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Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets

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Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets

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Abstract

This study examines competitive conditions, including regulatory conditions, affecting U.S. sales and trade of medical devices in Japan and other principal foreign markets during 2001–5. An examination of regulatory cost and approval data by the U.S. International Trade Commission suggests that average total approval times for new medical devices were higher in Japan during the period than in other principal global markets, including the United States and the European Union (EU). Despite Japan's limited success in reducing these times in 2005 after reforms to Japan's Pharmaceutical Affairs Law took effect, significant challenges remain. Innovative, advanced technology medical devices are the most adversely affected by the Japanese regulatory process. U.S. medical device firms are the leading developers and exporters of such products and may be disproportionately affected. Medical device firms generally prefer the EU medical device approval system over the U.S. and Japanese approval systems, due to its shorter approval times. Although medical device regulation in the United States remains tightly controlled, it has become more predictable in recent years, and review times have steadily declined.

The United States, the EU, and Japan together account for about 90 percent of global production and consumption of medical devices. The study finds that the U.S. medical device industry is the most competitive in the world, recognized for its ability to continually design, develop, and place innovative medical devices in U.S. and foreign markets. This can be attributed in part to a higher level of research and development investment and greater availability of venture capital, compared with the EU and Japanese industries. While both U.S. and EU firms produce a broad variety of medical devices, ranging from general hospital supplies to more advanced technology products, including advanced cardiovascular devices, Japanese firms are more narrowly focused on medical imaging devices and commodity hospital supplies. Government healthcare and regulatory policies appear to have inhibited the growth of the Japanese medical device industry, and Japan's global share of related manufacturing has declined throughout the past decade.

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Acronyms

ABHI	Association of British Healthcare Industries
ACCJ	American Chamber of Commerce in Japan
AIMDD	Active Implantable Medical Device Directive (EU)
BLA	Biologics License Application
CABs	conformity assessment bodies
CBERA	Caribbean Basin Economic Recovery Act
CDC	Centers for Disease Control and Prevention
CDRH	Center for Devices and Radiological Health
CE mark	Conformite Europeene mark
CFDA	China Food and Drug Administration
CMS	Centers for Medicare & Medicaid Services
CT	computerized tomography
DRGs	diagnosis-related groups
ECG	electrocardiograph
EEG	electroencephalogram
EMC	electromagnetic compatibility
EU	European Union
FDA	Food and Drug Administration
FDAMA	FDA Modernization Act of 1997
GAO	U.S. Government Accountability Office
GCP	good clinical practices
GDP	gross domestic product
GEMS	General Electric Medical Systems
GHTF	Global Harmonization Task Force
GLPs	good laboratory practices
GMPs	good manufacturing practices
GPOs	group purchasing organizations
GSP	Generalized System of Preferences
GVP	good vigilance practice
HMOs	health maintenance organizations
HTA	health technology assessment
ICC	in-country caretaker
IDA	Investment Development Agency (Ireland)
IPO	initial public offering
IUDs	intrauterine devices
IVDs	in vitro diagnostics
IVDD	In Vitro Diagnostics Directive (EU)
JAAME	Japan Association for the Advancement of Medical Equipment
JCCT	U.S.-China Joint Commission on Commerce and Trade
JETRO	Japan External Trade Organization
M&A	mergers and acquisitions
MAH	market authorization holder
MDD	Medical Device Directive (EU)
MDDI	Medical Device and Diagnostic Industry
MDP	Medical Devices and Pharmaceutical Subgroup
MDR	medical device reporting
MDUFMA	Medical Device User Fee and Modernization Act

Acronyms—*Continued*

MHLW	Ministry of Health, Labour and Welfare (Japan)
MOSS	market-oriented, sector-selective
MRA	Mutual Recognition Agreement
MRI	magnetic resonance imaging
NAICS	North American Industry Classification System
NAS	National Academy of Sciences
NASA	National Aeronautics and Space Administration
NBER	National Bureau of Economic Research
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICE	National Institute for Health and Clinical Excellence
NIH	National Institutes of Health
NRC	National Research Council
OECD	Organisation for Economic Co-operation and Development
OPSR	Organization for Pharmaceutical Safety and Research (Japan)
PAL	Pharmaceutical Affairs Law (Japan)
PDP	Product Development Protocol
PMA	premarket approval
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PMDEC	Pharmaceutical and Medical Devices Evaluation Center (Japan)
PMOA	primary mode of action
PMR	premarket report
R&D	research and development
RAPS	Regulatory Affairs Professionals Society
RFD	requests for designation
STED	Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices
TBT	Technical Barriers to Trade (WTO)
U.K.	United Kingdom
UN	United Nations
USPTO	United States Patent and Trademark Office
WHO	World Health Organization
WTO	World Trade Organization

Executive Summary

This report examines competitive conditions affecting U.S. sales and trade of medical devices and equipment in Japan and other principal foreign markets, for 2001–5, with a focus on comparing the regulatory conditions in the Japanese market with those of the other major foreign markets for U.S.-made medical devices.[1] The United States, the European Union (EU), and Japan together account for about 90 percent of global production and consumption of medical devices. Medical devices range from relatively homogeneous, commodity-type items — such as tongue depressors, syringes, intravenous and blood administration apparatus, and other general hospital supplies — to more advanced products, including cardiac pacemakers, defibrillators, and stents; electromedical therapeutic, monitoring, and imaging devices and apparatus; in vitro diagnostics; and implantable orthopedic and prosthetic devices and appliances.

Overview of Japan's Regulatory System and Impact on U.S. Industry

U.S. medical device firms are the world's leading developers and exporters of high-technology products and may be disproportionately affected compared to other major producers by Japan's regulatory approval system. Although the Japanese approval system does not discriminate in its treatment of domestic and foreign-made medical devices, medical device firms that specialize in innovative products are more adversely affected by the regulatory delays and other unique costs of the Japanese approval system because of the shorter product life cycles (as short as 18 months) and more rigorous regulatory scrutiny of such products compared to less advanced medical technologies.

Specifically, U.S. firms incur three types of unique costs in Japan: opportunity costs associated with much longer product approval times; requirements for conducting additional clinical trials to acquire safety data equivalent to that obtained in previous trials and accepted by regulators in other markets; and new requirements for firms to separate marketing and safety operations from production functions, thereby requiring expensive organizational changes and associated ongoing maintenance costs not required in other principal markets. U.S. industry officials estimate that complying with recent changes in Japan's regulatory system has cost U.S. companies $350 million and that U.S. firms will incur an additional $1.2 billion in compliance costs over the next five years.

The Japanese government enacted major amendments to its Pharmaceutical Affairs Law (PAL) in 2002 to reform its medical device regulatory approval system. These new changes to Japan's regulatory system came in response to pressures both from within and outside of Japan, including the U.S. government. The most significant goals of the reform were to improve efficiency and shorten product approval times. Despite some limited success in reducing product approval times in 2005 after these reforms took effect, significant challenges remain.

[1] On March 9, 2006, the Commission received a request from the Committee on Ways and Means of the U.S. House of Representatives and instituted investigation No. 332-474, Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets, under section 332(g) of the Tariff Act of 1930.

Average total approval times for new medical devices during 2001–5 were much lengthier in Japan than in other major markets, including the United States and the EU. In 2004 (the most recent year for which comparable data are available), the average total review time for approval of a new medical device was 1,083 days in Japan compared with 356 days in the United States for similarly regulated devices. While average total approval times in Japan declined by 60 percent to 678 days in 2005, they remained higher than their average level prior to the reform (176 days in 2002, 565 days in 2003).

Two major reasons for the longer medical device approval times in Japan are (1) too few experienced reviewers to handle approval applications, and (2) a backlog of applications inherited from the previous system. With a review staff of 28 compared to about 300 at the U.S. regulatory agency, the Food and Drug Administration, the Japanese staffing level is well below that of the United States with minimal planned increases.

However, Japanese government data indicate that while the new approval agency did not meet its own performance target of processing 90 percent of its medical device approval applications within 12 months of administrative time, the figure improved from 50 percent in 2004 to 82 percent in 2005. The Japanese government also reported that 100 percent of applications filed in or after 2004 were approved within the 12 month target time; however, this figure does not include those applications filed before the reform that are part of the backlog.

Despite the improvement in Japanese approval times in 2005, total new medical device applications from U.S. companies submitted for review in Japan reportedly decreased from 132 in 2003 to only 8 applications in 2005. U.S. medical device industry officials cited burdensome applications and an unpredictable approval process as reasons for the decline.

Comparison of the U.S., EU, and Japanese Regulatory Systems

Medical device firms generally prefer the EU medical device approval system over the U.S. and Japanese approval systems, due to its shorter approval times. Although medical device regulation in the United States remains tightly controlled, it has become more predictable in recent years, and review times have steadily declined. Meanwhile, despite improvements in 2005, Japan maintains the slowest, least transparent, and most difficult regulatory system of the major markets for medical devices.

Because of the potential health and safety risks intrinsic to medical technology, medical device firms have faced strict regulatory measures in the United States, the EU, and Japan for several decades. These three markets all classify medical devices according to risk, and require approval of riskier devices before they can be marketed. The most important differences among the three systems are those pertaining to the role of government. In the United States and Japan, the government retains final authority for approval of medical devices. In contrast, premarket review and approval in the EU is principally conducted by independent third-party testing laboratories accredited by member state health ministries to review and approve medical devices for the EU market. Although both U.S. and Japanese regulatory bodies use third parties for the preliminary assessment of low- and medium-risk devices, they retain final authority over device approval.

Global Supply and Demand

Worldwide sales of medical devices reached $180 billion in 2005, with U.S. producers accounting for an estimated 51 percent, EU firms 30 percent, and Japanese producers 10 percent. The U.S. medical device industry is the most competitive in the world, recognized for its ability to continually design, develop, and place innovative medical devices in U.S. and foreign markets. This can be attributed in part to a higher level of R&D investment and greater availability of venture capital, compared with the EU and Japanese industries. While both U.S. and EU firms produce a broad variety of medical devices, ranging from general hospital supplies to more advanced technology products, including advanced cardiovascular devices, Japanese firms are more narrowly focused on medical imaging devices and commodity hospital supplies. Government healthcare and regulatory policies appear to have inhibited the growth of the Japanese medical device industry, and Japan's global share of medical device manufacturing has declined throughout the past decade.

The most significant supply and demand factors for the medical device industry were identified and used to analyze the markets of the United States, the EU, and Japan. Table ES-1 provides a summary of these factors with respect to the medical device markets of the United States, the EU, and Japan.

Trade in Medical Devices

The U.S. medical device trade surplus declined steadily, from $5.9 billion in 2001 to $957 million in 2004, before rebounding modestly in 2005 to $1.8 billion. Despite steady growth in U.S. exports (which reached $25.5 billion in 2005), uninterrupted growth in U.S. demand and increased foreign outsourcing by U.S. firms contributed to the decline. Japan continued its historical trend of running a trade deficit in medical devices, while the EU maintained a trade surplus.

Several multilateral and bilateral trade agreements have facilitated U.S. trade in medical devices, as they focus on issues of concern to the medical device industry, including the harmonization of medical device regulatory systems. These agreements and initiatives include the World Trade Organization Agreement on Technical Barriers to Trade (TBT), the market-oriented sector-specific (MOSS) talks and the Regulatory Reform and Competition Policy Initiative with Japan, the medical devices annex of the U.S.-European Union Mutual Recognition Agreement (MRA), the U.S.-China Joint Commission on Commerce and Trade (JCCT) Medical Devices and Pharmaceuticals Subgroup, and the Global Harmonization Task Force (GHTF).

Table ES-1 Summary of the U.S., EU, and Japanese medical device markets

		United States	European Union	Japan
General information	**Products**	Produces a wide variety of medical devices	Produces a wide variety of medical devices	Limited production of medical devices, focused on diagnostic imaging and endoscopy
	Share of global production (estimated)	51 percent	30 percent	10 percent
	Industry	6,000-7,000 small, medium, and large companies	8,500-10,000 companies. Most are small and medium size.	750 large and small companies
	Trade balance	Maintains a trade surplus ($1.8 billion - 2005)	Maintains a trade surplus ($4.5 billion - 2005)	Maintains a trade deficit (-$4.9 billion - 2004)
Supply factors	**Innovation, research and development (R&D), and intellectual property**	High R&D spending leads to much innovation (10-13 percent of sales)	Lower R&D spending leads to less innovation (6 percent of sales)	Lower R&D spending leads to less innovation (6 percent of sales)
	Access to capital	Wide availability of venture capital	Limited access to capital	Limited access to capital
	Industry structure and consolidation	Recent merger and acquisition (M&A) activity has somewhat consolidated the industry	Recent global consolidation has affected the industry, but there are relatively lower levels of intra-EU M&As	Lower levels of consolidation
	Global marketing and distribution networks	Direct distribution system	Direct distribution system	Complex distribution system
	Skilled workforce	Highly skilled workforce High productivity ($297, 938 per worker - 2005)	Highly skilled workforce Relatively lower productivity ($98, 149 per worker - 2005)	Good technical skills in workforce Moderate productivity ($173, 460 per worker - 2004)
	Standards and regulations	Transparent regulatory system	Transparent, efficient regulatory system	Complex government regulatory policies place constraints on market growth
Demand factors	**Healthcare spending**	Large and growing healthcare expenditures (15% of gross domestic product (GDP))	Constrained healthcare expenditures (7-8% of GDP)	Constrained healthcare expenditures (8% of GDP)
	Cost containment policies	Government and private insurers try to contain costs	Government tries to contain costs	Government and private insurers try to contain costs
	Demographics	Population is 298.4 million. 12% of population age 65 or older in 2005. This is expected to reach 18% by 2025.	Population is 457.0 million. 17% of population age 65 or older in 2004. This is expected to reach 23% by 2025.	Population is 127.5 million. 20% of population age 65 or older in 2004. This is expected to reach 30% by 2025.

Data Sources

Industry definitions and product coverage for the medical device industry vary between countries. The information used in preparing this report was obtained through interviews with industry associations, government regulators, companies, market analysts, venture capital firms, economists, and hospital purchasing officials throughout the United States, the EU, and Japan. In addition to fieldwork and telephone interviews, information was gathered through published sources, testimony at the Commission's July 11, 2006 public hearing, and written submissions from interested parties. The Commission's review of the literature identified few studies, with the exception of a comprehensive study completed in 2005 for the European Commission, with direct relevance to assessing the effects of regulation and other conditions of competition on the U.S. medical device industry. This report provides, to the extent possible, an in-depth examination of the role and impact of regulatory approval systems in principal markets on trade and competitiveness in the medical device industry. It also presents and analyzes production and trade information for the United States and its principal foreign competitors at a more detailed product and segment level than previous studies.

CHAPTER 1
Introduction and Overview

This report examines the competitive conditions affecting U.S. sales and trade of medical devices and equipment (medical devices) in Japan and other principal foreign markets throughout the most recent 5-year period. The report focuses on those medical devices that accounted for the largest shares of U.S. exports to these markets throughout this period, and compares the competitive conditions in the Japanese market with those of other major foreign markets for U.S.-made medical devices, paying particular attention to regulatory conditions. The report was prepared in response to a request from the Committee on Ways and Means.[1]

For purposes of this study, medical devices include in vitro diagnostics (IVDs); electromedical equipment; surgical and medical instruments; orthopedic devices and hospital supplies; and dental equipment.[2] These devices are all used in professional medical practice for the prevention, diagnosis, and treatment of diseases and injuries, and the correction of physical deformities of the body. Such medical devices range from relatively homogeneous, commodity-type items — such as tongue depressors, syringes, intravenous and blood administration apparatus, and other general hospital supplies — to more advanced products, including cardiac pacemakers, defibrillators, and stents; electromedical therapeutic, monitoring, and imaging devices and apparatus; and implantable orthopedic and prosthetic devices and appliances.[3] Table 1-1 provides examples of specific medical devices.

The United States, the European Union (EU), and Japan are the three largest producers and consumers of medical devices in the world. Together, they account for almost 90 percent of both total global production and global consumption (valued at an estimated $180 billion in 2005) of such equipment (figures 1-1 and 1-2).[4]

[1] On March 9, 2006, the Committee on Ways and Means (Committee) requested that the U.S. International Trade Commission (Commission) prepare a report under section 332(g) of the Tariff Act of 1930 (19 U.S.C. 1332(g)) that examines the competitive conditions affecting U.S. sales and trade of medical devices and equipment in Japan, and other principal foreign markets, for the most recent 5-year period. The Committee requested that the Commission submit its report no later than March 9, 2007. A copy of the request letter is included in app. A, and the Commission's notice of investigation, published in the Federal Register of April 6, 2006 (71 FR 17496), is in app. B.

[2] The United States, European Union (EU), and Japan define the medical device industry differently. These categories, although used for U.S. data and EU trade data, cannot be utilized for EU production data or for Japan trade and production data. The definitional differences are explained, where necessary, throughout the report.

[3] Ludwig, hearing transcript, 7.

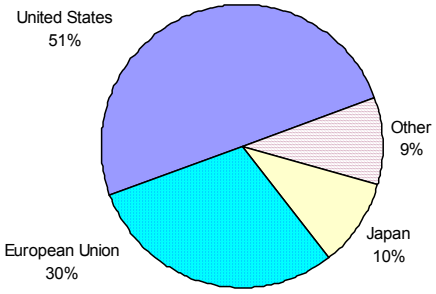
[4] Estimated by Commission staff based on official data of the U.S. Department of Commerce, the European Union (Eurostat), and the Japanese Ministry of Health, Labour and Welfare (MHLW); U.S., EU, and Japanese medical device trade associations; and other sources.

Table 1-1 Examples of medical devices

Abdominal stent grafts	Dental instruments	Arthroscopic instruments
Anesthesia machines	Denture adhesive cream	Pacemakers
Ankle braces	Disposable needles	Patient monitoring systems
Artificial heart valves	Drug-eluting stents	Prostheses
Bandages	Endoscopes	Splints
Blood gas monitors	Forceps	Surgical clamps
Blood glucose meters	Hearing aids	Surgical gloves
Blood transfusion apparatus	Implantable infusion pumps	Syringes
Bone screws	In-vitro diagnostics	Ultrasound equipment
Catheters	Knee braces	Urinary catheters
Chisels	Liquid disinfectors	Ventilators
Coils to treat aneurysm	Magnetic resonance imaging (MRI) equipment	X-rays
Computed tomography (CT) equipment	Medical lasers	
Defibrillators	Neuromuscular stimulators	
Dental chairs	Orthopedic implants (hip, knee, spinal, etc.)	

Source: Compiled by Commission staff from various sources.

Figure 1-1 Global production in the medical device industry, by major producers, 2005

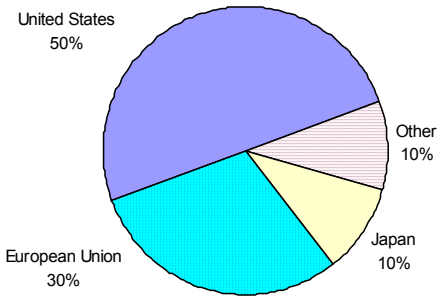


Total = $180 billion

Source: Estimated by Commission staff based on official data of the U.S. Department of Commerce, the European Union (Eurostat), and the Japanese Ministry of Health, Labour and Welfare; U.S., EU, and Japanese medical device trade associations; and other sources.

Note.—Because of regional differences in industry definitions and product coverage, these estimates are not directly comparable to the official statistics presented in chapter 3.

Figure 1-2 Global consumption in the medical device industry, by major markets, 2005



Total = $180 billion

Source: Estimated by Commission staff based on official data of the U.S. Department of Commerce, the European Union (Eurostat), and the Japanese Ministry of Health, Labour and Welfare; U.S., EU, and Japanese medical device trade associations; and other sources.

Note.—Because of regional differences in industry definitions and product coverage, these estimates are not directly comparable to the official statistics presented in chapter 3.

Total trade in medical devices was valued at nearly $190 billion in 2005 (figure 1-3).[5] The largest producers are also the largest traders of medical devices with the EU, United States, and Japan accounting for 68 percent of total trade in 2005. Switzerland and China are other large traders of medical devices, with more than $8 billion each. These estimates may not match official national data that appear in other parts of this report, as industry definitions and product coverage for the medical device industry vary amongst countries; data limitations are discussed in box 1-1.

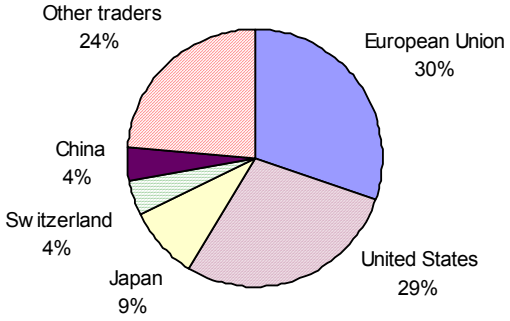
U.S.-based companies dominate global sales of medical devices. As shown in table 1-2, 15 of the leading 20 global firms in terms of medical device revenue in 2005 were U.S.-headquartered firms, while the remaining 5 companies were EU-based.[6] Terumo, the leading Japanese-based firm in terms of medical device revenue in 2005, ranked 24th worldwide.

The U.S. industry is responsible for more than one-half of world production and manufactures a wide variety of medical devices, ranging from commodity hospital supplies and general medical and surgical instruments and apparatus, to advanced medical imaging

[5] Global Trade Information Services, *World Trade Atlas 2006*. World Trade Atlas statistics likely underestimate trade in medical devices. See chapter 4 for more information on trade in this industry. Global production is less than total trade as a result of different data sources.

[6] "The Top 30 Global Medical Device Companies," *Medical Product Outsourcing*, 1-2; company annual reports and forms 10-K, and other sources.

Figure 1-3 Global trade in the medical device industry, by major traders, 2005



Total = $190 billion

Source: Global Trade Information Services, Inc., *World Trade Atlas Database 2006*.

Box 1-1 Data limitations

Industry definition and product coverage for the medical device industry vary among countries. Although the Commission was able to improve upon past industry reports and provide global estimates, data for this industry and across the three major markets are not directly comparable. Specifically, EU production data are understated for at least two reasons. First, production data from Eurostat, the official data source, does not include missing values (where individual countries have failed to report) or suppressed values (where data are not publicly reported to protect confidential business information). Second, Eurostat reports production totals for the category NACE 33.1, medical and surgical equipment and orthopedic appliances. This category does not include chemical and biochemical devices, such as in vitro diagnostics, which are classified under "chemicals," and medicine-impregnated products, such as gauzes, which are classified as "pharmaceutical preparations." Moreover, these particular types of medical devices are extremely difficult to separate out from chemical and pharmaceutical preparation classifications in the Eurostat database, while the United States and Japan were able to include them in their statistics. EU trade data, gathered using Global Trade Atlas, were available only at the 6-digit HS level, and, therefore, may underestimate EU trade in medical devices. While there are fewer concerns with the Japanese production and trade data, they are also understated to some extent compared with the U.S. data, as Japan's industry definition and product coverage are not identical to those of the United States.

In addition to collecting official government regulatory and other data for use in this report, U.S. International Trade Commission (Commission) staff met with industry associations, government regulators, companies, market analysts, venture capital firms, economists, and hospital purchasing officials in the United States, the European Union, and Japan to gain their perspective on the issues addressed in the request. In addition to fieldwork and telephone interviews, information was gathered through published sources, a July 11, 2006 public hearing, and written submissions from interested

Table 1-2 Top global manufacturers of medical devices, 2005[a]

Rank	Company	2005 medical device revenues	Headquarters
1	Johnson and Johnson	$17.7 billion	United States
2	GE Healthcare	$12.1 billion	United States
3	Medtronic	$10.1 billion	United States
4	Baxter International	$9.8 billion	United States
5	Cardinal Health	$9.8 billion	United States
6	Tyco Healthcare	$9.5 billion	United States
7	Siemens Medical Solutions	$9.2 billion	Germany
8	Philips Medical Systems	$7.5 billion	Netherlands
9	Boston Scientific[b]	$6.3 billion	United States
10	Stryker	$4.9 billion	United States
11	B. Braun	$3.9 billion	Germany
12	Guidant Corp.[b]	$3.6 billion	United States
13	3M Healthcare	$3.5 billion	United States
14	Zimmer Holdings	$3.3 billion	United States
15	Becton Dickinson & Co.	$3.0 billion	United States
16	St. Jude Medical	$2.9 billion	United States
17	Kodak Health Group	$2.7 billion	United States
18	Hospira	$2.6 billion	United States
19	Fresenius	$2.5 billion	Germany
20	Smith & Nephew	$2.4 billion	United Kingdom

Source: *Medical Product Outsourcing*.

[a] In vitro device companies are not included in this list.
[b] Boston Scientific and Guidant merged in 2006.

and therapeutic devices, including computed tomographic (CT) equipment; digital ultrasound, nuclear, and magnetic resonance imaging (MRI) equipment; coronary pacemakers; defibrillators; and stents.[7] The U.S. industry distinguishes itself from its EU and Japanese competitors through its ability to continually design, innovate, and place leading-edge, high-technology medical devices in U.S. and foreign markets.[8] Notwithstanding these strengths, a longstanding U.S. trade surplus in medical devices declined steadily throughout 2001–4, before modestly rebounding in 2005, as demand growth in the U.S. market for medical devices outpaced growth in principal foreign markets, causing U.S. imports to increase more than U.S. exports.[9]

[7] Diller and Gold, "Healthcare: Products and Supplies," February 2006, 1-17; and U.S. industry official, interviews by Commission staff, United States, June 5-16, 2006.

[8] Diller and Gold, "Healthcare: Products and Supplies," February 2006, 1-17; Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 1-60; and Pammolli et al. in *Medical Devices, Competitiveness and Impact on Public Health Expenditures*, 116-159.

[9] OECD, "How Does the United States Compare," 1; OECD, "Total Expenditures on Health-% of Gross Domestic Products"; and OECD, "Special Report: America's Health-Care Crisis, Spending on Health as % of GDP" (table), 25.

The EU, which accounts for almost one-third of global production and world consumption, also produces a broad scope of medical goods and generally has maintained global surpluses in medical device trade. Germany, by far the largest EU producer, excels in the production of high quality precision medical and surgical instruments and electromedical equipment. Ireland has become an increasingly important producer of advanced medical devices in the past 5 years because of tax incentives and a low-cost labor pool, attracting substantial investment in manufacturing operations by leading U.S.-based producers of implantable cardiac pacemakers and defibrillators, drug eluting stents, and orthopedic implants.[10]

Japan, whose share of total global medical device manufacturing declined from approximately 13 to 15 percent in the mid 1990s to about 10 percent in 2005,[11] is highly specialized in the production of medical imaging and optical medical devices. The country imports a significant portion of its other medical device needs from the United States and the EU, including high-technology medical devices.[12] Japan has historically run a trade deficit in medical devices, including a deficit of approximately $1.3 billion with the United States in 2005.[13]

In recent years, there has been an increase in advanced medical goods manufacturing and assembly in countries such as Switzerland and Ireland, as well as an increase in final assembly of commodity hospital supplies by developing-country affiliates of U.S. firms. In addition, China's rapidly expanding economy and large population are drawing increasing investment from medical device manufacturers.[14]

Demographics (such as an aging population), income growth, and an increased range of health conditions that utilize medical devices are the main drivers of medical device demand.[15] New technologies resulting from investment in research and development (R&D), and increased outsourcing have further contributed to industry growth.[16] However, in recent years, cost-containment strategies by U.S. and overseas healthcare providers have constrained medical device markets.[17] For example, rising healthcare expenditures, coupled with government and private budget constraints, have led insurers to control pricing more tightly.[18]

The report includes, to the extent possible, for 2001–5, (1) an overview of the global market for medical devices, including production, consumption, and trade; (2) profiles of the medical device industries in the United States and principal foreign producer countries;

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[10] IDA Ireland, "Industry Profile-Medical Devices," 1; Irish industry and government officials and experts, interviews by Commission staff, European Union, September 28-29, 2006; and annual reports and forms 10-K, of Abbott Laboratories, Baxter International, Boston Scientific, Johnson & Johnson (DePuy), and Medtronic Inc. See textbox 4-2 for further information on Ireland as a production location and on outsourcing in the medical device industry.

[11] Some public sources continue to estimate Japan at 11-15 percent of global production. Commission staff estimates, which are low in comparison, are based on official Japanese data.

[12] JETRO, *Japanese Market Report No. 69: Medical Equipment*, 6-11; Hanawa, "Medical Devices," 1-4; Hanawa, *US&FCS Market Research Report*, 1-10; and Pammolli et al., "Competitiveness, Productivity and Industry Structure" and "R&D and Innovation," chs. in *Medical Devices, Competitiveness and Impact on Public Health Expenditure*, 90-115 and 116-159.

[13] Based on statistics of the U.S. Department of Commerce.

[14] See textbox 4-1 for further information.

[15] Pammoli, et al., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 17.

[16] Diller and Gold, "Healthcare: Products and Supplies," August 31, 2006, 10.

[17] Pammoli, et al., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 17.

[18] Diller and Gold, "Healthcare: Products and Supplies," August 31, 2006, 3.

(3) an analysis of U.S. trade in medical devices with major competitor countries, including a description of trade practices, regulatory measures such as those regarding product approvals, and government and private expenditures on medical research; (4) an examination of bilateral and multilateral trade agreements that address regulatory issues in major foreign markets, and their implications for the U.S. medical device industry; and
(5) a comparison of regulatory conditions in Japan with those in other major foreign markets.

Chapter 2 of this report identifies the principal competitive factors affecting the medical device market. Profiles of the U.S., EU, and Japanese medical device industries can be found in chapter 3. Chapter 4 analyzes trade in medical devices, focusing on key markets and products. Chapter 5 describes trade agreements that address issues related to medical devices and the implications of those agreements for U.S. exports. Chapter 6 describes Japan's regulatory approval system for medical devices and compares that system with those of the United States and the EU. Appendices A through D contain copies of the request letter from the Committee on Ways and Means, the Commission's *Federal Register* notice, a list of participants at the Commission's July 11, 2006 hearing, and a glossary, respectively.

CHAPTER 2
Principal Competitive Factors

This chapter identifies the principal competitive factors in the global medical device market.[1] On the supply (production) side, the competitiveness of the medical device industry is tied most closely to the innovation, development, and protection of new and existing technologies. Access to capital, through both private financing and government support; industry structure and consolidation; and the delicate regulatory balance between protecting health and safety and allowing new products to enter the market are also important supply side factors. Important demand (consumption) factors include levels of healthcare spending, reimbursement policies, and demographics (figure 2-1).

Figure 2-1 Medical devices: Factors of competitiveness

Supply factors:
- Innovation, research and development, and intellectual property
- Access to capital
- Consolidation and strategic alliances
- Global marketing and distribution networks
- Highly skilled workforce
- Standards and regulations

Demand factors:
- Healthcare spending
- Reimbursement policies
- Demographics

Source: Compiled by Commission staff based on information gathered from a literature review, interviews with U.S.-, Japan-, and EU-based companies and associations, a public hearing, and written submissions of interested parties.

Supply Side Factors

Innovation, research and development, and intellectual property

Innovation and a strong commitment to R&D are principal competitive factors for this industry and were the factors most frequently cited as critical to firm success.[2] The medical device industry is R&D-intensive, driven by constant innovation and short product life cycles.[3] According to the National Academy of Sciences (NAS), most advanced medical devices tend to undergo continual product improvements that eventually render the products

[1] These factors were identified through a literature review; interviews with U.S.-, Japan-, and EU-based companies, associations, and market analysts; a public hearing; and written submissions by interested parties.

[2] U.S., EU, and Japanese industry officials and market analysts, interviews by Commission staff, United States, European Union, and Japan, June–September 2006.

[3] AdvaMed, *The Medical Technology Industry at a Glance*; and U.S. industry officials, interview by Commission staff, United States, April 19, 2006.

obsolete, often within 2 years or less.[4] The U.S. medical device industry is particularly R&D-intensive; U.S. firms spend more than 10 percent of their total revenues on R&D, approximately twice the average of those in the EU and Japan.[5]

The technological innovation process in the medical device industry is often based on applied research and product engineering problem-solving by firms (many of them small), university and hospital doctors, and other medical workers, all of whom contribute to the modification, upgrading, and incremental improvement of existing medical devices.[6] Much innovation, in fact, occurs after products have been used in clinical settings; medical professionals can then interact closely with producers to refine, improve, and develop new applications for medical devices (figure 2-2).

Many studies have examined the determinants of innovation in the health technology industries.[7] According to the NAS, for example, innovation requires both a strong commitment to science and significant financial resources. Long development times, burdensome regulations, and uncertainty about reimbursement may hinder access to necessary capital.[8] Thus, regulatory procedures and reimbursement affect not only whether a medical device is marketed and becomes accessible to patients, but also the process of innovation in the industry. If the regulatory process is perceived as being slow and expensive for innovative devices, then incentives shift to producing more "me-too"[9] or derivative devices, which are usually subject to a less rigorous and less lengthy review process and generally have much lower profit margins than the newer devices.[10]

The medical device industry includes both large global firms and a large number of small entrepreneurial companies and startups.[11] Small, innovative companies may be particularly sensitive to regulatory and other requirements that can divert their limited resources and cash flow. The risk profiles of these small companies often are closely tied to the success of one or a few products. Providing opportunities for earlier revenue streams through

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[4] This contrasts with pharmaceuticals whose basic formulations usually remain unchanged for the commercial lifetime of the product, which can be as long as 5 to 50 years. Gelijns and Halm, eds., *The Changing Economics of Medical Technolo*gy, 93; and Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 4.

[5] Pammolli, et al., *Medical Device Competitiveness and Impact on Public Health Expenditure*, 116–135; Gold and Diller, "Healthcare: Products and Supplies," February 2006, 19 and 25; and Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 31–46 and 49–60.

[6] Roberts, "Technological Innovation and Medical Devices," 4–13.

