Industry & Trade Summary

Antibiotics

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UNITED STATES INTERNATIONAL TRADE COMMISSION

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PREFACE

In 1991 the United States International Trade Commission initiated its current *Industry and Trade Summary* series of informational reports on the thousands of products imported into and exported from the United States. Each summary addresses a different commodity/industry area and contains information on product uses, U.S. and foreign producers, and customs treatment. Also included is an analysis of the basic factors affecting trends in consumption, production, and trade of the commodity, as well as those bearing on the competitiveness of U.S. industries in domestic and foreign markets.[1]

This report on antibiotics covers the period 1988 through 1992 and represents one of approximately 250 to 300 individual reports to be produced in this series during the first half of the 1990s. Listed below are the individual summary reports published to date on the chemicals and textiles sectors.

USITC publication number	*Publication date*	*Title*
Chemicals:		
2458	November 1991	Soaps, Detergents, and Surface-Active Agents
2509	May 1992	Inorganic Acids
2548	August 1992	Paints, Inks, and Related Items
2578	November 1992	Crude Petroleum
2588	December 1992	Major Primary Olefins
2590	February 1993	Polyethylene Resins in Primary Forms
2598	March 1993	Perfumes, Cosmetics, and Toiletries
2736	February 1994	Antibiotics
Textiles and apparel:		
2543	August 1992	Nonwoven Fabrics
2580	December 1992	Gloves
2642	June 1993	Yarns
2695	November 1993	Carpets and Rugs
2703	November 1993	Coated Fabrics
2702	November 1993	Fur Goods

[1] The information and analysis provided in this report are for the purpose of this report only. Nothing in this report should be construed to indicate how the Commission would find in an investigation conducted under statutory authority covering the same or similar subject matter.

CONTENTS

INTRODUCTION

Antibiotics are chemical substances produced by or derived from various living microorganisms. These substances, even in small concentrations, are capable either of inhibiting the growth of or killing bacteria or microorganisms.[1] Although many antibiotics are effective against a wide range of microorganisms and are, therefore, classified as broad-spectrum antibiotics, many others are effective only against specific microorganisms. This report addresses certain features and trends of the U.S. antibiotics industry over the past 5 years. Products covered include antibiotics in bulk form (i.e., active ingredients) and antibiotics that have been formulated into dosage-form, or end-use, products. The report contains three major sections: a discussion of the antibiotics industry in the United States and overseas; a discussion of domestic and foreign trade measures; and a discussion of domestic and foreign markets for antibiotics. An appendix is also included that provides an explanation of tariff and trade agreement terms.

Penicillin was the first antibiotic to be isolated and developed for commercial use. The commercialization of penicillin was one of the primary catalysts behind the rapid development of the U.S. pharmaceutical industry after World War II. An Englishman, Alexander Fleming, discovered penicillin in 1928, but lacked the time and money to develop his discovery. Research on the product was continued by scientists from universities and the chemical industry in the United States during World War II as part of a wartime project to develop penicillin and to produce it in large quantities to supply the allied forces. The U.S. Government sponsored much of the research, investing about $3 million in the project. The penicillin plants were then sold to private firms at one-half cost after the war.[2] New discoveries in the field of antibiotics occurred at a relatively rapid pace from 1938 to 1953; as a result, this period subsequently became known in the industry as the "Age of Antibiotics."[3]

Today, antibiotics are produced in nearly all developed countries and many developing countries. Several thousand antibiotics have been discovered and developed worldwide. New antibiotics are continuously needed as more microorganisms become resistant to the antibiotics currently available. Antibiotics are classified in several categories, depending on the chemical structure of the product, microbial source, and mechanism of action. Examples of such categories include natural penicillins, semisynthetic penicillins, aminoglycosides, cephalosporins, tetracyclines, quinolones, and macrolides.

Antibiotics are generally produced, at least in part, by batch aerobic fermentation processes.[4] The process, as illustrated in figure 1 for the production of penicillin G, consists of cultivating antibiotics in a fermentation medium housed in a large climate-controlled tank. Typical fermentation media consist of corn steep liquor to which carbohydrates, nitrogen sources, and any compound(s) needing to be incorporated into the final structure have been added. Once the fermentation process is complete, the antibiotic is recovered from the resulting broth by techniques, used either singly or in combination, such as solvent extraction, ion-exchange chromatography, or precipitation.[5]

Antibiotics not manufactured by fermentation include semisynthetic penicillins, cephalosporins, tetracyclines, and the quinolones. These antibiotics are generally produced from intermediate chemical products that, in many cases, are themselves either the product of fermentation or derived from the chemical modification of fermentation products. Alternatively, products such as chloramphenicol, cycloserine, and the quinolones are examples of antibiotics produced completely by chemical synthesis.[6]

U.S. INDUSTRY PROFILE

Industry Structure

Antibiotics are included among the many products classified under the three-digit Standard Industrial Classification (SIC) Group No. 283 "Drugs." Depending on their form, antibiotics are further classified in one of two four-digit industry codes included in SIC 283: SIC 2833 "Medicinal Chemicals and Botanical Products" or SIC 2834 "Pharmaceutical Preparations." These industry codes traditionally have covered the majority of shipments under SIC 283. As reflected in the SIC classifications, drugs are produced in two major manufacturing stages:

1. the production of pure pharmacologically active chemicals (often called "active ingredients") in bulk form either by conventional methods or through use of bioengineering procedures (SIC 2833); and

[1] *Encyclopedia of Chemical Technology*, edited by Raymond Eller Kirk and Donald Frederick Othmar, 1978, 3d ed., vol. 2, p. 809.

[2] National Academy of Engineering, *The Competitive Status of the U.S. Pharmaceutical Industry: The Influences of Technology in Determining International Industrial Competitive Advantage*, National Academy Press, 1983, p. 9.

