dr. Kostas that if it conclusively appeared from the face of the information and factual analysis in his request for a hearing that there was no genuine and substantial issue of fact that precluded the order of debarment, FDA would enter summary judgment against him and deny his request for a hearing in accordance with procedures set forth at part 12 (21 CFR part 12).

Dr. Kostas requested a hearing in a letter dated February 12, 1993, based upon three grounds. His request, in its entirety, states:

> Dr. Kostas, by his attorney, requests a hearing on the following grounds:
>
> (1) The law, as applied to Dr. Kostas, violates the expost facto clause of the Constitution of the United States. Art. I, Sec. 9, cl. 3 of the Constitution. Debarment is, in effect, a criminal forfeiture and an increased punishment which could not have been imposed at the time of Dr. Kostas' conviction.
>
> In addition, Dr. Kostas' offer of plea of guilty to the criminal charges was tendered and accepted with no mention of P.L. 102–282 [GDEA]; and
>
> (2) The pleas of guilty which prompted your letter of December 9, 1992, were based upon conduct last occurring in 1985. The conduct was not discovered by the government, but was reported voluntarily by Dr. Kostas. In addition, Dr. Kostas immediately, that is in 1985, returned all funds to [the pharmaceutical company]. The pleas of guilty did not result in any incarceration and Dr. Kostas did not lose his license to practice. Since in excess of seven years has passed, application of 21 U.S.C. § 335a would be violative of both the ex post facto and due process clauses of the Constitution.
>
> (3) Dr. Kostas hereby incorporates all of the reasons in the preceding paragraph and states additionally that precepts of constitutional law require statutes such as 21 U.S.C. § 335a to be applied prospectively and with the rule of lenity.
>
> For all of the foregoing reasons, pursuant to 21 C.F.R. § 12.22, Dr. Kostas requests a hearing on the above issues. Undersigned contemplates that briefing of issues and argument may be necessary, insofar as the facts are not in dispute.

Although Dr. Kostas concedes that he was convicted of felonies under Federal law and that no facts are in dispute, he argues that FDA's proposal to debar him is unconstitutional. The Deputy Commissioner for Operations has considered Dr. Kostas' claims and, for the reasons discussed below, concludes that they are unpersuasive and fail to raise a genuine and substantial issue of fact requiring a hearing.

II. Dr. Kostas' Claims in Support of His Hearing Request

A. The Ex Post Facto Argument

In his hearing request, Dr. Kostas argues that the ex post facto clause of the U.S. Constitution prohibits FDA from retrospectively applying section 306(a)(2) of the act to him. He states that ''debarment is, in effect, a criminal forfeiture and an increased punishment which could not have been imposed at the time of Dr. Kostas' conviction.''

An ex post facto law is one that reaches back to punish acts that occurred before enactment of the law or that adds a new punishment to one that was in effect when the crime was committed. (*Ex Parte Garland*, 4 Wall. 333, 377, 18 L. Ed. 366 (1866); *Collins* v. *Youngblood*, 497 U.S. 37 (1990).)

Dr. Kostas' argument that application of the mandatory debarment provisions of the act is prohibited by the ex post facto clause is unpersuasive, because the intent of debarment is remedial, not punitive. Congress created the GDEA in response to findings of fraud and corruption in the generic drug industry. Both the language of the GDEA and its legislative history reveal that the purpose of the debarment provisions set forth in the GDEA is ''to restore and ensure the integrity of the abbreviated new drug application approval process and to protect the public health.'' (See section 1, Pub. L. 102–282, GDEA of 1992.) In a suit challenging a debarment order issued by FDA (58 FR 69368, December 30, 1993), the constitutionality of the debarment provision was upheld against a challenge under the ex post facto clause. The reviewing court affirmed the remedial character of debarment:

> Without question, the GDEA serves compelling governmental interests unrelated to punishment. The punitive effects of the GDEA are merely incidental to its overriding purpose to safeguard the integrity of the generic drug industry while protecting public health.

(*Bae* v. *Shalala*, 44 F.3d 489, 493 (7th Cir. 1995); see also *DiCola* v. *Food and Drug Administration*, 77 F.3d 504 (D.C. Cir. 1996).) Because the intent of the GDEA is remedial rather than punitive, Dr. Kostas' argument that the GDEA violates the ex post facto clause must fail. (See *Bae* v. *Shalala*, 44 F.3d at 496–497.)

Dr. Kostas also states that his ''offer of plea of guilty to the criminal charges was tendered and accepted with no mention or contemplation of [debarment].'' It is not the function of the plea agreement to provide notice of any subsequent civil or administrative actions. Nor do the terms of the plea agreement preclude subsequent civil or administrative actions against Dr. Kostas. Therefore, Dr. Kostas' claim that the plea agreement does not mention debarment fails to raise a genuine and substantial issue of fact.