[7] See, for example, Aspden, ed., *Medical Innovation in the Changing Healthcare Marketplace: Conference Summary*; Hanna, et. al., eds., *Innovation and Invention in Medical Devices*; and Gelijns and Halm, eds., *The Changing Economics of Medical Technology.*

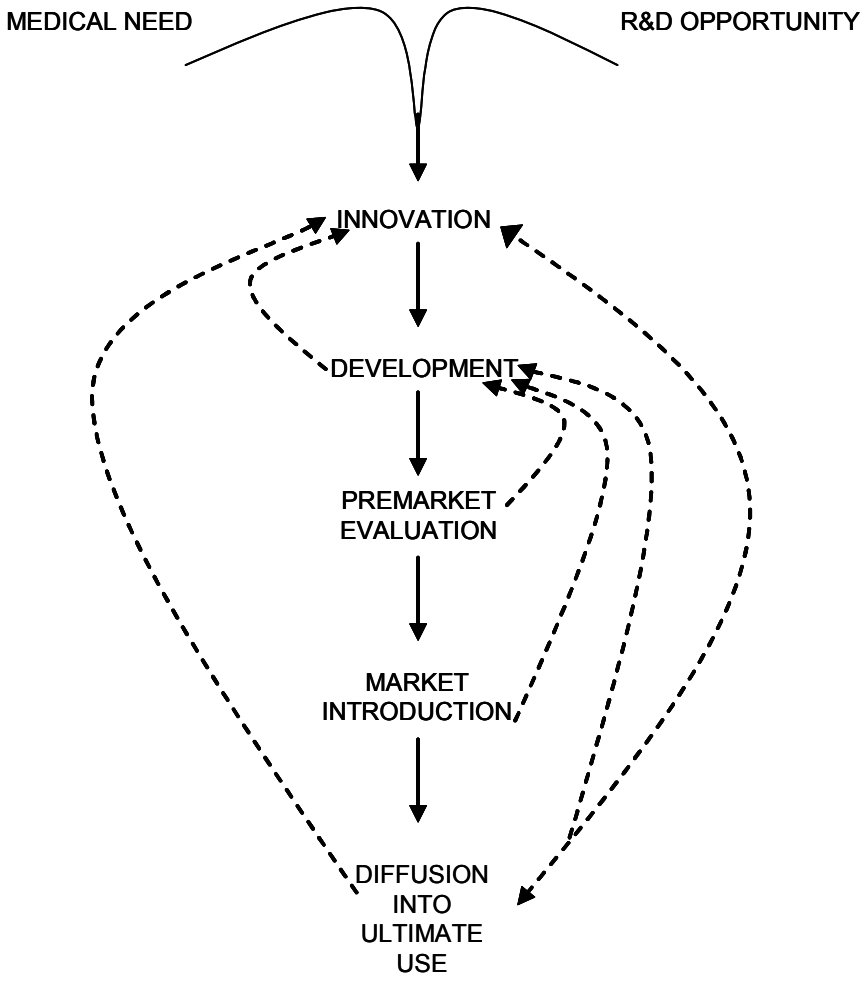
[8] Hanna, et. al., eds., *Innovation and Invention in Medical Devices*, 56.

[9] "Me-too" devices refer to those that are comparable to already approved medical devices, or predicate devices. In most instances, the process for gaining approval of a me-too medical device is much less lengthy than that for new medical devices. It usually only requires a manufacturer to provide information demonstrating equivalence to already approved products that pose no special safety concerns. PMDA Annual Report, 2005; and Japanese government officials, interview with Commission staff, Japan, August 8, 2006.

[10] U.S. and Japanese industry and government officials, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[11] According to data cited at a 2001 NAS workshop, of the 6,000 companies and 3,000 product lines covered by the medical device industry, only 1,000 companies had revenues over $100 million and only 64 product groups had revenues over $150 million. Hanna, et. al., eds., Innovation and Invention in Medical Devices, 54.

Figure 2-2 Innovation and new product introduction in the medical device industry



Source: William W. Lowrance, *New Medical Devices* (Washington, DC: National Academy Press, 1988).

efficient and predictable regulatory and reimbursement requirements may play an important role in improving the innovation outlook for these small companies.[12]

The development and marketing of medical devices involve complex sequential decision making, which can be conceptualized through "real options analysis."[13] Each new product creation incurs development costs, takes time, and has a projected net cash flow over its product life. If demand conditions or production cost estimates change after the onset of the initial R&D effort, the firm may elect to minimize losses and discontinue the process. Longer approval times will lower the value of the effort because they prolong the period of costs and delay the beginning of the revenue stream.

Medical device innovation is risky and replete with regulatory hurdles; intellectual property protection can offset some of these downside risks. Intellectual property protection provides an incentive to invest in research by providing property rights to the inventor. By granting a limited monopoly, a patent may enable a better return on successful research and provide the incentive to invest when payoffs are uncertain.[14] However, the utility of medical device patents is somewhat limited by the nature of innovation in the field. According to industry officials, because devices often can be designed in a number of different ways, competitors can more easily "build around" patents for medical devices as compared to pharmaceuticals.[15]

Notwithstanding these limitations, there is substantial medical device patent activity in the United States, the country where medical device firms are most likely to seek patent protection. Approximately 140,000 medical device patents were filed with the U.S. Patent and Trademark Office (USPTO) from 1977 to 2004. Of these, 71 percent were of U.S. origin; Japan ranked a distant second, with 7 percent of all patents granted; and Germany third, with 5 percent.[16] Leading firms, such as Medtronic, Boston Scientific, and Johnson & Johnson, each received more than 250 U.S. patents in 2005.[17] Thus, despite the challenges presented by the relative ease of "build arounds," patent protection remains critical to industry leaders. Patents are often extremely important to smaller firms, whose most valuable assets may be inventions in the early stages of development. Venture capitalists consider well-protected intellectual property a necessary, although not sufficient, condition for funding.[18]

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[12] Hanna, et. al., eds., *Innovation and Invention in Medical Devices*, 49; and Gelijns and Halm, eds., *The Changing Economics of Medical Technology*, 91.

[13] Real options analysis uses techniques adapted from financial options to generalize traditional capital budgeting or cash flow analysis. Real options can incorporate uncertainty, investor flexibility, and the limited ability to expand or reverse previous decisions. Recent books on real options analysis include Dixit and Pindyck, Trigeorgis, and Copeland and Antikarov.

[14] Hahn, ed., *Intellectual Property Rights in Frontier Industries*, 11.

[15] Ludwig, hearing transcript, 116–117; Agress, hearing transcript, 117; Italian industry officials, interviews by Commission staff, Italy, September 28, 2006; and Gold and Diller, "Healthcare: Products and Supplies," August 2006, 26. Moreover, in the in vitro diagnostics (IVD) segment, where discoveries may be used for further research, there are legal and practical limitations to the availability of patent protection. U.S. industry officials, interviews by Commission staff, United States, June 9, 2006; and Truong and Levy, "U.S. Patents on Medical Diagnostics: Valid...For Now," June 2006.

[16] U.S. Patent and Trademark Office (USPTO), *Technology Profile Report*.

[17] Kratzer, "Medtech's Patent Strongholds."

[18] U.S. industry officials, interviews by Commission staff, United States, June 6 and 7, 2006; and German industry officials, interviews by Commission staff, Germany, September 22, 2006.

Access to capital

Adequate funding for R&D, through both private and government expenditures, is critical to the development and commercialization of new medical technology. A robust venture capital industry, combined with strong government support of medical research, provides U.S. medical device firms with important competitive advantages over those in Europe and Japan.[19] The aging population's growing demand for medical device products, among other factors, has increased the attractiveness of the medical device industry for venture capital funds.[20] Venture capital funding to U.S. medical device firms totaled approximately $1.7 billion in 2004, climbed to $2.1 billion in 2005, and is on track to exceed these levels in 2006.[21] Many companies also obtain funding through initial public offerings (IPOs). Nineteen U.S. medical technology firms undertook IPOs in 2004 and 12 in 2005; the median amount raised per IPO was $60 million.[22] Venture capital and equity financing may be used to fund R&D, to facilitate mergers and acquisitions (M&A), and to create and maintain the distribution channels needed to market medical devices domestically and overseas.

A strength of the U.S. medical device industry is the significant amount of research conducted by its national government.[23] The National Institutes of Health (NIH) and the National Aeronautics and Space Administration (NASA) contribute significantly to the development of U.S. medical technology.[24] The EU's framework programmes for research and technological development are the main vehicle for government funding of medical device firms in Europe. Japan's National Institute of Health Science conducts its own medical research and provides its research results to the medical and scientific community. However, it does not provide the same sort of university and private sector grants that exist in the United States and the EU. Government-financed medical research allows industry to devote less revenue toward R&D while maintaining the level and extent of research necessary to improve medical technology and place new products on the market.[25]

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[19] U.S., EU, and Japanese industry officials and market analysts, interviews by Commission staff, United States, European Union, and Japan, June-September 2006.

[20] Loftus, "Medical Device Venture-Capital Funding on the Rise."

[21] These totals include investments by venture capital firms, venture arms of corporations, institutions, investment banks and entities whose primary activity is financial investing. Where there are other participants in a verified financing round, such as wealthy individuals or "angel investors," their contributions are included. PricewaterhouseCoopers, "Money Tree Report, Historical Trend Data: Medical Devices and Equipment" and "Report Definitions and Methodology."

[22] Navarro, "The Changing Landscape of the Medical Technology Industry."

[23] Pammolli, et al., "R&D and Innovation," 116–159; Nelson, M.D., "Innovation and Invention in Medical Devices: Implantable Defibrillators," 21–25; Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 31–38; National Academy of Science, Institute of Medicine official, telephone interview by Commission staff, May 17, 2006; and U.S. industry officials, personal and telephone interviews by Commission staff, United States, June 5–26, 2006.

[24] For further information on NIH and NASA funding related to their support for basic and applied R&D with relevance to medical technology, see their annual reports at *http://www.nih.gov* and *http://www.nasa.gov*, respectively. For background and history of U.S. government research and expenditures strengthening the medical technology industry, see Thomas, Jr., "Federal Support of Medical Device Innovation," 51–57; and Hanna, et al., *Innovation and Invention in Medical Devices*, 31–38.

[25] U.S., EU, and Japanese industry officials and market analysts, interviews by Commission staff, United States, European Union, and Japan, June–September 2006.

Consolidation and strategic alliances

M&A and strategic alliances[26] are important tools that affect both large and small companies in the medical device industry. The industry has undergone significant consolidation in the past 10 years. Key acquisitions in the global medical device industry totaled approximately $37 billion in 2006 (including Boston Scientific's $25 billion acquisition of Guidant), compared with approximately $10 billion in 2005.[27] A principal driving force behind M&A activity has been market expansion, as many large medical device firms seek to complement their product mix by acquiring smaller firms producing new, innovative medical devices or serving niche markets.[28] Smaller companies benefit from M&A activity by gaining access to funding for the development and marketing of their products, in addition to the regulatory expertise necessary to place their product on the market.[29] Brand recognition and the wider product and service selection offered by more established firms also provide competitive advantages over smaller and less well-known firms. Further, by producing medical devices in high volumes, large firms are able to achieve manufacturing cost efficiencies that are unavailable to small and medium size firms.[30]

Global marketing and distribution networks

Effective marketing and distribution networks are important determinants of medical device industry competitiveness. Companies with strong marketing networks are able to establish long-term supply contracts with their customers, enabling future sales. In Japan, which is characterized by a highly complex medical device distribution system, an effective network requires a relationship with experienced and well-connected dealers who maintain effective distribution networks and access to hospitals and who may assist manufacturers to develop long-term supply relationships.[31] Nearly all industry analysts and distributors interviewed by Commission staff in Japan noted that Japan's relatively complex distribution system has increased both supply inefficiencies and prices.[32]

Highly skilled workforce

A highly skilled workforce, which includes researchers, engineers, and staff with regulatory expertise, is an important competitive factor in the medical device industry.[33] Medical device companies continually seek the latest skills in engineering, electronics, and materials science, among other disciplines.[34] Expertise in regulatory affairs and reimbursement is critical to the

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[26] An example of a strategic alliance in medical devices is the May 2006 collaboration agreement between GE Healthcare and St. Jude Medical to develop a cardiovascular ultrasound imaging system. *Wireless News*, "GE Healthcare and St. Jude Medical Join to Help Fight Heart Disease and Stroke"; and U.S. industry official, interview by Commission staff, United States, June 12, 2006.

[27] Burkhardt and Tardio, "Converging Trends Drive Industry Consolidation," December 2006.

[28] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and Mergent, *The North America Medical Instruments & Equipment Sectors: A Company and Industry Analysis,* 5.

[29] Diller, "Healthcare: Products and Supplies: Asia," 28.

[30] Ibid.

[31] Japanese dealers tend to be regional or product-specific rather than national and broad-based, so manufacturers have to build multiregional networks. Diller, "Healthcare: Products and Supplies: Asia," 25; and U.S. industry official, interview by Commission staff, United States, June 12, 2006.

[32] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

[33] U.S. and EU industry officials, interviews by Commission staff, United States and Europe, June 5–16, 2006 and September 18–29, 2006.

[34] Diller and Gold, "Healthcare: Products and Supplies," August 2006, 22.

medical device industry, as each new and improved product must be approved in every country in which it is to be sold and the requirements for approval are constantly evolving. Large numbers of staff often are devoted to regulatory affairs. Reimbursement experience can help a firm boosts its returns. Expertise in other regulatory areas, such as environmental, import/export, and transportation policies, are also important for competitive success.[35] However, the need to devote substantial resources to regulatory matters often reduces resources that would otherwise be available to support product development and commercialization.[36]

Standards and regulations

Understanding a country's standards and regulations and its regulatory process is pivotal in securing approval to sell medical devices in that market. Complex standards and regulatory requirements add to the cost of bringing products to market and delay product approval, and thus, may impede the success of medical device firms in that market. At the same time, standards and regulations are designed to ensure health and safety and serve critical consumer protection functions (box 2-1).

One aspect of product regulation is the amount of premarket testing and clinical trials that a regulatory agency requires, given that full information is often infeasible. Premarket testing reduces health costs in the event that the device may be unsafe or ineffective but raises approval costs and opportunity costs resulting from missed chances to sell the device. The expected return on a device limits the amount of testing that a firm is willing to perform because the costs of testing are high. Clinical trials increase fixed costs and may make it infeasible to develop devices for small markets. The FDA has special procedures that apply to medical devices whose estimated market is less than 4,000 individuals per year. To date, EU regulators have not routinely required clinical trials for most medical devices. Japan, on the other hand, reportedly requires extensive domestic clinical trials even when these trials have already been conducted abroad.[37] Larger firms often perform clinical trials on new products with safety concerns and for expensive items, but small and medium size firms rarely perform clinical trials on medical devices that they develop. If clinical trials were required for all launches of medical devices, the cost structure of small and medium size firms could change and make them targets for takeovers.[38]

[35] U.S. industry official, interview by Commission staff, United States, June 7, 2006.

[36] Chapter 6 contains further information on the impact of regulatory measures on sales. U.S. industry officials, personal and telephone interviews by Commission staff, United States, June 5–26, 2006.

[37] U.S. industry officials, interviews by Commission staff, United States, June 5–26, 2006.

[38] Cookson and Hutton, "Regulating the Economic Evaluation of Pharmaceuticals and Medical Devices," 175.

Box 2-1 Medical devices: Balancing commerce and regulation

The economic criterion for establishing the appropriate regulatory level is to equate the marginal costs of regulation with its marginal benefits. To estimate benefits, a value must be placed on what the regulation produces, which in this case is better health and improvements in the quality, and possibly the length of life because of medical devices. Uncertainty over the future and the complexity of multiple influences on health and life expectancy make the costs and benefits of regulation difficult to measure. Analysis of costs and benefits typically requires estimating the statistical value of life. Estimates of the statistical value of life are also employed in risk-risk analyses that make explicit how policy changes affect the different types of risks.

A stringent approval process not only prevents the use of some medical devices that may have adverse effects, but also deprives society of devices with potentially beneficial effects; the tradeoffs are depicted in table 2-1. Although some claim that regulatory agencies are too lenient, others, such as Campbell, argue that the marketing of safe and effective devices has been delayed or prevented (type I error) because so much emphasis is placed on preventing the marketing of unsafe and ineffective devices (type II errors).[a] One reason for this situation is that potential beneficiaries of new devices cannot generally be identified ex ante, but specific people will be linked to error where a product was unsafe and ineffective, but accepted.

Table 2-1 Approval tradeoffs

		State of the World	
		Device safe and effective	Device unsafe and ineffective
Regulatory policy decision	Accept	Correct policy decision	Type II error - Device unsafe and ineffective, but accepted
	Reject	Type 1 error - Device safe and effective, but rejected	Correct policy decision

Source: Adapted by Commission staff from Viscusi and Aldy, "The Value of a Statistical Life," and Viscusi, Vernon, and Harrington, *Economics of Regulation and Antitrust,* 757.

Note.—Placing a statistical value on death and injury has a long history in economics. Viscusi and Aldy review more than 60 studies of mortality risk and 40 studies of injury risk premiums. They find that the income elasticity of the value of a statistical life is in the range of 0.5 to 0.6.

[a] Campbell, "Exploring Free Market Certification of Medical Devices," 313–344.

Demand Side Factors

Healthcare spending

In recent years, expenditures for healthcare as a share of gross domestic product (GDP) in the EU, Japan, and the United States have risen and are projected to continue to increase, although at a declining rate. In the EU, medical devices account for an estimated 6 percent of total health expenditures, and health expenditures account for 8 percent of GDP.[39] The United States and Japan are estimated to spend about 5 percent of health expenditures on

[39] This includes medical and surgical equipment and orthopedic appliances, but not other devices such as chemical and biochemical devices that are classified under "chemicals" and medical-impregnated products that are classified under "pharmaceutical preparations." The EU national accounting framework does not provide a clean breakout of medical devices.

medical devices, and their health expenditures account for 14 and 8 percent of GDP, respectively. The amount of money a country spends on healthcare is a key factor affecting the market for medical devices. National levels of healthcare expenditures are a strong indicator of potential success for the industry.[40]

Technological advances lead to the development of more innovative medical devices, which, in turn, enables a number of medical problems to be treated, thereby increasing demand and expenditures on medical devices. Technical change has been the largest driver of growth in healthcare spending over the past 50 years; it has resulted in annual increases in per capita spending on healthcare of approximately 2 percent, which is about half of the total real growth in healthcare spending from 1950–2000.[41]

Reimbursement

Adequate reimbursement rates and transparent reimbursement policies are important demand factors in the medical device market.[42] Reimbursement rates are determined by government and private payers after a medical device has been approved for use in a particular market. If medical devices are not reimbursed at a rate that enables the medical device consumer to recoup its cost or if rates are not predictable or transparent, the consumer then may not purchase the device.[43] Cost containment policies being adopted by healthcare systems that face growing budget deficits also put substantial monetary constraints on potential consumers of medical devices. These policies may take the form of budgetary caps (at the national, regional, or local level) or the adoption of payment systems that classify particular devices or treatments in categories for which the associated payment does not adequately cover the total cost of the device, innovation, testing, and/or marketing.[44]

Most sector revenue comes from the sale of surgical and medical equipment to institutional purchasers rather than from the sale of expensive devices to individuals. Institutional purchasers, including public and private sector hospitals, have made efforts to trim costs by standardizing treatment protocols, making purchasing more rational, and forming group purchasing organizations (GPOs). The GPOs attempt to use their size to negotiate lower prices and possibly to counter market power on the seller's side. The increasing presence of GPOs in the United States and the EU has been met with some controversy and reported concerns about their impact on small and medium size suppliers and on the adoption of new technology.[45]

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[40] Diller, "Healthcare: Products and Supplies: Asia," 28.

[41] Aspden, ed., *Medical Innovation in the Changing Healthcare Marketplace, 16.*

[42] EU industry officials, interviews by Commission staff, European Union, September 17–29, 2006; and Walterskirchen, *The U.S. Market for Medical Devices: Opportunities and Challenges for Swiss Companies*, 17.

[43] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and Gold, "Healthcare: Products and Supplies," 23.

[44] Prospective payment systems, including diagnosis related groups (DRGs), are in place in varying forms in the United States, Japan, and many European countries. Depending on how technologies are classified, and the payment rates associated with the classification, the systems may either encourage or discourage the uptake of a particular device. OECD Health Project, *Health Technologies and Decision Making*, 33.

[45] U.S. and U.K. industry officials, interviews by Commission staff, United States and United Kingdom, June and September 25–27, 2006.

Demographics

Demographics and income levels influence demand for medical devices, as aging populations and high incomes are expected to enhance the growth of the medical device industry. Organisation for Economic Cooperation and Development (OECD) data show that population levels increased in the EU, Japan, and the United States over the last 10 years,[46] and that the elderly generally represent an increasing share of the population.[47] The proportion of Japan's population age 65 or older is growing faster than in the United States and EU,[48] and stood at 20 percent in 2005 (compared with 17 percent in 2004 in the EU and 12 percent in 2005 in the United States).[49] Income also increased in the EU, Japan, and the United States between 2000 and 2005.[50] The greater the average age and income of a population, the more advanced medical treatments that market is likely to demand.[51]

[46] OECD, Table on "Total Population," *OECD Factbook 2006*.

[47] The elderly's share of the U.S. population is smaller than its share in the EU and Japan, and the U.S. share has been relatively steady over the past 10 years. OECD, Table on "Population Aged 65 and Over," *OECD Factbook 2006*.

[48] United Nations (UN), *World Population Prospects - 2000 Revisions*.

[49] Statistics Bureau & Statistics Center, Ministry of Public, Management, Home Affairs (Japan), Demographic Data. Accessed via CEIC database; Japan's Ministry of Internal Affairs and Communication's Statistical Bureau and Statistical Research and Training Institute, *Statistical Handbook of Japan*, chapter 2-Population.

[50] OECD, table on GDP per capita, *OECD Factbook 2006*.

[51] Diller, "Healthcare: Products and Supplies: Asia," 13.

CHAPTER 3
Profiles of U.S. and Foreign Industries and Markets

The United States, the EU, and Japan dominate the global medical device industry and market (table 3-1). The U.S. medical device industry is widely acknowledged to be the most competitive in the world in a broad range of product lines. It benefits from supply side factors, such as above-average expenditures on R&D, innovative products, ready access to capital, a well-trained and productive workforce, and a strong global marketing and distribution network. The U.S. industry also benefits from strong demand factors, such as a large and growing U.S. market, which spends about twice the percentage of its gross domestic product (GDP) on healthcare as its major trading partners, favorable private and public insurance reimbursement policies, and relatively high market pricing.

Although EU firms tend to be smaller than U.S. firms, several of the largest and most prominent medical device companies in the world are headquartered in EU member countries. However, on the supply side, while an efficient regulatory approval system is an important factor favoring the medical device industry in the EU market, the EU has relatively lower expenditures on R&D, less innovative products, and less access to venture capital. This has inhibited the development of leading-edge, high-technology medical device firms that can compete effectively with the most advanced U.S.-based firms. On the demand side, public policies of many EU member states aimed at strictly controlling healthcare expenditures impact industry reimbursement and profit.

Despite Japan's traditional strengths in certain segments of the medical device industry, such as diagnostic imaging and general hospital products, less favorable factors on the supply side, including lower expenditures on R&D, lower technology products, and less access to venture capital, have made Japan more dependent on imports for higher technology medical device products. Despite favorable demographic factors, including the highest proportion of elderly persons in the world, other demand factors, such as lower per capita expenditures and less favorable government healthcare and regulatory policies, have inhibited the growth of the Japanese market for medical devices. The Japanese medical device industry experienced little growth in production from 2001 through 2005, and accounts for a decreasing share of the global industry. Profiles of the U.S., EU, and Japanese medical device markets appear below.

Table 3-1 Highlights of medical devices for the United States, EU, and Japan

Medical devices	United States	EU	Japan
Production • Global share • Value (2005) • Dominant products	 51% $92.0 billion - Interventional cardiology (coronary stents, pacemakers, defibrillators) - Diagnostic imaging - Orthopedic implants - Patient monitoring - Medical and surgical instruments - In vitro diagnostics (IVD)	 30% $38.0 billion - Diagnostic imaging - IVD - Orthopedic implants - Dialysis - Commodity hospital supplies	 10% $14.2 billion (2004) - Diagnostic imaging - Optical (endoscopic) - Commodity hospital supplies
Consumption • Global share • Value (2005) • Population	 50% $90.2 billion 298.4 million	 30% $38.1 billion 457.0 million	 10% $19.0 billion (2004) 127.5 million
Trade Balance *(2005)*	$1.8 billion	$4.5 billion	- $4.9 billion (2004)
Total Employment *(2005)*	388,449	393,000	68,000
National Healthcare Expenditures *(percent of GDP)*	15%	7-8%	8%
Research & Development Expenditures[a]	10-13%	6%	6%

Source: Compiled by Commission staff from official government and industry sources. Population figures from CIA, *The World Factbook*, July 2006.

[a] Reported research and development expenditures as a share of sales.

United States

The United States continues to maintain a large advantage over its principal foreign trading partners in the design, manufacture, and marketing of medical devices and equipment. Compared to their EU and Japanese rivals, U.S. medical device companies spend significantly more on R&D, typically place innovative products on the market at a faster rate, enjoy higher profit margins, and benefit from enduring reputations among healthcare professionals around the world for high quality products and services.[1]

Notwithstanding these advantages, the trade surplus held by the U.S. medical device industry has declined in recent years despite continued steady growth in U.S. exports. This decline is largely due to rapidly increasing demand in the U.S. healthcare market, which has resulted in higher growth rates of imports relative to exports,[2] and to a lesser extent, to supply side factors, such as U.S. firms' increased outsourcing of labor-intensive assembly and production activities to Costa Rica, the Dominican Republic, Malaysia, and Mexico.[3] In recent years, several major U.S. companies have also transferred some higher-value production to Europe in order to benefit from market proximity and to take advantage of investment incentives and highly skilled workers in Ireland and Switzerland, while maintaining engineering, design, and other capabilities in the United States.[4] Further, the manufacture and assembly of medical devices in China by U.S.-headquartered firms continues to rise due to the increasing importance of maintaining a presence in that market,[5] where healthcare demand is growing rapidly.[6]

Supply

Overall, there are an estimated 6,000–7,000 small, medium, and large medical device and equipment manufacturers operating in the United States, many of which produce for both the U.S. and international markets.[7] Major U.S. industry participants and their major products (table 3-2) in the global market for medical devices include (1) Boston Scientific/ Guidant, Cordis,[8] Medtronic, and St. Jude (major developers of advanced cardiovascular products); (2) Abbott Laboratories, Baxter International, Becton Dickinson, C.R. Bard, Inc., and Johnson & Johnson (large suppliers of a broad range of medical and hospital supplies);

[1] European and Japanese government and industry officials and market analysts, interviews by Commission staff, United States, June 5–16, 2006; Japan, July 31–August 8, 2006; and EU, September 18–29, 2006; Diller and Gold, "Healthcare: Products and Supplies," February 2006, 1–17; Mergent, Inc., *The North America Medical Instruments & Equipment Sectors*, 1–6, and 10–13; and Pammolli, et al., *Medical Devices, Competitiveness and Impact on Public Health Expenditure*, 116–159.

[2] Official statistics of the U.S. Department of Commerce; and U.S. industry representatives, personal and telephone interviews by Commission staff, 2002–5, and March–April 2006.

[3] For more information on U.S. medical equipment trade see USITC, *Shifts in U.S. Merchandise Trade 2003*, 60–64; USITC, *Shifts in U.S. Merchandise Trade 2004*, 55–59; and chapter 4 of this report.

[4] See USITC, *Shifts in U.S. Merchandise Trade 2003*, 60-64;and USITC, *Shifts in U.S. Merchandise Trade 2004*, 55–59.

[5] See box 4-1 for more information on China.

[6] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and General Electric Corporation and Medtronic, Inc., annual reports and forms 10-K.

[7] U.S. Census Bureau, "Statistics for Industry Groups and Industries, 2005 and earlier years."

[8] A subsidiary of Johnson & Johnson.

Table 3-2 Medical device NAICS segments and U.S. shipments, 2005

NAICS code	Name of segment	Product examples	Major companies	2005 shipments *($ millions)*
325413	In vitro diagnostic substances and devices	Reagents, substances, devices, and systems for use in diagnosis of disease or other conditions through collection, preparation, and examination of blood, urine, tissue, other specimens taken from the human body	Abbott, Bayer, Beckman Coulter, Becton Dickinson, Dade Behring, Johnson & Johnson, Newport Medical, Roche	8,741
334510; 334517	Electromedical equipment	Cardiac defibrillators and pacemakers, electrocardiographs, electrosurgical instruments, hearing aids, medical imaging and therapeutic apparatus (CT, MRI, nuclear, ultrasound, and X-ray), medical lasers, patient monitoring systems	Accuscope, Beltone, Boston Scientific, General Electric, Laserscope, Medtronic, Philips, Siemens, Spacelabs, St. Jude, Varian	26,526
339112	Surgical and medical instruments	Anesthesia apparatus, arthroscopic instruments, cardiac and urological catheters, drug-eluting stents, forceps, hypodermic needles, heart valves, intravenous and blood administration apparatus, surgical scalpels and other related instruments, surgical clamps, syringes	Abbott, Bard, Biomet, Baxter, Becton Dickinson, Boston Scientific, DePuy, Johnson & Johnson, St. Jude, Stryker, Wolf, Zimmer	25,872
339113	Orthopedic devices and hospital supplies	Crutches, orthopedic implants (hip, knee, spine), prosthetic appliances, surgical dressings, surgical gloves, sutures	Abbott, Bard, Baxter, Becton Dickinson, Boston Scientific, DePuy Orthopaedics, Inc., Johnson & Johnson, Stryker, and Zimmer	27,296
339114	Dental equipment	Dental chairs, dental hand instruments, dental drills, other instrument delivery systems	Align Technology, Dentsply, Great Lakes Dental, Summit, Sybron	3,566

Source (of shipment data): U.S. Census Bureau, "Value of Product Shipments: 2005," *Annual Survey of Manufactures*, M05(AS)-2, November 2006; Diller and Gold, "Healthcare: Products and Supplies," February 2006; and Mergent, Inc., *The North America Medical Instruments & Equipment Sectors*.

(3) General Electric Medical Systems (GEMS), Philips Medical Systems,[9] Siemens Medical Solutions,[10] and SpaceLabs Medical (producers of electromedical diagnostic imaging and complete patient monitoring systems); and (4) Biomet, DePuy Orthopaedics, Inc.,[11] Stryker Corp., and Zimmer Holdings, Inc. (four of the five leading orthopedic manufacturers in the world).[12] Almost all of these firms supply U.S. and foreign markets through both U.S. exports and overseas manufacturing.[13]

Shipments

Newly developed high-technology electromedical, interventional cardiology, and orthopedic products led strong growth in U.S. producers' shipments of medical devices and equipment for 2001–5. Such shipments increased at an average annual rate of 5 percent during 2001–5 to $92 billion (table 3-3) due to favorable demand by U.S. and foreign doctors and patients for less-invasive, innovative products that improve the quality of patients' lives and the diagnosis and treatment of disease.[14] U.S. shipments posted the largest increase in 2005, rising by 11 percent over the previous year, principally as the result of cyclical factors as U.S. and foreign healthcare providers replaced aging equipment with newer technologies.[15] Figure 3-1 illustrates the shares of total U.S. shipments accounted for by each of the major medical device segments of the industry in 2005.

Among the five industry segments, U.S. shipments of electromedical equipment for diagnosis and treatment of cardiovascular disease and orthopedic devices and hospital supplies grew at the fastest rates during 2001–5, each reaching $27 billion in 2005, increasing at annual rates of growth of 10 percent and 7 percent, respectively. Specific products that contributed significantly to this growth were implantable defibrillators (devices which are programmed to deliver shocks to resuscitate failing hearts), neurostimulators (used for non-pharmaceutical treatment of Parkinson's Disease, mental depression, and other therapeutic purposes), and orthopedic hip, knee, and spinal implants (which utilize biologics to enhance adhesion of the implants to bone cartilage).[16]

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[9] Philips, the large Dutch electronics firm, acquired the patient monitoring equipment operations of Agilent (Hewlett-Packard), the leading U.S. producer of complete patient monitoring systems. These operations remain in Andover, MA.

[10] This major U.S. manufacturer of nuclear medical imaging systems in Illinois is owned by German-based Siemens Medical Systems.

[11] A subsidiary of Johnson & Johnson.

[12] London-based Smith & Nephew is the other major orthopedic manufacturer.

[13] U.S. industry representatives, interviews by Commission staff, United States, June 15–16, 2006; and company annual reports and forms 10-K.

[14] U.S. Census Bureau, "Value of Product Shipments: 2005." The five North American Industry Classification System (NAICS) medical device segments on which these data are based are In Vitro Diagnostics (NAICS 325413), Electromedical and Irradiation Equipment (NAICS 334510 and 334517), Surgical and Medical Instruments (339112), Surgical Appliances and Supplies (including Orthopedic) (339113), and Dental Equipment and Supplies (339114).

[15] U.S. industry analysts, telephone interviews by Commission staff, October 3–5, 2006.