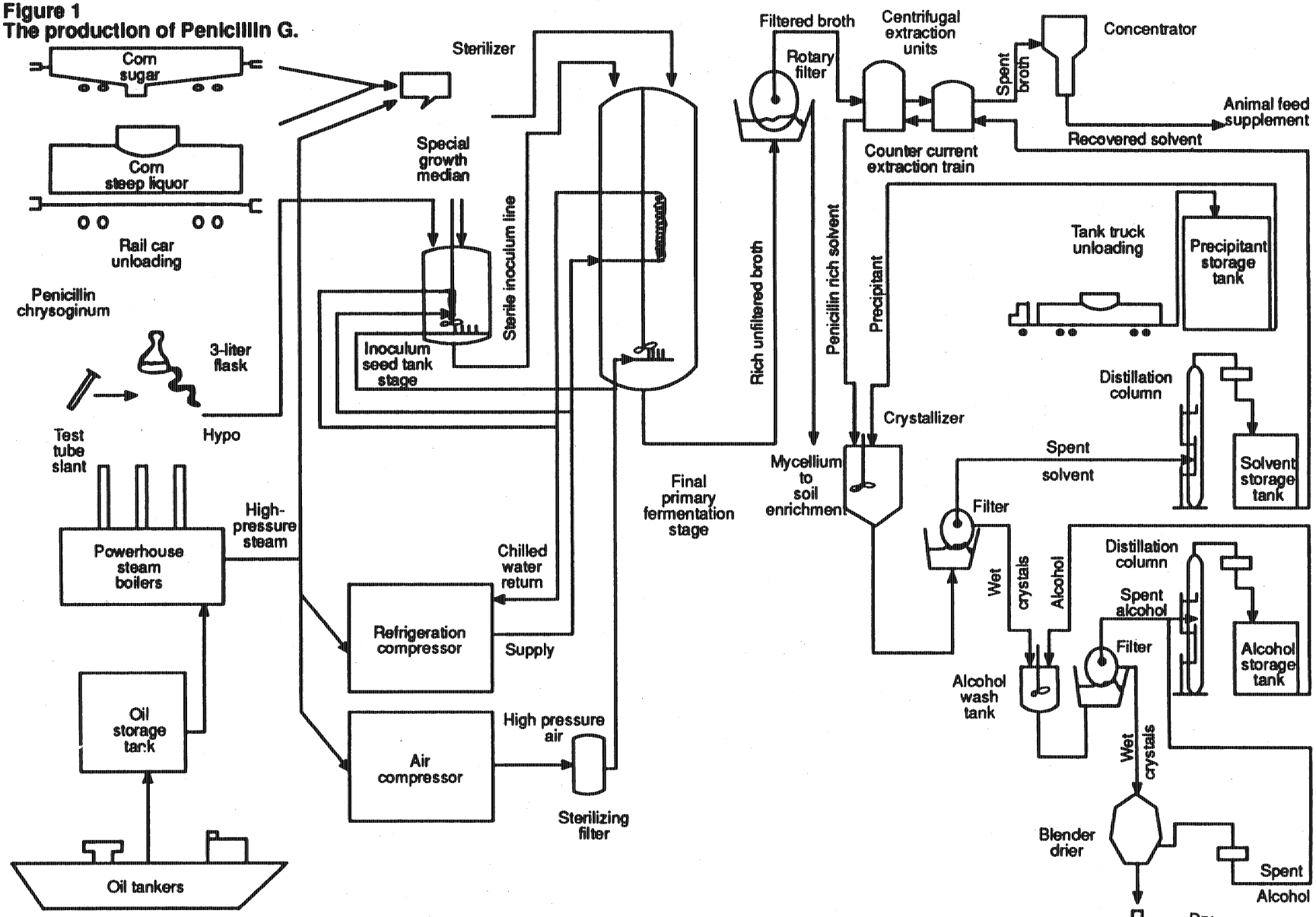
[3] The word "antibiotic" was only introduced in 1942. Prior to that time, these products were called toxins, lysins, or bacteriostatic or bacteriolytic agents. In 1948, the U.S. Patent Office granted a patent on streptomycin, paving the way "for a new form of competition—competition through product development." *Encyclopedia of Chemical Technology*, p. 811; *The Competitive Status of the U.S. Pharmaceutical Industry: The Influences of Technology in Determining International Industrial Competitive Advantage*, 1983, p. 9.

[4] It should be noted that fermentation is considered one of the older biotechnology processes. According to the Office of Technology Assessment, "biotechnology, broadly defined, includes any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses."

[5] *Encyclopedia of Chemical Technology*, vol. 2, p. 814.

[6] Ibid.

Figure 1
The production of Penicillin G.



Source: Courtesy of Pfizer Inc.

2. the formulation of these concentrated pharmacologically active chemicals into dosage form (or pharmaceutical preparations) (SIC 2834).[7]

Antibiotics, either in bulk form or as pharmaceutical preparations, are produced by innovative companies (i.e., those companies involved in research and development (R&D) of new pharmaceutical products) and by companies that manufacture generics (see figure 2).[8] Multinationals account for a relatively high percentage of the innovative companies. Multinationals generally have operations in most of the developed countries and in many developing countries.[9] Within the United States, many of the firms are concentrated geographically in New York, New Jersey, Pennsylvania, and California.

Although no information is readily available as to the share of total sales held by the largest firms (i.e., the level of concentration) within the antibiotics industry, the level of concentration within the U.S. pharmaceutical industry in general is not very high, according to official and industry statistics.[10] For example, the average four-firm concentration ratio on the basis of sales was valued at about 25 percent during the past 10 years.[11] In recent years, the pharmaceutical industry has experienced increasing consolidation, ranging from mergers to strategic alliances. This consolidation is reportedly the result of companies trying to expand their portfolios and their geographic reach, and to spread the risks and costs associated with R&D expenditures.

Because of the batch nature of production of these and many other pharmaceutical products and because employees in pharmaceutical firms are often involved with the production of more than one class of product, employment data for this segment of the industry are not readily available. However, such data are available for SIC 283, SIC 2833, and SIC 2834 during 1988-92. Total U.S. employment in firms classified under SIC 283 increased from 175,000 in 1988 to an estimated 193,000 workers in 1992, or by about 10 percent.[12] The majority of these employees during this period, or about 77 percent, were involved in the manufacture of dosage form products (SIC 2834). Within SIC 2834, production workers accounted for about 75-80 percent of the total. Of the total for SIC 283 in 1989, production workers accounted for about 30 percent of all employees; marketing, about 30 percent; medical R&D, about 23 percent; and administrative, about 10 percent.[13]

As is the case with the pharmaceutical industry overall, Government policies, domestic and foreign,[14] have a cumulative impact on the competitiveness and viability of the antibiotics industry. Such policies include regulatory and tax policies, intellectual property right systems, and product liability. In some cases, the impact can be negative if industry revenues are decreased, often resulting, in turn, in reduced R&D activity. A recent Commission study found that the ability of a pharmaceutical firm and, ultimately, the industry, to remain competitive "hinges on its capability to develop innovative and profitable products."[15] The U.S. pharmaceutical industry annually reinvests about 16-17 percent of its revenues into R&D activities, or about three times the level allocated by the remainder of the chemical and related industries sector.[16]

Regulatory policies and practices, intended to protect the consumer from unsafe and nonefficacious products, provide one example. Lengthy delays in the granting of product approvals can shorten a product's market lifetime and effective patent term, thereby decreasing the time in which a company can recoup its R&D expenditures. Such delays are partially offset by patent restoration programs such as those enacted in the United States in 1984 and in Japan in 1988. Nonetheless, many companies reportedly seek approval of pharmaceutical products overseas first because of the perceived differential in approval times.[17]

Product liability laws and judgments can also have a significant impact on the antibiotics industry. U.S. firms reportedly face more exposure to the risks

[7] Pharmaceutical preparations are typically the pure chemicals plus inert substances such as diluents or extenders. Pharmaceutical preparations are available in several forms, including pills, capsules, tablets, creams, and lotions.

[8] The term "generic" refers to nonproprietary products. Denoting a drug name not protected by a trademark, the term is usually descriptive of the drug's chemical structure. Innovative companies, in addition to producing brandname products, also often manufacture generic drugs. Innovative and generic companies are represented in almost all of the statistics presented in this report. Many of the discussions, however, such as those on nontariff barriers, primarily address innovative companies.

[9] Such operations include facilities focussing on production, formulation, R&D, marketing, or a combination of these functions.

[10] The U.S. pharmaceutical industry, as referred to in this report, includes firms based in the United States and firms of foreign parentage operating in the United States.

[11] Pharmaceutical Manufacturers Association, *Fact Book*, 1991, p. 14. The statistics presented in the fact book are sourced from both the U.S. Department of Commerce and from the National Prescription Audit (IMS America, Ltd.). No one pharmaceutical firm holds more than about 7-8 percent of the domestic pharmaceuticals market.