B. The Due Process Argument

Dr. Kostas argues that, because his debarment is based upon conduct

occurring over 7 years before the agency proposed to debar him, and because of other mitigating factors, his debarment also violates the due process clause (presumably the fifth amendment) of the U.S. Constitution. Under the fifth amendment, no person shall be deprived of life, liberty, or property without due process of law. Dr. Kostas' due process claim appears grounded upon an alleged retroactive deprivation of future employment.

The Supreme Court has said that retroactive legislation must be supported by ''a legitimate legislative purpose furthered by rational means.'' (*Pension Benefit Guar. Corp*. v. *R. A. Gray & Co*., 467 U.S. 717, 729 (1984).) The ''judgments about the wisdom of such legislation remain within the exclusive province of the legislative and executive branches.'' *Id*. As discussed above, Congress intended the GDEA to be remedial. The GDEA prohibits certain individuals from providing services to a person who has an approved or pending drug application in order to meet the legitimate regulatory purpose of restoring the integrity of the drug approval and regulatory process and protecting the public health. In addition, the remedial nature of the GDEA is not diminished simply because the GDEA deters debarred individuals from future misconduct. (*U.S*. v. *Halper*, 109 S.Ct. 1892, 1901, n.7 (1989); *Bae* v. *Shalala*, 44 F.3d 489, 493 (7th Cir. 1995).)

Dr. Kostas argues that because he was not incarcerated and did not lose his ''license to practice,'' and because he voluntarily reported his conduct and provided restitution to the pharmaceutical company, debarment under the GDEA would violate the due process clauses of the Constitution. This list of mitigating circumstances suggests a ''takings'' argument based upon an expectation of future employment. However, the expectation of employment is not recognized as a protected property interest under the fifth amendment. (*Hoopa Valley Tribe* v. *Christie*, 812 F.2d 1097, 1102 (9th Cir. 1986); *Chang* v. *United States*, 859 F.2d 893, 896–897 (Fed. Cir. 1988).) One who voluntarily enters a pervasively regulated industry, such as the pharmaceutical industry, and then violates its regulations, cannot successfully claim that he has a protected property interest when he is no longer entitled to the benefits of that industry. (*Erikson* v. *United States*, 67 F.3d 858 (9th Cir. 1995).) Thus, debarment for a 1985 felony conviction does not violate the ex post facto or due process clauses of the Constitution. In addition, Dr. Kostas' list of mitigating circumstances does not raise a genuine or substantial issue of disputed fact.

C. Prospective Application and the Rule of Lenity Arguments

Finally, Dr. Kostas argues that constitutional law requires that the GDEA be applied ''prospectively'' and with ''the rule of lenity.'' Again Dr. Kostas' arguments are unpersuasive. The GDEA, as remedial legislation, was intended by Congress to be applied, in part, to conduct that occurred before enactment of the legislation. The express language of section 306(a)(1) of the act requires that mandatory debarment apply only prospectively to a person ''other than an individual'' who has been convicted of a Federal felony offense ''after the date of enactment of this section [section 306(a)(1)].'' By contrast, section 306(a)(2) of the act, which applies only to individuals, omits the limiting language regarding prospective application, indicating a legislative intent to apply this provision retrospectively. When one of two closely related subsections within the same act contains particular language that is omitted from the other subsection, ''it is generally presumed that Congress acted intentionally and purposely in the disparate inclusion or exclusion.'' (*Russello* v. *U.S*., 464 U.S. 16, 24 (1983) (citations omitted); *USA* v. *Olin Corp*., 107 F.3d 1506, 1513 (11th Cir. 1997).) Such retrospective remedial legislation is not unlawful so long as the ''retroactive application of the legislation is itself justified by a rational legislative purpose.'' (*Pension Benefit Guar. Corp*. v. *R. A. Gray & Co*., 467 U.S. at 730.) As discussed previously, debarment under the GDEA meets the legitimate regulatory purpose of restoring the integrity of the drug review process and protecting the public health.

Dr. Kostas also states that constitutional law requires that the ''rule of lenity'' apply to his case. The rule of lenity applies in criminal cases and requires a sentencing court to impose the lesser of two penalties where there is an actual ambiguity over which penalty should apply. (*U.S*. v. *Canales*, 91 F.3d 363 (2nd Cir. 1996).) The rule of lenity is not applicable here because debarment under the GDEA is neither a criminal law nor a penalty. It is a civil, remedial law intended to protect the drug review process and the public health. Moreover, section 306(a)(2) of the act requires debarment in this case and does not provide the agency with discretion to implement a different remedy.

None of Dr. Kostas' arguments raises a genuine and substantial issue of fact regarding his conviction. Instead, Dr. Kostas concedes that there are no facts in dispute. Moreover, Dr. Kostas' constitutional arguments are without merit. Accordingly, the Deputy Commissioner for Operations denies Dr. Kostas' request for a hearing under 21 CFR 12.28.