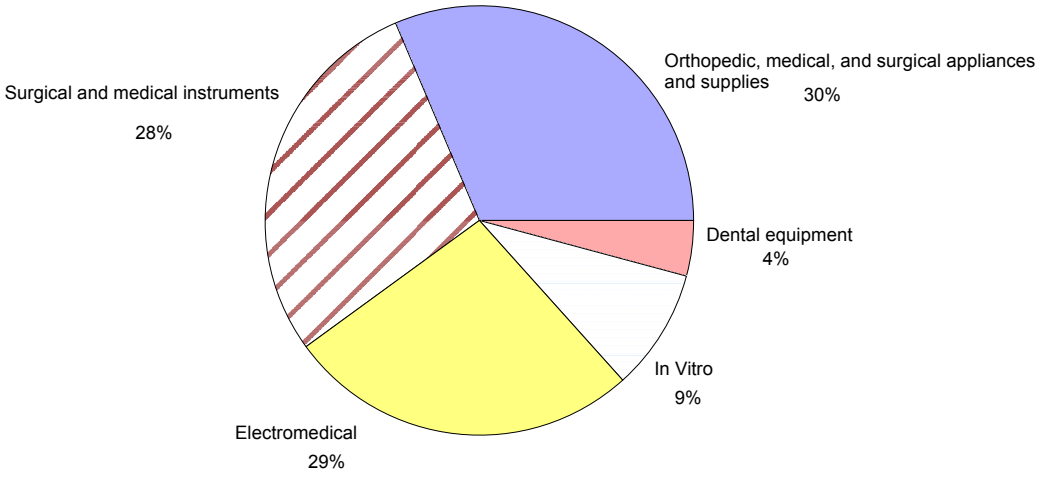
[16] Diller and Gold, "Healthcare: Products and Supplies," February 2006, 1–17; Mergent, Inc., *The North America Medical Instruments & Equipment Sectors*, 1–6 and 10–13; and Boston Scientific, Johnson & Johnson (Cordis and DePuy), Medtronic, St. Jude, Stryker, and Zimmer, annual reports and forms 10-K.

Table 3-3 U.S. shipments of medical devices, 2001–5

NAICS segment	2001	2002	2003	2004	2005	Absolute change 2001–5	Percent change 2001–5
	million dollars						*percent*
In vitro diagnostic substances and devices	11,026	9,172	8,417	8,730	8,741	-2,285	-21
Electromedical equipment	17,968	19,267	19,994	23,117	26,526	8,558	48
Surgical and medical instruments	23,560	22,396	21,417	22,337	25,872	2,312	10
Orthopedic devices and hospital supplies	20,860	22,036	24,732	24,634	27,296	6,436	31
Dental equipment	3,175	2,965	3,085	3,393	3,566	391	12
Total	76,589	75,836	77,645	82,211	92,001	15,412	20

Source: U.S. Census Bureau, "Value of Product Shipments: 2005," *Annual Survey of Manufactures*, M05(AS)-2, November 2006.

Figure 3-1 Shares of U.S. shipments by major segment, 2005



Total shipments 2005 = $92 billion

Source: Compiled by Commission staff based on official statistics of the U.S. Department of Commerce.

Meanwhile, shipments of surgical and medical instruments exhibited much smaller growth, rising by an average annual rate of 2 percent throughout the period.[17] Despite an unremarkable performance by the surgical and medical devices segment, especially in low-price margin, high-volume commodity products, such as disposable syringes, forceps, tongue depressors, and surgical hand instruments, shipments of certain products within the segment, including interventional cardiovascular products, such as angioplasty catheters and drug-eluting stents, exhibited above average growth. Dental equipment shipments also registered little growth over the period.

Finally, shipments of IVDs were variable during the period, declining in the first 2 years of the period but increasing in the last 3 years of the period, as increasingly sophisticated testing methods and products came on the market in those years.[18]

Employment

Labor productivity in the U.S. medical device industry improved from 2001 through 2005 (table 3-4) while U.S. employment in this industry declined by 5 percent, to 308,792 workers, over the same period (table 3-5).[19] Employment decreased in every year during the period except 2005, when such employment posted a slight increase of 2 percent. According to U.S. government and industry representatives, the overall decline in U.S. employment is largely attributed to (1) use of more advanced manufacturing technology in segments of the industry producing high-technology medical devices such as drug-eluting stents, cardiac defibrillators, and advanced orthopedic implants, which accounted for a significant portion of the growth in shipments throughout the period; and (2) outsourcing of more labor-intensive assembly and production abroad while maintaining more advanced research and engineering activities in the United States, which increased the average productivity of U.S. workers in the industry.[20]

Table 3-4 U.S. manufactured output per employee, 2001–5

Year	U.S. production	Employment	Derived output per worker
	million dollars		*dollars*
2001	76,589	325,805	235,076
2002	73,836	324,936	227,232
2003	77,645	312,149	248,743
2004	82,211	302,068	272,161
2005	92,001	308,792	297,938

Source: US Census Bureau, "Statistics for Industry Groups and Industries: 2005," *Annual Survey of Manufactures*, M05(AS)-1, November 2006, and "Statistics for Industry Groups and Industries: 2001," *Annual Survey of Manufactures,* M01(AS)-1, January 2003.

[17] IVD production declined sharply between 2001 and 2002, before steadily increasing by 5 percent annually from 2003–5.

[18] U.S. and Japanese industry representatives, interviews by Commission staff, Japan, July 31–August 9, 2006.

[19] Estimated by Commission staff based on U.S. Census Bureau, "Statistics for Industry Groups and Industries: 2001" and "Value of Product Shipments: 2005."

[20] U.S. government and industry officials, telephone interviews by Commission staff, April 3–14, 2006.

Table 3-5 Employment in the U.S. medical device industry, 2001–5

NAICS code	Name of segment	2001	2002	2003	2004	2005	Absolute change, 2001–5	Percent change, 2001–5
		number of employees						*percent*
325413	In vitro diagnostic substances and devices	40,960	27,233	28,901	27,294	26,324	-14,636	-36
334510, 334517	Electromedical equipment	67,924	71,548	66,994	65,491	67,602	-322	0
339112	Surgical and medical instruments	102,273	101,960	93,796	95,549	97,799	-4,474	-4
339113	Orthopedic devices and hospital supplies	96,914	107,200	105,873	96,695	98,993	2,079	2
339114	Dental equipment	17,734	16,995	16,585	17,039	18,074	340	2
	Total	325,805	324,936	312,149	302,068	308,792	-17,013	-5

Source: U.S. Census Bureau, "Statistics for Industry Groups and Industries: 2005," *Annual Survey of Manufactures*, M05(AS)-1, November 2006, and "Statistics for Industry Groups and Industries: 2001," *Annual Survey of Manufactures,* M01(AS)-1, January 2003.

Factors of competition

Several supply factors contribute to U.S. firms' competitive advantage in the global medical device market, including significant investment in R&D (reflected in the large numbers of patents owned by U.S. medical device companies); access to venture capital and other funding sources; high barriers to entry; M&A strategies; and an increasingly efficient and predictable regulatory approval system that facilitates the placement of new medical devices on the U.S. market.[21]

It is estimated that U.S. medical device companies have spent more than 10 percent of their total revenues on R&D in recent years, over twice the average for U.S. manufacturers as a whole.[22] Although large U.S. hospital supply firms producing mature commodity products spend a relatively small percentage of their revenues on R&D,[23] firms producing

[21] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and Diller and Gold, "Healthcare: Products and Supplies," February 2006, 22.

[22] Company annual reports and Forms 10-K, 2004–5; U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; Diller and Gold, "Healthcare: Products and Supplies," February 2006, 19 and 25; and Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 31–46 and 49–60.

[23] The National Science Foundation, Survey of Industrial Research and Development, shows that the percentage of R&D to net sales for medical equipment and supplies under NAICS 3391 (which includes 3 of the 6 NAICS categories covered by this investigation, but does not include statistics for generally more high-

(continued...)

high-technology products (such as IVD reagents and testing devices, interventional cardiovascular and combination products, and implantable electromedical and orthopedic devices) often spend 15 to 20 percent of their revenues on R&D.[24] Some newly established small firms reportedly spend significantly higher portions of their revenues on R&D.[25] A 2004 study conducted by the Boston Consulting Group, which examined publicly available information for 40 medical device companies, suggests that the relatively higher R&D expenditures by U.S. firms may significantly improve U.S. competitiveness in this industry.[26] The study indicated that gains from higher levels of R&D spending "translate into higher revenue growth, profit margins, and stock valuations."[27] A recent European Commission report examining U.S., EU, and Japanese government and trade association statistics finds that U.S. medical device firms' expenditures on R&D as a percentage of sales were, on average, roughly twice as high as such expenditures by medical device firms in the EU and Japan in recent years.[28]

A strength of the U.S. medical device industry is the significant amount of research conducted by its national government.[29] Two federal agencies that contribute to the development of U.S. medical technology are the National Institutes of Health (NIH) and the National Aeronautics and Space Administration (NASA).[30] NIH is the principal U.S. government agency responsible for the support of medical research.[31] In recent years, NIH has supported U.S. medical device and equipment companies by funding basic and applied research in medical technologies through its bioengineering grant program, and by sponsoring both intramural research at NIH and extramural research conducted by scientists in universities, institutes, and organizations outside of NIH. In 2005, the total value of NIH bioengineering grants for applied research related to medical technology amounted to $1.3 billion, representing an increase of 30 percent from 2003 (figure 3-2). Cardiac

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[23] (...continued)
technology-intensive NAICS segments such as electromedical equipment (NAICS 334510) or IVDs (NAICS 325413) ranged from a high of 13.1 percent to a low of 6.6 percent from 1999–2003, averaging 9.2 percent for the period. National Science Board, "Company and Other (Nonfederal) R&D Fund Share of Net Sales in R&D-Performing Companies, by Industry and Company Size: 1999–2003," A4–41.

[24] Company annual reports and SEC filings; and U.S. industry officials, investment analysts, and venture capital specialists, personal and telephone interviews by USITC staff, United States, April 10–14 and June 5–16, 2006.

[25] Mergent, Inc., *The North America Medical Instruments & Equipment Sectors,* 11; and U.S. industry officials, investment analysts, and venture capital specialists, personal and telephone interviews by USITC staff, United States, April 10–14, and June 5–16, 2006.

[26] Lawyer, et al., "High Science: A Best-Practice Formula for Driving Innovation: The Boston Consulting Group Reveals Results of a Study on How Medical Technology Firms Can Cultivate and Manage their R&D to Boost Revenue, Profits–and Stock Valuations," 1–5.

[27] Ibid.

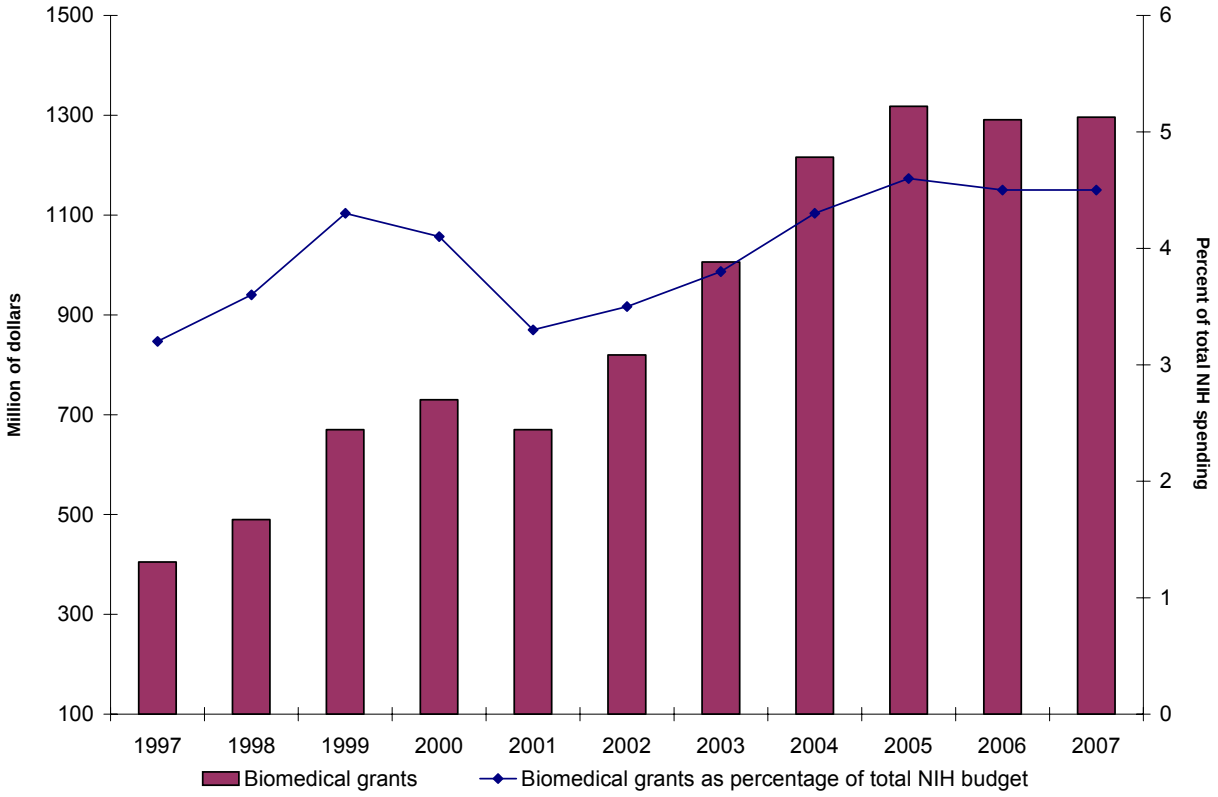
[28] Pammolli, et al., *Medical Device Competitiveness and Impact on Public Health Expenditure,* 116–159; and OECD, *Science Technology and Industry Outlook 2005*.

[29] Pammolli et al., *Medical Device Competitiveness and Impact on Public Health Expenditure,* 116–159; Hanna, et al., eds., *Innovation and Invention in Medical Devices,* 21–25 and 31–38; NAS, Institute of Medicine official, telephone interview by Commission staff, May 17, 2006; and U.S. industry representatives, personal and telephone interviews by Commission staff, United States, June 5–26, 2006.

[30] For further information on NIH and NASA funding related to their support for basic and applied R&D with relevance to medical technology, see their annual reports at http://www.nih.gov and http://www.nasa.gov, respectively. For background and history of U.S. government research and expenditures benefitting the medical technology industry, see Thomas, "Federal Support of Medical Device Innovation," 51–57; and Hanna, et al., eds., *Innovation and Invention in Medical Devices,* 31–38.

[31] See *NIH Budget* and *NIH Almanac* at http://www.nih.gov/about/budget.htm.

Figure 3-2 NIH bioengineering grant awards, 1997–2005, and estimated 2006–7



Source: National Institutes for Health (NIH), "[Actual] and Estimated Funding for Various Diseases, Conditions, and Research Areas," March 10, 2006, http://grants1.nih.gov/grants/award/award.htm.

defibrillators, magnetic resonance equipment, and nuclear imaging devices are a few examples of the numerous types of medical device technologies whose development has benefitted from NIH-sponsored research.[32] A relatively new source of NIH funding directly relevant to medical device and equipment firms is the National Institute of Biomedical Imaging and Bioengineering (NIBIB), which was established by Congress in 2000 as the newest NIH institute.[33]

[32] Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 21–25 and 31–38; NAS, Institute of Medicine official, telephone interview by Commission staff; and U.S. industry representatives, personal and telephone interviews by Commission staff, United States, June 5–26, 2006.

[33] The NIBIB mission is to bring together researchers in the imaging, physical sciences, bioengineering, computer science, and informatics fields to support research on a broad variety of technologies. Such technologies include molecular imaging tools that integrate imaging data from multiple sources, unique imaging research tools, and low-cost imaging and diagnostic technologies that may be "widely deployed to improve human health." Congressional appropriations for the new program increased by 166 percent to $298 million during 2002–6. Public Law 106-580, signed into law on December 29, 2005, authorized the establishment of NIBIB. NIH, *About NIBIB*; Zerhouni, *National Institute of Biomedical Imaging and Bioengineering Five-Year Professional Judgment Budget*, 1–19; and NIH, "[Actual] and Estimated Funding for Various Diseases, Conditions, and Research Areas."

The U.S. industry also has derived significant side benefits from U.S. space program efforts to fund or engage in the development of medical technology.[34] NASA programs were critical to the development of advanced patient monitoring technologies by such U.S. firms as Spacelabs,[35] Hewlett-Packard, and Marquette Electronics. These firms took advantage of NASA research and NASA-supported grants in such areas as telemetry, for example, and developed wireless technologies for medical and physiological monitoring of astronauts using NASA-customized components and packaging designed to withstand the difficult conditions of space flight.[36] Overall, NASA-supported research has led to the development of a number of devices that have been adapted for commercial purposes, including heart imaging systems, heart pumps, telemedicine instrumentation systems, and ingestible temperature sensing pills.[37] NASA continues to support such research efforts in connection with the International Space Station.

Another important resource unique to the U.S. medical device industry is a strong venture capital industry.[38] Venture capital funds provide many U.S. companies with significant financial resources, enabling them to focus on funding key activities such as R&D.[39] Growing demand for medical device products from an aging population has increased the attractiveness of the medical device industry for venture capital funds.[40] According to a Moneytree Survey by the consulting firm PriceWaterhouseCoopers, venture capital investments in the U.S. medical device industry reached $2.1 billion in 2005, up from $1.7 billion in the previous year. In 2006, through the third quarter of the year, investments in the industry were approximately $1.9 billion.[41]

The competitive strengths possessed by the U.S. medical device industry create high barriers to entry in the imperfectly competitive medical device market,[42] making it difficult for new firms to challenge established firms.[43] These advantages have especially benefitted large, well-established U.S. firms that supply a large selection of commodity hospital supplies and other medical devices and equipment, as well as U.S. manufacturers of high-technology cardiac rhythm products (pacemakers and defibrillators), interventional cardiology products (cardiovascular catheters and stents), diagnostic imaging equipment (CT, MRI, nuclear), and orthopedic devices (hip, knee, and spinal implants), allowing them to maintain their dominant positions in U.S. and global markets for medical devices.

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[34] Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 31–38.

[35] U.S.-based Spacelabs was founded in 1958 to develop monitoring of astronauts during NASA space travel. In 1974, Spacelabs launched the first monitoring system to incorporate microprocessor technology. For further information on Spacelabs history, see Spacelabs Medical, "A Pioneering History," at http://www.spacelabs.com.

[36] Philips Medical Systems acquired Agilent's (formerly Hewlett-Packard's) patient monitoring operations in Andover, MA in 2003 and General Electric Medical Systems reacquired those of Marquette Electronics in 2004, which it had divested in the 1970s. Company annual reports and Internet sites.

[37] Hanna, et al., eds., *Innovation and Invention in Medical Devices*, 31–38.

[38] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006.

[39] Agress, hearing transcript, 74.

[40] Loftus, "Medical Device Venture-Capital Funding on the Rise."

[41] PriceWaterhouse Coopers, "MoneyTree Report, Historical Trend Data, Medical Devices and Equipment," Q1 2005–Q3 2006 data.

[42] Diller and Gold, "Healthcare: Products and Supplies," February 2006, 22; and U.S. industry officials, interviews by Commission staff, United States, January–June 2006.

[43] U.S. industry officials, interviews by Commission staff, United States, January–June 2006; and Diller and Gold, "Healthcare: Products and Supplies," February 2006, 22.

Some medical device industry representatives argue that barriers to entry in the U.S. medical device and equipment industry are reinforced and exacerbated by the power of group purchasing organizations (GPOs). While GPOs were originally established to help hospitals contain price growth for medical devices, some small and medium size company officials state that long-term contracts large medical device firms have been able to negotiate with GPOs, which include discounted pricing scales based on volume and compliance requirements, dampen competition and opportunities for sales of innovative products by smaller companies.[44]

Another factor affecting the competitiveness of the U.S. industry is the strategic use of M&As by companies to create synergies. For example, established companies may engage in M&As to strengthen themselves by increasing scale or diversifying their product lines. They may also use M&As to increase shareholder value and reduce their risk by acquiring smaller start-up firms after they have developed promising technologies. In such cases, the start-up firms benefit by being acquired by more established firms which have greater marketing capabilities, extensive distribution networks, and the experience and resources necessary to take innovative technologies through the complex regulatory approval process and onto the market. A number of notable M&As were completed by U.S.-based companies during the period (box 3-1).

U.S. government regulation of medical devices and equipment is another important factor affecting U.S. supply of such devices. The U.S. Food and Drug Administration (FDA) is the principal federal regulatory agency responsible for protecting the public from unsafe and ineffective medical products.[45] As such, obtaining FDA approval to market new medical devices is critical to the success of U.S. and foreign medical equipment suppliers in the U.S. market. The FDA requires medical device producers to provide extensive documentation of their products' safety and effectiveness before granting approval. The agency also has the authority to require producers to recall products, deny approval to manufacturers' new products, suspend sales of devices that it believes to be harmful, and levy fines and penalties on companies that violate its regulations inside the U.S. market.[46]

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[44] Healthcare GPOs, which have become a dominant feature of the U.S. distribution landscape in the United States in recent years, were provided protection against antitrust laws under a "safe harbor" from Congress in an attempt to provide leverage for relatively small hospitals and clinics against market power held by large manufacturers of medical products and to help reduce price growth of medical devices. However, one industry group, the Medical Device Manufacturers Association (MDMA), representing small to mid size companies, indicates that, instead, GPO business has been captured by dominant U.S. manufacturers, reducing sales opportunities for smaller companies. Rasmussen, "Is America's Health Care Hindered by 'Group Purchasing Organizations?'," 1; Medical Device Manufacturers Association (MDMA), "Group Purchasing Organizations," 1; Department of Health and Human Services, "Review of Revenue From Vendors at Three Group Purchasing Organizations and Their Members," 1; and U.S. industry representatives, interview by Commission staff, United States, June 23, 2006.

[45] U.S. government officials, interview by Commission staff, United States, May 31, 2006; and Diller and Gold, "Healthcare: Products and Supplies," February 2006, 19–22.

[46] U.S. government officials, interview by Commission staff, United States, May 31, 2006; and Diller and Gold, "Healthcare: Products and Supplies," February 2006, 19–22.

Box 3-1 Merger and acquisition (M&A) activity in the U.S. market in 2001–6

One notable M&A deal in the U.S. market, resulting in the merger of two prominent U.S.-based firms with domestic and global ramifications, was the 2006 purchase of Guidant (a major producer of cardiac pacemakers and defibrillators, as well as interventional cardiovascular products) by Boston Scientific (a major producer of interventional cardiovascular products such as catheters and stents).The acquisition, estimated at approximately $27 billion, is expected to enable Boston Scientific to offer a much more complete line of products to cardiologists and implant physiologists. However, according to some market analysts, the undertaking also includes significant risks for Boston Scientific, which needs to settle some potentially expensive regulatory issues related to product failures of Guidant products reported just after the acquisition. To address antitrust concerns, Boston Scientific and Guidant each divested portions of their interventional cardiovascular product lines to Abbott Laboratories.

Other notable mergers and acquisitions throughout 2001–5 include Dutch-based Philips' acquisition of U.S.-based Agilent's (formerly Hewlett-Packard) patient monitoring manufacturing facilities in Andover, MA, and General Electric Medical System's (GEMS) re-acquisition of Marquette Electronics, a major patient monitoring producer spun off by GEMS some years ago. Patient monitoring and medical imaging traditionally constituted distinct subsets of the electromedical equipment segment of the medical device industry. Thus, these acquisitions represent a major consolidation, offering further scope and scale and, thus, potential competitive advantage in an already fairly concentrated medical device segment. Market analysts contend that the medical device and equipment market "continues to be ripe for mergers and acquisitions."

Source: Boston Scientific Form 10-K, 2; Boston Scientific and Abbott Laboratories, press releases and SEC filings, 2005 and 2006; "Medical Goods" writeups in USITC, *Shifts in U.S. Merchandise Trade 2003,* 60–64 and *2004*, 55–59; Tully, "The Second Worst Deal Ever," 1; Boston Scientific 2005 Form 10-K; Diller and Gold, "Healthcare: Products and Supplies," 7; Mergent, Inc., *The North America Medical Instruments & Equipment Sectors*, 1–6 and 10–13; investment analysts, telephone interviews by Commission staff, May 22 and June 7, 2006; and U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006.

Although the FDA's primary role is the regulation of medical devices in the United States, it has gradually become more involved in collaborating with other U.S. and foreign government agencies that address international trade issues. According to FDA officials, the agency realizes the implications of its regulatory policies on international commerce,[47] even though the FDA's purpose is not to promote international trade. As the U.S. medical device regulatory system, along with the regulatory policies of its major foreign competitors, can have a significant effect on U.S. sales of medical equipment, it will be discussed in more detail and compared with the regulatory systems of the EU and Japan in chapter 6.

Demand

Consumption

Demand conditions in the U.S. market are particularly favorable to the medical device industry. The United States is, by far, the world's largest consumer of medical devices, accounting for nearly half of the global market in 2005. Apparent U.S. consumption increased by an average annual rate of 6 percent during 2001–5, from $71 billion to $90 billion (table 3-6). In 2005, U.S. consumption was dominated by products in three

[47] Holston, "An Overview of International Cooperation," 1; and Kelly and Bachorik, "Promoting Public Health and Protecting Consumers in a Global Economy: An Overview of HHS/FDA's International Activities," 339-346.

sectors: electromedical equipment (28 percent), orthopedic devices and hospital supplies (27 percent), and surgical and medical instruments (26 percent) (table 3-7). Increased demand for the latest cardiovascular technologies, such as coronary stents and implantable defibrillators, promoted growth in the medical instruments and electromedical device segments of the medical device market. Meanwhile, the orthopedics market has experienced robust growth in the United States, due to significant increases in the number of senior citizens taking advantage of new developments in minimally invasive joint reconstruction procedures, hip and knee replacements, and spinal implant surgeries. Such procedures enable them to continue to participate as active adults in normal recreational and social activities.[48]

Table 3-6 U.S. medical device shipments, exports, imports, apparent consumption, and the ratios of exports to shipments and imports to consumption, 2001–5

Year	U.S. shipments	U.S. exports	U.S. imports	Apparent U.S. consumption	Ratio of exports to shipments	Ratio of imports to consumption
	million dollars				*percent*	
2001	76,589	18,759	12,826	70,656	24	18
2002	73,836	18,806	15,390	70,420	25	22
2003	77,645	20,997	18,854	75,502	27	25
2004	82,211	22,709	21,752	81,854	28	27
2005	92,001	25,501	23,700	90,200	28	26

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

Table 3-7 U.S. medical device shipments, exports, imports, apparent consumption, and the ratios of exports to shipments and imports to consumption, by segment, 2005

NAICS Code	Name of segment	U.S. shipments	U.S. exports	U.S. imports	Apparent U.S. consumption	Ratio of exports to shipments	Ratio of imports to consumption
		million dollars				*percent*	
325413	In vitro diagnostic substances and devices	8,741	3,798	1,470	6,413	43	23
334510, 334517	Electromedical equipment	26,526	7,894	9,030	27,662	30	33
339112	Surgical and medical instruments	25,872	7,286	7,373	25,959	28	28
339113	Orthopedic devices and hospital supplies	27,296	5,658	4,866	26,504	21	18
339114	Dental equipment	3,566	866	961	3,661	24	26
	Total	92,001	25,501	23,700	90,200	28	26

Source: Compiled from official statistics of the U.S. Department of Commerce. Source (of shipment data): U.S. Census Bureau, "Value of Product Shipments: 2005," *Annual Survey of Manufactures*, M05(AS)-2, November 2006.

Note.—Due to rounding, figures may not add up to totals.

An important factor influencing U.S. consumption of medical device products is increasing healthcare expenditures. Aggregate healthcare expenditures traditionally have been a major

[48] U.S. industry representatives and market analysts, personal and telephone interviews by USITC staff, United States, June 15–16, and October 11, 2006.

determinant of demand for medical devices; such goods have historically accounted for about 5 to 6 percent of total U.S. healthcare expenditures, and sales of such equipment have risen proportionally with increases in overall healthcare expenditures.[49] In recent decades, the United States has outspent other major countries on health and medical care by a large margin as U.S. doctors and their patients have demanded more technologically sophisticated and expensive procedures. Healthcare expenditures currently account for 15 percent of U.S. GDP, about twice the OECD average of 7 to 8 percent (figure 3-3).[50] The largest customers for medical devices and equipment in the U.S. market are hospitals, followed by physician offices and other outpatient facilities, including freestanding imaging centers and ambulatory surgical centers.[51]

Demographic trends in the United States also have influenced growth in the U.S. market for medical devices and equipment. U.S. citizens aged 65 and above accounted for approximately 12 percent of the population in 2005 (figure 3-4), up from over 8 percent since 1950.[52] This figure is projected to rise to almost 20 percent by 2030[53] with the aging of the "baby boomer" generation. As people age, the incidence of disease and injury increases, leading to growth in the intensity of demand for medical services. U.S. medical device companies benefit from these trends.[54]

Health insurance

U.S. medical device and equipment manufacturers sell the largest portion of their products to hospitals and physicians who typically bill various third-party payers, such as the Medicare and Medicaid programs, private insurance plans, and health maintenance organizations (HMOs), for the healthcare provided to their patients.[55] As the largest single insurer in the United States, the Federal Medicare and Medicaid program has a profound influence on the healthcare market.[56] About one-third of funding for hospitals, or approximately $125 billion a year, is from Medicare, and much of the balance is from

[49] Russell, *Technology in Hospitals*, 80; and healthcare analyst, Center for Medicare and Medicaid Services, telephone interviews by Commission staff, March 3, 2005, and June 7, 2006.

[50] OECD, "How Does the United States Compare," 1; OECD, "Total Expenditures on Health-% of Gross Domestic Products;" and OECD, "Special Report: America's Health-Care Crisis, Spending on Health as % of GDP (table)," 25.

[51] Diller and Gold, "Healthcare: Products and Supplies," August 2006, 2; and Bian and Morrisey, "HMO Penetration, and Growth of Ambulatory Surgery Centers," 111-122.

[52] U.S. Census Bureau, "Statistical Abstract of the United States, Table No. HS-3"; U.S. Census Bureau, "2004 American Communities Survey, S0101"; and U.S. Census Bureau, "2005 American Communities Survey, S0101."

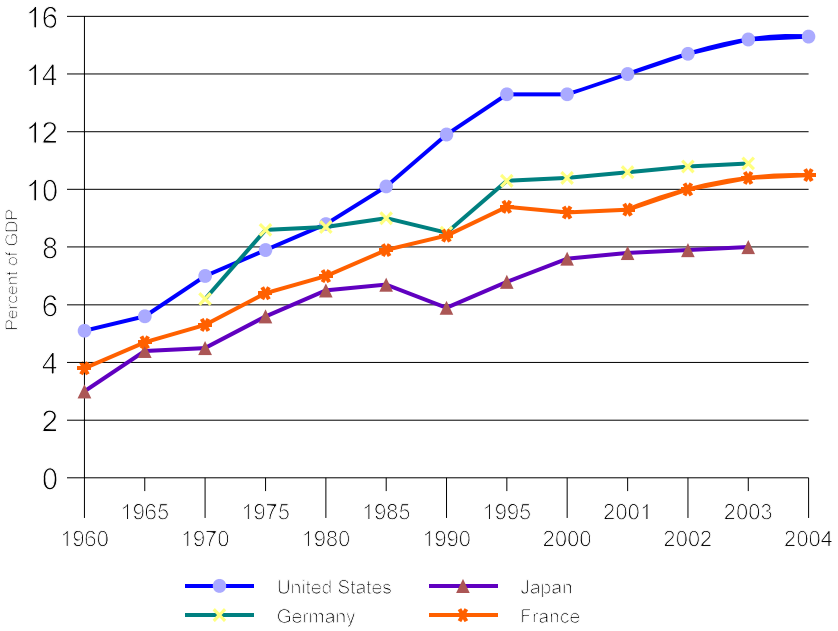
[53] U.S. Census Bureau, "U.S. Interim Projections by Age, Sex, Race, and Hispanic Origin."

[54] The U.S. Center for Disease Control and Prevention (CDC) estimates that healthcare cost per capita for persons 65 and older is three to five times the cost for younger people. For further information and statistics on these trends, see the CDC Internet site at http://www.cdc.gov.

[55] Center for Medicare and Medicaid Services (CMS) official, personal and telephone interviews by Commission staff, United States, 2003, and June 6, 2006; and company forms 10-K.

[56] Company forms 10-K.

Figure 3-3 Total expenditures on healthcare as a percentage of gross domestic product



Source: OECD Health Data, June 2006, at http://www.oecd.org/dataoecd/60/28/35529791.xls (accessed October 16, 2006).

Note.— For Germany, data provided up to 1990 are for West Germany. For some countries, data were not available for specific years or were estimated in OECD figures.

private insurers and HMOs.[57] Thus, the ability of customers (healthcare providers) to obtain reimbursement from third-party payers is critical to the success of medical device producers because it determines which products a customer can purchase and the price it is willing to pay.

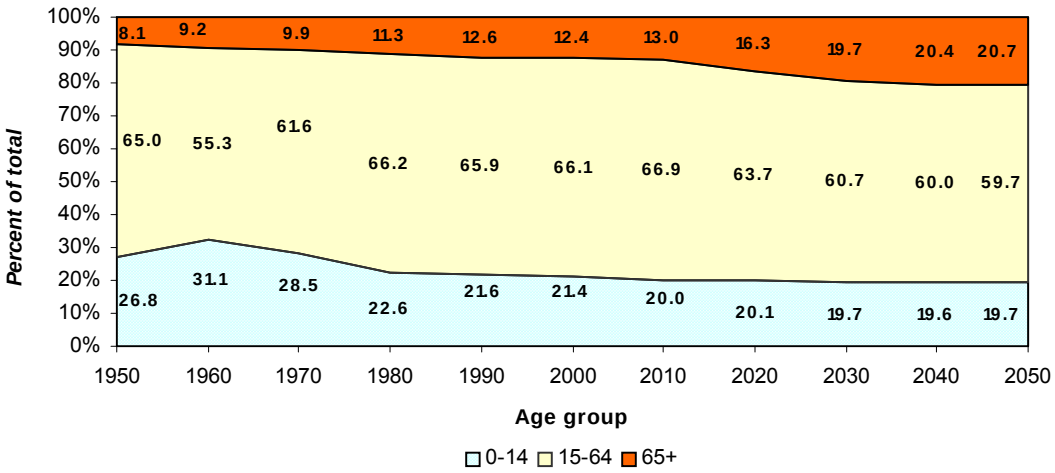
According to U.S. industry representatives, the processes through which medical device firms obtain desired levels of reimbursement under Medicare and private health insurers are complex.[58] Initially reimbursement was based primarily on "usual and necessary costs" incurred by healthcare providers in providing treatment. However, with healthcare expenditures contributing to a rapidly growing federal deficit, in an effort to contain costs, Congress approved legislation in 1983 to replace Medicare's cost-based system with a prospective payment plan based on diagnosis-related groups (DRGs).[59] After adoption of the

[57] Diller and Gold, "Healthcare: Products and Supplies," August 2006, 2; and Bian and Morrisey, "HMO Penetration, and Growth of Ambulatory Surgery Centers," 111–122.