[12] Derived from information provided in the U.S. Department of Commerce's *U.S. Industrial Outlook 1993*, p. 43-2. Total employment is defined as all employees, including production workers and R&D scientists.

[13] PMA, *Annual Survey Report: 1989-1991*, 1991, p. 16.

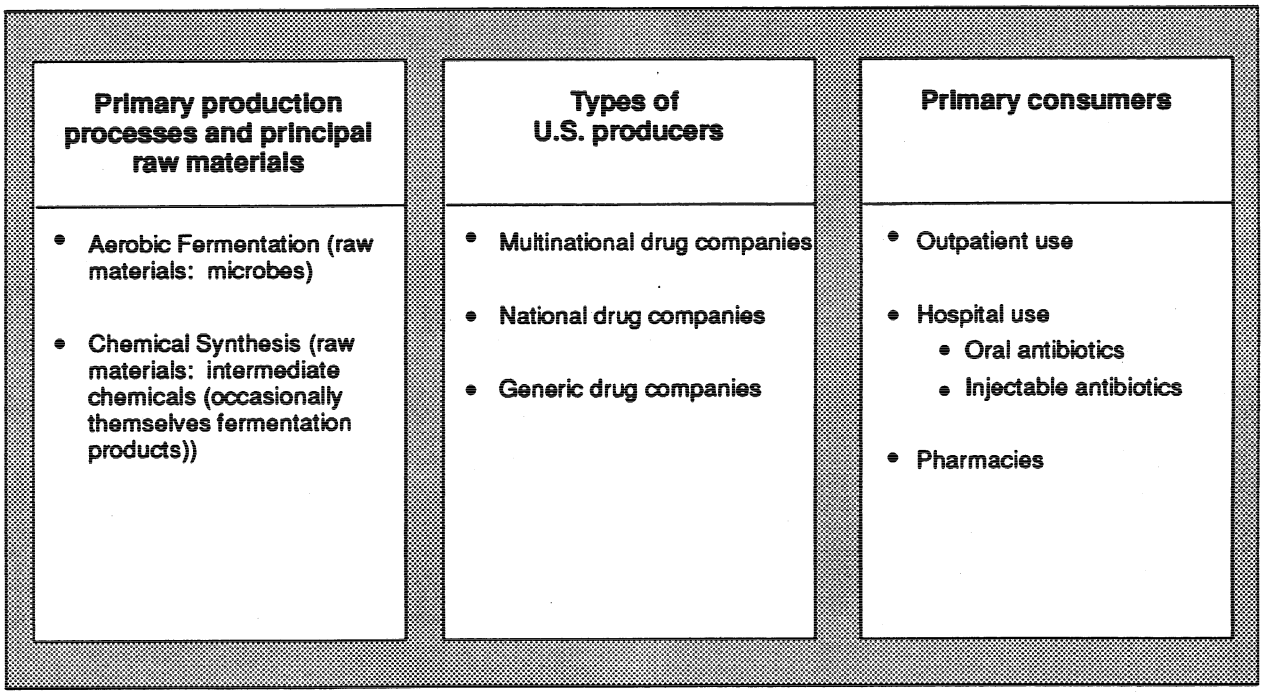
[14] See "Foreign Trade Measures" section for a brief discussion of other Government policies that affect the U.S. antibiotics industry.

[15] U.S. International Trade Commission, *Global Competitiveness of U.S. Advanced-Technology Manufacturing Industries: Pharmaceuticals*, (investigation Number 332-302), USITC publication 2437, Sept. 1991, p. vii.

[16] PMA, *Annual Survey Report: 1989-1991*, p. 18.

[17] During 1984-90, 121 of the 159 new drugs approved by the FDA during 1984-90 were first approved in a foreign country. In 1990, 14 of the 23 new drugs approved were first approved overseas. PMA, *Facts at a Glance*, 1991, p. 21.

Figure 2
Antibiotics: Primary production processes and principal raw materials, types of producers, and primary consumers



Source: Compiled from various sources.

of liability suits than foreign firms with U.S. operations since, in the case of litigation, only the U.S. assets of the foreign companies can be seized. In addition, U.S. firms must also factor in the higher cost of liability claims into the prices of their products.[18]

Consumer Characteristics and Factors Affecting Demand

Distinctly separate consumer groups purchase antibiotics in bulk form as compared with dosage form. Antibiotics in bulk form are more likely to be consumed internally by producing companies in the manufacture of dosage form products or marketed to other companies for formulation into dosage form products. Antibiotics in dosage form, however, are generally marketed directly to wholesalers, who then supply pharmacies and hospitals.[19] The final consumer generally obtains these products either from a hospital, on an inpatient or an outpatient basis; from a pharmacy with a doctor's prescription; or from a retailer as an over-the-counter product.

Anti-infectives (including antibiotics), the second-largest class of prescription pharmaceutical products sold in the United States in 1972, accounting for almost 16 percent of the total, declined to the third-largest class by the late 1980s. Overseas, however, anti-infectives (including antibiotics) maintained their premier position in the market during this time period, accounting for about 22 percent of the total overseas market for prescription pharmaceutical products. Differences in the leading categories of products in the United States and overseas primarily reflect differences in marketing or consumer information, and in socioeconomic and demographic factors.

FOREIGN INDUSTRY PROFILE

The antibiotics industry, like the pharmaceutical industry in general, is multinational. Many of the major producers of antibiotics in the United States have operations overseas; conversely, many foreign-based firms have operations in the United States. According to industry sources, the three largest producing countries or regions are the United States, Western Europe, and Japan. Western European subsidiaries of U.S.-based firms accounted for approximately 25 percent of all pharmaceuticals, including antibiotics, which were produced, formulated, or both, in Western Europe during 1988-92. In Japan, antibiotics represented about 13 percent, by value, of pharmaceuticals produced in that country. As in other countries, however, the geriatric population in Japan is

[18] Peter Huber and Robert E. Litan, *The Liability Maze: The Impact of Liability Law on Safety and Innovation*, Washington, DC (The Brookings Institution), 1991, p. 18.

[19] Sales of all dosage form prescription pharmaceuticals to wholesalers in 1989 represented about 71 percent of total such sales. In some cases, pharmacies and hospitals obtain dosage form prescription pharmaceuticals directly from the manufacturer.

increasing, resulting in a shift in production and research in Japan towards products consumed by older people.[20]

U.S. TRADE MEASURES

Tariff Measures

The provisions of the *Harmonized Tariff Schedule of the United States* (HTS) applicable to antibiotics, as of January 1993, are shown in table 1. The table shows the column-1 general rates of duty for countries eligible for most-favored-nation (MFN) treatment, as well as duty rates under column 1 for countries qualifying under special tariff programs.[21] The column-1 general rates of duty for these products ranged from almost 2 percent ad valorem to slightly over 7 percent ad valorem in 1992. The aggregate trade-weighted, average rate of duty for all products covered based on full-year 1992 trade was almost 5 percent ad valorem.