III. Findings and Order

Therefore, the Deputy Commissioner for Operations, under section 306(a) of the act and under authority delegated to him (21 CFR 5.20), finds that Dr. Constantine I. Kostas has been convicted of felonies under Federal law for conduct: (1) Relating to the development or approval, including the process for development or approval, of a drug product (section 306(a)(2)(A) of the act); and (2) relating to the regulation of a drug product (306(a)(2)(B)) of the act)).

As a result of the foregoing findings, Dr. Kostas is permanently debarred from providing services in any capacity to a person with an approved or pending drug product application under sections 505, 507, 512, or 802 of the act (21 U.S.C. 355, 357, 360b, or 382), or under section 351 of the Public Health Service Act (42 U.S.C. 262), effective June 25, 1998 (sections 306(c)(1)(B) and (c)(2)(A)(ii) and 201(dd) of the act (21 U.S.C. 321(dd))). Any person with an approved or pending drug product application who knowingly uses the services of Dr. Kostas in any capacity, during his period of debarment, will be subject to civil money penalties (section 307(a)(6) of the act (21 U.S.C. 335b(a)(6))). If Dr. Kostas, during his period of debarment, provides services in any capacity to a person with an approved or pending drug product application, he will be subject to civil money penalties (section 307(a)(7) of the act). In addition, FDA will not accept or review any abbreviated new drug application or abbreviated antibiotic drug application submitted by Dr. Kostas or with his assistance during his period of debarment (section 306(c)(1)(B) of the act).

Dr. Kostas may file an application to attempt to terminate his debarment under section 306(d)(4)(A) of the act. Any such application, if filed, will be reviewed under the criteria and processes set forth in section 306(d)(4)(C) and (D) of the act. Any such application should be identified with Docket No. 92N–0429 and sent to the Dockets Management Branch (address above). All such submissions are to be filed in four copies. The public availability of information in these submissions is governed by 21 CFR 10.20(j). Publicly available submissions

may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: June 18, 1998.

Michael A. Friedman,

Acting Commissioner of Food and Drugs.

[FR Doc. 98–16850 Filed 6–24–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Anti-Infective Drugs Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Anti-Infective Drugs Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on July 29, 30, and 31, 1998, 8 a.m. to 5 p.m.

Location: Gaithersburg Hilton, Grand Ballroom, 620 Perry Pkwy., Gaithersburg, MD.

Contact Person: Ermona B. McGoodwin, Center for Drug Evaluation and Research (HFD–21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7001, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), code 12530. Please call the Information Line for up-to-date information on this meeting.

Agenda: The committee will discuss documents on ''Guidance to Industry'' being developed by the Office of Drug Evaluation IV's Division of Anti-Infective Drug Products and the Division of Special Pathogens and Immunologic Drug Products. Copies of these draft guidance documents can be obtained from the Center for Drug Evaluation and Research (HFD–210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4573, or requested by FAX at 301–827–4577. Electronic versions of these guidance documents will be available via Internet using the World Wide Web (www). To access the documents on the www, connect to CDER Home Page at http://www.fda.gov/cder/guidance.htm.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by July 22, 1998. Oral presentations from the public will be scheduled between approximately 1 p.m. and 1:30 p.m. on July 29, 30, and 31, 1998. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before July 22, 1998, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: June 18, 1998.

Michael A. Friedman,

Deputy Commissioner for Operations.

[FR Doc. 98–16934 Filed 6–24–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Arthritis Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Arthritis Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA regulatory issues.

Date and Time: The meeting will be held on August 7, 1998, 8 a.m. to 5 p.m.

Location: Bethesda Holiday Inn, Versailles Ballrooms I and II, 8120 Wisconsin Ave., Bethesda, MD.

Contact Person: Kathleen R. Reedy or LaNise S. Giles, Center for Drug Evaluation and Research (HFD–21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–5455, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), code 12532. Please call the Information Line for up-to-date information on this meeting.

Agenda: The committee will discuss the safety and efficacy of new drug application 20–905 Arava (leflunomide, Hoechst Marion Roussel, Inc., Germany) for the treatment of rheumatoid arthritis.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by July 30, 1998. Oral presentations from the public will be scheduled between approximately 11 a.m. and 12 m. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before July 30, 1998, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: June 15, 1998.

Michael A. Friedman,

Deputy Commissioner for Operations.

[FR Doc. 98–16837 Filed 6–24–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Ophthalmic Drugs Subcommittee of the Dermatologic and Ophthalmic Drugs Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Ophthalmic Drugs Subcommittee of the Dermatologic and Ophthalmic Drugs Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on July 22, 1998, 8 a.m. to 5 p.m.

Location: Holiday Inn, Versailles Ballrooms I and II, 8120 Wisconsin Ave., Bethesda, MD.