[58] U.S. industry officials, personal and telephone interviews by Commission staff, United States, June–July 2006.

[59] Russell, *Medicare's New Hospital Payment System*, 2.

Figure 3-4 Composition of the U.S. population (by age)[a]



Source: U.S. Census Bureau, Statistical Abstract: Historical Statistics, No. HS-3; and U.S. Census Bureau, "U.S. Interim Projections by age, sex, and race, and Hispanic origin."

[a] Numbers may not add to 100 percent due to rounding.

new prospective payment cost-containment program, hospitals have become much more cost-conscious in their purchases of medical devices, and demand for such equipment has consequently become more price sensitive.[60]

The U.S. Center for Medicare and Medicaid Services (CMS) has been tasked by Congress to implement further cost containment policies in an effort to reduce the growth in healthcare reimbursement. One recent example of such a policy is the 2005 Deficit Reduction Reconciliation Act,[61] which reduced Medicare reimbursement for medical imaging procedures.[62] Industry representatives in the medical imaging equipment area estimate that the change could result in losses of $8.9 billion in the next 10 years, due to cancelled orders for nuclear medicine, CT, and MRI devices.[63]

CMS and private health insurance cost-containment efforts also have used technology assessment and cost-benefit analyses as the basis for a larger number of medical device reimbursement decisions. Such efforts have required firms to demonstrate the cost

[60] Under prospective payment, rates of reimbursement are set in advance of the period to which they applied. The prospective rates are set for over 500 diagnosis-related groups (DRGs) (i.e., groups of patients with similar conditions) used for coding reimbursement claims. Developed from costs historically associated with diagnosis and treatment for each condition, the rates for the groups would cover all hospital operating costs. Under the DRG system, the rates constitute payment in full to the hospital. Hospitals can keep any profits but have to absorb any losses. Russell, *Medicare's New Hospital Payment System*, 2.

[61] Pub. L. No. 109-171, 120 Stat. 4.

[62] Ku, et al., "Survey Indicates Deficit Reduction Act Jeopardizes Medicaid Coverage for 3 to 5 Million U.S. Citizens," 1.

[63] U.S. industry officials, personal and telephone interviews by Commission staff, United States, June–July 2006.

effectiveness of their medical devices, and largely benefitted manufacturers supplying less-invasive medical innovations that enable patients to be treated in outpatient settings rather than more expensive hospital settings. As a result of U.S. medical device firms' competitive advantages in such technologies compared to their principal foreign rivals, they have profited more from these trends. Finally, efforts to reduce the growth in healthcare costs also have included the use of private high-deductible healthcare plans and health savings accounts, and experimentation with other new proposals, such as gainsharing.[64]

Trade practices

U.S. and foreign medical device industry representatives state that there are few, if any, formal trade barriers to the marketing of medical devices in the United States.[65] Some foreign industry representatives suggest that preferences for U.S.-made medical equipment among U.S. doctors and hospitals may have a negative effect on foreign firm sales, but acknowledge that healthcare providers in foreign markets often have similar preferences for certain brands.[66] Moreover, leading European and Japanese firms with well-known reputations and brands—such as Philips, Siemens, and Toshiba —also may benefit from U.S. market preferences for certain medical equipment.

European Union

Firms operating in the EU[67] sell a broad array of products ranging from inexpensive commodity items to large-scale capital equipment. The EU medical device industry largely comprises small and medium size companies, many of which employ less than 20 people. With few exceptions, EU firms are not market leaders within the European or global market; large U.S. multinational firms dominate most industry segments. While production and employment in the EU medical device industry grew during 2001–5, outsourcing to other European countries and Asia is becoming increasingly important for the EU industry as competitive pressures intensify.

The competitive conditions in the EU market vary widely according to product type; companies that produce commodity products adapt strategies that are qualitatively different than the R&D focused strategies of firms in advanced product segments. The M&A activities of EU-headquartered companies are typically driven by corporate strategies aimed at acquiring new product lines, technologies, and distribution channels. On the demand side,

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[64] Gainsharing offers financial incentives to physicians and other employees who can reduce hospital expenditures by using less costly procedures or purchasing methods. For example, under gainsharing, physicians can "order less expensive treatment options or agree to work with fewer vendors so that their hospitals [can] obtain better discounts on high-volume supplies." In return, the doctors may be reimbursed for a portion of the savings their treatment decisions yield. Diller and Gold, "Healthcare: Products and Supplies," 12; MDMA, "Gainsharing;" and Accenture, "Using Gainsharing to Align Incentives for Medical Management," 2.

[65] U.S., European, and Japanese government and industry officials and experts, interviews by Commission staff, United States, June 5–16, 2006; Japan, July 31–August 8, 2006; and EU, September 18–29, 2006.

[66] U.S., European, and Japanese industry representatives, personal and telephone interviews by Commission staff, June–July 2006.

[67] The terms EU, Europe, and EU-25 are used interchangeably throughout the report and, unless otherwise indicated, refer to the 25 member states of the EU. The analysis does not address the two new states that entered the EU in 2007, Bulgaria and Romania.

demographic trends, such as aging populations and rising incomes, may lead to increases in demand, and increased prices and sales in some EU countries. On the other hand, divergent and constrained reimbursement policies across EU member countries substantially limit demand and the uptake of new technologies.

Supply

The EU medical device and equipment industry comprises between 8,500 and 10,000 companies.[68] Firms in the European medical device industry range from suppliers of commodity products, such as syringes and gloves, to cardiology companies producing pacemakers, to electronics firms producing X-ray and MRI machines. Although firms operating in Europe include large and diversified multinational companies such as Johnson & Johnson, most firms operating in the EU are small and medium size companies.[69] According to the industry trade association Eucomed, more than 80 percent of the medical device firms in Europe employ less than 250 people.[70] Further, an estimated 40 percent of employees in the European medical device sector work in firms with less than 20 employees, compared with 6 percent in the United States.[71]

European-based medical device firms generally focus on sales in Europe, although some firms sell medical devices throughout the world.[72] Europe's leading medical device product groupings, in terms of revenues and/or technological distinction, include advanced wound care, cardiovascular, diagnostic imaging, dialysis, IVD, and orthopedic devices.[73] Although industry leaders vary by country and industry segment and no single firm dominates all product segments, large U.S. multinational firms account for the vast majority of sales in most medical device product segments in Europe (table 3-8).[74] Large U.S. firms are particularly active in highly profitable segments characterized by technologically advanced, high-value-added products, particularly cardiovascular and orthopedic devices. U.S. firms also own a relatively large proportion of the medical device firms located in Europe. U.S. ownership is particularly high in Ireland, where approximately 60 percent of medical device companies registered with the FDA are owned by U.S. parent companies (box 3-2). Similarly, U.S. parent companies own large shares of medical device firms located in Finland (17 percent), Hungary (15 percent), the United Kingdom (12 percent), the Netherlands (11 percent), France (10 percent), and Germany (7 percent). By contrast,

[68] Belgian industry official, interview by Commission staff, Belgium, September 19, 2006; Marchant, "Europe's Medical Device Market Braces for an Era of Change"; "Medical Devices Sector Seeks Innovation Boost;" Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure,* 90; and Diller, "Healthcare: Products and Supplies: Europe," 18.

[69] Belgian, German, and UK industry officials, interviews by Commission staff, Belgium, Germany, and the United Kingdom, September 19–27, 2006.

[70] Eucomed, *Medical Technology Brief.*

[71] Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure,* 109–110.

[72] Diller, "Healthcare: Products and Supplies: Europe," 18.

[73] Belgian industry official, interview by Commission staff, Belgium, September 19, 2006.

[74] Diller, "Healthcare: Products and Supplies: Europe," 9 and 12.

Table 3-8 Major EU medical device product groupings and leading firms

Product grouping	Leading firms
Advanced wound care	3M (U.S.), Coloplast (Denmark), Johnson & Johnson (U.S.), Smith & Nephew (U.K.)
Cardiovascular	Abbott (U.S.), Biotronik (Germany), Boston Scientific (U.S.), Johnson & Johnson (U.S.), Medtronic (U.S.), St. Jude/Guidant (U.S.), Sorin (Italy)
Dental implants	AstraZeneca (U.K.), Lifecore Biomedica (U.S.), Nobel Biocare (Switzerland), Straumann (Switzerland), Zimmer (U.S.)
Diagnostic imaging	General Electric (U.S.), Philips (Netherlands), Siemens (Germany)
Dialysis	Fresenius Medical Care (Germany), Gambro (Sweden)
Hearing devices	Amplifon (Italy), GN Store Nord (Denmark), Logitech (U.S.), Phonak (Switzerland), Plantronics (U.K.), William Demant (Denmark), Siemens (Germany)
In vitro diagnostics	Abbott Labs (U.S.), Bayer Diagnostics (Germany), Becton Dickinson (U.S.), Beckman Coulter (U.S.), BioMerieux (France), Dade-Behring (U.S.), Ortho-Clinical Diagnostics (U.S.), Roche Diagnostics (Switzerland)
Lab equipment	Affymetrix (U.S.), Applied Biosystems (U.S.), Biacore (Sweden), Invitrogen (U.S.), Millipore (U.S.), Qiagen (Germany)
Orthopedic devices and hospital supplies	B. Braun (Germany), Biomet (U.S.), Encore Medical (U.S.), Medtronic (U.S.), Smith & Nephew (U.K.), Stryker (U.S.), Synthes (Switzerland), Wright Medical (U.S.), Zimmer (U.S.)

Source: Compiled by Commission staff from Belgian industry official, interview by Commission staff, Belgium, September 19, 2006; and Diller, "Healthcare: Products and Supplies: Europe," 18.

Box 3-2 The Irish medical device cluster

Medical device firms have been establishing operations in Ireland since 1974, when Abbott Laboratories established its first facility. It was not until 1994, however, when Boston Scientific set up operations in Galway, that Ireland's medical device cluster began to take shape. Following Boston Scientific's investment, other global medical device firms began to establish operations in Galway, including Bausch & Lomb, Medtronic, and Johnson & Johnson. Overall, investment in the medical devices segment has centered in the west of Ireland, largely due to efforts by the Investment Development Authority (IDA) to target high regional unemployment.

One of the primary catalysts for investment in the medical device sector was the government's policy of waiving corporate taxes for firms establishing manufacturing facilities in Ireland. Although Ireland still maintains one of the lowest corporate tax rates in Europe, it was increased to 12.5 percent in 2003 to comply with EU regulations. Other important factors leading global medical device firms to locate manufacturing facilities in Ireland included relatively low labor costs, a well-educated, English-speaking population, and proximity to the EU market.

To date, approximately 91 separate medical device companies have established facilities in Ireland, including 15 of the world's top 25 medical device firms. The medical devices industry in Ireland generates approximately $5 billion in annual sales and employs nearly 25,000 people. Over the years, a large support infrastructure has evolved to support Ireland's medical device industry, including both multinational companies and indigenous Irish firms. Large multinational companies such as Medtronic typically tend to produce advanced, high technology products such as pacemakers and arterial stents. By contrast, indigenous Irish firms such as Creganna tend to produce disposable medical devices and/or inputs, such as guidewires, for multinational companies.

Over the past several years, Ireland's medical device industry has expressed concern that it is losing its cost advantage relative to countries in Eastern Europe and Asia, largely due to increasing labor costs, tax rates, and energy costs, as well as costs associated with complying with increasing levels of regulation, particularly environmental laws. As a result, the IDA is increasingly emphasizing Ireland's experienced, well-trained workforce and high levels of labor productivity. The IDA is also highlighting Ireland's growing R&D capacity: approximately 50 percent of medical device firms located in Ireland now conduct R&D within Ireland.

Source: Irish industry officials, interviews by Commission staff, Ireland, September 28–29, 2006; and Ludwig, hearing transcript, 70.

European parent companies own approximately 1 percent of medical device firms located in the United States.[75]

Although Europe's many small firms tend to focus on commodity/disposable products and relatively low-value-added niche products, several large European firms compete successfully in high-value-added product segments, notably advanced wound care, dialysis, diagnostic imaging, and orthopedic devices. However, in terms of sales, few European firms are leaders in the European market. In 2003, for example, one of Europe's leading orthopedic firms, UK-based Smith & Nephew, ranked fifth in the European market for hip and knee implants, behind four U.S. firms.[76] Leading European-headquartered medical device firms include Fresenius (Germany), Philips (Netherlands), Siemens (Germany), Smith & Nephew (United Kingdom), and Synthes (Switzerland) (table 3-9). With the exception of Siemens and Philips, however, few European-based companies are active in non-European markets, and only a small number are global leaders in their respective medical device segments.

Production

EU production of medical devices totaled approximately €31 billion ($38 billion) in 2005 (table 3-10).[77] Production grew at a compound annual growth rate of approximately 8 percent from 2001-5, with particularly strong growth in 2002 (12 percent) and 2005 (20 percent). Overall, production at the end of the period was 34 percent higher than at the beginning. In 2004, five countries accounted for nearly 87 percent of total EU-25 production, with Germany (45 percent) accounting for the largest share, followed by France (13 percent), the United Kingdom (12 percent), Italy (11 percent), and Ireland (5 percent).[78]
Historically, European medical device companies have been reluctant to outsource production activities. However, shorter product life-cycles, competitive pressures to reduce costs, and currency risks are forcing European firms to consider outsourcing strategies.[79]

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[75] Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 109–110.

[76] In 2003, market share for the top five firms in the European hip and knee market included Zimmer (19 percent), DePuy/Johnson & Johnson (15 percent), Biomet (12 percent), Stryker (12 percent), and Smith & Nephew (9 percent). Medtech Insight Report #A305, cited in Diller, "Healthcare: Products and Supplies: Europe," 21.

[77] Eurostat, *Prodcom Database 2006*. Table 3-10 understates production in the EU for at least two reasons. First, production data from Eurostat, the official data source, does not include missing values (where individual countries have failed to report) or suppressed values (where data are not publicly reported to protect confidential business information). Second, Eurostat reports production totals for the category NACE 33.1, medical and surgical equipment and orthopedic appliances. This category does not include chemical and biochemical devices, such as IVDs, which are classified under "chemicals," and medicine-impregnated products, such as gauzes, which are classified as "pharmaceutical preparations." Moreover, these particular types of medical devices are extremely difficult to separate out from chemical and pharmaceutical preparation classifications. Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 161.

[78] Eurostat, *Prodcom Database 2006*. Production shares for 2004 are provided because 2005 production data for the United Kingdom and Ireland, while included in the aggregate, were suppressed at the country level in 2005.

[79] Marchant, "Outsourcing Outlook"; U.S. industry officials, interviews by Commission staff, United States, June 13, 2006; German, Irish, and UK industry officials, interviews by Commission staff, Germany, Ireland, and the United Kingdom, September 21–29, 2006.

Table 3-9 Selected EU-headquartered medical device companies

Company	Country	Main market segments	2005 Revenue
			billion dollars
Siemens Medical Systems	Germany	Imaging equipment, in vitro diagnostics, and hearing aids	$9.5
Philips Medical Systems	Netherlands	Imaging equipment and healthcare information systems	$7.6
B. Braun Melsungen	Germany	Orthopedics and surgical instruments	$3.8
Smith & Nephew	United Kingdom	Orthopedics, wound treatment, and endoscopy	$2.4
Synthes	Switzerland	Orthopedics	$2.1
BioMerieux	France	In vitro diagnostics equipment	$1.2
Sorin Group	Italy	Cardiovascular and dialysis	$0.9
Carl Zeiss Meditec	Germany	Ophthalmology products	$0.4
Gyrus Group	United Kingdom	Surgical instruments and ear, nose, throat instruments	$0.3
Ambu	Denmark	Life support systems	$0.1
Bayer Diagnostics	Germany	In vitro diagnostics	([a])
Elektra	Sweden	Radiation oncology and neurosurgery equipment	([a])
Fiab	Italy	Electromedical devices	([a])
Maersk Medical	Denmark	Disposable medical supplies	([a])
Roche Diagnostics	Switzerland	In vitro diagnostics	([a])

Source: Compiled by Commission staff from Diller, "Healthcare: Products and Supplies: Europe," 18.

[a] Not available.

Table 3-10 EU production of medical devices, 2001–5

	2001	2002	2003	2004	2005	Absolute change 2001–5	Percent change 2001–5
	million euros						*percent*
Total	22,854	25,555	24,209	25,495	30,657	7,803	34.1
	million dollars						*percent*
Total	20,451	24,050	27,323	31,657	38,125	17,674	86.4

Source: Eurostat, *Prodcom Database*; IMF Exchange Rate.

Note.—The 2001–2002 aggregates were obtained as the sum of available national data reported by Eurostat's Prodcom. Aggregates for 2003–2005 were obtained as a sum of available EU 25 8-digit code totals. The differences between the data in euros and dollars is a result of exchange rate fluctuations that occurred in this period.

According to a survey by *European Medical Device Manufacturer*, for example, approximately 75 percent of responding firms maintained outsourcing contracts with firms located in Western Europe, followed by Central and Eastern Europe (29 percent), North America (26 percent), and Asia (23 percent). Within Central and Eastern Europe, Hungary, Poland, and the Czech Republic were the preferred country locations for outsourcing production, largely due to their low labor costs and geographic proximity to Western European markets. With respect to Asia, nearly 70 percent of firms with outsourcing contracts in the region identified China as the source country, followed by Malaysia, India, Taiwan, and Thailand. The most commonly outsourced activities include production (70 percent), packaging and/or sterilization (45 percent), surface treatment and other

specialized processes (37 percent), electronics (34 percent), logistics (13 percent), product design (13 percent), research and development (7 percent), and regulatory compliance (7 percent).[80]

Employment

Employment in the EU medical device industry has steadily increased, from 341,020 employees in 2001 to 388,449 in 2005 (table 3-11). With nearly 158,000 employees, Germany has, by far, the largest number of persons employed in the sector.[81] France maintains the second highest level of employment, followed by the United Kingdom, Italy, and Ireland. Together, these five countries are estimated to account for 73 percent of 2005 employment in the EU medical device industry. The countries of Central and Eastern Europe generally experienced strong employment growth during the period, although most began from employment levels that were much lower than those in Western Europe.

Productivity measures, particularly the derived output per employee, indicate that apparent labor productivity in the EU is substantially lower (table 3-12) than that recorded in either the United States or Japan. EU labor productivity varies among countries; value-added per employee is low in Central and Eastern Europe, whereas other countries, such as Ireland and Finland, report levels that are closer to those of Japan and the United States.[82]

Factors of competition

Competitive conditions in the European medical device market vary widely by product type. For example, companies that manufacture commodity products typically face high levels of competition and price sensitive markets, due largely to relatively low barriers to entry and the relative ease of manufacturing low-tech, undifferentiated products.[83] To remain profitable in such a highly competitive environment, companies selling commodity/disposable products typically sell high volumes at the lowest possible price, and focus on minimizing manufacturing costs and increasing sales and distribution efficiencies. To stay competitive, such firms must produce a broad range of products, maintain high quality standards, develop high levels of brand recognition, and cultivate strong relationships with buyers. In commodity segments, R&D and technological innovation play a relatively small role in developing and maintaining industry competitiveness.[84]

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[80] Sparrow, "Outsourcing Outlook." Totals exceed 100 percent because survey participants were allowed to select multiple categories.

[81] The German diagnostics industry association, VDGH, reports that 21,500 persons were employed in the diagnostics sector in Germany in 2005, a 16 percent increase over employment in 2001. Verband der Diagnostica-Industrie e.V. (VDGH), "The VDGH and its Companies."

[82] Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 94 and 199.

[83] Examples of such products include trays, gloves, bandages, syringes, and disposable medical devices such as catheters. Diller, "Healthcare: Products and Supplies: Europe," 18.

[84] German industry officials, interview by Commission staff, Germany, September 22, 2006; and Diller, "Healthcare: Products and Supplies: Europe," 28.

Table 3-11 Employment in the EU medical device industry, by country, 2001–5

Country	2001	2002	2003	2004	[a]2005	Absolute change, 2001-5	Percent change, 2001-5
Austria	6,249	6,335	6,622	6,986	7,233	984	16
Belgium	2,980	([b])	3,273	[a]3,368	3,465	985	16
Cyprus	([b])	([b])	([b])	155	168	([b])	([b])
Czech Republic	8,649	9,106	9,649	[a]10,654	11,764	3,115	36
Denmark	7,142	7,397	7,338	7,435	7,638	496	7
Estonia	528	685	785	[a]957	1,167	639	121
Finland	5,115	5,156	4,663	[a]4,447	4,241	-874	-17
France	42,527	43,297	43,916	44,734	46,071	3,544	8
Germany	145,037	140,328	153,639	154,416	157,959	12,922	9
Greece	([b])	([b])	([b])	([b])	([b])	([b])	([b])
Hungary	7,019	7,682	8,043	8,092	9,130	2,111	30
Ireland	14,770	15,093	15,133	16,883	17,789	3,019	20
Italy	25,692	26,769	26,296	28,676	28,663	2,971	12
Latvia	564	587	591	[a]599	607	43	8
Lithuania	1,415	1,451	1,545	1,755	1,928	513	36
Luxembourg	290	301	341	[a] 361	382	92	32
Malta	489	([b])	([b])	([b])	([b])	([b])	([b])
Netherlands	([b])	10,742	10,131	11,218	11,352	([b])	([b])
Poland	10,621	12,675	13,109	14,515	15,682	5,061	48
Portugal	2,223	2,084	1,959	[a]1,944	1,929	-294	-13
Slovakia	2,600	2,764	2,824	2,352	2,408	-192	-7
Slovenia	827	1,010	1,059	[a]1,212	1,387	560	68
Spain	11,845	13,014	13,662	13,635	15,303	3,458	29
Sweden	9,356	9,287	([b])	10,426	10,804	1,448	15
United Kingdom	35,082	33,023	33,894	31,066	31,379	-3,703	-11
Total	341,020	348,786	358,472	[a]375,827	388,449	47,429	14

Source: Eurostat, *Structural Business Statistics Database*.

[a] Estimated values. All 2005 values are estimated based on average annual growth.
[b] Not available.

Table 3-12 EU manufactured output per employee, 2001–5

Year	EU production	Employment	Derived output per worker
	million euros		*euros*
2001	22,854	341,020	67,018
2002	25,555	348,786	73,268
2003	24,209	358,472	67,534
2004	25,495	375,827[a]	67,838
2005	30,657	388,449[a]	78,921
	EU production	Employment	Derived output per worker
	million dollars		*dollars*
2001	20,451	341,020	59,970
2002	24,050	348,786	68,955
2003	27,323	358,472	76,220
2004	31,657	375,827[a]	84,233
2005	38,125	388,449[a]	98,149

Source: Eurostat, *Prodcom* and *Structural Business Statistics Databases*, and IMF exchange rates.

[a] Estimated values.

By contrast, companies attempting to sell more complex, technologically advanced products in Europe typically face lower levels of competition and less severe pricing pressures, largely due to high barriers to entry and short product life cycles.[85] Although competitive conditions in Europe require companies to control costs, produce high-quality products, and maintain strong ties with customers, one of the most crucial factors in maintaining industry competitiveness is the maintenance of cutting-edge medical technology research, and/or the development of such research into marketable products. In many cases, companies in such segments utilize R&D-driven technological innovation to differentiate their products from those of competitors. Successful products typically improve clinical outcomes while simultaneously allowing hospitals to reduce costs and operate more efficiently. In an attempt to achieve first-mover advantages,[86] many firms release high-technology products in rapid succession, leading to product life cycles as short as 18–24 months. In contrast, some companies reportedly adopt second-mover strategies as a means to reduce large, up-front costs associated with product development and customer education/training.[87]

For companies in advanced product segments, R&D expenditures and the effectiveness of that spending are extremely important to maintaining competitiveness. European companies

[85] Examples of such products include advanced wound care products, defibrillators, diagnostic imaging, hip and knee implants, and pacemakers. Diller, "Healthcare: Products and Supplies: Europe," 18.

[86] First-mover advantage is the potential advantage gained by the initial occupant of a market segment. Such advantages include the acquisition of substantial market share because of a lack of competition; the preemption of scarce resources (e.g., occupation of prime retail locations); the ability to reinvest early profits; and reputational benefits (e.g., supplier, distributor, and customer familiarity and loyalty). Second-mover advantages are created by the drawbacks of first-mover initiatives, largely high up-front costs (first-movers often face high R&D and marketing costs) and risk (first-movers may fail and/or cannot capitalize on the experience/mistakes made by others). In some cases, such drawbacks permit second-movers to gain a larger share of the market than first-movers, often by focusing their resources on developing a superior product or by taking the first-mover's niche product to the mass market. Grant, *Contemporary Strategy Analysis,* 2003.

[87] German industry officials, interview by Commission staff, Germany, September 21, 2006.

spend approximately 6 percent of sales on R&D compared with, on average, above 10 percent for U.S. medical device firms.[88] Lower R&D expenditures on the part of European firms, a frequently cited weakness of the European medical device industry, likely reflect the European industry structure, which is dominated by small and medium size companies that tend to have fewer financial resources than large, multinational firms. Nonetheless, companies in Germany (10 percent) and Sweden (9 percent) record average R&D expenditures closer to U.S. averages.[89]

Most government funding for R&D in the EU occurs through the Framework Programmes, which provide for R&D funding across different thematic areas. The European Council recently adopted the 7th Framework Programme, which covers the period 2007–13, and identifies various thematic areas of relevance to the medical device field including health, nano-sciences, and research infrastructures.[90] Few of the EU industry officials interviewed, however, reported receiving any substantial government funding to support their R&D efforts.[91]

Increasing competition in most segments of the European medical device industry is driving industry consolidation and leading to the creation of ever-larger firms, mainly because size conveys important competitive advantages. As discussed in chapter 2, large firms, in general, are often better at accessing capital markets, managing regulatory approval processes, achieving manufacturing efficiencies, taking innovative products to market, developing distribution channels, and managing global supply chains. In Europe, the well-developed, experienced administrative bureaucracy of most large corporations also provides an advantage in navigating divergent reimbursement schemes across the EU.[92] Overall, the many advantages of size and scale provide many advantages unavailable to small and medium size firms in Europe, limiting the ability of small and medium size firms to break into markets and/or develop substantial market share.

Mergers and acquisitions are becoming an important feature of the global medical device marketplace, including Europe. Although most high-profile acquisitions in the past three years have involved U.S. companies, the M&A activities of European-headquartered companies tend to involve other European companies, with small to medium size firms

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[88] Pammolli, et al., eds., *Medical Devices Competitiveness and Impact on Public Health Expenditure*, 130.

[89] Ibid.

[90] As part of the 7th Framework Programme, the European medical device trade association, Eucomed, is pursuing the establishment of so-called Medical Technology Innovation Centres. If initiated, such centers would assist companies with many aspects of commercializing new technologies, including advisory services related to obtaining appropriate financing, developing business plans, and protecting intellectual property. Eucomed, "Position Paper on FP7." A similar model already has been adopted in Oxford, United Kingdom, where DiagnOx, a company funded initially by the U.K. Department of Trade and Industry, seeks to improve the commercialization of R&D in the U.K. diagnostics sector by providing laboratory facilities as well as services and advice related to start-up financing and intellectual property protection. Arthur D. Little Limited, *UK Sector Competitiveness*, 69. Such initiatives address a commonly cited weakness in the EU medical device sector – the difficulty of commercializing new technologies.

[91] Belgian, German, U.K, and Italian industry officials, interviews by Commission staff, Belgium, Germany, the United Kingdom, and Italy, September 18–29, 2006.

[92] "Medical Devices Sector Seeks Innovation Boost," *European Innovation*.

acting as either acquirer and/or target.[93] In Europe, as in the United States, M&A activity is typically driven by corporate strategies aimed at acquiring new product lines, technologies, and distribution channels.[94]

Another important supply-side factor is the regulatory system under which a company operates. Many U.S. industry representatives state that the EU system for medical device approval is more predictable, efficient, and transparent than those in the United States, Japan, and other global markets.[95] Industry representatives in Europe also rate the EU regulatory system positively, noting that the governing standards, time lines, and costs generally are reasonable and predictable.[96] IVD manufacturers, in particular, have noted that the EU regulatory system encourages innovation and the development of new products because, unlike in the United States and Japan, many new products may be self-certified by the manufacturer.[97] As a result, many U.S. and European companies introduce innovative medical devices and equipment in the EU prior to the United States, Japan, and other global markets.[98] Chapter 6 presents additional information concerning the EU regulatory system.

Demand

Consumption

Apparent EU consumption of medical devices grew at a compound annual rate of 5 percent during 2001-5, ranging from €22.2 billion ($19.9 billion) to €27.4 billion ($34.1 billion). During 2003, apparent consumption began to decline, falling by 11 percent in euro terms by the end of 2004, before rebounding by 30 percent in 2005. Overall, consumption at the end of the period was approximately 23 percent higher than at the beginning (table 3-13).

[93] On occasion, European firms also purchase companies based in the United States. In 2005, for example, Philips (Netherlands) bought joint venture partner Agilient's share of Lumiled for $948 million. Similarly, in 2006, Coloplast Group (Denmark) bought U.S.-based Mentor Corporation's urology business for $463 million, while Siemens (Germany) announced plans to acquire IVD firm Diagnostic Products for $1.9 billion. Diller, "Healthcare: Products and Supplies: Europe," 6; and Landesbank Baden-Wurttemberg, *Sector Analysis: Medical Technologies 2006*, 12 and 35.

[94] Belgian, German, and U.K. industry officials, interviews by Commission staff, Belgium, Germany, and the United Kingdom, September 19–27, 2006.

[95] U.S. industry officials, interviews by Commission staff, United States, June 2006; Agress, hearing transcript, 51; and Ludwig, hearing transcript, 51–2.

[96] German and U.K. industry officials, interviews by Commission staff; and Germany and the United Kingdom, September 20–27, 2006.

[97] German industry officials, interviews by Commission staff, Germany, September 22, 2006.

[98] U.S. industry officials, interviews by Commission staff, United States, June 2006; and German and U.K. industry officials, interviews by Commission staff, Germany and the United Kingdom, September 20–27, 2006.

Table 3-13 EU medical device production, exports, imports, apparent consumption, and the ratios of exports to production and imports to consumption, 2001–5

Year	EU production	EU exports	EU imports	EU apparent consumption	Ratio of exports to shipments	Ratio of imports to consumption
	million euros				*percent*	
2001	22,854	14,705	14,095	22,244	64	63
2002	25,555	16,198	14,467	23,824	63	61
2003	24,209	17,291	14,922	21,840	71	68
2004	25,495	19,521	15,297	21,272	77	72
2005	30,657	20,474	17,262	27,446	67	63
	million dollars				*percent*	
2001	20,451	13,159	12,612	19,905	64	63
2002	24,050	15,245	13,616	22,421	63	61
2003	27,323	19,515	16,842	24,649	71	68
2004	31,657	24,238	18,994	26,413	77	72
2005	38,125	25,461	21,467	34,131	67	63

Source: Global Trade Information Services, Inc. *Global Trade Atlas Database;* Eurostat, *Prodcom Database*; and IMF exchange rates.

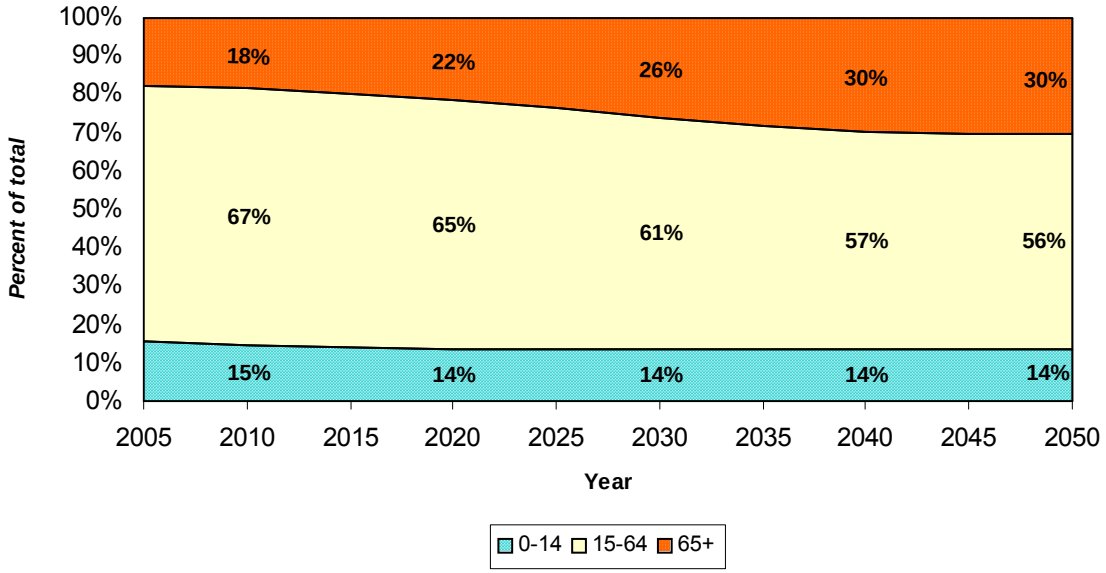
Note.—Imports and exports do not include the in vitro diagnostics segment to harmonize with production data. Totals may not add due to rounding.