A proposed initiative on pharmaceuticals is currently being negotiated under the Uruguay Round market access negotiations of the General Agreement on Tariffs and Trade (GATT). The "zero-for-zero" initiative would allow for reciprocal duty-free treatment for those pharmaceuticals, in bulk and in dosage forms, having an international nonproprietary name and for certain intermediate chemical products (used primarily in the production of pharmaceuticals), as specified by the United States Trade Representative.[22]

The pharmaceutical industry is generally expected to benefit from the North American Free Trade Agreement (NAFTA)[23] through the improvement of intellectual property rights (IPR) in Canada and the opening of the government procurement market in Mexico. The IPR provisions of NAFTA will end compulsory licensing for pharmaceuticals in Canada; extend product and process patent protection for pharmaceuticals; and codify for future signatories to NAFTA "pipeline"[24] protection for pharmaceuticals in the R&D and regulatory process.[25] Mexico already provides patent rights for pharmaceuticals "at a level and standard of the OECD [Organization for Economic Cooperation and Development] industrial trading partners" as a result of Mexico's implementation of "The Law for the Development and Protection of Industrial Property" on June 28, 1991.[26]

Nontariff Measures

Except that Food and Drug Administration (FDA) approval is required for most imports of these products, there are no known significant domestic nontariff import restrictions. FDA approval is required for all pharmaceutical products entering the United States for commercial use, regardless of the country of origin.

U.S. Government Trade-Related Investigations

In recent years the Commission has conducted two investigations involving antibiotic products, one under the U.S. antidumping law[27] and the other under section 337 of the Tariff Act of 1930.[28] In addition, the Commission recently completed an investigation under section 332 of the Tariff Act of 1930[29] concerning the competitiveness of the U.S. pharmaceutical industry; that industry includes producers of antibiotics.

The antidumping investigation, USITC investigation No. 731-TA-423 final), concerned imports of generic cephalexin capsules from Canada and was conducted, following the filing of a petition by Biocraft Laboratories, Inc., Elmwood Park, NJ, on October 27, 1988, with the U.S. Department of Commerce and the U.S. International Trade Commission. Commerce subsequently found that such imports from Canada were being sold at less than fair value within the meaning of the antidumping law. The Commission, however, made a negative injury determination. Accordingly, no antidumping order was issued and no antidumping duties were collected.[30]

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[20] USITC, *Pharmaceuticals*, USITC publication 2437, p. 4-9.

[21] See appendix A.

[22] The GATT Uruguay Round of trade negotiations was recently completed in December 1993.

[23] The North American Free Trade Agreement (NAFTA), as implemented by the North American Free Trade Agreement Implementation Act (Pub. Law 103-182, approved Dec. 8, 1993), provided for the elimination of U.S. duties, effective Jan. 1, 1994, on certain antibiotics imported from Mexico, including penicillin G salts, streptomycins and their derivatives, tetracyclines and their derivatives, erythromycin and its derivatives, and certain other natural and synthetic antibiotics. It also provides for the phaseout of U.S. duties on U.S. imports of all other antibiotics from Mexico over 10-15 years. Mexico eliminated its duties on imports on many antibiotics imported from the United States effective Jan. 1, 1994, and is obligated to phaseout its duties on imports of all other antibiotics from the United States over 10-15 years. The NAFTA became effective for both the United States and Mexico on Jan. 1, 1994.

[24] "Pipeline" protection refers to the protection of products that have been previously patented in other NAFTA countries (i.e., country of origin). Those products would be entitled to protection for the unexpired terms of their patents in any given NAFTA country, provided that the product has not been previously marketed in that country.

[25] USITC, *Potential Impact on the U.S. Economy and Selected Industries of the North American Free-Trade Agreement*, USITC publication 2596, Jan. 1992, pp. 9-1 and 9-2.

[26] Mexican Investment Board, "Intellectual Property: Increased Protection for Business in Mexico," Oct. 1991, pp. 6 and 11, and the American Bar Association, International Trade Committee, "The North American Free Trade Agreement," Mar. 1992, p. 288.

[27] 19 U.S.C. 1673 et seq.

[28] 19 U.S.C. 1337.

[29] 19 U.S.C. 1332.

[30] USITC, *Generic Cephalexin Capsules from Canada*, inv. No. 731-TA-423, USITC publication 2211, Aug. 1989.

Table 1
Antibiotics: Harmonized Tariff Schedule subheading; description; U.S. col. 1 rate of duty as of January 1, 1993; U.S. exports, 1992; and U.S. imports, 1992

HTS subheading	Description	Col. 1 rate of duty as of Jan. 1, 1993		U.S. exports, 1992	U.S. imports, 1992
		General	Special[1]		
				— *Million dollars* —	
2941.10.10	Ampicillin and its salts	6.9%	Free (CA,E,IL,J)	8	17
2941.10.20	Penicillin G salts	6.9%	Free (A*,CA,E,IL,J)	20	24
2941.10.30	Certain other penicillins	5.8%	Free (CA,E,IL,J)	(2)	2
2941.10.50	Other penicillins and their derivatives with a penicillanic acid structure; salts thereof	7.4%	Free (CA,E,IL,J)	(2)	54
2941.20.00	Streptomycins and their derivatives; salts thereof	3.5%	Free (A*,CA,E,IL,J)	394	1
2941.30.00	Tetracyclines and their derivatives	3.7%	Free (A*,CA,E,IL,J)	27	49
2941.40.00	Chloramphenicol and its derivatives; salts thereof	6.6%	Free (A*,CA,E,IL,J)	2	1
2941.50.00	Erythromycin and its derivatives; salts thereof	3.7%	Free (A*,CA,E,IL,J)	217	10
2941.90.10	Other natural antibiotics	1.8%[4]	Free (A*,CA,E,IL,J)	43	23
2941.90.30	Other synthetically-derived aromatic or modified aromatic antibiotics	6.6%[4]	Free (CA,E,IL,J)	(2)	70
2941.90.50	Other synthetically-derived antibiotics	3.7%[4]	Free (A*,CA,E,IL,J)	(2)	203
3003.10.00	Medicaments containing penicillins or derivatives thereof, with a penicillanic acid structure, or streptomycins or their derivatives (excluding goods of heading 3002, 3005, or 3006) consisting of two or more constituents which have been mixed together for therapeutic or prophylactic uses, not put up in measured doses or in forms or packings for retail sale	6.9%	Free (E,IL,J) 3.4% (CA)	17	23
3003.20.00	Medicaments containing antibiotics other than penicillins or derivatives thereof, with a penicillanic acid structure, or streptomycins or their derivatives, (excluding goods of heading 3002, 3005, or 3006) consisting of two or more constituents which have been mixed together for therapeutic or prophylactic uses, not put up in measured doses or in forms or packings for retail sale	3.7%	Free (E,IL,J) 1.8% (CA)	61	58
3004.10.10	Medicaments (excluding goods of heading 3002, 3005, or 3006) containing penicillin G salts, consisting of mixed or unmixed products for therapeutic or prophylactic uses, put up in measured doses or in forms or packings for retail sale	6.9%	Free (A*,E,IL,J) 3.4% (CA)	49	12
3004.10.50	Medicaments (excluding goods of heading 3002, 3005, or 3006) containing penicillins (other than penicillin G salts), or derivatives thereof, with a penicillanic acid structure, or streptomycins or their derivatives, consisting of mixed or unmixed products for therapeutic or prophylactic uses, put up in measured doses or in forms or packings for retail sale	6.2%	Free (E,IL,J) 3.1% (CA)	66	14

See footnotes at end of table.