As in all markets, demographic trends are an important driver of demand for medical devices in the EU. The age structure of the European population, for example, is shifting upward due to low birthrates and greater longevity (figure 3-5). Since older people typically require higher levels of medical treatment, many observers speculate that the aging of Europe's relatively active and wealthy population will drive demand for medical devices and equipment over the next two or three decades.[99] Consumption is also driven by the application of both new and existing technologies to new markets, notably the move by some medical device companies to penetrate younger age groups. In the orthopedic device segment, for example, young patients are increasingly seeking orthopedic implants for the treatment of sports injuries.[100] In order to take advantage of this trend, for example, UK-based Corin Group plc, a developer, manufacturer, and distributor of reconstructive

[99] Belgian, German, and U.K. industry officials, interviews by Commission staff, Belgium, Germany, and the United Kingdom, September 19-27, 2006; Diller, "Healthcare: Products and Supplies: Europe," 16; Marchant, "Europe's Medical Device Market Braces for an Era of Change."

[100] Marchant, "Europe's Medical Device Market Braces for an Era of Change."

Figure 3-5 Projected composition of the EU's population (by age)



Source: United Nations Economic Commission for Europe, Population Activities Unit. Demographic Database.

Note.—Numbers may not add to 100 percent due to rounding.

orthopedic devices, is pursuing a deliberate strategy of focusing on "young, active" patients.[101] Budget-cutting initiatives across Europe also affect demand for medical devices. Large national budget deficits in nearly all European countries, for example, have put pressure on national governments to reduce healthcare expenditures, including spending on medical devices. Since European governments, through publicly funded national health plans, are overwhelmingly the largest purchasers of medical devices in Europe, many companies in Europe, both large and small, expect reimbursement cuts to negatively affect the pricing and sales environments. Such reforms are likely to have a disproportionate impact on small to medium size companies, the core of Europe's medical device industry, as such firms typically have fewer financial resources and staff to deal with new reimbursement rules and procedures. Companies producing high-volume/low-margin commodity products are also expected to be negatively affected by such reforms.[102]

[101] Corin Group PLC, *Annual Report 2005*, 7; and U.K. industry officials, interview by Commission staff, United Kingdom, September 27, 2006.

[102] Diller, "Healthcare: Products and Supplies: Europe," 13; and Belgian, German, and U.K. industry officials, interviews by Commission staff, Belgium, Germany, and the United Kingdom, September 19–27, 2006.

Health insurance

EU residents have access to universal health care through two main types of systems: national health service and social insurance models. The main difference between the two is whether the system is funded primarily from taxation (e.g., the national health service model typified by the UK system), or from some form of social insurance (e.g., the German system where employers and employees contribute and the state pays the contributions of the unemployed and the elderly).[103] Initiatives intended to cut costs and improve efficiency are prevalent in the EU, including a recent shift away from the global budgeting of healthcare spending to activity-based methods of payment, such as diagnosis-related groups (DRGs),[104] and the increased use of health technology assessments (HTAs).

Under DRGs, governments reimburse hospitals in a fixed amount based on the diagnosis and treatment category in which the illness falls.[105] DRGs may have a positive or negative effect on demand based on whether reimbursement classifications and rates accurately reflect the costs of care. In general, EU industry officials assert that funding constraints present much more severe barriers to the sale of medical devices in Europe than regulatory approval requirements.[106] They raise particular concerns about the negative impact of DRGs on the uptake of new technologies and the incentives that they provide for the use of the least expensive rather than the best products. In Germany, for example, it has reportedly been 5 years since the Ministry of Health has approved an application for reimbursement of a new IVD test by the statutory health insurance system.[107] In France, reimbursement authorization must be obtained not only for each product code, but also for each indicated use of the product, an expensive process that typically lasts years, limits authorized uses, and keeps new technologies off the market.[108] In general, the efficiencies that have been gained from the harmonization of regulatory requirements throughout the EU are not present in the area of funding and reimbursement.

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[103] The national health service model is generally present in Denmark, Finland, Greece, Ireland, Italy, Portugal, Sweden, Spain, and the United Kingdom. The social insurance model is followed in Austria, Belgium, France, Germany, Luxembourg, and the Netherlands. Grimmeeisen and Rothgang, "The Changing Role of the State in Europe's Health Care Systems," 7.

[104] The DRG system, initiated in the United States in 1983, has different variants around the world. The German DRG system, for example, is modeled after that in place in Australia. German government officials, interview by Commission staff, Germany, September 20, 2006.

[105] The rate of adoption of activity-based payment methods varies across EU countries. Such methods are currently in place in Austria, Belgium, Italy, Ireland, Portugal, and Spain, while France, Germany, the United Kingdom, and several Nordic countries are currently in the process of implementing variations of activity-based payment methods. Diller, "Healthcare: Products and Supplies: Europe," 13.

[106] Belgian, French, German, Italian, and U.K. industry officials, interviews by Commission staff, Belgium, France, Germany, Italy, and the United Kingdom, September 18–29, 2006.

[107] New tests have been only sporadically funded through an escape valve mechanism contained in the health insurance legislation. German industry official, interview by Commission staff, Germany, September 22, 2006.

[108] French industry officials, interview by Commission staff, France, September 19, 2006.

Throughout Europe, the expanding use of HTAs[109] to determine reimbursement or clinical use places additional burdens on medical device firms.[110] Although a favorable HTA should result in the adoption of a new technology by public sector practitioners, industry officials state that they are often ignored in practice.[111] Most HTA agencies in Europe do not have a budgetary link – that is, a technology may be recommended with no money allocated to pay for it. Without this link, industry officials assert that HTA often operates as a barrier, rather than a gateway, to market access.[112]

Trade practices

U.S. and Japanese industry officials interviewed by Commission staff indicated that, as in the United States, there are very few, if any, tariff barriers, non-tariff barriers, and/or burdensome customs procedures that affect exports of medical devices and equipment to the EU.[113]

Japan

Japan's medical device market is the second largest single-country market in the world,[114] and it imports over half of its medical devices from the United States.[115] Despite the large size of its market, Japanese production and consumption growth was sluggish between 2001 and 2004, while the country's global medical device trade deficit widened.[116]

Japan's share of global medical device production has decreased in recent years, given faster manufacturing growth from medical device firms in the United States and EU. Despite its traditional strengths in selected segments of the medical device industry, such as diagnostic imaging and general hospital supplies, overall production growth in Japan declined from 2001–4 as government healthcare and regulatory policies inhibited the growth of its domestic market for medical devices.[117] Slower growth in Japan also reflected limited product innovation, as Japanese medical device firms spent a lower proportion of their sales on R&D than their counterparts in the United States. Other factors contributing to slower production by Japan over the period included macroeconomic phenomena, such as Japan's slow industrial activity and GDP growth, and the exposure of Japanese firms to more risk than

[109] HTA means different things in different countries. In the United Kingdom, for example, the National Institute for Health and Clinical Excellence (NICE) – considered the preeminent HTA agency by European industry officials – provides recommendations on the use of new and existing technologies based on clinical and economic evidence that addresses how well the technology works in relation to its cost. NICE, "About Technology Appraisals."

[110] French, German, Italian, and U.K. industry officials, interviews by Commission staff, France, Germany, Italy, and the United Kingdom, September 19–29, 2006.

[111] AdvaMed, "United Kingdom Medical Technology Issues: CEO Tool Kit."

[112] Italian industry officials, interviews by Commission staff, Italy, September 28, 2006; and Bridges, "Lean Systems Approaches to Health Technology Assessment," 103.

[113] U.S. and Japanese industry officials, interviews by Commission staff, United States, June 13–17, 2006; and Japan, July 31–August 9, 2006.

[114] Ludwig, hearing transcript, 8–9.

[115] Japan Ministry of Health, Labour and Welfare (MHLW), *Annual Statistics on Production by Pharmaceutical Industry*.

[116] Official MHLW 2005 production and trade data will not be available until April 2007.

[117] U.S. and Japanese industry officials and market analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

U.S. companies, given limited venture capital funding and less protective domestic bankruptcy laws.[118]

Consumption in Japan also grew at a slower pace than in the U.S. and EU markets between 2001 and 2004 despite relatively long life spans and rising demand for medical devices from Japan's rapidly growing elderly population. Slow demand growth[119] is attributed to Japan's complex distribution network, government cost-containment strategies (in light of rising public debt), and relatively low aggregate and per-capita healthcare spending, which have cumulatively inhibited consumption growth.[120] The Japanese government made an effort to reform its regulatory process in 2004 and to address significant approval delays that keep the latest medical technology from reaching the Japanese public. Meanwhile, cost- containment efforts will continue to be a major priority for the Japanese government.[121]

Supply

The medical device industry in Japan consists of approximately 750 firms with licenses to manufacture domestically.[122] Despite slow domestic production growth in Japan, several Japanese-based companies have remained highly competitive worldwide,[123] including Toshiba Medical Systems, which derives 60 percent of its sales of diagnostic imaging devices from overseas,[124] and Olympus Optical, which holds 70 percent of the global market for medical endoscopes.[125] While not as dominant in overseas markets as Toshiba and Olympus, Terumo, the leading Japanese-based firm in terms of revenues in 2005, is the largest Japanese supplier of a broad range of general and commodity hospital supplies (including syringes, catheters, cardiovascular guidewires, intravenous apparatus, blood purification devices, and dialysis apparatus). While Terumo faces competition from imports from major U.S. suppliers of hospital supplies, the market for dialyzers and other dialysis apparatus in Japan is supplied predominantly by Terumo, Asahi Medical, and other domestic companies. Table 3-14 provides a more comprehensive list of Japanese medical device companies.

Several major U.S.-based companies manufacture medical devices in Japan. Notable among these, GE-Yokogawa Medical Systems, a majority-owned affiliate of U.S.-based General Electric, is a significant Japanese producer of medical imaging devices. The American

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[118] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

[119] Relative to the U.S., the EU, and other highly industrialized markets. Ludwig, hearing transcript, 10–14; and U.S., EU, and Japanese industry officials and market analysts, interviews by Commission staff, United States, EU, and Japan, June–September, 2006.

[120] U.S. and Japanese industry officials and market analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

[121] MHLW, posthearing statement, 2-13.

[122] Based on survey data provided by MHLW officials, e-mail message to Commission staff, November 2006.

[123] U.S. and Japanese industry officials and market analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

[124] "Overseas Sales Account for 60% of Sales-Toshiba Medical Systems," *Pharma Japan*, 19.

[125] "The Top 30 Global Medical Device Companies," *Medical Product Outsourcing*; and company annual reports.

Table 3-14 Leading manufacturers of medical devices in Japan

Rank	Company	Primary segment	Headquarters
1	Aloka Co., Ltd.	Instruments, gauges, and meters	Japan
2	Asahi Medical Co., Ltd.	Dialyzer equipment	Japan
3	Baxter Limited	Medical, surgical, & dental supplies	United States
4	Boston Scientific Japan K.K.	Medical, surgical, & dental supplies	United States
5	Fuji Photo Optical	Diagnostic imaging	Japan
6	GE Yokogawa Medical Systems, Ltd.	Diagnostic imaging	Japan
7	Goodman Co., Ltd.	Cardiac goods	Japan
8	Hitachi Medical Corporation	Diagnostic imaging	Japan
9	Hogy Medical Corporation	Disposable hygienic products	Japan
10	Johnson & Johnson K.K.	Diversified	United States
11	JMS	Medical processing	Japan
12	Kawamoto Sangyo Corporation	Disposable hygienic products	Japan
13	Medtronic Japan Co., Ltd.	Medical, surgical, & dental supplies	United States
14	Mochida Pharmaceutical Co., Ltd.	Diagnostic imaging	Japan
15	Nihon Mathys K.K.	Medical, surgical, & dental supplies	Japan
16	Nipro Corporation	Medical processing	Japan
17	Nipuru Corporation	Dialyzer equipment	Japan
18	Olympus Optical Corporation	Diagnostic imaging	Japan
19	Philips Medical Systems Japan Corp.	Diagnostic imaging	Netherlands/United States
20	Siemens	Diagnostic imaging	Germany
21	Shimadzu Corporation	Diagnostic imaging	Japan
22	St. Jude Medical, Inc.	Medical, surgical, & dental supplies	United States
23	Stryker Japan K.K.	Medical, surgical, & dental supplies	United States
24	Terumo Corporation	Medical processing	Japan
25	TOP Corporation	Medical processing	Japan
26	Toray Medical Co., Ltd.	Dialysis devices	Japan
27	Toshiba Medical Systems Corporation (Tokyo Office)	Digital imaging	Japan
28	Zimmer K.K.	Orthopedic products	United States

Source: *Medical Product Outsourcing*, Wright Reports, company annual reports and websites, 10-K reports, and other sources.

Chamber of Commerce in Japan (ACCJ) estimated the combined annual sales of its 54 members who produce medical devices in Japan to be roughly $8.5 billion in 2003.[126]

Shipments

As shown in table 3-15, total shipments of medical devices in Japan amounted to ¥1.53 trillion ($14.2 billion) in 2004, representing an average annual growth rate of

[126] Hanawa, "Medical Devices" (Japan).

0.4 percent from 2001 through 2004 (or 0.6 percent after correcting for deflation).[127] Japan's relatively slow shipment growth during the period resulted in a decline in its share of global production of medical devices to 10 percent, down from an estimated 11 percent in 2004 (and from an average of 13–15 percent in the 1990s).[128] Slow industry growth over the period was attributable to industry-specific determinants, such as limited technical innovation, as well as macroeconomic factors, such as Japan's recessionary and deflationary environments during that period. The decline in Japanese market growth was also a principal factor contributing to slow Japanese production growth.[129]

The composition of medical device production in Japan did not change markedly between 2001 and 2004. Shipments were concentrated in diagnostic imaging systems (20 percent), operating equipment and supplies (15 percent), artificial internal organ assisting devices (12 percent), and electronic measurement and monitoring systems (11 percent).[130] Medical devices that contributed most to the overall growth in the domestic industry in the period were medical devices for home use (such as inhalers and hearing aides), and IVDs (such as blood testing devices). Table 3-16 provides more information on Japanese device categories.

Employment

According to official data, employment in the Japanese medical device industry in 2004 was 81,759, or approximately 0.1 percent of the country's total workforce in that year (table 3-17).[131] Manufactured output per employee in this industry, which amounted to ¥18.8 million ($173,460) in 2004, declined by about 5 percent between 2001 and 2004 in yen denominated terms. Independent labor productivity estimates on data ending in 2001 show that the workforce in Japan provided less gross value added per employee than the U.S. workforce, but more than the European workforce.[132]

Factors of competition

Japan's sluggish production growth in its medical device industry is attributable, in part, to limited R&D and venture capital spending that have impeded innovation and inefficient distribution and regulatory systems. Private Japanese medical device manufacturing companies spend less on R&D relative to sales than their U.S. counterparts, according to MHLW's survey of the medical device industry.[133] According to the survey, larger Japanese companies with capital in excess of $425 million allocate an average of 6 percent of sales to research and development funding, compared with U.S. firms, which average over 10 percent. To stimulate domestic R&D, the Japanese government has recently revised its tax guidelines to allow for 8-10 percent of a domestic company's R&D expenditures to be tax-exempt (which has enhanced incentives relative to the United States).

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[127] Based on Commission staff estimations using Japan's consumer price index, as published by Japan's Statistics Bureau, Ministry of Internal Affairs and Communication.

[128] Based on Commission staff estimates.

[129] U.S. and Japanese industry officials and Japanese market analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

[130] Institute for Trade and Commercial Diplomacy, "Deregulation of the Medical Equipment Industry in Japan International Trade Negotiations"; and MLHW, *Annual Statistics on Production by Pharmaceutical Industry*.

[131] Based on survey data provided by MHLW officials, e-mail message to Commission staff, November 2006.

[132] Pammolli, et al., *Medical Devices: Competitiveness and Impact on Public Health Expenditure*.

[133] MLHW, *Annual Statistics on Production by Pharmaceutical Industry.*

Table 3-15 Japanese shipments of medical devices, 2001–4

Segment	2001	2002	2003	2004	Absolute change, 2001–4	Percent change, 2001–4
			million yen			*percent*
Diagnostic imaging systems	309,552	264,178	324,875	305,045	-4,507	-1.5
Related diagnostic X-ray equipment	115,267	118,700	100,080	110,475	-4,792	-4.2
Measuring and monitoring systems for biophenomena	156,709	147,976	154,704	167,458	10,749	6.9
In vitro clinical test equipment	78,484	92,564	81,089	89,067	10,583	13.5
Operating equipment and supplies	226,684	235,724	227,121	233,323	6,639	2.9
Clinical equipment and supplies	28,731	26,569	29,234	28,736	5	([a])
Artificial internal organ and assisting devices	184,656	182,572	177,569	189,979	5,323	2.9
Therapeutic and surgical equipment	51,319	60,301	49,422	40,335	-10,984	-21.4
Dental equipment	34,476	34,667	33,949	37,843	3,367	9.8
Dental material	98,585	96,117	86,026	87,900	-10,685	-10.8
Steel products for medical use	8,469	8,728	8,003	8,979	510	6.0
Ophthalmic and related products	79,188	76,937	74,885	78,411	-777	-1.0
Surgical dressing/hygienic products	4,328	4,722	4,152	4,740	412	9.5
Medical devices for home use	140,541	153,752	147,809	152,047	11,506	8.2
Total	1,516,989	1,503,507	1,498,918	1,534,338	17,349	1.1
			million dollars			*percent*
Diagnostic imaging systems	2,547	2,107	2,802	2,820	272	10.7
Related diagnostic X-ray equipment	948	947	863	1,021	73	7.7
Measuring and monitoring systems for biophenomena	1,289	1,180	1,334	1,548	258	20.0
In vitro clinical test equipment	646	738	699	823	177	27.5
Operating equipment and supplies	1,865	1,880	1,959	2,157	291	15.6
Clinical equipment and supplies	236	212	252	266	29	12.3
Artificial internal organ and assisting devices	1,519	1,456	1,532	1,756	237	15.6
Therapeutic and surgical equipment	422	481	426	373	-49	-11.7
Dental equipment	284	276	293	350	66	23.3
Dental material	811	767	742	812	1	0.2
Steel products for medical use	70	70	69	83	13	19.1
Ophthalmic and related products	652	614	646	725	73	11.2
Surgical dressing/hygienic products	36	38	36	44	8	23.0
Medical devices for home use	1,156	1,226	1,275	1,405	249	21.5
Total	12,482	11,991	12,930	14,182	1,699	13.6

Source: Japan's Ministry of Health, Labour and Welfare and IMF exchange rates.

[a] Less than 0.05 percent.

Table 3-16 MHLW medical device categories and examples of their components

Official category	Medical device product examples
Artificial internal organ and assisting devices	Dialyzers, cardiac pacemakers, artificial blood vessels, artificial joints, intraocular implants, artificial lungs, artificial respirators, anesthesia devices, etc.
Clinical equipment and supplies	Drug sprayers, medical suction units, inhalers, medical irrigators, etc.
Dental equipment	Dental surgery, units, and related equipment, orthodontic material and related equipment, etc.
Dental material	Dental metals, tooth crown materials, denture baseplate materials, dental model materials, etc.
Diagnostic imaging systems	X-ray diagnostic devices, CT, MRI, diagnostic ultrasound imaging devices, etc.
In vitro clinical test equipment	Clinical laboratory test equipment, blood testing devices, serum testing devices, etc.
Measuring & monitoring systems for biophenomena	Thermometers, blood pressure gauges, stethoscopes, cardiac output monitors, tonometers, electrocardiographs, electroencephalographs, monitoring equipment, endoscopes, etc.
Medical devices for home use	Massage and bath devices, electric/light-ray therapy devices, inhalers, hearing aids, etc.
Operating equipment and supplies	Syringes, tubes, catheters, blood collection/transfusion/infusion devices, suture machines, etc.
Ophthalmic and related products	Sight-correcting spectacles, cataract spectacles, contact lenses, optometric instruments, etc.
Related diagnostic X-ray equipment	X-ray imaging equipment, protective devices, etc.
Steel products for medical use	Amputators, snares/excisers, sharp/blunt curettes, retractors, aperture-opening devices, etc.
Surgical dressing/hygienic products	Sterile products, sterile materials, etc.
Therapeutic and surgical equipment	Radiation and laser therapy equipment, lithotripters, infrared ray therapy devices, low frequency electric therapy devices, ultrasound and short wave therapy devices, etc.

Source: Compiled by Commission staff from MHLW and JETRO information.

Table 3-17 Japanese manufactured output per employee, 2001–4

Year	Japanese production	Employment	Derived output per worker
	million yen		*yen*
2001	1,516,989	77,195	19,651,389
2002	1,503,507	80,361	18,709,411
2003	1,498,918	100,525	14,910,898
2004	1,534,338	81,759	18,766,595
	Japanese production	Employment	Derived output per worker
	million dollars		*dollars*
2001	12,482	77,195	161,700
2002	11,991	80,361	149,210
2003	12,900	100,525	128,326
2004	14,182	81,759	173,460

Source: MHLW. Employment data is likely higher, given that consolidated data only represents information from firms that responded to MHLW surveys.

Although Japan's National Institute of Health Science conducts its own medical research and provides its research results to the medical and scientific community, it does not provide the same sort of university and limited private sector grants that exist in the United States. Moreover, industrial-academic or medical-industrial research linkages are significantly less prevalent in Japan relative to the United States, so information does not easily flow across medical disciplines. Compared with the United States and the EU, medical practitioners in Japan also collaborate considerably less with those involved with medical training and design engineering.

The lower level of innovation in Japan's medical device industry is mainly evidenced by its low number of patents compared to its U.S. and EU counterparts.[134] According to U.S. and Japanese industry representatives, Japan's medical device industry is not firmly rooted in a pro-growth business environment, and its venture capital market is not as accessible, does not bear the risk, and/or is not as proactively involved in product development as it is in the United States and the EU.[135] The limited venture capital market in Japan has ultimately impeded the industry's ability to innovate. This is particularly true for small and medium size companies, which do not have critical funding during early product development that is necessary to continue research and sustain a business in a short product life-cycle industry. Moreover, given the limited venture capital firm presence in this highly regulated industry, innovation in Japan will likely continue to lag other major producers.[136] According to the MHLW, the Japanese venture capital market is not supportive of the medical device industry since firms in the venture capital industry are primarily funded by financial or security companies with very low risk thresholds. Moreover, entrepreneurs' home and family assets are not guaranteed in bankruptcy cases, which provide further innovation disincentives.[137] Recent bilateral government negotiations through the U.S.-Japan Regulatory Reform and

[134] MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

[135] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

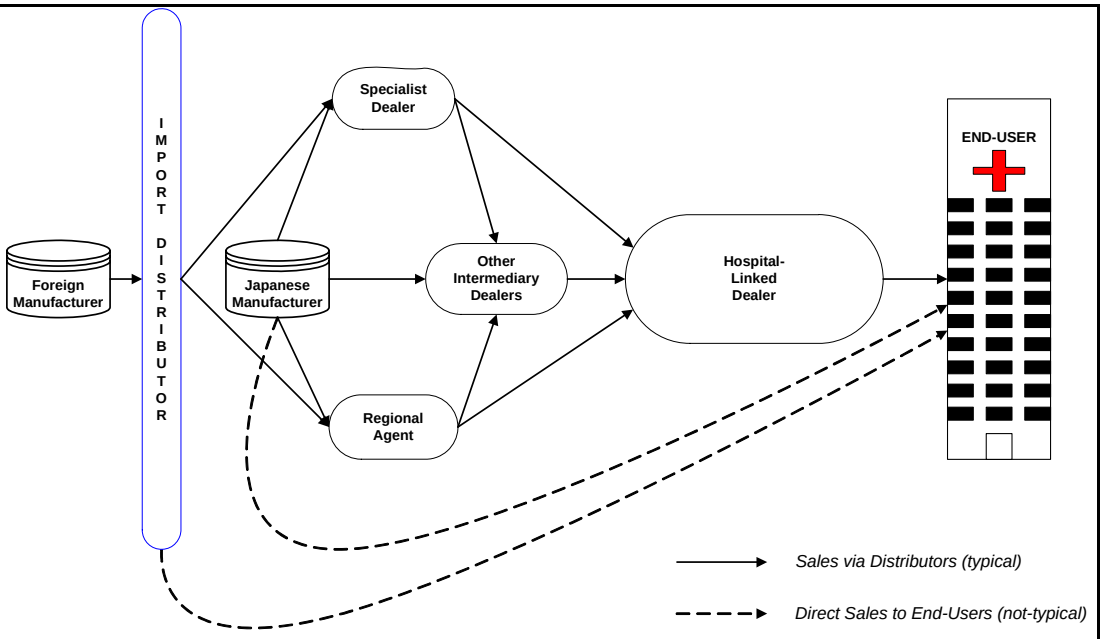
[136] U.S. Department of Commerce, International Trade Administration, *Medical Device Outlook 2005.*

[137] MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

Competition Initiative suggest that the Japanese government may provide greater innovation incentives in the near future.[138]

Japan's complex distribution system also makes it difficult for the industry to remain competitive. The system is characterized by various distribution layers employing numerous intermediary agents between manufacturers and end users (figure 3-6). More than 80 percent of foreign or domestic manufacturers' medical device sales are filtered through a series of regional agents (who often serve rural areas), specialist dealers (who possess highly technical training, such as for cardiac-related medical devices), intermediary dealers (whose purpose and business dealings are ill-defined), and/or hospital-linked dealers (who directly service hospitals by monitoring daily inventory records and matching hospital needs with other dealer offerings). Additionally, foreign manufacturers usually also sell through Japan's import distributors, who are considered the most expensive intermediary dealers by Japanese industry analysts interviewed by Commission staff.[139]

Figure 3-6 Japan's distribution system for medical devices



Source: Japan External Trade Organization; and industry analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

[138] Fontanazza, "Japanese Reform Brings More Access to Innovation."
[139] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

Japan's larger number of intermediary agents along typical supply routes is a key difference in its distribution system compared with the distribution systems in other advanced countries. Distributors of medical devices were estimated to account for between ¥100-¥200 billion (less than $1 billion) of business in Japan in 2003. They are smaller and more numerous than in other highly industrialized countries and sell a wide variety of products.[140]

Nearly all industry analysts and distributors interviewed by Commission staff in Japan suggested that Japan's relatively complex distribution system has increased supply inefficiencies and prices, since product training and price markups are added at each level of the distribution chain.[141] Although the number of agents used by the medical device industry was estimated to total nearly 2,500 in Japan, Japanese industry officials, analysts, and distributors suggest that increased consolidation among industry distributors over the past few years may have reduced that number.[142]

Only a minority of Japan's producers (e.g., those selling large expensive equipment such as MRIs)[143] supply their products directly to their healthcare customers, including hospitals, clinics, and physicians. The R&D Corporation, a research subsidiary of JFE Holdings, Inc., estimated that between 1997 and 2001, roughly 19 percent of manufacturers' sales went directly to end users,[144] though industry officials suggest that share has probably decreased in recent years.[145]

Another strategy foreign businesses have used to penetrate Japan's medical device market, other than through distributors, involves mergers, acquisitions, and/or the establishment of joint-venture operations. While this latter strategy has generally been rare in Japan, several prominent partnerships have recently been created. Boston Scientific Japan, for example, has continued to buy several domestic Japanese companies since its 1995 acquisition of SciMed Life Systems, to increase its domestic market presence.[146] St. Jude Medical, Inc. acquired the import retailer Getz Bros. in April 2003, largely in an effort to secure domestic distribution routes. Finally, GE entered the Japanese market by forming a joint-venture operation with Yokogawa Electric to form GE Yokogawa Medical, in which GE currently holds a 75 percent ownership position.[147]

Japan's system for regulatory review of medical devices, another supply-side factor of competition, has come under widespread criticism for its excessive delays, complicated requirements, non-transparency, insufficient number of qualified reviewers and limited number of product categories, and expense in gaining product approvals.[148] Delays associated with regulatory review inhibit consumption and often result in Japanese patients gaining access to new medical technologies years after the products have come into use in

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[140] JETRO, *Japanese Market Report-Medical Equipment*; and MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

[141] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

[142] Ludwig, hearing transcript, 93; U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006; and MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

[143] JFMDA, *Report on the Investigation Into the Distribution of Medical Devices.*

[144] R&D Corporation, *Medical Equipment/Supplies Yearbook.*

[145] U.S. and Japanese industry officials and market analysts, interviews by Commission staff, Japan, July 31–August 9, 2006.

[146] JETRO, *Japanese Market Report No. 69: Medical Equipment.*

[147] General Electric Form 10-K.

[148] U.S. and Japanese government and industry officials, interviews by Commission staff, United States, May 31, 2006, and Japan, July 31–August 9, 2006.

the United States or in the EU. Industry officials suggest that the standard review process in Japan is generally much longer than in the United States and the EU.

In the most recent legislative revision of the Pharmaceutical Affairs Law (PAL) on July 25, 2002, the Japanese government streamlined the regulatory review process of medical devices and pharmaceuticals.[149] U.S. and Japanese officials indicate that while these reforms may help expedite the regulatory review process in the future, the inclusion of additional regulatory review requirements (e.g., plant inspections), and the existing backlog of applications that preceded the creation of the PMDA, reportedly have compromised the agency's present ability to significantly decrease review times.[150]

Demand

According to several industry sources, growth in medical device demand in Japan, relative to other prominent markets, remains constrained by the government's broader cost-containment strategy[151] and the populations' relatively low aggregate and per-capita spending on healthcare compared with other OECD countries.[152] Japan's lower healthcare spending appears to reflect weaker domestic demand from doctors and patients who are not as likely to use more advanced medical technologies as in other highly developed industrialized countries,[153] as well as Japanese cultural preferences (such as higher product safety expectations and a relative reluctance to undergo physically invasive procedures).[154]

Nevertheless, the rapidly growing proportion of Japan's aging population has placed upward pressure on overall consumption of medical devices. The average life span of the Japanese population was 82.1 years by 2006, longer than in any other OECD country.[155] Moreover, the proportion of the country's population aged 65 or older is rising faster than any other advanced industrial country,[156] and increased from 18 percent in 2001 to 20 percent in 2004 (figure 3-7).[157] These factors are expected to continue to have a positive impact on medical device industry growth in Japan. Healthcare expenditures for Japanese citizens over 65 account for nearly 40 percent of overall healthcare spending, and have been estimated to reach 50 percent of total spending by 2011.[158] Moreover, the percentage of the population exceeding age 65 is projected to increase to 30 percent by 2025.[159]

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[149] Chapter 6 provides further detail on the Japanese regulatory system.

[150] U.S. and Japanese government and industry officials, interviews by Commission staff, United States, May 31, 2006, and Japan, July 31–August 9, 2006.

[151] Diller and Gold, *Industry Survey-Healthcare: Products & Supplies*.

[152] OECD, Health Data Database, 2006; and U.S. and Japanese government and industry officials, interviews by Commission staff, United States and Japan, May–August 2006.

[153] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

[154] U.S. and Japanese industry officials; and Japanese healthcare economist, interviews by Commission staff, Japan, July 31–August 9, 2006.

[155] OECD, Health Data Database, 2006; and JETRO, "Attractive Sectors-Medical Care."

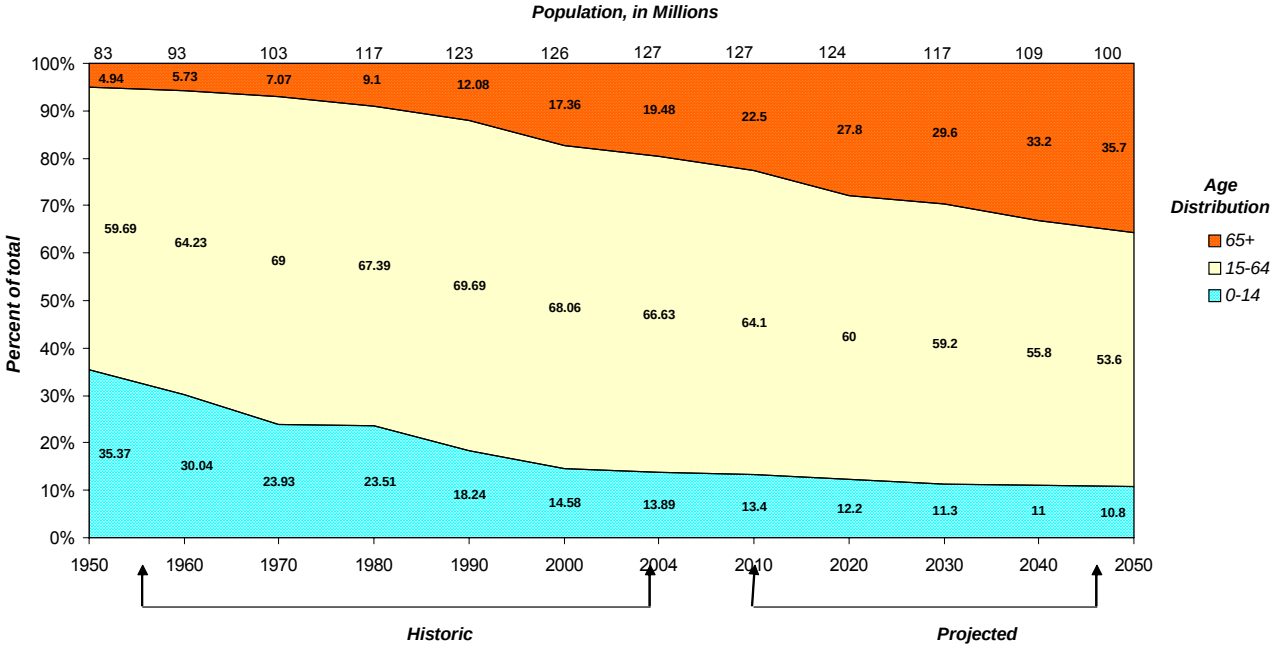
[156] United Nations (UN). *World Population Prospects-2000 Revisions*.

[157] Statistics Bureau & Statistics Center, Ministry of Public, Management, Home Affairs (Japan), Demographic Data, accessed via CEIC database, Japan's Ministry of Internal Affairs and Communication's Statistical Bureau and Statistical Research and Training Institute, *Statistical Handbook of Japan*, accessed via CEIC database.

[158] AdvaMed/ACCJ, "Japan Medical Technology Issues CEO Tool Kit."