Table 1—Continued
Antibiotics: Harmonized Tariff Schedule subheading; description; U.S. col. 1 rate of duty as of January 1, 1993; U.S. exports, 1992; and U.S. imports, 1992

HTS subheading	Description	Col. 1 rate of duty as of Jan. 1, 1993		U.S. exports, 1992	U.S. imports, 1992
		General	Special[1]	— *Million dollars* —	
3004.20.00	Medicaments (excluding goods of heading 3002, 3005, or 3006) containing antibiotics other than penicillins or derivatives thereof, with a penicillanic acid structure, or streptomycins or their derivatives, consisting of mixed or unmixed products for therapeutic or prophylactic uses, put up in measured doses or in forms or packings for retail sale	3.7%[4]	Free (A*,E,IL,J) 1.8% (CA)	291	578

[1] Programs under which special tariff treatment may be provided, and the corresponding symbols for such programs as they are indicated in the "Special" subcolumn, are as follows: Generalized System of Preferences (A); Automotive Products Trade Act (B); Agreement on Trade in Civil Aircraft (C); United States-Canada Free-Trade Agreement (CA); Caribbean Basin Economic Recovery Act (E); United States-Israel Free Trade Area (IL); and Andean Trade Preference Act (J).

[2] Official statistics for U.S. exports of those products classified under this HTS subheading are not collected at a similar level of aggregation. The total value of exports for all products covered in this summary was about $1.4 billion during 1992.

[3] Less than $500,000.

[4] Certain temporary duty-free provisions apply to one or more of the products classified under this HTS subheading.

Source: U.S. exports and imports compiled from official statistics of the U.S. Department of Commerce.

In March 1989, the Commission instituted investigation No. 337-TA-293, *Certain Crystalline Cefadroxil Monohydrate*, following the filing of a complaint by Bristol-Myers Co. (now Bristol-Myers Squibb Co.). The complaint alleged that imports of crystalline cefadroxil monohydrate (CCM), an antibiotic drug, infringed a patent owned by Bristol. On March 15, 1990, the Commission determined that there was a violation of section 337 and issued (1) a permanent limited exclusion order directed to all infringing CCM products of the three named foreign respondents and (2) permanent cease-and desist-orders directed to the three domestic respondents named.[31]

The section 332 investigation on pharmaceuticals, Commission investigation No. 332-302, *Global Competitiveness of U.S. Advanced-Technology Manufacturing Industries: Pharmaceuticals*, was instituted in November 1990, following receipt of a request from the Senate Committee on Finance. The Commission transmitted its report to the Committee in September 1991.

FOREIGN TRADE MEASURES

Tariff Measures

The general rates of duty associated with antibiotics in many of the developed countries are similar to or lower than those in the United States. In the European Union (EU),[32] for example, the general rates of duty for antibiotics in bulk form (including mixtures) and in dosage form in 1992 ranged from 5.3 percent to 10 percent ad valorem, with many at the 5.3-percent and 6.3-percent level.[33]

In Canada, the general rates for imports of these products from the United States in 1992 ranged from zero to about 1.8 percent ad valorem.[34] The United States is on a staged duty-elimination schedule under the provisions of the United States-Canada Free-Trade Agreement Implementation Act of 1988.

In recent years, Japan unilaterally instituted a schedule falling under the temporary category that includes rates of duty that are lower than those in its GATT schedule. The temporary schedule is up for review every year on March 31 (the end of the Japanese fiscal year). Under this schedule, the rates of duty for these products in bulk (including mixtures) and dosage forms range from zero to 3.0 percent ad valorem.[35]

Nontariff Measures

Government policies considered to have the most significant effect on the industry, in addition to regulatory concerns, include intellectual property rights protection and price controls/cost-containment programs. Although the patent systems in the United States, Western Europe, and Japan are generally viewed by industry representatives as offering comparable protection and enforcement, concern exists about inadequate patent protection systems in a number of other countries, including many developing countries.[36] Inadequate patent protection in a country can result in losses to companies from patent infringement and can reduce a company's market share and presence in the country.[37]

Price controls, cost-containment programs, or both, have been implemented throughout Western Europe and Japan, primarily in an effort to offset growing national health-care expenditures. The enactment of such programs on a national level, however, often results in decreased R&D spending because these programs often reduce revenues to companies that could be reinvested in R&D programs. Some countries, requiring national price approval prior to marketing pharmaceutical products in the country, also set prices for these products based in part on negotiation and in part on consideration of factors such as exports, investments, research, wages, raw material costs, and employment levels.[38]

U.S. MARKET

Consumption

U.S. consumption of antibiotics, in bulk and in dosage form, increased from about $5.6 billion in 1988 to about $7.3 billion in 1992, or by about 30 percent (see table 2 and figure 3).[39] The growth in the U.S. market was attributable to several factors, including—(1) the increasing size of the domestic geriatric population; (2) the growing use of antibiotics in treating chronic infectious diseases; and (3) the increasing number of over-the-counter products containing antibiotics. Although price differentials exist (primarily between brandname and generic products), consumption of these products by the final consumer is relatively price-insensitive in that such consumption is generally considered necessary for the treatment of a particular disease or condition.

The import-to-consumption ratio for these products generally trended upward during 1988-92, ranging from a low of 8.7 percent in 1989 to a high of

[31] 55 FR 10512, Mar. 21, 1990.

[32] Formerly known as European Community.

[33] Telephone conversation with a representative of the U.S. Department of Commerce on Sept. 15, 1992; and from the *Official Journal of the European Communities*, Sept. 10, 1990, vol. 33, pp. 225 and 228.

[34] Telephone conversation with a representative of the U.S. Department of Commerce on Sept. 15, 1992.

[35] Telephone conversation with a representative of the U.S. Department of Commerce on Oct. 27, 1993; and from the *Customs Tariff Schedules of Japan*, 1992.

[36] Countries, regions, or both, in which inadequate patent protection is of the greatest concern to the pharmaceutical industry include Canada, Latin America, East Asia, and the Pacific Rim.

[37] USITC, *Pharmaceuticals*, USITC publication 2437, p. 3-38.

[38] Ibid.

[39] One source estimated that the market for oral dosage form antibiotics was valued at about $3 billion in 1991. ("Upjohn to Launch *Vantin* Antibiotic Next Month," *European Chemical News*, Sept. 7, 1992, p. 41.)