[159] Hanawa, "Medical Devices" (Japan).

Figure 3-7 Composition of Japan's population (by age)



Source: National Institute of Populaiont and Social Security Research (Japan), "Population for Japan: 2001-2050, January 2006.

The Japanese government has sought to curb healthcare spending in recent years, and has viewed a reduction in medical device prices as a critical component in controlling healthcare expenditures. Japan's sluggish economic performance since the early 1990s[160] has only recently begun to rebound, and has encumbered the government with large public debt currently exceeding 160 percent of GDP.[161]

Consequently, Japan has recently sought to limit public spending, which includes healthcare expenditures. However, since 1992, Japan's public healthcare expenditures have progressively increased, largely due to an increase in the country's retired population, who account for a greater share of government healthcare spending. By 2002, expenditures reached nearly ¥30 trillion ($250 billion), which represented approximately 8 percent of Japan's GDP in that year.[162] The Japanese public's perception that medical device prices in Japan significantly exceed foreign prices has increased pressure to reduce medical device and equipment pricing.[163]

[160] Citrin and Wolfson, "Japan's Back!," *Finance and Development;* and Economist Intelligence Unit, *Country Report (Japan*), 19.

[161] Economist Intelligence Unit, *Country Report (Japan*), 19.

[162] OECD, Health Data Database, 2006.

[163] AdvaMed/ACCJ, "Japan Medical Technology Issues CEO Tool Kit."

Consumption

While Japan's medical device market is the second largest single country market in the world behind the United States, valued at ¥2.1 trillion ($19.0 billion) in 2004 (table 3-18),[164] relatively low average growth of 2 percent (even after correcting for deflation) per year since 2001 has resulted in loss of global market share.

The leading segments of the Japanese market are artificial internal organ and assisting devices (implantable medical devices) (21 percent), operating equipment/supplies (20 percent), diagnostic imaging systems (13 percent), and ophthalmic devices (10 percent).[165] The contribution of each of these segments to overall consumption in Japan has remained virtually unchanged since 2001, with the exception of ophthalmic devices whose market share grew by 2 percentage points.

Health insurance

Since 1961, Japan's healthcare system has provided universal coverage and equality of benefits to its citizens. It currently maintains this system through three basic sources of insurance: municipal government (which includes coverage for the unemployed and retired); national government (which includes coverage for employees of small and medium size enterprises); and private companies (which provide coverage for employees of large enterprises).[166] Citizens pay insurance premiums into a public health insurance system, and can receive medical care at any medical facility in the country providing insurance-covered care.[167] Under this system, the national government, local governments, and unions pay reimbursement for medical care to medical facilities and pharmacies directly.[168] The national government is fully involved in reimbursement decisions, as well as some purchasing decisions of medical equipment. Those purchasing decisions affect the type and cost of equipment deemed necessary, which ultimately influences market conditions faced by Japanese and foreign manufacturers.[169] The situation is further exacerbated by the financial burdens imposed on the government from an increasing elderly proportion of the population (mostly retiring from large private firms) who are less able to pay insurance premiums. Moreover, a growing proportion of patients is not paying its supplementary medical charges to hospitals, thereby further constraining hospitals' medical device purchasing decisions.[170]

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[164] MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

[165] MLHW, *Annual Statistics on Production by Pharmaceutical Industry*.

[166] MHLW, "Medical Device Industry Vision-Aiming to Provide Even Better, Safer, and Innovative Medical Devices."

[167] JETRO, *Japanese Market Report No. 69: Medical Equipment.*

[168] Ibid.

[169] Diller and Gold, "Healthcare: Products & Supplies."

[170] U.S. and Japanese government and industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

Table 3-18 Japanese medical device shipments, exports, imports, apparent consumption, and the ratios of exports to shipments and imports to consumption, 2001–4

Year	Japanese shipments	Japanese exports	Japanese imports	Apparent Japanese consumption	Ratio of exports to shipments	Ratio of imports to consumption
	billion yen					*percent*
2001	1,517	397	836	1,956	26	43
2002	1,504	377	840	1,967	25	43
2003	1,499	421	884	1,962	28	45
2004	1,534	430	955	2,059	28	46
	billion dollars					*percent*
2001	12.5	3.3	6.9	16.1	26	43
2002	12.0	3.0	6.7	15.7	25	43
2003	12.9	3.6	7.6	16.9	28	45
2004	14.2	3.9	8.8	19.0	28	46

Source: Japan's Ministry of Health, Labour and Welfare and IMF exchange rates.

Note.—Official 2005 Japanese production and trade data will not become available until early 2007.

Trade practices

Several U.S. and other foreign manufacturers state that the most prominent Japanese trade barriers revolve around regulatory delays, reimbursement policies, and market entry restrictions. According to a U.S. government report, the regulatory reform priority that would most benefit U.S. industry and government is a faster product approval process in Japan.[171] While most U.S. and EU medical device manufacturing firms agreed that this is the main obstacle to accessing the Japanese market, Japanese firms also indicated that they were adversely affected by Japan's slow review process.[172] This suggests that although Japan's relatively slow regulatory process has hampered the introduction of new products, the regulatory review process does not appear to be discriminatory against foreign manufacturers.[173] Rather, complex regulations, the low number of qualified medical device reviewers, overseas audits, and factory inspection procedures appear to be the principal causes of more lengthy medical device reviews in Japan.[174]

Another high priority issue for U.S. and foreign businesses, according to U.S. industry and government officials, is the establishment of a reimbursement system in Japan that sufficiently accounts for product differentiation through its reimbursement schedule. U.S. industry officials contend that the number of product categories in the MHLW's reimbursement schedule is too limited, and thereby incapable of effectively differentiating products for reimbursement purposes.

[171] USTR, *National Trade Estimate Report on Foreign Trade Barriers.*
[172] U.S. and Japanese industry officials, interviews by Commission staff, Japan, July 31–August 9, 2006.
[173] Ludwig, hearing transcript, 35.
[174] USTR, *National Trade Estimate Report on Foreign Trade Barriers.*

CHAPTER 4
Trade in Medical Devices

The EU, the United States, and Japan accounted for 68 percent of total global trade in medical devices in 2005, which was valued at nearly $190 billion.[1] The United States and the EU both maintained a trade surplus, in dollar terms, during 2001–5. Japan, on the other hand, maintained a trade deficit throughout the period. National trade data for medical devices are not directly comparable between the United States, the EU, and Japan, as industry definitions and product coverage vary.

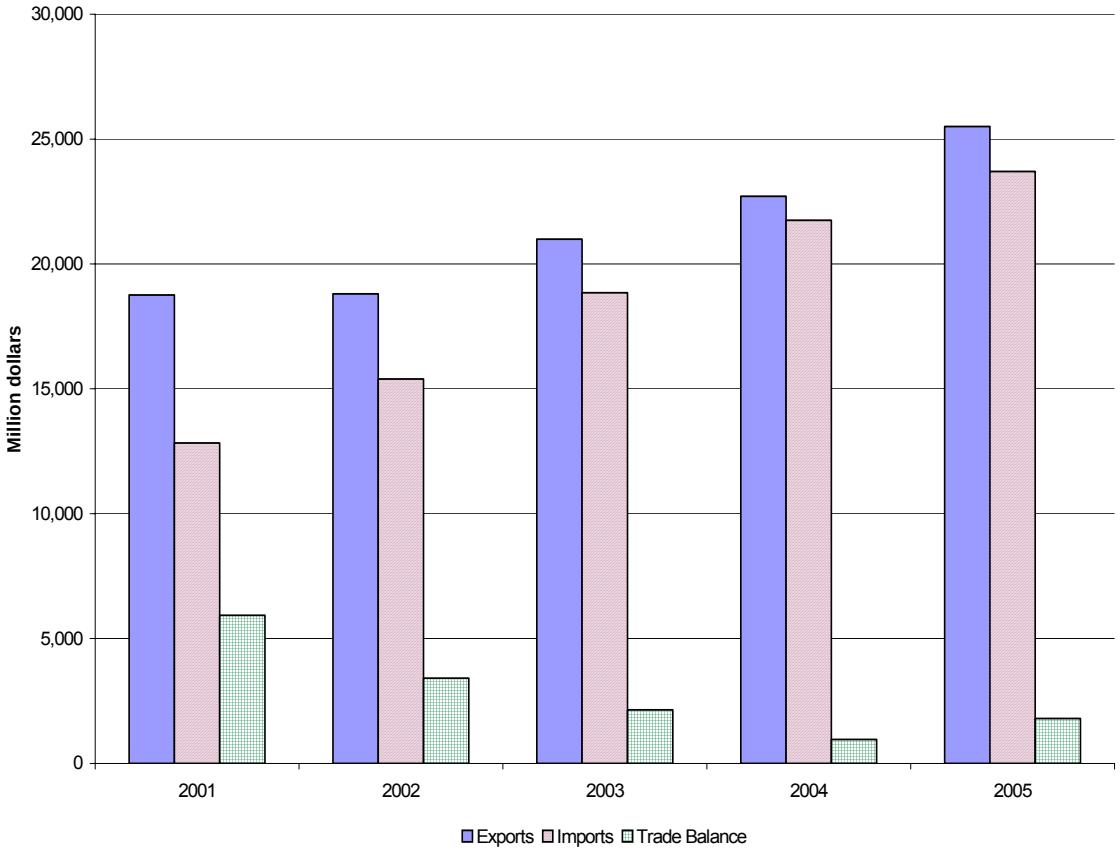
United States

The U.S. medical device industry has posted a trade surplus every year during 2001–5. However, the surplus declined steadily from 2001 through 2004, before rebounding modestly in 2005 (figure 4-1). Healthcare analysts attribute the decline largely to continuing strong demand for medical devices in the United States, both the largest healthcare market in the world and fastest-growing among the more advanced economies.[2] Despite steady growth in exports, which increased by 36 percent from 2001 through 2005, the uninterrupted growth in U.S. demand led to even greater increases in imports over the period, which rose by 85 percent. Increased foreign outsourcing, especially to foreign affiliates of U.S. firms in the EU (particularly Ireland), has also been a significant contributor to the decline in the trade balance (figure 4-2).

[1] Global Trade Information Services, *World Trade Atlas Database 2006.* Global Trade Atlas statistics likely underestimate trade in medical devices.

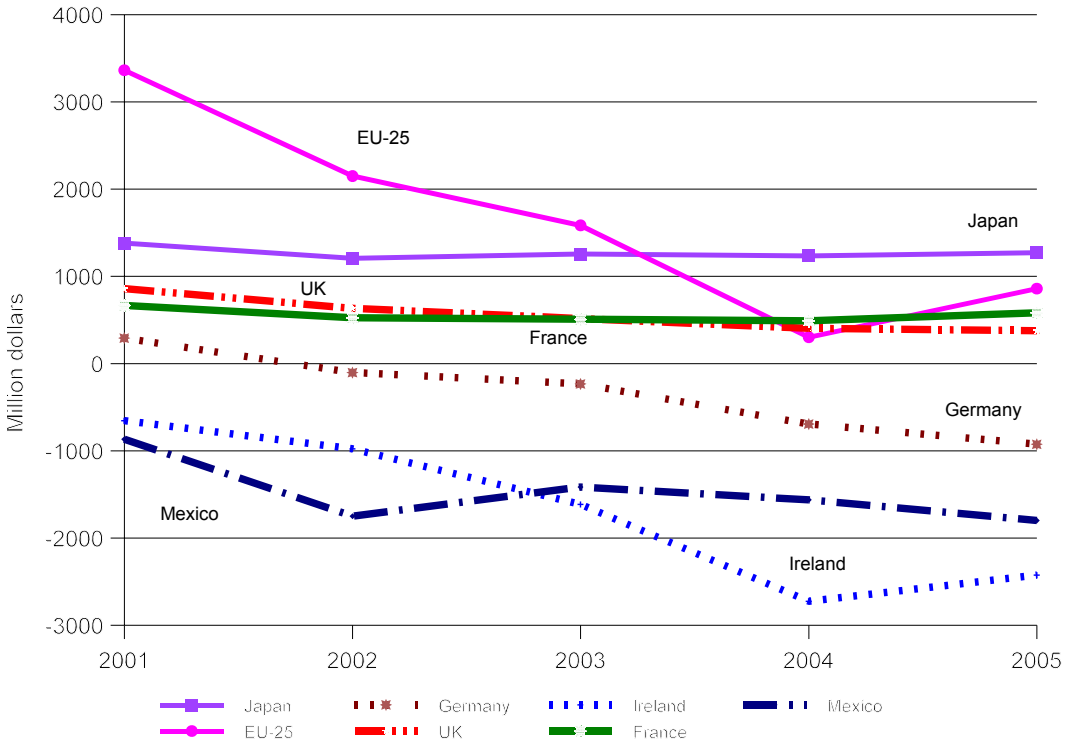
[2] Yeo, *North America Medical Instruments*, 3; and U.S. healthcare analysts, telephone interviews by Commission staff, October 17, 2006.

Figure 4-1 U.S. exports, imports, and merchandise trade balance in medical devices, 2001–5



Source: Compiled by Commission staff based on official statistics of the U.S. Department of Commerce.

Figure 4-2 U.S. bilateral trade balance in medical devices with selected trading partners, 2001–5



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

Among the major medical device segments, electromedical equipment, followed by surgical and medical instruments, and dental equipment, contributed the most to the decline in the U.S. trade surplus for 2001–4, which decreased from $5.9 billion in 2001 to $957 million in 2004, before turning up again in 2005 to $1.8 billion (table 4-1). Conversely, orthopedic devices and hospital supplies accounted for a large portion of the rebound in the trade surplus in 2005. However, selected products from all five major medical device segments influenced the turnaround in the trade balance as overseas demand picked up for innovative U.S.-made medical devices after gaining regulatory approval in Europe and Japan, contributing to a 12 percent rise in U.S. exports in the final year of the period. Among these were new versions of IVDs, implantable cardiac defibrillators, drug-eluting stents, and advanced orthopedic products, such as hip, knee, and spinal implants.[3]

[3] Diller and Gold, "Healthcare: Products and Supplies"; 3–7, 30, and 31; and Zimmer, "Spinal Fusion," 1–8.

Table 4-1 U.S. medical device trade balance, by segment, 2001–5

NAICS code	Product segment	2001	2002	2003	2004	2005	Absolute change, 2001–5	Percent change, 2001–5
		million dollars						*percent*
325413	In vitro diagnostic substances and devices	2,086	2,028	2,408	2,324	2,328	242	12
334510, 334517	Electromedical equipment	1,191	-453	-1,195	-1,363	-1,136	-2,327	-195
339112	Surgical and medical instruments	1,746	1,071	677	-273	-88	-1,834	-105
339113	Orthopedic devices and hospital supplies	739	618	264	297	792	53	7
339114	Dental equipment	171	151	-11	-28	-95	-266	-156
	Total	5,933	3,415	2,143	957	1,801	-4,132	-70

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

U.S. exports of medical devices increased by 36 percent from 2001 through 2005 to $25.5 billion, influenced by changes in foreign government policies and growing demand from China. Although Japan continued to be the most important single country market for U.S.-manufactured medical devices (table 4-2), growth in exports to Japan lagged other markets as U.S. exports to that country grew by just 13 percent from 2001–5.[4] However, in the final year of the period, U.S. exports to Japan rose by 9 percent as U.S. medical device makers benefitted from efforts in 2005 by the Japanese government to address growing imbalances in its healthcare expenditures compared to other OECD countries.[5] According to a major U.S. trade association, "U.S. companies are the major suppliers of many critical products in Japan such as pacemakers, orthopedic implants such as hips and knees, and drug-eluting stents." [6]

U.S. exports to the EU increased by a total of 39 percent for the 2001–5 period, led by exports to Germany, the EU's largest market for medical devices.[7] U.S. exports to the United Kingdom rose by 14 percent in 2005, largely as a result of the "UK government's commitment to increase public spending on health."[8] U.S. exports to Ireland grew by 84 percent over the period to $1.4 billion. However, such exports declined by one percentage point in 2005, as U.S.-owned operations in Ireland, which account for a large portion of the trade with the United States, produced more parts and components themselves, relying less on their parent companies.[9]

[4] Alch, *The U.S. Market for Medical Devices,* 8.

[5] "How Does Japan Compare," *OECD Health Data 2005,* 1.

[6] Ludwig, hearing transcript, 7.

[7] Diller, "Healthcare: Products and Supplies: Europe," 8–12.

[8] "How Does the United Kingdom Compare," *OECD Health Data 2005,* 1–2; and UK government and industry officials, interviews by Commission staff, United Kingdom, September 25–27, 2006.

[9] U.S. industry officials, telephone interviews by Commission staff, August 21–23, 2006.

Table 4-2 U.S. imports and exports of medical devices, by selected countries, 2001–5

Country	2001	2002	2003	2004	2005
			million dollars		
Imports:					
Ireland	1,409	1,881	2,951	4,120	3,811
Germany	1,751	2,108	2,578	3,154	3,582
Mexico	1,693	2,097	2,506	2,726	3,134
Japan	1,494	1,550	1,585	1,761	1,989
United Kingdom	578	747	775	947	1,163
Switzerland	428	734	1,230	1,173	1,113
China	396	533	689	805	1,049
France	450	512	567	683	730
Netherlands	478	502	471	532	608
Canada	347	421	493	554	607
Exports:					
Japan	2,876	2,756	2,841	2,996	3,259
Germany	2,043	2,004	2,344	2,461	2,656
Netherlands	1,241	1,428	1,776	2,087	2,410
Canada	1,592	1,561	1,700	1,840	2,070
United Kingdom	1,437	1,382	1,291	1,350	1,538
Ireland	753	905	1,336	1,395	1,387
Mexico	825	948	1,091	1,165	1,335
France	1,118	1,036	1,075	1,173	1,312
Belgium	713	602	667	967	1,122
Australia	523	579	621	743	845

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

U.S. exports to China (box 4-1) doubled to $661.0 million over the period, making it the fastest growing among the top 10 U.S. export markets, as demand for better healthcare by China's growing middle class led to increased expenditures on medical devices, including U.S.-made medical devices.

U.S. imports of medical devices also increased from 2001 through 2005, mainly based on growing U.S. demand and transfers from U.S. affiliate companies abroad. The EU, Mexico, Switzerland, China, and Japan accounted for a significant amount of the increase. U.S. imports from the EU increased to $11.5 billion in 2005. Ireland remained the leading supplier of U.S. imports of medical devices. However, imports from Ireland declined by 8 percent in the final year of the period, as Irish subsidiaries of U.S. high-tech producers[10] directed a greater portion of their sales to fast-growing markets in other EU countries and to Japan.[11] U.S. imports from both Germany and the United Kingdom more than doubled during the period, while U.S. imports from Switzerland, which included cardiac pacemakers manufactured in a Swiss subsidiary of a U.S.-based manufacturer and orthopedic devices from a major Swiss producer, increased to $1.1 billion.[12]

[10] Whitney, "Innovation Ireland," 1.

[11] U.S. industry officials, telephone interviews by Commission staff, March 20–21, 2006; Irish industry officials, interviews by Commission staff, Ireland, September 28 and 29, 2006; and official trade data of MHLW.

[12] Alch, *The U.S. Market for Medical Devices*, 8; Medtronic, Inc., *Medtronic Switzerland at a Glance*, 1*;* and Medtronic Inc., form 10-K.

Box 4-1 Growing importance of China's medical device market

China's market is generally recognized as among the fastest growing in the world, growing 15–20 percent annually, and is the second largest market in Asia, after Japan. Estimates of the size of China's medical device market vary widely, ranging from $2.5 billion to $9.4 billion. Nevertheless, a strong driver of market growth is demand for IVDs. Notably, Frost and Sullivan project the estimated value of the Chinese IVD market to grow at 14 percent annually through 2010, the fastest IVD market growth rate worldwide. The Chinese market for devices is primarily concentrated in large east coast cities, such as Beijing and Shanghai.

Growing imports of medical devices reflect in part the general increase in market demand. Imports supply an estimated 75 percent of the Chinese market. Underscoring the importance of the Chinese market in terms of growth, U.S. exports to China have more than doubled from 2001 through 2005.

Factors driving increased consumption in China include an increasingly wealthy and growing middle class, an expanding elderly population, and a state-sponsored push to extend access to quality healthcare. As part of China's most recent five-year plan, the government plans to invest 21.7 billion RMB ($2.8 billion) in healthcare. Funding from the central government is expected mainly to channel into rural hospitals, providing them with the means to buy more advanced medical equipment. In fact, about 6.8 billion RMB ($877 million) is earmarked for medical device and equipment purchases. The Chinese elderly population is also increasing and is projected to reach nearly 400 million in 2050. Finally, the expanding Chinese middle class has the potential to augment these growth prospects in their ability to afford increasing expenditures on healthcare.

To meet current and anticipated demand, industry players have stepped up production. Currently, foreign firms dominate the production and sale of high-end devices, while smaller Chinese firms are more price-competitive in low-tech, commodity-type items. At the end of 2003, approximately 2,900 domestic manufacturers were producing basic medical supplies, such as bandages, patient aids, and medical or surgical instruments. The number of Chinese manufacturers is reportedly expanding, with sales estimated at over $5 billion in 2005, 75 percent of which represented exports.

Sources: Agress, hearing transcript, 46; "China Rural Medical Market Target for GE Healthcare"; "J&J Targets Medical Device Sector"; Biggs, "China's Medical Device Market"; Chang-Hong, "Regulators Continue to Tighten Control over Med-Tech Companies"; Cowan, "Chinese Medical-Device Maker's IPO Rises 30%"; Cleaveland, "Critical Outsourcing Questions"; Lipson, "Healthcare Market in China"; Hassell and Bella, "Diagnosing China's Medical Device Market"; *The Global Plastics Magazine;* Mindray Medical Form 10-K; and Zamiska,"Beijing Policy Shift May Boost Local Medical Device Companies."

U.S. imports from Mexico also rose during 2001–5 to $3.1 billion in 2005. Mexico continues to be a major base for manufacturing operations of U.S.-headquartered companies. U.S. firms originally established operations there to take advantage of U.S. and Mexican tax and tariff incentives and relatively low wage costs. However, Mexico has moved up the supply chain to manufacture more advanced products, while U.S. firms outsource more labor-intensive manufacturing activities to less-developed Latin American countries such as Costa Rica and the Dominican Republic. Together, these two countries accounted for over $1 billion in U.S. imports in 2005 and represent an increase of 52 percent over the period (box 4-2).

Meanwhile U.S. imports from Japan increased by 33 percent from 2001 through 2005 to just under $2 billion. A significant portion of the U.S. imports from Japan consisted of diagnostic imaging apparatus, endoscopic instruments, and commodity hospital supplies from firms such as Toshiba, Olympus, and Terumo.

Box 4-2 Outsourcing by the U.S. medical device industry

As in other industries, most medical device companies outsource some aspect of operations to independent firms to reduce operating costs and focus on core strengths. In recent years, many U.S. industries have successfully broadened their outsourcing model to include U.S. and foreign firms with offshore production facilities.

Transportation costs, speed to market issues, and vast differences in individual market demand have created overall structural incentives for medical device firms to locate manufacturing facilities near customer bases. Medical device firms adopt offshore outsourcing as a strategy to boost competitiveness in terms of both cost and market access. In addition to internal efforts to control expenditures, companies confront external downward price pressures on their products. A global trend of healthcare cost-containment combined with intra-industry competition has created significant momentum for medical device firms to actively pursue cost-reducing strategies. As well, companies are looking to offshore outsourcing as a preliminary step in entering new markets. By strategically positioning themselves in these developing markets now, they hope to reap the future returns associated with expanding their customer base.

When firms decide to outsource their manufacturing to offshore plants, tax incentives, proximity to important markets, or low production costs dictate where operations are located. Outsourcing by U.S. companies largely consists of (1) exporting parts and subassemblies of low-end commodity hospital supplies, such as intravenous and blood administration sets, to be assembled in Latin America and Asia to reduce labor costs for products to be consumed in the United States; and (2) more sophisticated components for such devices as pacemakers, defibrillators, and magnetic resonance imaging equipment exported to foreign manufacturing subsidiaries and partners in the European Union and Switzerland, for purposes of proximity to those important overseas markets for medical goods.

A number of U.S. companies also maintain manufacturing facilities in Mexico, the Dominican Republic, Costa Rica, Singapore, and Malaysia. Large U.S. hospital supply companies began substantive assembly and manufacture in Mexico in the 1970s. They benefited from relatively lower wages and from preferential duty treatment provided by both the United States and Mexico in the *maquiladora* program. Since that time, even as its wages and production costs have gone up, Mexico has advanced itself to become an outsourcing partner with higher-technology U.S. firms, assembling such sophisticated products as self-expanding and drug-eluting stents. The Dominican Republic replaced Mexico as a leading low-cost assembler of commodity medical devices in the 1990s, taking advantage of tax and infrastructure incentives provided by the Dominican Republic government and preferential tariff treatment under the U.S. GSP and CBERA programs, which lowered the cost of exporting finished products back to the United States. More recently, Costa Rica has emerged as a major competitor for U.S. investment in manufacturing and assembly facilities as the Dominican Republic has begun to face capacity constraints. Products imported by the United States from the Dominican Republic and Costa Rica consist primarily of high volume, price-sensitive hospital products, such as intravenous and blood administration sets, assembled for large U.S. hospital supply companies. Other countries serving as outsourcing partners for U.S. companies for similar products include Singapore and Malaysia.

More advanced countries, such as Ireland and Switzerland, have become major outsourcing partners for leading U.S.-based suppliers of advanced cardiovascular and orthopedic implant devices. Ireland, especially, has become a major outsourcing partner for leading U.S. high-tech firms who have substantial investment in Irish facilities.

Sources: Agress, hearing transcript, 46; Andrews, "10 Reasons to Outsource Design and Development;" Bell, "Have It Your Way: Full Service Outsourcing Firms Offer OEMs Broader Menus of Capabilities;" Conkey, "Made in USA? Now, Customers Get to Choose;" Davies, "Outsourcing Goes to a Deeper Level;" "Healthcare Trends: Medical Device Outsourcing;" *Medtech Insight*, May 2005; Kerber, "Medical Device Makers Increasingly Send Work to Contract Manufacturers;" Nyberg, "International Outsourcing: When Outsourcing in Asia, a Cornucopia of Options Exists;" "Outsourcing in Asia: As China's Capabilities Grow, OEMs Face Pros and Cons of Sourcing from Chinese Market;" Sparrow, "Outsourcing Outlook;" US industry officials, interviews by Commission staff, June 5–16, 2006; Cordis de Mexico VPO Victor Chance; and Irish industry officials, interviews by Commission staff, Ireland, September 28–29, 2006.

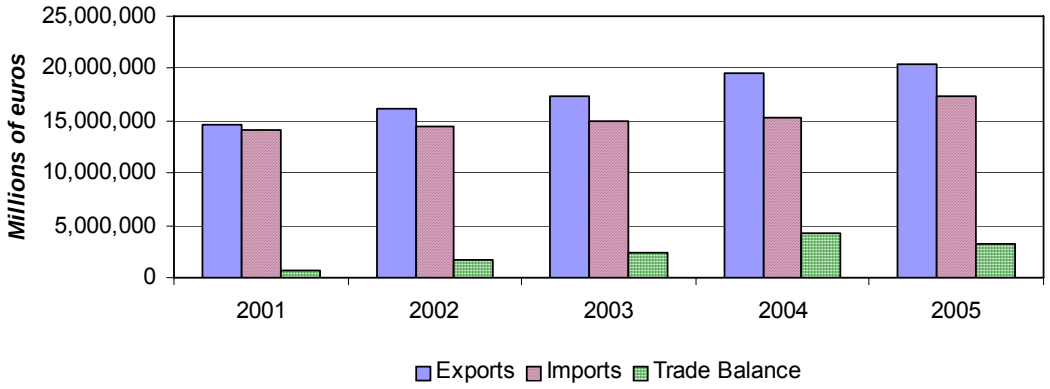
European Union

The EU medical device industry experienced a rapidly growing trade surplus from 2001–4 (figure 4-3). Although that surplus declined in 2005, exports still exceeded imports by €3.6 billion ($4.5 billion), driven by a surplus of €2.6 billion ($3.2 billion) in the electromedical equipment segment (including irradiation and diagnostic imaging equipment such as MRI and CT apparatus). Surgical and medical instruments, in vitro diagnostics, and dental equipment sectors all posted surpluses in 2005 (table 4-3). European-headquartered global leaders, such as Siemens and Philips, are active in the electromedical segment and B. Braun in the surgical and medical instruments segment. By contrast, orthopedic and surgical supplies recorded a consistent, albeit declining, trade deficit from 2001–5, ranging from -€618 million to -€186 million (-$553 million to -$232 million).

At the individual country level, Germany and Ireland lead the EU in exports of medical devices. In 2005, Germany reported trade surpluses across all segments, with particularly large balances in the areas of surgical and medical instruments and orthopedic and surgical supplies, and an overall surplus of €4.6 billion ($5.8 billion). Ireland reported large trade surpluses in the surgical and medical instruments and electromedical equipment segments, and an overall surplus of €4.3 billion ($5.4 billion). By contrast, Italy, France, and the United Kingdom reported overall deficits of -€2.3 billion (-$2.8 billion), -€96 million (-$741 million) and -€20 million (-$24 million), respectively, in 2005. The large trade surpluses of Germany and Ireland drive the EU's positive trade balance (figure 4-4).

The United States is, by far, the most important trading partner of the EU; it is the top export destination (42 percent of all exports) and the top foreign source (54 percent of all imports) for medical devices across all segments. The EU has recorded a consistent deficit, albeit declining, in its medical device trade with the United States. Japan, Switzerland, and China are the EU's next largest trading partners, with the EU reporting surpluses in its medical device trade with Japan and China and a deficit with Switzerland in 2005. Russia and Australia also are important export destinations for EU medical devices (table 4-4).

Figure 4-3 EU exports, imports and merchandise trade balance in medical devices, 2001–5



Source: Global Trade Information Services, Inc., *Global Trade Atlas Database*.

Note.—Imports and exports do not include the in vitro diagnostics segment.

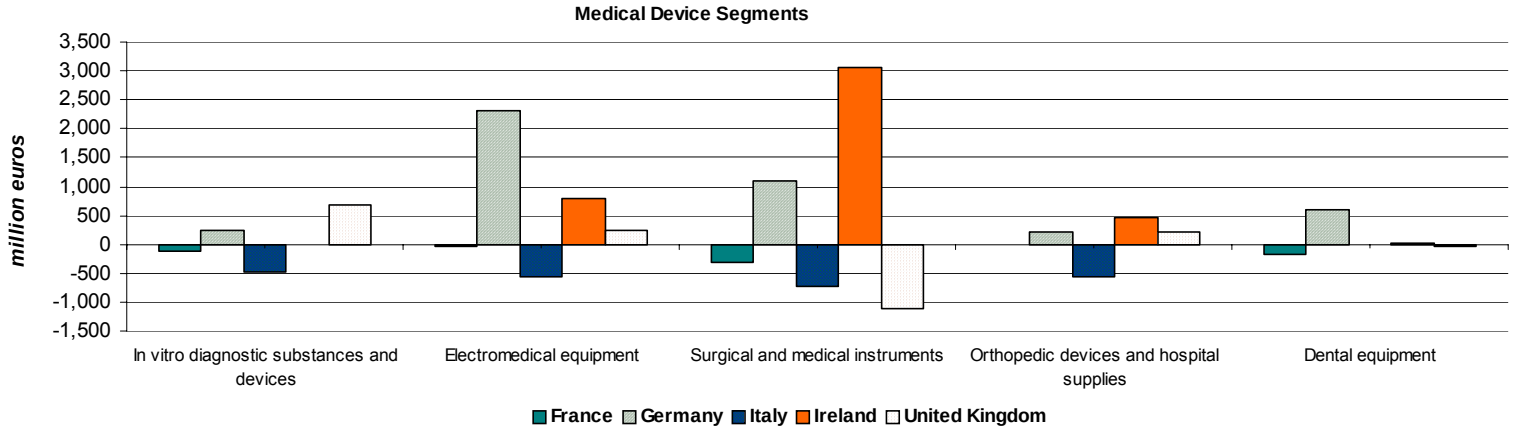
Table 4-3 EU medical device trade balance, by segment, 2001–5

Segment	2001	2002	2003	2004	2005	Absolute change 2001–5	Percent change 2001–5
			million euros				
In vitro diagnostic substances and devices	-270	-152	69	244	404	673	250
Electromedical equipment	1,566	1,874	1,780	2,948	2,553	988	63
Surgical and medical instruments	-425	324	763	1,324	667	1,092	257
Orthopedic devices and hospital supplies	-618	-607	-377	-245	-186	432	70
Dental equipment	88	139	203	196	178	89	101
Total	341	1,579	2,438	4,468	3,616	3,274	960
			million dollars				
In vitro diagnostic substances and devices	-241	-143	78	303	502	743	308
Electromedical equipment	1,401	1,764	2,009	3,661	3,175	1,774	127
Surgical and medical instruments	-381	305	862	1,644	829	1,210	318
Orthopedic devices and hospital supplies	-553	-571	-426	-304	-232	321	58
Dental equipment	79	131	229	243	221	142	180
Total	305	1,486	2,752	5,548	4,496	4,191	1,373

Source: Global Trade Information Services, Inc. Global Trade Atlas Database; and IMF exchange rate.

Note.—The 2001–2002 aggregates were obtained as the sum of available national data reported by Eurostat's Prodcom. Aggregates for 2003–2005 were obtained as a sum of available EU 25 8-digit code totals. The differences between the data in euros and dollars is a result of exchange rate fluctuations that occurred in this period.

Figure 4-4 Trade balance, by segment, 2005: Germany, France, Italy, United Kingdom, and Ireland



Source: Global Trade Information Services, Inc. *Global Trade Atlas Database*.

Note.—Due to scaling, countries' sectoral medical device trade balances less than 10,000 euros may appear as zero.

Table 4-4 EU imports and exports of medical devices, by selected countries, 2001–5

Country	2001		2002		2003		2004		2005	
	million euros	*million dollars*	*million euros*	*million dollars*	*million euros*	*million dollars*	*million euros*	*million dollars*	*million euros*	*million dollars*
Imports:										
United States	10,216	9,142	10,360	9,750	9,926	11,203	9,814	12,185	10,416	12,955
Switzerland	2,003	1,792	2,262	2,129	2,722	3,072	2,680	3,328	2,980	3,706
Japan	1,420	1,271	1,391	1,309	1,433	1,617	1,431	1,777	1,475	1,834
Mexico	87	78	102	96	234	264	411	510	1,011	1,257
China	298	267	350	329	425	480	500	621	631	785
Israel	379	339	323	304	296	334	291	361	331	412
Singapore	207	185	229	216	257	290	274	340	313	389
Malaysia	254	227	254	239	233	263	219	272	232	288
Australia	127	114	145	136	153	173	161	200	199	247
Canada	145	130	144	136	128	144	147	183	169	211
Exports:										
United States	6,082	5,442	7,342	6,910	8,265	9,328	9,559	11,869	9,696	12,059
Japan	1,661	1,486	1,731	1,629	1,712	1,932	1,970	2,446	2,068	2,572
Switzerland	743	665	984	926	993	1,121	1,044	1,296	1,071	1,333
China	359	321	426	401	554	625	620	770	670	833
Russia	604	540	527	496	522	589	561	697	667	830
Australia	400	358	476	448	498	562	622	772	649	807
Turkey	333	298	330	311	356	402	514	638	627	780
Canada	365	327	415	391	420	474	491	610	567	705
Norway	381	341	444	418	463	523	527	654	514	640
Singapore	125	112	185	174	264	298	370	459	424	527

Source: Global Trade Information Services, Inc. *Global Trade Atlas Database.*

Japan

Japan has remained a net importer of medical devices for many years (figure 4-5), as a result of growing differentials between national consumption and production levels. As shown in table 4-5, its medical device trade deficit widened to ¥525.1 billion ($4.9 billion) in 2004, from ¥438.8 billion ($3.6 billion) in 2001, while its import to consumption ratio increased from 43 to 46 percent in that period.

Exports of Japanese medical devices amounted to ¥430.1 billion ($3.9 billion) in 2004, compared with ¥397.4 billion ($3.3 billion) in 2001. Export growth, which averaged 3 percent annually from 2001 to 2004, was mostly driven by overseas demand for Japanese-made in vitro clinical test equipment (such as blood testing devices), whose share of Japan's medical device export market grew by 2 percentage points over the period. Overall export growth in this period was also attributable to exports of diagnostic imaging equipment (such as MRI and CT), Japan's largest medical device export segment. The recent discontinuation by Hitachi and Shimadzu of the manufacture of high-end CT and MRI devices in 2006 may lower exports of these products over the course of the next few years.

The United States, historically the largest export market for Japanese-made medical devices, accounted for approximately 26 percent of Japan's exports in 2004 (table 4-6). Germany was the second largest market for Japanese exports of such devices, accounting for 9 percent in 2004, while China, the Netherlands, and Switzerland rounded out the top five leading export markets for Japan. China's growth as an export destination for Japanese medical devices has been the most pronounced in recent years.

Japan's medical device market has increasingly been supplied by imports, which accounted for ¥955.3 billion yen ($8.8 billion) in 2004, compared to ¥836.3 billion yen ($6.9 billion) in 2001. Import growth in this sector has averaged 5 percent per year since 2001, and was mainly driven by ophthalmic devices (such as ophthalmic lasers and sight test equipment), internal organ devices (implantable devices such as orthopedic implants and cardiac pacemakers), and diagnostic imaging systems (such as MRI and CT devices).

The United States has also historically been the largest source of Japanese medical device imports, accounting for 58 percent in 2004. U.S. firms are the major suppliers of many critical products in Japan, such as pacemakers, defibrillators, and orthopedic implants, including artificial hips and knees, which are not made in Japan. Other Japanese imports from the United States primarily consist of catheters, diagnostic X-ray equipment, MRI systems, laser surgical equipment, and cardiac valve prostheses. In some cases, such as the drug-eluting stent, U.S. companies are the only approved supplier in Japan. Medical device imports from the United States grew by 4 percent in 2004, though their share of Japan's import market fell because of faster growth from such countries as Ireland. Between 2003 and 2004, Japan's medical device imports from Ireland grew by 31 percent, and gained nearly 2 percentage points in Japanese market share, as major U.S.-based firms increased manufacture and assembly of medical devices in majority-owned affiliate operations in Ireland.

Figure 4-5 Japanese exports, imports, and merchandise trade balance in medical devices, 2001–4

Source: Japan's Ministry of Health, Labour and Welfare.

Note.—Official 2005 Japanese production and trade data will not become available until early 2007.

Table 4-5 Japanese merchandise trade balance in medical devices, by segment, 2001–4

Segment	2001	2002	2003	2004	Absolute change, 2001–4	Percent change, 2001–4
			million yen			*percent*
Diagnostic imaging systems	50,444	38,811	70,033	46,722	-3,722	-7.4
Related diagnostic X-ray equipment	14,143	17,804	12,539	15,455	1,312	9.3
Measuring and monitoring systems for biophenomena	41,429	23,744	44,022	48,515	7,086	17.1
In vitro clinical test equipment	5,250	2,200	4,771	17,705	12,455	237.2
Operating equipment and supplies	-170,102	-145,662	-164,684	-171,054	-952	-0.6
Clinical equipment and supplies	-2,535	-2,567	-1,973	-1,527	1,008	39.8
Artificial internal organ and assisting devices	-223,069	-221,992	-260,312	-267,852	-44,783	-20.1
Therapeutic and surgical equipment	-31,483	-37,970	-27,425	-33,964	-2,481	-7.9
Dental equipment	-3,270	1,341	2,904	3,057	6,327	193.5
Dental material	-17,975	-20,153	-19,009	-21,187	-3,212	-17.9
Steel products for medical use	-20,587	-21,172	-21,411	-26,607	-6,020	-29.2
Ophthalmic and related products	-69,287	-90,274	-97,122	-127,314	-58,027	-83.8
Surgical dressing/hygienic products	-8,331	-9,415	-7,440	-7,875	456	-5.5
Medical devices for home use	-3,442	2,155	1,795	777	4,219	122.6
Total	-438,815	-463,150	-463,312	-525,149	-86,334	-19.7
			million dollars			*percent*
Diagnostic imaging systems	415	310	604	432	17	4.0
Related diagnostic X-ray equipment	116	142	108	143	26	22.8
Measuring and monitoring systems for biophenomena	341	189	380	448	108	31.5
In vitro clinical test equipment	43	18	41	164	120	278.8
Operating equipment and supplies	-1,400	-1,162	-1,421	-1,581	-181	13.0
Clinical equipment and supplies	-21	-20	-17	-14	7	-32.3
Artificial internal organ and assisting devices	-1,836	-1,770	-2,245	-2,476	-640	34.9
Therapeutic and surgical equipment	-259	-303	-237	-314	-55	21.2
Dental equipment	-27	11	25	28	55	205.0
Dental material	-148	-161	-164	-196	-48	32.4
Steel products for medical use	-169	-169	-185	-246	-77	45.2
Ophthalmic and related products	-570	-720	-838	-1,177	-607	106.4
Surgical dressing/hygienic products	-69	-75	-64	-73	-4	5.8
Medical devices for home use	-28	17	15	7	36	-125.4
Total	-3,611	-3,693	-3,998	-4,855	-1,243	34.4

Source: Japan's Ministry of Health, Labour and Welfare; and IMF exchange rate.

Note.—The differences between the data in yen and dollars is a result of exchange rate fluctuations that occurred in this period.

Table 4-6 Japanese imports and exports of medical devices, by selected countries, 2001–4

Country	2001		2002		2003		2004	
	billion yen	*billion dollars*	*billion yen*	*billion dollars*	*billion yen*	*billion dollars*	*billion yen*	*billion dollars*
Imports:								
United States	527	4.34	511	4.08	536	4.62	555	5.13
Ireland	35	0.29	53	0.42	77	0.66	100	0.92
Germany	58	0.48	71	0.57	66	0.57	69	0.64
China	23	0.19	26	0.21	31	0.27	34	0.31
Switzerland	14	0.12	17	0.14	30	0.26	33	0.31
Thailand	18	0.15	15	0.12	18	0.16	22	0.20
Netherlands	37	0.30	26	0.21	22	0.19	22	0.20
Sweden	12	0.10	13	0.10	14	0.12	13	0.12
France	11	0.09	14	0.11	12	0.10	12	0.11
United Kingdom	([a])	([a])	([a])	([a])	10	0.09	12	0.11
Exports:								
United States	104	0.86	884	7.05	110	0.95	112	1.04
Germany	34	0.28	31	0.25	39	0.34	38	0.35
China	15	0.12	15	0.12	17	0.15	21	0.19
Netherlands	20	0.16	16	0.13	20	0.17	18	0.17
Switzerland	([a])	([a])	7	0.06	9	0.08	11	0.10
Korea	11	0.09	12	0.10	11	0.09	10	0.09
Taiwan	8	0.07	9	0.07	11	0.09	9	0.08
Belgium	7	0.06	7	0.06	7	0.06	7	0.06
Italy	([a])	([a])	5	0.04	([a])	([a])	6	0.06
France	5	0.04	([a])	([a])	5	0.04	5	0.05

Source: Japan's Ministry of Health, Labour and Welfare.

[a] Not available.

CHAPTER 5
Relevant Multilateral and Bilateral Trade Agreements

Several multilateral and bilateral trade agreements have direct implications for U.S. trade in medical devices, as they focus on issues of concern to the medical device industry including the harmonization of medical device regulatory systems. These include a World Trade Organization (WTO) agreement for addressing standards and regulatory issues, two related U.S.-Japan initiatives for addressing regulatory and other market access issues, an agreement between the United States and the EU to recognize one another's regulatory requirements and procedures, a more recent U.S.-China initiative to address important trade issues of concern, and a major voluntary agreement between the United States and several of its major trading partners to harmonize global medical device standards and regulatory approval procedures (table 5-1).

Table 5-1 Relevant medical device trade agreements and initiatives

Agreement/Initiative	Country	Issues
WTO Agreement on Technical Barriers to Trade	WTO members	Tries to ensure that standards, technical regulations, and conformity assessment measures do not constitute unnecessary trade barriers
Regulatory Reform and Competition Policy Initiative	Japan	Regulatory and market access
U.S.-EU Mutual Recognition Agreement	EU	Reciprocal recognition policies
U.S.-China Joint Commission on Commerce and Trade	China	Regulatory, certification, and pricing issues
Global Harmonization Task Force	Australia, Canada, Japan, EU, and United States	Standards harmonization

Source: Compiled by Commission staff.

Each of these agreements and initiatives focuses on issues of concern to the U.S. medical device industry that have the potential to impede U.S. sales and exports of medical devices. Following is a brief overview of these agreements and initiatives and an examination of the implications of each for the U.S. medical device industry.

WTO Agreement on Technical Barriers to Trade

As WTO members, the United States, Japan, the EU, and other signatories are bound by the WTO Agreement on Technical Barriers to Trade (TBT). The TBT agreement is significant to medical device companies because it can impact regulatory issues confronting the industry. The TBT tries to ensure, inter alia, that mandatory technical regulations and conformity assessment requirements, such as product approval procedures, do not constitute

unnecessary trade barriers.[1] Generally, under the TBT agreement, national governments are to apply their technical regulations and conformity assessment procedures on a nondiscriminatory basis[2] and develop regulations and procedures in such a manner that they are no more trade-restrictive than necessary to meet legitimate objectives, which may include the protection of human health, safety, and the environment, and the prevention of deceptive practices.[3]

Strict transparency provisions[4] that require members to notify the WTO in advance of adoption of all proposed new regulations that have a potential to impact trade are an important mechanism to ensure that members' regulatory policies adhere to TBT principles.[5] Such transparency provisions provide WTO members with an opportunity to review and comment on proposed new regulations and have their views taken into account before final regulations are adopted. Such was the case in a recent European Commission decision to increase the regulatory scrutiny of certain orthopedic implant devices, a leading product segment for the U.S. industry. The TBT's transparency provisions provided the United States and other concerned WTO members an opportunity to carefully review, comment on, and request the European Commission to explain its reasons for its proposal.[6] After adoption of the proposed EU regulation, U.S. industry officials indicated that while they were disappointed with the adoption of the proposed directive, they are pleased that some of their comments, which addressed ways to comply with the directive, were taken into account.[7]

Although the TBT procedures do not guarantee that all members' concerns regarding proposed regulations will be completely resolved in their favor, there has been broad consensus among WTO members, including the United States, that the TBT provisions have greatly enhanced the opportunity of all members to learn about and influence the final decisions of WTO member country regulators before they become final.[8]

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[1] WTO TBT, Article 2-2.

[2] WTO TBT Articles 2.1 and 5.1.1.

[3] WTO TBT Articles 2.2 and 5.1.2.

[4] WTO TBT Articles 2.9 and 5.6.

[5] Draft regulations should be received by the WTO Secretariat, if possible, sixty days prior to their formal adoption so as to allow time for other Members to make comments. The required process is analogous to the U.S. *Federal Register* process in the United States and similar processes in many other developed countries, requiring that all new proposed regulations first go through a review and comment process to ensure transparency and careful consideration of the views of all interested parties to decrease the likelihood that ineffective and costly new rules are adopted that result in more costs than benefits than intended by the proponents of the original draft regulation.

[6] AdvaMed, "Comments to the World Trade Organization (WTO) on the European Commission's Notification Under the Technical Barriers to Trade (TBT) Agreement of its Draft Directive to Up-Classify Total Joint Implants."

[7] U.S. industry officials, interviews by Commission staff, United States, June 15–16 and September 20, 2006.

[8] U.S. government officials, interviews by Commission staff, United States, September 27, 2006; and U.S. and foreign government officials, interviews by Commission staff, WTO TBT Committee Meeting, Geneva, Switzerland, March 21–23, 2005.

U.S.-Japan Trade Agreements Related to Medical Devices and Equipment

Over the past two decades, the United States has entered into trade talks with Japan through market-oriented, sector-selective (MOSS) negotiations[9] and a Regulatory Reform and Competition Policy Initiative (Regulatory Reform Initiative) to address key regulatory and other market access issues for U.S. industries, including the medical device industry.[10] In general, bilateral discussions between U.S. and Japanese government officials have provided opportunities to address industry concerns regarding issues such as the Japanese regulatory system structure.

Although U.S. government and industry officials state that substantial progress was achieved in these discussions, they indicate that U.S. companies still face complex and slow regulatory approval procedures for medical devices sold in Japan.[11]

Progress in the Regulatory Reform Initiative discussions is reported to Japanese and U.S. leaders twice a year. Recommendations by the United States to Japan in December 2005 and June 2006 focused on progress in the reform of the Japanese medical device regulatory system and on new Japanese medical device reimbursement and pricing proposals.[12] Although the April 2005 reorganization of Japan's medical device regulatory system was purportedly to boost efficiency, U.S. government and industry officials continue to express frustration regarding continued delays in processing of applications for medical device approvals and other elements of the new regulatory system which reportedly increase U.S. exporters' costs in marketing medical devices in Japan.[13] Further, U.S. industry and government officials have expressed opposition to a new Japanese policy aimed at reducing the natural rate of growth of healthcare costs by reducing insurance reimbursement rates on medical devices.

The June 2006 report on the Regulatory Reform Initiative does include agreements by Japan to increase staff at Japan's new regulatory approval agency to help shorten review and approval times and to establish a system to expedite regulatory approval of partial changes to medical devices, many of which are currently reviewed as completely new applications. The report also acknowledges Japan's agreement to carefully review industry studies examining the costs of Japan's regulatory and distribution systems, with a view toward taking such costs into account when determining new reimbursement rates for medical devices.[14] Another issue being discussed within the framework of the U.S.-Japan Regulatory Reform Initiative is what U.S. medical device companies perceive as insufficient use by

[9] USTR, "Fact Sheet on Fifth Report to the Leaders on the U.S.-Japan Regulatory Reform and Competition Policy Initiative," 1.

[10] USDOC, Trade Compliance Center, "Report on the U.S.-Japan Market-Oriented, Sector-Selective Discussions on Medical Equipment and Pharmaceuticals."

[11] U.S. government and industry officials, interviews by Commission staff, United States, March-June 2006.

[12] USTR, "Fact Sheet on Fourth Report to the Leaders on the U.S.-Japan Regulatory Reform and Competition Policy Initiative," 1; and "Fact Sheet on Fifth Report to the Leaders on the U.S.-Japan Regulatory Reform and Competition Policy Initiative," 1.

[13] USDOC, "Medical Devices and Pharmaceuticals," and U.S. industry officials, interviews by Commission staff, United States, June 5-16, 2006.

[14] USTR, "Fact Sheet on Fifth Report to the Leaders on the U.S.-Japan Regulatory Reform and Competition Policy Initiative."

Japanese regulators of non-Japanese clinical data to demonstrate safety and efficacy of medical devices, which they indicate requires U.S. producers to duplicate trials previously conducted in the United States or the EU. The Medical Device Resource Group, a coalition of medical device industry companies, estimated that, in 2005, only 20 percent of submissions relying entirely on foreign data were accepted by Japan.[15]

U.S.-European Union Mutual Recognition Agreement–Medical Devices

On May 18, 1998, the United States and the EU signed a mutual recognition agreement (MRA), which became effective in December of that year.[16] The MRA consists of a framework agreement and six sectoral annexes, one of which covers medical devices and equipment. The medical device MRA specifies conditions under which U.S. and EU regulatory bodies will recognize the results of conformity assessment (or product approval) by the other party's conformity assessment bodies (CABs).[17]

Under the medical device MRA, the relevant regulatory authority can conduct reviews for the sale of medical devices in the other country (or countries in the case of the EU) to assess their conformance with the importing party's requirements and make recommendations. This may include premarket reviews of select low- to medium-risk devices. In the United States, third-party CABs are to evaluate products and conduct inspections with respect to EU requirements as specified in the EU's medical device directive (MDD). Conversely, in the EU, CABs are to test to U.S. requirements. Regulatory reviews conducted in the United States for the EU market and in the EU for the U.S. market by the CABs do not constitute final approvals but only provide recommendations to regulatory authorities to grant approval in the respective markets.[18]

Although government and industry officials interviewed indicate that the U.S.-EU medical device MRA has not fully met initial expectations, they state that it has improved cooperation and understanding between regulatory officials in the two largest global markets for medical devices.[19] They indicate that it has significantly contributed to the movement towards international harmonization and cooperation in medical device regulatory review and approval processes. For instance, the introduction of the new approach of using private third-party review and testing has since been incorporated in a number of other regulatory approval systems, including that of Japan.[20]

However, consolidation and globalization of the medical device supply chain has led to reduced interest in the medical device MRA by U.S. medical device companies. In 1998, one of the main objectives of the Agreement was to facilitate regulatory review of U.S. and EU firms' medical devices in their domestic markets. However, many U.S. firms now have a major presence in the EU[21] or can now gain EU approval by simply using U.S. subsidiaries

[15] Further discussion of this issue is contained in chapter 6 of this report.
[16] Devereaux, *International Trade Meets Domestic Regulation*, 1.
[17] Chai, "Medical Device Regulation in the United States and the European Union," 75–76.
[18] European Commission official, interviews by Commission staff, Belgium, September 18, 2006.
[19] U.S. and European Commission officials, telephone interviews by Commission staff, May 9 and 11, 2006; and U.S. industry official, interview by Commission staff, United States, September 20, 2006.
[20] U.S. and Japanese industry officials, and officials of third-party bodies accredited to the Pharmaceutical Affairs Law, Japan, July 31–August 9, 2006.
[21] U.S. government official, interview by Commission staff, United States, May 2006.

of EU accredited third-party bodies to complete much of the required testing and review in the United States, thereby bypassing use of the medical device MRA.[22]

Some U.S. industry representatives suggest that, in order to be effective, the medical device MRA would have to be conceptually different, allowing acceptance of foreign medical device approval without further evaluation.[23] In other words, they hope that FDA approvals will be considered as acceptable as CE-marked medical devices in the EU and vice versa. However, U.S. government officials suggest that significant policy, legislative, and regulatory changes would need to occur first.[24]

Still, the United States and the EU continue to work to make the medical device MRA fully operational. An area of current focus is joint inspections of medical device manufacturing facilities to ascertain compliance with both U.S. and EU regulatory requirements.[25] For such inspections to be accepted by both parties, regulatory authorities for both parties must have complete assurance that the other party's CABs will be able to effectively perform such inspections to meet their own specific guidelines.[26] To help achieve such confidence, regulators for each party are calling for companies to volunteer to have their facilities inspected to meet both U.S. FDA and EU manufacturing requirements.[27]

U.S.-China JCCT Medical Devices and Pharmaceuticals Subgroup

The U.S.-China Joint Commission on Commerce and Trade (JCCT),[28] chaired by the U.S. Secretary of State and USTR and China's Vice Premier for Foreign Trade, provides a forum for the United States and China to discuss trade concerns and expand commercial trade opportunities.[29] Within the JCCT, U.S. and Chinese government and industry officials employ the Medical Devices and Pharmaceuticals (MDP) Subgroup to discuss medical device regulatory and market access issues.[30]

Three major issues currently dominate the MDP discussions: China's decentralized regulatory system, redundant certification requirements, and proposed price controls on medical devices. Because of the growing importance of China as a major medical device market, U.S. industry officials state that China must address these issues if U.S. exports are

[22] AdvaMed, "US-EU Mutual Recognition Agreement (MRA)."

[23] U.S. industry representatives, personal and telephone interviews by Commission staff, May 9 and 11, 2006, and September 20, 2006.

[24] U.S. government officials, telephone interviews by Commission staff, November 21–22, 2006.

[25] GAO, *Medical Devices: Status of FDA Inspections*, 2-12; and Swain, "Euro-US Inspections to Begin by December," 21.

[26] Rudolph and Stigi, "FDA Third-Party Programs: Reality or Myth," 64.

[27] GAO, *Medical Devices: Status of FDA Inspections*, 9; and Rudolph and Stigi, "FDA Third-Party Programs: Reality or Myth," 64; and U.S. government officials, interview by Commission staff, United States, May 31, 2006.

[28] USTR, *Summary of JCCT Medical Devices Task Force Meeting.*

[29] USTR, "Trade Facts, The U.S.-China JCCT: Outcomes on Major U.S. Trade Concerns."

[30] USDOC, "U.S-China Joint Commission on Commerce and Trade (JCCT)."

to thrive in that market.[31] They claim that the JCCT subgroup for medical devices is an important vehicle to continue to address these issues.[32]

While China has created a separate regulatory agency for medical devices (the China Food and Drug Administration (CFDA), patterned on the U.S. FDA), U.S. industry officials contend that other Chinese agencies continue to impose their own approval requirements on medical devices,[33] often resulting in costly and duplicative testing and inspection requirements for U.S. medical device firms attempting to gain product approval.[34] China agreed to eliminate redundant certification requirements on imported medical devices by May 2006.[35] However, according to the U.S.-China Business Council, proposed regulations issued on April 30, 2006 to accomplish this do not appear to effectively address the redundancy issues.[36]

Global Harmonization Task Force

The Global Harmonization Task Force (GHTF) is a voluntary effort established in 1993 by government and medical device industry officials of Australia, Canada, Japan, the EU, and the United States. The primary purpose of the GHTF is to harmonize medical device standards to minimize regulatory barriers related to the safety, performance, and quality of medical devices and equipment; facilitate international trade; and improve access to new medical technologies.[37] The work of the GHTF is accomplished principally through publication and dissemination of harmonized guidance documents on basic regulatory practices, which are developed by four different GHTF study groups.[38] These documents may then be implemented or adopted by the regulatory authorities of members. The GHTF also serves as an information exchange forum for countries in the process of developing medical device regulatory systems so they can benefit from the experience of countries with existing systems.

One document adopted by the GHTF that may ease product registration for U.S. medical device companies is an internationally harmonized format for the submission of premarket applications by members, the Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED). GHTF member countries launched a pilot project in 2002 to test the viability and effectiveness of STED. In the United States, the FDA initiated its STED pilot program in June 2003[39] and has extended the deadline indefinitely in hopes of encouraging the industry

[31] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006.

[32] U.S. industry and government officials, interviews by Commission staff, September 20 and October 10, 2006.

[33] U.S. industry and government officials, interviews by Commission staff, United States, September 20 and October 10, 2006.

[34] USTR, *Summary of JCCT Medical Devices Task Force Meeting;* and U.S. government and industry officials, interviews by Commission staff, United States, June 5-16, 2006.

[35] U.S. Chamber of Commerce, "International Trade and Investment, Accomplishments and Ongoing Activities by Country."

[36] U.S.-China Business Council, "China's 2004, 2005, and 2006 JCCT Commitments," 6.

[37] World Health Organization (WHO), *Medical Device Regulations: Global Overview and Guiding Principles*, 15–17.

[38] GHTF, "Working Toward Harmonization in Medical Device Regulation," 1.

[39] FDA, "FDA Extends Pilot Program for Evaluation of Globally Harmonized Medical Device Premarket Applications Until July 2006 (STED Initiative)."

to utilize STED.[40] Meanwhile, Japan has made STED an integral component of its application process in its recently reformed medical device regulatory approval system.[41]

U.S. industry officials state that for GHTF documents to effectively minimize the inherent costs and redundancy resulting from firms' having to register products to different rules and regulations in multiple markets, there must be consistency in how each of the GHTF countries implements each document.[42] Often, member countries add their own specific provisions to GHTF documents, thus reducing the benefits of harmonization the documents are meant to provide.[43] For instance, they point out that U.S. and Japanese pilot STED applications require different information for product applications to the two countries. However, U.S. and Japanese regulatory authorities believe that as more experience is gained through the pilot efforts, some national deviations may be minimized or even eliminated.[44]

[40] U.S. government official, telephone interview by Commission staff, United States, November 2006.

[41] U.S. and Japanese government officials, interviews by Commission staff, Japan, July 31 and August 8, 2006.

[42] U.S. and Japanese government and industry officials, interviews by Commission staff, United States, May 31 and June 5–16, 2006, and Japan, July 31–August 9, 2006.

[43] U.S. government and industry officials, interviews by Commission staff, United States, June 5–16, 2006.

[44] U.S. and Japanese government officials, interviews by Commission staff, United States, May 31, 2006, and Japan, July 31 and May 8, 2006.

CHAPTER 6
Impact of Regulatory Approval Systems on U.S. Industry

To assess the impact of Japan's regulatory approval system on U.S. trade of medical devices, this chapter compares it with those of the United States and the EU, reviews relevant literature on the subject of medical device regulation, and examines regulatory data on product approvals. Regulatory cost and approval data indicate that while total fees paid by firms to gain approval in the United States appear to be higher than those in Japan, the average total length of time it takes to approve new medical devices is significantly higher in Japan. Even though average approval times in Japan declined substantially in 2005, the year in which a major reform of the Japanese regulatory approval system took effect, they still were more than three times the average level experienced in 2002. They also continued to be significantly higher than those in the United States and EU.

A qualitative assessment[1] of the potential impact on U.S. medical device producers of Japan's longer average approval times indicates that U.S. firms may be disproportionately affected compared to Japanese and EU rivals in terms of sales, exports, and profitability even though there is no evidence of discrimination. This is because U.S. medical device firms have a competitive advantage in higher-risk, more innovative products compared to their principal foreign rivals. Such innovative medical devices, which face approval times of up to 3 years in Japan, are characterized by much shorter product life cycles (as little as 18 months) than most other products. Thus, industry officials contend that delays in regulatory approvals in Japan result in significant opportunity costs for U.S. medical device firms during the time their products are undergoing review.

U.S. industry officials report that medical device firms also encounter some other significant costs in Japan not faced in other markets. For example, U.S. medical device firms reportedly have incurred substantial reorganization costs to comply with a new Japanese regulation requiring medical device firms to separate their manufacturing from their marketing operations for regulatory purposes. Neither the United States nor the EU has such a requirement. Further, U.S. industry officials report that Japan often requires medical device firms to conduct additional clinical trials to produce safety data that are equivalent to those obtained in clinical trials in other countries, while the United States and the EU commonly accept foreign clinical trial data for regulatory approval purposes. While such requirements do not discriminate against U.S. companies, industry officials state they still add significant costs to their operations that adversely affect their sales and trade with Japan. Industry officials also indicate that medical devices do not reach patients in Japan until several years after they are approved for sale in the United States and the EU, thus depriving Japanese patients of the latest medical technologies.[2]

[1] For reasons explained in the qualitative assessment section of this chapter, Commission staff determined that a quantitative analysis measuring the impact of foreign regulatory approval systems on U.S. sales and exports could not be adequately and reliably completed for purposes of this investigation.

[2] Ludwig, hearing transcript, 9-10; Agress, hearing transcript, 109; and U.S. and Japanese industry officials, market analysts, and a Japanese healthcare economist, interviews by Commission staff, Japan, July 31–August 9, 2006.

Comparison of the U.S., EU, and Japanese Regulatory Systems

U.S. medical device firms have faced strict regulatory measures in the United States, the EU, and Japan for several decades given the potential health and safety risks intrinsic to medical technology. All three of these markets have medical device regulations with broadly similar purposes.[3] All classify medical devices according to risk, and a regulatory organization must approve the riskier devices before they can be marketed. All have postmarket monitoring systems for surveillance of approved products but place more emphasis on premarket approval. Given the broad similarities in regulations across regions, the efficiency of regulatory agencies' implementation of them becomes a central concern to medical device firms. The scant literature identified by the Commission on this issue is inconclusive and mainly addresses distinctions between different aspects of EU and U.S. regulations.[4]

Despite differences in the number of risk categories[5] of the U.S., EU, and Japanese medical device regulatory systems, they are conceptually the same (table 6-1). The most important differences among the three systems are those pertaining to the role of government. In the United States and Japan, the government retains final authority for approval of medical devices. In contrast, premarket review and approval in the EU is principally conducted by independent third-party testing laboratories accredited by member state health ministries to review and approve medical devices for the EU market.[6] Although the U.S. and Japanese systems do not grant third parties as much discretion as the EU system, both the U.S. and Japanese regulatory bodies use third parties for the preliminary assessment of low- and medium-risk devices but retain the final authority over device approval.[7]

Another important difference is that while the United States and Japan review devices for safety and effectiveness, which includes providing a benefit to patients, EU accredited testing and certification bodies review medical devices for safety and performance according to the manufacturer's specifications.[8] The EU's mandate is thus more limited than that of the U.S. and Japanese regulatory bodies.[9]

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[3] U.S., Japanese, and European industry and government officials, interviews by Commission staff, United States, June 5–16, 2006; Japan, July 31–August 9, 2006; and the EU, September 18–29, 2006.

[4] Efficiency in producing a public good, such as product safety, is difficult to measure. Input measurements, such as the number of employees per approved device, are straightforward, but do not measure the safety aspect of what the regulatory agency is supposed to produce. There is a nascent literature in economics on bureaucratic efficiency, such as Prendergast and Chan, but it does not address issues pertinent to this report.

[5] Although the U.S. classification system of products for regulatory purposes is technically broken into three risk categories, while Japan uses a four-class system, and the EU, a three-class system with two subparts in its second class, there is much overlap between the three systems.

[6] Diller, "Healthcare: Products and Supplies: Europe," July 2006, 25–26; European Commission officials, telephone interviews by Commission staff, March 6–10, 2006; and EU notified body official, interview by Commission staff, United States, May 4, 2006.

[7] Based on a review of the literature, Campbell is virtually alone in advocating that independent, privately funded organizations review and approve medical devices. Campbell, "Exploring Free Market Certification of Medical Devices." Preker and Harding advocate a strong governmental role that is restricted to stewardship and financing. Preker and Harding, "The Economics of Public and Private Roles in Health Care: Insights from Institutional Economics and Organizational Theory."

[8] GAO, "Medical Device Regulation," 6.

[9] Chai, "Medical Device Regulation in the United States and the European Union," 62–63.

Table 6-1 Medical device classification and regulation in the European Union, the United States, and Japan

<table>
<tr><th>International Classification[a]</th><th colspan="2">EU system guidelines</th><th>U.S. system guidelines</th><th>Japanese system guidelines</th></tr>
<tr><td>Class I

(extremely low risk– e.g. tongue depressors, X-ray film, sutures)</td><td colspan="2">No approval necessary</td><td>No approval necessary</td><td>No approval necessary</td></tr>
<tr><td>Class II

(low risk– e.g. MRI, urological catheters)</td><td rowspan="3">Third-party certification</td><td rowspan="2">Site inspection only</td><td rowspan="3">Government approval necessary

(limited 3rd-party initial review)</td><td>Third-party certification</td></tr>
<tr><td>Class III

(medium risk– e.g. dialysis apparatus, artificial bones)</td><td rowspan="2">Government approval necessary</td></tr>
<tr><td>Class IV

(high risk– e.g. implantable pacemakers/ defribrillators, coronary stents, heart valves)</td><td>Document examination necessary</td></tr>
</table>

Sources: Global Harmonization Task Force, U.S. Food and Drug Administration, European Commission, and Japanese Ministry of Health, Labour and Welfare.

[a] Global Harmonization Task Force translation of EU, U.S., and Japanese medical device classes for comparison purposes.

United States

The Federal Food, Drug, and Cosmetic Act [10] of 1938 (Act) laid the foundation for federal regulation of medical devices by authorizing the FDA to prosecute individuals and firms who misused or misbranded medical devices for commercial purposes.[11] However, it did not require firms to obtain approval before they placed medical devices on the market. Following a number of highly publicized incidents involving injuries from newly developed products, such as pacemakers and intrauterine devices (IUDs), Congress passed significant amendments to the Act in 1976, establishing a substantive FDA medical device regulatory approval system.[12]

Under the 1976 law, the FDA reviews all new medical devices for safety and efficacy prior to granting regulatory approval. Medical device firms are required to provide data to the FDA supporting their device claims. The amount of data required depends on the potential degree of risk to a patient using the medical device in question. The FDA has three general product classifications and related requirements based on level of risk (table 6-2).