Table 2
Antibiotics: U.S. producers' shipments, exports of domestic merchandise, imports for consumption, and apparent consumption, 1988-92

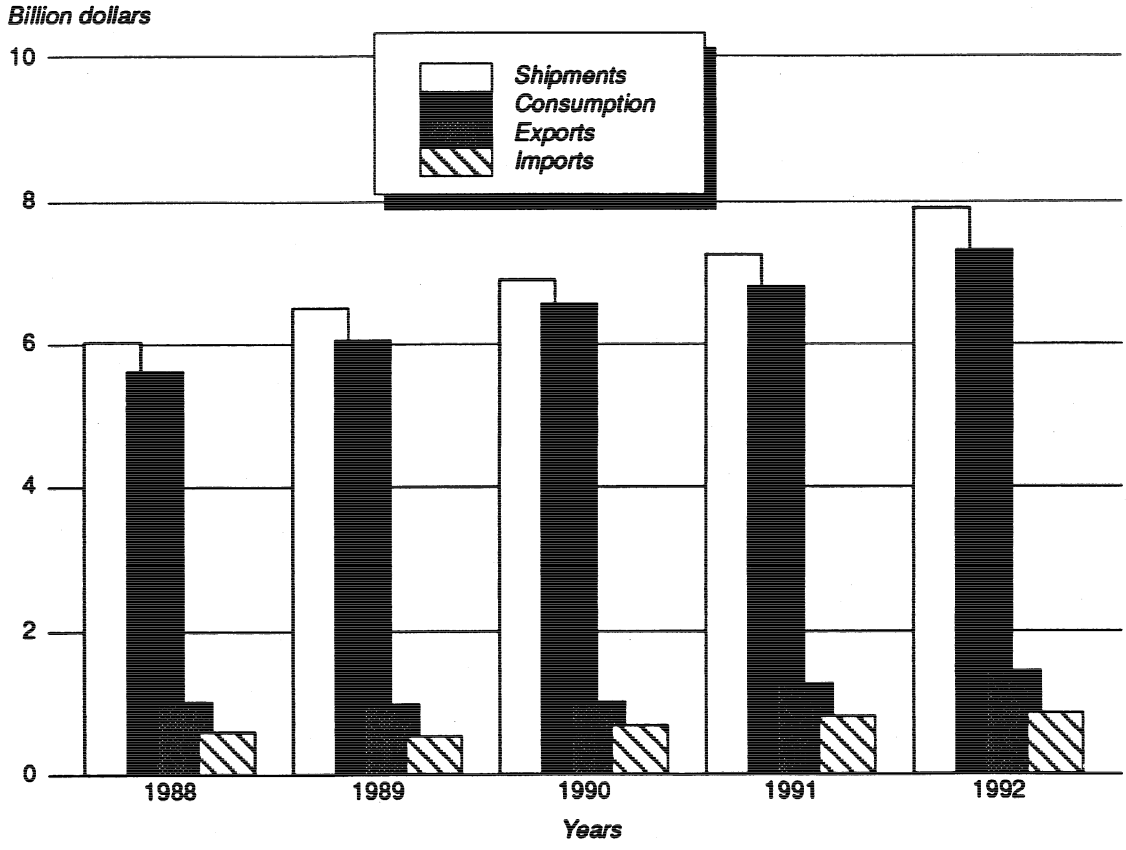
Year	U.S. shipments[1]	U.S. Exports	U.S. Imports	Apparent U.S. consumption	Ratio of imports to consumption
	Million dollars				*Percent*
1988	6,025	1,004	593	5,614	10.6
1989	6,500	973	525	6,052	8.7
1990	6,900	1,010	677	6,567	10.3
1991	7,250	1,254	806	6,802	11.8
1992	7,900	1,438	850	7,312	11.6

[1] Estimated by the staff of the U.S. International Trade Commission.

Note.—Includes production of bulk active ingredient and dosage-form products.

Source: Compiled from official statistics of the U.S. Department of Commerce, except as noted.

Figure 3
Antibiotics (including bulk and dosage forms): U.S. imports, exports, shipments, and apparent consumption, 1988-92



Apparent consumption = Producers' shipments + imports - exports.

Source: Official statistics of the U.S. Department of Commerce and estimates by the Commission.

11.8 percent in 1991. This increase is attributed largely to the increasing trend of pharmaceutical companies to manufacture bulk product overseas to supply foreign markets, particularly prior to receiving marketing approval for the product(s) in the United States,[40] and to the increasing value of the imports because of the declining value of the dollar.

Production

The value of U.S. shipments of antibiotics, in bulk and in dosage form, increased from about $6.0 billion in 1988 to about $7.9 billion in 1992, or by about 32 percent. The average annual rate of increase was about 7 percent. By value, antibiotics, in bulk and in dosage form, represented about 10 percent of all pharmaceuticals produced in the United States in 1992. Dosage form antibiotics accounted for a large share of total production of antibiotics in 1992, in terms of value, primarily because of the added value associated with the production of such products. Specific data on U.S. production of individual classes of antibiotics cannot be published because they would disclose confidential business information.

Imports

U.S. imports of antibiotics increased in value from $593 million to $850 million during 1988-92, or by almost 43 percent (see table 3). This increase is primarily attributable to both the declining value of the U.S. dollar during this period and, inasmuch as the industry is largely multinational and many of the newer products are more likely to be patent protected in the United States, increased related party trade in bulk antibiotics.[41] Moreover, since many multinational companies are reluctant to duplicate the capital expenditures associated with bringing onstream multiple production facilities, companies with production facilities overseas are more likely to import bulk active ingredient for formulation within the United States. This is reflected in the increasing numbers of temporary duty suspensions for individual products sought by companies. The three largest single sources of U.S. imports of antibiotics in 1992 were the United Kingdom (23 percent), Switzerland (22 percent), and Italy (16 percent) (see figure 4). As a group, the EU accounted for 52 percent of total imports of these products.

Duty-free trade under special tariff provisions such as the Generalized System of Preferences (GSP), the Caribbean Basin Economic Recovery Act (CBERA), the United States-Israel Free Trade Area Implementation Act of 1985 (IFTA), and the United States-Canada Free Trade Agreement (CFTA) accounted for about 4 percent of total imports of these products in 1992. As shown in the following tabulation, imports entering under the provisions of GSP and the IFTA accounted for the majority, or 74 percent, of the duty-free imports under consideration.

Type of provision	Value of imports, 1992	Share of duty-free imports under special tariff provisions[1]
	(millions dollars)	*(percent)*
Total imports	850	—
Duty-free imports under special tariff provisions:		
GSP	15	48
IFTA	8	26
CFTA	6	19
CBERA	2	6
Total	31	100

[1] May not equal 100 percent because of rounding.

FOREIGN MARKETS

Foreign Market Profile

Japan and Western Europe are the major overseas markets for antibiotics produced in the United States. The largest single markets by value for these exports in 1992 were Japan (17 percent), Italy (14 percent), and France (9 percent). As a group, the EU accounted for 49 percent of the value of total exports of antibiotics. A large percentage of these exports to Western Europe were bulk antibiotics, which were then formulated into dosage form in individual Western European countries. According to industry estimates, sales of antibiotics accounted for 5-15 percent of total pharmaceutical sales in several EU countries. In Japan, the second-largest world market for pharmaceuticals, antibiotics have traditionally been the major class of pharmaceuticals consumed. More recently, however, producers and importers have been diversifying into cardiovascular agents, central nervous system drugs, digestive system products, and anticancer drugs, echoing changing demographics.

U.S. Exports

The value of U.S. exports of these products increased from $973 million in 1988 to $1.4 billion in 1992, or by almost 50 percent (see table 4). The average annual increase was approximately 14 percent. The ratio of exports to U.S. producers' shipments remained relatively constant during 1988-92, ranging from 18 percent in 1989-90 to 19 percent in 1991.

Bulk antibiotics account for a large share of exports of these products. As mentioned in the section discussing import levels, many producers of antibiotics have production facilities concentrated in a few countries. They have, however, decentralized formulation facilities, locating them in or near most

[40] As mentioned earlier, many companies reportedly seek product approval overseas first because of a perceived differential in approval times overseas compared with those of the United States. USITC, *Global Competitiveness of U.S. Advanced-Technology Manufacturing Industries: Pharmaceuticals*, USITC publication 2437, p. 3-6.

[41] Until the U.S. patent on a product expires, only the company holding the U.S. patent and/or its licensee(s) can import the product.

Table 3
Antibiotics: U.S. imports for consumption, by principal sources, 1988-92

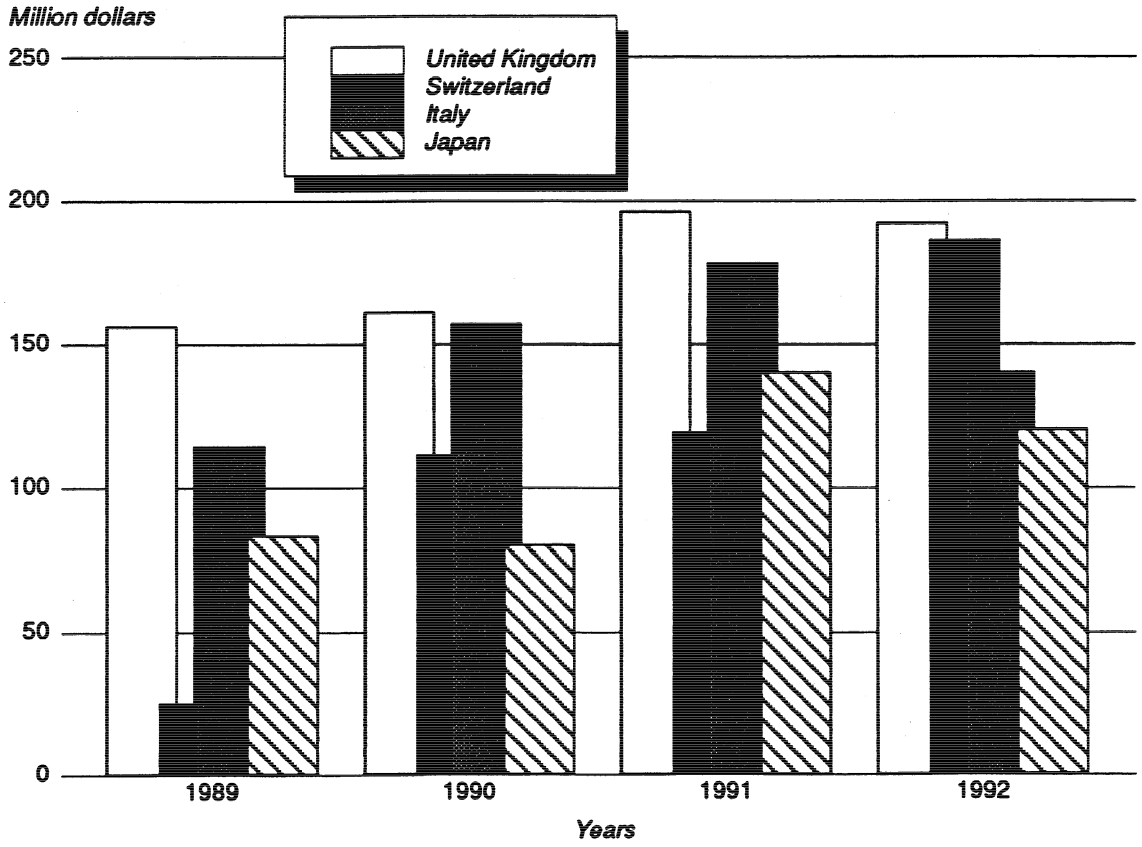
Source	1988	1989	1990	1991	1992
			Value *(Million dollars)*		
United Kingdom	(1)	156	161	196	192
Switzerland	(1)	25	111	119	186
Italy	(1)	114	157	178	140
Japan	(1)	83	80	109	120
Belgium	(1)	1	2	7	31
Germany	(1)	35	34	26	22
Singapore	(1)	1	7	25	22
Austria	(1)	10	12	18	15
Spain	(1)	28	19	17	14
Canada	(1)	5	6	7	14
All other	(1)	68	87	103	95
Total	593	525	677	806	850

[1] Country-level detail provided only for years in which there are actual trade data under the HTS.

Note.—Includes bulk active ingredient and dosage-form products. Because of rounding, figures may not add to the totals shown.

Source: Compiled from official statistics of the U.S. Department of Commerce.

Figure 4
Antibiotics (including bulk and dosage forms): U.S. imports for consumption, by principal sources, 1989-92



Source: Official statistics of the U.S. Department of Commerce and estimates by the Commission.

Table 4
Antibiotics: U.S. exports of domestic merchandise, by principal markets, 1988-92

Market	1988	1989	1990	1991	1992
	Value *(Million dollars)*				
Japan	(1)	254	245	258	250
Italy	(1)	86	71	111	202
France	(1)	84	102	107	128
United Kingdom	(1)	53	56	73	105
Belgium	(1)	54	57	79	79
Canada	(1)	38	48	74	73
Spain	(1)	42	38	54	63
Mexico	(1)	20	30	43	47
Germany	(1)	41	48	42	42
Australia	(1)	10	15	35	41
All other	(1)	291	301	377	408
Total	1,004	973	1,010	1,254	1,438

[1] Country-level detail provided only for years in which there are actual trade data under the new Schedule B (based on the HTS).

Note.—Includes bulk active ingredient and dosage-form products. Because of rounding, figures may not add to the totals shown.

Source: Compiled from official statistics of the U.S. Department of Commerce.

markets being accessed.[42] Bulk product is then shipped from the production facilities to the formulation facilities, resulting in a relatively high level of related-party trade.

[42] Investment in facilities in a particular country, whether involved with production, formulation, or marketing, can often result in better market access within that country. Transportation costs within this industry are relatively low, facilitating this structure. Other advantages of formulating and packaging products abroad include the need to label the products in the language of the country and the desire to meet the preferences of local doctors for certain dosage forms. PMA, *Fact Book*, 1991, p. 12.

U.S. TRADE BALANCE

The antibiotics industry, like the overall U.S. pharmaceutical industry, historically has incurred a positive overall trade balance (see table 5). On a country basis, the largest trade surpluses in antibiotics during 1989-92 have been those with Japan and France; negative trade balances have been incurred with the United Kingdom, Italy (1989-91), and Switzerland. A large share of the imports from the United Kingdom, Italy, and Switzerland are likely to be related-party transactions between the parent companies in these countries and their U.S. subsidiaries, affiliates, or both.

Table 5
Antibiotics: U.S. exports of domestic merchandise, imports for consumption, and merchandise trade balance, by selected countries and country groups, 1988-92[1]

(Million dollars)

Item	1988	1989	1990	1991	1992
U.S. exports of domestic merchandise:					
Japan	(2)	254	245	258	250
Italy	(2)	86	71	111	202
United Kingdom	(2)	53	56	73	105
Switzerland	(2)	23	20	16	24
France	(2)	84	102	107	128
Belgium	(2)	54	57	79	79
Canada	(2)	38	48	74	73
Spain	(2)	42	38	54	63
Germany	(2)	41	48	42	42
Mexico	(2)	20	30	43	47
All other	(2)	278	296	396	425
Total	1,004	973	1,010	1,254	1,438
EU-12	(2)	427	434	552	706
OPEC	(2)	16	17	27	26
ASEAN	(2)	23	22	26	26
CBERA	(2)	12	16	26	39
Eastern Europe	(2)	10	7	16	11
U.S. imports for consumption:					
Japan	(2)	83	80	109	120
Italy	(2)	114	157	178	140
United Kingdom	(2)	156	161	196	192
Switzerland	(2)	25	111	119	186
France	(2)	7	9	4	6
Belgium	(2)	1	2	7	31
Canada	(2)	5	6	7	14
Spain	(2)	28	19	17	14
Germany	(2)	35	34	26	22
Mexico	(2)	0	0	1	6
All other	(2)	71	97	141	120
Total	593	525	677	806	850
EU-12	(2)	368	415	461	438
OPEC	(2)	0	0	0	0
ASEAN	(2)	1	7	25	22
CBERA	(2)	0	0	1	1
Eastern Europe	(2)	7	12	24	16
U.S. merchandise trade balance:					
Japan	(2)	171	165	149	130
Italy	(2)	-28	-86	-67	62
United Kingdom	(2)	-103	-105	-123	-87
Switzerland	(2)	-2	-91	-103	-162
France	(2)	77	93	103	122
Belgium	(2)	53	55	72	48
Canada	(2)	33	42	67	59
Spain	(2)	14	19	37	49
Germany	(2)	6	14	16	20
Mexico	(2)	20	30	42	41
All other	(2)	207	199	255	305
Total	411	448	333	448	588
EU-12	(2)	59	19	91	268
OPEC	(2)	16	17	27	26
ASEAN	(2)	22	15	1	4
CBERA	(2)	12	16	25	38
Eastern Europe	(2)	3	-5	-8	-5

[1] Import values are based on customs value; export values are based on f.a.s. value, U.S. port of export. U.S. trade with East Germany is included in "Germany" but not "Eastern Europe."

[2] Country detail provided only for years in which there are actual trade data.

Source: Compiled from official statistics of the U.S. Department of Commerce.

APPENDIX A
EXPLANATION OF TARIFF AND TRADE AGREEMENT TERMS

TARIFF AND TRADE AGREEMENT TERMS

The ***Harmonized Tariff Schedule of the United States*** (HTS) replaced the *Tariff Schedules of the United States* (TSUS) effective January 1, 1989. Chapters 1 through 97 are based upon the internationally adopted Harmonized Commodity Description and Coding System through the 6-digit level of product description, with additional U.S. product subdivisions at the 8-digit level. Chapters 98 and 99 contain special U.S. classification provisions and temporary rate provisions, respectively.

Rates of duty in the ***general*** subcolumn of HTS column 1 are most-favored-nation (MFN) rates; for the most part, they represent the final concession rate from the Tokyo Round of Multilateral Trade Negotiations. Column 1-general duty rates are applicable to imported goods from all nonembargoed countries except those enumerated in general note 3(b) to the HTS plus Serbia and Montenegro, whose products are dutied at the rates set forth in ***column 2***. Goods from Albania, Armenia, Belarus, Bulgaria, the People's Republic of China, the Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Mongolia, Poland, Romania, Russia, Slovakia, Turkmenistan, Ukraine, and Uzbekistan are currently eligible for MFN treatment, as are the other republics of the former Socialist Federal Republic of Yugoslavia. Among articles dutiable at column 1-general rates, particular products of enumerated countries may be eligible for reduced rates of duty or for duty-free entry under one or more preferential tariff programs. Such tariff treatment is set forth in the ***special*** subcolumn of HTS column 1. Where eligibility for special tariff treatment is not claimed or established, goods are dutiable at column 1-general rates.

The ***Generalized System of Preferences*** (GSP) affords nonreciprocal tariff preferences to developing countries to aid their economic development and to diversify and expand their production and exports. The U.S. GSP, enacted in title V of the Trade Act of 1974 and renewed in the Trade and Tariff Act of 1984, applies to merchandise imported on or after January 1, 1976 and before September 30, 1994. Indicated by the symbol "A" or "A*" in the special subcolumn of column 1, the GSP provides duty-free entry to eligible articles the product of and imported directly from designated beneficiary developing countries, as set forth in general note 4 to the HTS.

The ***Caribbean Basin Economic Recovery Act*** (CBERA) affords nonreciprocal tariff preferences to developing countries in the Caribbean Basin area to aid their economic development and to diversify and expand their production and exports. The CBERA, enacted in title II of Public Law 98-67, implemented by Presidential Proclamation 5133 of November 30, 1983, and amended by the Customs and Trade Act of 1990, applies to merchandise entered, or withdrawn from warehouse for consumption, on or after January 1, 1984; this tariff preference program has no expiration date. Indicated by the symbol "E" or "E*" in the special subcolumn of column 1, the CBERA provides duty-free entry to eligible articles, and reduced-duty treatment to certain other articles, which are the product of and imported directly from designated countries, as set forth in general note 7 to the HTS.

Preferential rates of duty in the special subcolumn of column 1 followed by the symbol "IL" are applicable to products of Israel under the ***United States-Israel Free Trade Area Implementation Act*** of 1985 (IFTA), as provided in general note 8 to the HTS. Where no rate of duty is provided for products of Israel in the special subcolumn for a particular provision, the rate of duty in the general subcolumn of column 1 applies.

Preferential nonreciprocal duty-free or reduced-duty treatment in the special subcolumn of column 1 followed by the symbol "J" or "J*" in parentheses is afforded to eligible articles the product of designated beneficiary countries under the ***Andean Trade Preference Act*** (ATPA), enacted in title II of Public Law 102-182 and implemented by Presidential Proclamation 6455 of July 2, 1992 (effective July 22, 1992), as set forth in general note 11 to the HTS.

Preferential rates of duty in the special subcolumn of column 1 followed by the symbol "CA" are applicable to eligible goods of Canada, and those followed by the symbol "MX" are applicable to eligible goods of Mexico, under the **North American Free Trade Agreement**, as provided in general note 12 to the HTS, effective January 1, 1994.

Other special tariff treatment applies to particular ***products of insular possessions*** (general note 3(a)(iv)), goods covered by the ***Automotive Products Trade Act*** (APTA) (general note 5) and the ***Agreement on Trade in Civil Aircraft*** (ATCA) (general note 6), and ***articles imported from freely associated states*** (general note 10).

The ***General Agreement on Tariffs and Trade*** (GATT) (61 Stat. (pt. 5) A58; 8 UST (pt. 2) 1786) is a multilateral agreement setting forth basic principles governing international trade among its signatories. The GATT's main obligations relate to most-favored-nation treatment, the maintenance of scheduled concession rates of duty, and national (nondiscriminatory) treatment for imported products; the GATT also provides the legal framework for customs valuation standards, "escape clause" (emergency) actions, antidumping and countervailing duties, and other measures. Results of GATT-sponsored multilateral tariff negotiations are set forth by way of separate schedules of concessions for each participating contracting party, with the U.S. schedule designated as Schedule XX.

Officially known as "The Arrangement Regarding International Trade in Textiles," the ***Multifiber Arrangement*** (MFA) provides a framework for the negotiation of bilateral agreements between importing and producing countries, or for unilateral action by importing countries in the absence of an agreement. These bilateral agreements establish quantitative limits on imports of textiles and apparel, of cotton and other vegetable fibers, wool, man-made fibers and silk blends, in order to prevent market disruption in the importing countries—restrictions that would otherwise be a departure from GATT provisions. The United States has bilateral agreements with many supplying countries, including the four largest suppliers: China, Hong Kong, the Republic of Korea, and Taiwan.