All domestic and imported medical devices, regardless of classification, are also subject to postmarket controls by the FDA, i.e., monitoring the safety of medical devices already in use and taking required remedial actions. Important components of the FDA's postmarket program include mandatory medical reports from manufacturers under the Medical Device Reporting (MDR) system, reports from hospitals, and FDA inspections of manufacturing facilities.[13] Postmarket information on devices also is compiled through FDA recall-notification reports, FDA bio-research monitoring investigations, user complaints, international vigilance reports, and studies carried out by manufacturers after their products have been approved. Based on data and other information developed from these sources, FDA staff and outside experts identify the nature, magnitude, and public health significance of any problems regarding certain medical devices to determine whether actions are required to protect the public, such as issuing urgent alerts or instituting administrative or judicial enforcement actions.[14]

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[10] 21 U.S.C. § 301 *et seq*.

[11] See 21 U.S.C. § 352.

[12] 21 U.S.C. § 360c *et seq*.; Diller and Gold, "Healthcare: Products and Services," 22–25; and U.S. industry analysts and government officials, personal and telephone interviews by Commission staff, May-June 2006.

[13] FDA/CDHR, *CDHR's Medical Device Postmarket Safety Program*, 6–20.

[14] FDA, "Overview: FDA Regulation of Medical Devices," 1.

Table 6-2 FDA medical device classification system and regulatory clearance requirements

FDA class	Device types and requirements	Regulatory clearance procedure
I	Commodity medical devices posing least potential risk to patients. Examples: Tongue depressors, stethoscopes, X-ray film, and sutures.	Most class I devices similar to ones already on the market require no regulatory clearance or approval, and manufacturers may place them directly on the market 90 days after notifying and listing products with the FDA, registering manufacturing facilities, and conforming to good manufacturing practices (GMPs). A few class I devices are required to undergo more rigorous demonstration of equivalence to products already on the market, such as required with a 510(k) filing, the most common FDA filing for approval of medical devices.
II	Devices constituting moderate potential risk to patients. Examples: X-ray, MRI, CT, endoscopes, and surgical lasers.	Most class II devices are cleared through the FDA 510(k) process. Manufacturers must demonstrate substantial equivalence of their products to predicate devices already on the market, provide evidence of product safety and efficacy, and meet certain other standards. They are also responsible for registering their facilities, conforming to GMPs, postmarket surveillance, and maintenance of patient registries.
III	Technologically advanced products constituting significant potential risk to patients. Examples: Cardiac pacemakers, implantable defibrillators, angioplasty (balloon) catheters, coronary stents, replacement heart valves, and silicone gel-filled breast implants.	Most class III devices employing new methods of treatment and not similar to medical devices already on the market require FDA premarket approval (PMA), a more complex and lengthier process than 510(k) filing. Submission usually requires significant clinical testing data, manufacturing information, and other data supporting firms' claims of safety and efficacy for the new product. Producers are also responsible for the same GMP and postmarket surveillance requirements as class I and II devices. (A few class III devices similar to devices already on market only require 510(k) review.)

Source: FDA, "Overview: FDA Regulation of Medical Devices," 1; FDA/CDHR, *CDHR's Medical Device Postmarket Safety Program*, 6–20; and Diller and Gold, "Healthcare: Products and Services," 22–25.

Although the FDA traditionally has been responsible for both the review and approval of medical devices, the FDA Modernization Act of 1997 (FDAMA) created a third-party review program referred to as the "Accredited Person Program."[15] Under this program, third-party testing bodies accredited by the FDA are authorized to conduct primary reviews of selected 510(k) applications, which are applications for devices substantially equivalent to devices already on the market.[16] The third-party conducts the primary review of the 510(k), then forwards its review, recommendation, and 510(k) to the FDA. The FDA is required to issue a final determination within 30 days of receiving the recommendation of the accredited third party. It is important to note that like Japan, but unlike the EU, a third-party decision in the United States must be reviewed and approved by the government authority, the FDA, before a device may be placed on the U.S. market.

Rapid developments in emerging technologies are challenging the FDA as well as foreign regulators, particularly with respect to the classification and regulation of medical products

[15] GAO, *Medical Devices: Status of FDA Inspections*, 3.
[16] FDA/CDHR, "What is a Third Party Review," 1.

that combine elements that were previously subject to differing regulatory regimes, such as medical devices, drugs, and biologics.[17] Significant issues presented by such combination devices are discussed in box 6-1.

Box 6-1 Combination products: Questions and answers

What are combination products?

In brief, combination medical devices are defined in the United States as regulated drugs, devices, or biologics, whether already approved or investigational, that are either mixed with, packaged with, or required for use with one or more other such products to provide delivered, metered doses in potentially safer, more efficient, and/or more convenient form than that of the individual products.[a]

Examples of recently approved combination devices in the United States include products to deliver medications directly to users in measured doses (e.g., metered-dose inhalers, transdermal patches, inhaled insulin, and an inhaled flu vaccine), as well as products intended to enhance and/or facilitate the effectiveness of various procedures (e.g., drug-eluting coronary stents and surgical mesh with antibiotic coating).

How large is the market for combination products?

The global market for combination medical devices is rapidly evolving. The estimated value of this market totaled $5.4 billion in 2004, and is expected to more than double to $11.5 billion by 2010. The U.S. market accounted for 65 percent of the world market in 2004 (compared with 24 percent for Europe and 7 percent for Japan), largely because of the rapid U.S. adoption of drug-eluting stents. Drug-eluting stents accounted for about $4.0 billion of the 2004 global market, a 100 percent increase from 2003, their introductory year. The worldwide drug-eluting stent market is expected to double again by 2010 to $8.0 billion, paralleling double-digit annual growth projected through 2010 for the overall combination products market.[b]

What regulatory issues face combination products?

The regulation of such products creates unique challenges for manufacturers and regulators because, by definition, the devices involve disparate products that often fall under the jurisdiction of two or more regulating organizations.[c] Also, many are innovative products with unique doses and delivery methods that present new safety and efficacy issues and make it difficult to generalize across product categories.[d] Such issues, when combined with differences in national regulatory systems, can result in additional testing requirements and, in turn, additional paperwork, time, and expenditures for manufacturers.

The two principal differences between the EU and Japanese regulatory systems, and the regulatory system of the United States is that neither the EU nor Japan has an official definition of combination products nor do they have centralized mechanisms to allow for jurisdictional decisions related to the regulation of combination products. Japan reportedly has no specific provisions for the regulation of combination medical devices. Also, whereas medicinals and medical devices marketed in the United States undergo a centralized review by the FDA, under the EU's New Approach, combination products classified as medical devices undergo third-party certification (although incorporation of a medicinal in such a device requires that the Notified Body consult with a competent authority).

Country/regional profiles

United States–Regulatory challenges have been addressed through numerous initiatives, including 1990 amendments to the Federal Food, Drug and Cosmetic Act (21 U.S.C.21 U.S.C. §301 *et seq.*), which introduce the concept of combination products as part of a larger effort to clarify product jurisdiction issues, as well as through structural changes within the FDA. These structural changes resulted from the implementation of the Medical Device User Fee and Modernization Act of 2002 (PL 107–250, 116 Stat. 1588), which, among other things, established the Office of Combination Products. Although this office does not review products itself, it makes timely jurisdictional decisions regarding the appropriate center within FDA to review/approve such products,[e] oversees reviews and resolves associated disputes, develops regulations, and responds to issues raised by interested parties. Companies

[17] See Massa, in Hanna et al., *Innovation and Invention in Medical Devices*; Fox and Shapiro, "Combination Products;" Sall, Lassoff, and Babbit, "Getting Started with a Combination Product Part 1"; and FDA, "Intercenter Agreements."

Box 6-1 Combination products: Questions and answers *(Continued)*

EU– In the EU, combination products are covered by either the medicinals directive or the medical devices directive,[f] generally depending on their mode of action and intended purpose.[g] If any doubt exists, the product would reportedly be addressed as a medicinal and would be subject to what has been characterized as a more rigorous regulatory review. The manufacturer has sole and ultimate responsibility for the conformity of the product to the applicable directives.

The medical devices directive provides three potential classifications for combination products. Products that administer medicinals (e.g., empty syringes) are classified as medical devices, although the pharmaceutical delivered must be approved for use in the EU. One-time use devices that deliver prepackaged medicinals (e.g., prefilled syringes) are covered by the medicinal directive, although the device must meet the conditions of the medical devices directive addressing safety and performance. Combination products in which both the device and the medicinal play an integral therapeutic role are subject to approval by a notified body under the auspices of the medical devices directive; however, the notified body must also consult with the proper competent authority either through the centralized procedure (via the European Medicines Evaluation Agency) — particularly if the product contains human blood or derivatives, or through the decentralized procedure (via the competent authorities of individual member states).

Japan– In Japan, there are reportedly no special provisions for regulating combination products. Although the revised Japanese regulatory system for medical devices is reportedly evolving, industry sources do not expect combination products to be addressed immediately, given many other priority issues facing the PMDA.

Sources: Compiled by Commission staff using information gathered from U.S. industry officials, telephone interviews by Commission staff, May–August 2006; U.S. government official in Belgium, e-mail messages to Commission staff, February–October, 2006; U.S. government official in Japan, e-mail message to Commission staff, April 12, 2006; EU government official, e-mail message to Commission staff, April 25, 2006; EU industry officials, interviews by Commission staff, September 17–29, 2006; Japanese government official, e-mail message to Commission staff, December 8, 2006; Massa, in Hanna et al., *Innovation and Invention in Medical Devices*; Fox and Shapiro, “Combination Products”; Sall, Lassoff, and Babbit, "Getting Started with a Combination Product Part 1”; and FDA, “Intercenter Agreements;” among others.

[a] The complete U.S. definition, dating to 1991, can be found in 21 *CFR* §3.2(e).

[b] The market value information was obtained from Gray, “B-205 Drug-Device Combinations,” *Press Release.*

[c] Industry cites the FDA’s Office of Combination Products’ list of newly approved products as providing helpful regulatory information on certain types of products, giving insight into regulatory issues of new products.

[d] Industry sources note that U.S., EU, and Japanese reviewing authorities may consider review findings for products already approved in foreign markets but are not bound by the results.

[e] The FDA centers responsible for review remain the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, or the Center for Devices and Radiological Health, depending largely on the product’s primary mode of action (PMOA). Additional factors are considered if the PMOA cannot be determined with reasonable certainty. Although generally maintaining full responsibility for the product, the designated lead FDA Center may consult with other FDA centers on specific components of the product. According to the FDA, intercenter consultation requests almost tripled between early FY2003 and FY2005.

[f] “Borderline” products are subject to the Demarcation Guidelines. If any ambiguity still remains, companies may seek guidance from a competent authority in a procedure described as being similar to the U.S. RFD. Also, representatives of the EU state that the pending European Regulation on Advanced Therapies, which addresses advanced therapy combination products containing human cell and other tissue-based products as well as other advanced therapy devices, is generating questions among member states as to whether such combination products should be considered devices or pharmaceuticals. Implementation of the registration is expected in 2007.

[g] EU representatives note this is likely to change to PMOA once pending medical device directive revisions are implemented.

European Union

The EU medical device regulatory approval process is unique among the three major markets. Although it includes many of the same features – such as premarket review of devices based on risk and postmarket surveillance activities – as those contained in the U.S. and Japanese regulatory systems, the manner in which these activities are conducted and the entities that perform them differ in the EU system. Independent third-party test laboratories,[18] rather than government reviewers and inspectors, generally are the key entities responsible for determining if new medical devices and their manufacturing processes meet essential EU requirements of safety, thus allowing them to be placed on the market.[19]

EU requirements, or technical regulations, for different types of medical devices are specified in several European Council directives: the medical device directive (MDD),[20] the active implantable medical device directive,[21] and the in vitro diagnostics directive (figure 6-1).[22] Each of these directives contains a legislative statement of EU "essential requirements," which are further defined by technical standards for each directive.[23] Medical device manufacturers are responsible for meeting and documenting how they meet these essential requirements.

For certain less risky medical devices, including most EU class I products (table 6-3), a declaration of conformity by the producer is sufficient. For higher risk products – ranging from class II "me too" devices, such as diagnostic imaging devices, that require evidence comparing them to devices already on the market, to the highest risk class III devices, such as implantable cardiac pacemakers or drug-eluting stents – firms are required to obtain a third-party assessment from a registered EU notified body regarding their conformity to regulatory requirements.[24] In general, the manufacturer may choose among different methods of assessing the conformity of a product or manufacturing system.[25] The conformity assessment determines whether the product complies with the applicable directives and technical standards.[26] Once conformity is demonstrated, the manufacturer may apply a European conformity mark (CE mark) to the medical device to indicate that the device meets

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[18] Diller, "Healthcare: Products and Supplies: Europe," 25–26.

[19] European Commission officials, telephone interviews by Commission staff, March 6–10, 2006; and EU notified body official, interview by Commission staff, United States, May 4, 2006.

[20] European Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ L 169, 12.7.1993.

[21] European Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical equipment.

[22] European Council Directive 98/79/EC of 27 October 1998 on in vitro diagnostic medical devices.

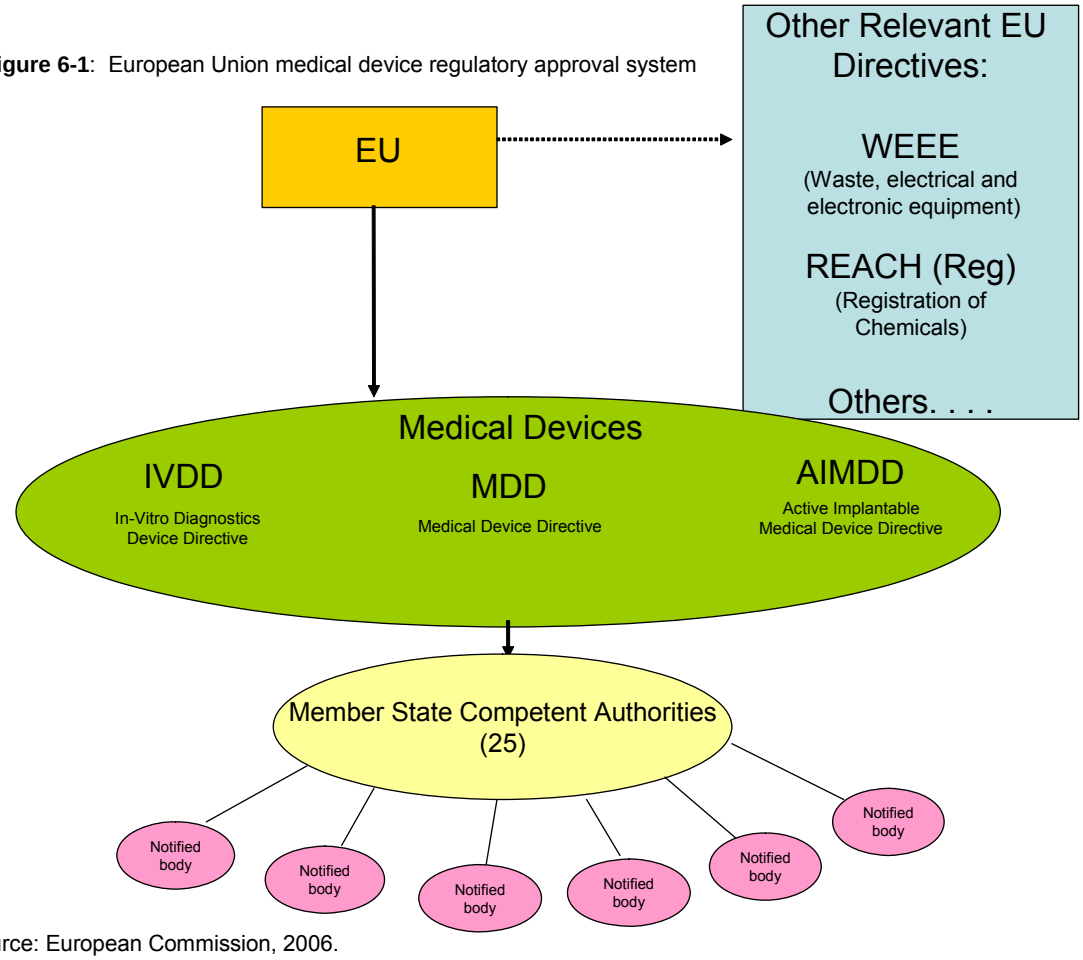
[23] Horton, *European Union Pharmaceutical & Medical Device Regulation*, 44–50.

[24] Ibid.

[25] Under the EU system, manufacturers usually have a choice between having their products approved through a quality management systems approach or one of several specific product testing and approval approaches specified in the relevant directives. For larger firms, the quality systems approach is often preferred because by having their quality management systems certified by a notified body to the ISO 13485 international standard, a number of firms' products may be made eligible for marketing in the EU by a supplier's declaration of conformity by the manufacturer. At the conclusion of a conformity assessment, the notified body either issues a certificate of conformity or provides an explanation of the problems that preclude certification. EU notified body official, interview by Commission staff, United States, May 4, 2006; and European regulatory officials, interviews by Commission staff, Belgium, Germany, and France, October 19–29, 2006.

[26] Diller, "Healthcare: Products and Supplies: Europe," 25–26.

Figure 6-1: European Union medical device regulatory approval system



Source: European Commission, 2006.

Table 6-3 European Union medical device classification system and regulatory clearance requirements

EU class	Device types and requirements	Regulatory clearance procedure
I	Class I medical devices are those that pose a low risk to the patient and, except for sterile products or measuring devices, such devices generally do not enter into contact or interact with the body. Examples: Stethoscopes, EEG and ECG electrodes, body liquid collection devices, syringes without needles, wheelchairs.	Class I devices can be placed on the market, as a general rule, under the sole responsibility of the manufacturer in view of the low level of risk associated with these products. The devices can be self-certified by the manufacturer as meeting relevant EU directives.
IIA	Class IIA devices are of a medium risk that are invasive in their interaction with the human body, but that interact with the body only through natural body orifices. The category may also include therapeutic devices used in diagnosis or in wound management. Examples: Syringes and tubing intended for use with infusion pumps, blood transfusion devices, nonmedicated gauze dressings, urinary catheters, CT devices.	Class IIA devices require that an EU notified body assess the compliance of medical device manufacturers' quality systems to the ISO 9000/EN46000 standards.
IIB	Class IIB devices are of a medium risk that are either partially or totally implantable within the human body, and may modify the biological or chemical composition of body fluids. Examples: Dialysis apparatus, medicated gauze dressings.	Class IIB devices require third-party certification by a EU notified body with regard to the design and manufacture of the devices, as well as an assessment of quality systems to ISO 9000/EN46000 standards.
III	Class III devices are of high risk, and generally affect the functioning of vital organs and/or life-support systems. Examples: Cardiac pacemakers and defibrillators, drug-eluting stents, breast implants, hip, knee, and spinal implants.	Class III devices require explicit prior authorization certifying conformity to required technical regulations to be placed on the market. All third-party product and system certification must be conducted by an EU notified body (or designee through formal agreement). They require design/clinical trial reviews, product certification, and an assessed quality system.

Source: European Commission, Enterprise Directorate-General, 2006.

EU safety and manufacturing quality standards and, thus, may be marketed throughout the European Union.[27]

In the EU, third-party conformity assessment is carried out by independent conformity assessment bodies that member state health ministries, known as "competent authorities," have accredited as having the required technical competence to review specified types of medical devices.[28] Each member state must notify the European Commission of all third-

[27] Ibid.
[28] EU notified body official, interview by Commission staff, United States, May 4, 2006.

party testing and certification bodies (notified bodies) it has accredited to review specific categories of medical devices under the different directives. Unlike in the United States or Japan, where third-party bodies may only make recommendations to the FDA or MHLW regulatory officials regarding conformity assessment approvals, in the EU, neither the European Commission nor the competent authorities in individual member states play a role in the premarket review of medical devices.[29] The third-party notified body conducts the entire review and certification. However, even though they are not as deeply involved in the premarket authorization stage of medical device regulation as their counterparts in the United States and Japan, competent authorities in EU member states are responsible for approving and overseeing the notified bodies, regulating medical device clinical trials, and overseeing postmarket surveillance, including adverse event reporting, product recalls, and enforcing penalties when required.[30]

Although most U.S. and foreign industry officials continue to favor the EU regulatory system, they have concerns that the European Commission is considering increasing its regulatory scrutiny.[31] In 2005, for example, the European Commission issued a directive that reclassified hip, knee, and shoulder implants from class II to class III, at the behest of the healthcare authorities in France and the United Kingdom despite the objections of many industry participants. Moreover, revisions that clarify and tighten the MDD are currently under review in the European Parliament and European Council. These revisions would require clinical data to support all medical device applications (except where demonstrated to be inappropriate) and clarify when notified bodies must sample such data of the devices reviewed.[32]

Some EU regulators are also considering options for more extensive premarket evaluation of medical devices, particularly in the area of new and emerging technologies, where there is a concern that technological developments have outpaced regulatory review (box 6-2).[33] However, the opinions of industry and regulatory officials in the EU vary on the question of how to improve the evaluation of the newest technologies; some assert that premarket review by competent authorities may be necessary, while others believe that enhanced scrutiny should be implemented by designated third-party notified bodies.[34] Those taking the latter position indicate that requiring "competent authority" approval could undermine the fundamental philosophy and strength of the EU system – e.g., its reliance on qualified third parties who act in a timely manner and possess particular strengths and expertise.

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[29] However, government regulators are involved in the premarket review and approval of combination devices. EU notified body official, interview by Commission staff, United States, May 4, 2006; and European regulatory and third-party testing body officials, interviews by Commission staff, European Union, September 19–29, 2006.

[30] Horton, *European Union Pharmaceutical & Medical Device Regulation*, 44–50.

[31] U.S. and EU industry officials, interviews by Commission staff, United States, June 5–16, 2006, and Belgium, France, Germany and the United Kingdom, September 18–27, 2006.

[32] Horton, *European Union Pharmaceutical & Medical Device Regulation*, 47; and Lacerda de Queiroz, *EU-China Cooperation Seminar*.

[33] U.S. and EU industry officials, interviews by Commission staff, United States, June 5–16, 2006, and Belgium, France, Germany and the United Kingdom, September 18–27, 2006.

[34] EU industry and member state government officials, interviews by Commission staff, Belgium, France, Germany, and the United Kingdom, September 18–27, 2006.

Box 6-2 New regulatory challenges in the EU

New regulatory challenges in such areas as advanced therapies and nanotechnology have sparked debate in the EU among stakeholders – including device makers, clinicians, regulators, notified bodies, and patient advocates – about how to achieve the best balance between promoting innovation and ensuring patient safety.

• Advanced therapies include gene therapy, somatic cell therapy and human tissue engineering. These therapies are based on innovative manufacturing processes that seek to modify genetic or structural properties of cells or tissues. Important therapies that presently or in the future are expected to rely on tissue engineering include treatments for skin, cartilage, and bone disease and the latest heart valve and blood vessel replacements. Gene and somatic cell therapies are classified as medicinal products, and thus subject to more stringent regulation than medical devices. The treatment of human tissue engineered products (hTEPs) has not yet been decided. The lack of EU regulation in this emerging area has resulted in divergent national approaches that may impact innovation because the path for product approval is uncertain. The European Commission proposed a new regulatory framework for advanced therapies in November 2005, after sponsoring three years of debate on the issue. A new Committee for Advanced Therapies would be set up at the European Medicines Evaluation Agency (which currently regulates pharmaceuticals but not medical devices in the EU market) to evaluate the products. The proposal is under consideration in the European Parliament, where its progress also has been delayed.

• Risk assessment of the potential environmental and health impacts associated with nanomaterials is receiving increasing attention at the European Commission, in the member states and in European and international standards bodies. Nanotechnology involves working with matter on an extremely small scale. New medical technologies incorporating nanotechnology include bone replacement materials that incorporate nanostructured materials for better integration into the body and wound dressings that include antibacterial nanoparticles. As with advanced therapies, industry advocates a level of regulation that protects safety while still promoting innovation.

Sources: Horton & Giles, "Changing Regulatory Landscape in the European Union"; EurActiv, "Advanced Therapies"; EurActiv, "Nanotechnology;" Eucomed, "Nanotechnology"; Diller, "Healthcare: Products and Supplies -Europe"; and EU industry, government and notified body officials, interviews by Commission staff, Belgium, France, Germany, and the United Kingdom, September 18–27, 2006.

Japan

The Pharmaceutical Affairs Law (PAL), enacted in 1943, is the principal law for regulating medical devices and pharmaceuticals in Japan, although legislative amendments taking effect in 2005 have significantly restructured the regulatory approval process.[35] The MHLW is the agency responsible for administering and ensuring compliance with medical device regulations in that country in concert with the new independent regulatory agency, the Pharmaceuticals and Medical Devices Agency (PMDA), which was created in 2004.[36] On July 25, 2002, the Japanese legislature enacted major amendments to reform and improve the efficiency of the regulatory approval system for medical devices and drugs.[37] The reform included over 150 new regulations and guidance documents that were to be fully implemented by April 2005. Major changes focused on the introduction of a four-tier, risk-based classification system, the adoption of a third-party review system for class II devices, the implementation of quality systems requirements, and the enhancement of postmarket surveillance requirements.[38]

[35] *Guide to Medical Device Registration in Japan*, 1; and PMDA, *Annual Report FY 2005*, 1.

[36] Gross and Loh, "Medical Device Regulatory Update: China and Japan," 112–114; and Diller, "Healthcare: Products and Supplies: Asia," 25.

[37] MHLW, "Statement by the Government of Japan on Trade Issue Concerning Medical Devices," posthearing statement, 3.

[38] Advamed/American Chamber of Commerce in Japan (ACCJ), "Japan Medical Technology Issues."

In 2004, to prepare for the April 2005 implementation of the amended PAL, an independent agency, PMDA, was created to consolidate three previously separate functions served by different organizations in the MHLW regulatory approval process (figure 6-2).[39] With the consolidation, PMDA is now the cornerstone of Japan's medical device and pharmaceutical regulatory system. This quasi-governmental body is financed by a combination of general government revenues and industry "user fees" for product reviews and postmarket surveillance activities and consultations. Funds are intended to augment staff size (for both premarket reviews and postmarket activities) and expertise, including the utilization of external experts.[40]

While PMDA now has the primary responsibility for conducting medical device reviews (and overseeing other related activities), MHLW retains final authority for approval of drugs and medical devices.[41] Thus, PMDA will make approval recommendations to MHLW based on its reviews. MHLW also will maintain a council of outside experts to advise it on the most difficult reviews. One of the most significant PAL revisions includes the introduction of third-party certification by registered bodies for certain controlled "generic medical devices"[42] of moderate risk, while maintaining governmental reviews of higher-risk medical devices.[43] Like PMDA, third-party bodies will make recommendations to MHLW based on their reviews, with MHLW retaining final approval authority.

Similar to the United States and the EU, Japan has a regulatory classification system based on potential risk of devices (table 6-4). PMDA is responsible for evaluating the quality, safety, and effectiveness of all class III and IV premarket approval (PMA) applications for "new medical devices" and for developing standards for class II medical devices to be reviewed by third-party testing bodies.[44] Currently, there are three application categories for medical devices, which include (1) "new" devices,[45] (2) "improved or modified" devices,[46] and (3) generic or "me-too" devices (box 6-3). Each year some 3,000 medical devices are

[39] Nakai and Yahiro, "Japan's New Organization and Review Process," 1–4; *Guide to Medical Device Registration in Japan*, 1; and PMDA, *Annual Report FY 2005*.

[40] Advamed/ACCJ, "Japan Medical Technology Issues," 1.

[41] PMDA, *Annual Report FY 2005*, 1.

[42] PMDA's use of the term "generic medical devices" is different from usage of "generic" for drugs. Generic devices are devices that are similar to those already on the market. They are comparable to 510(k) medical devices in the United States.

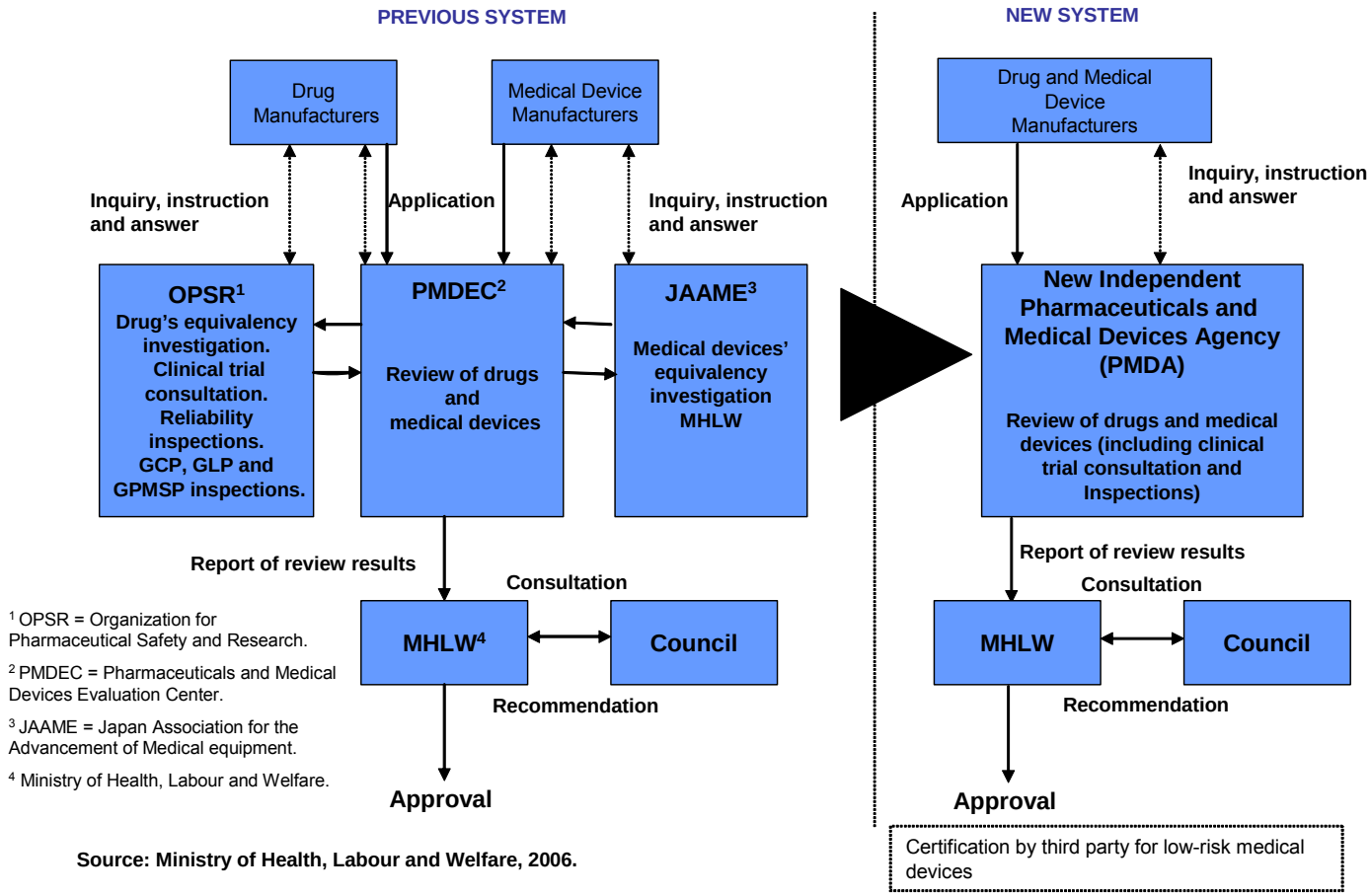
[43] Japanese regulatory experts, interviews by Commission staff, Japan, July 31-August 9, 2006; and MHLW, "Statement by the Government of Japan on Trade Issue Concerning Medical Devices," posthearing submission, 3.

[44] Nakai and Yahiro, "Japan's New Organization and Review Process," 1-4; and *Guide to Medical Device Registration in Japan*, 1.

[45] The definition of a "new medical device" is a product whose structure, usage, efficacy, effectiveness, or performance is clearly different from that of products that have already been approved. It is most comparable to those products requiring PMA approval in the United States.

[46] The definition of an "improved" device is a product whose structure, usage, efficacy, effectiveness, or performance are improvements on already approved products.

Figure 6-2: Reform of Japanese medical device regulatory approval system



Source: Ministry of Health, Labour and Welfare, 2006.

Table 6-4 Japanese medical device classification system and regulatory clearance requirements

Japan Class	Device types and requirements	Regulatory clearance procedure
I	Uncontrolled device: If malfunction or side effect occurs, risk to patient is insignificant. Examples: Stethoscopes, syringes without needles, wheelchairs.	No regulatory approval or marketing authorization needed.
II	Controlled device: Malfunction or side effect creates low possibility of serious or life-threatening injury to patient. Examples: Syringes with needles, blood transfusion devices, nonmedicated gauze dressings, urinary catheters, MRI, CT.	Third-party certification required. Only those class II devices for which PMDA has completed standards may utilize the third-party certification process. Third-party certification body reviews application and compliance with PMDA essential requirements and new GMP regulation. If found in compliance, the third-party body recommends approval to MHLW.
III	Highly controlled device: Very high risk in the case of malfunction. Examples: Dialysis apparatus, artificial bones, medicated gauze dressings.	Requires PMDA review of application and check of factory compliance to essential requirements and good manufacturing practices through documentation or factory inspection. If found in compliance, PMDA recommends approval to MHLW.
IV	Highly controlled device: Invasive devices; malfunction could cause life threatening effects. Examples: Cardiac pacemakers and defibrillators, drug-eluting stents, breast implants, hip, knee, and spinal implants.	Requires PMDA review of application and check of factory compliance to essential requirements and good manufacturing practices through documentation or factory inspection. If found in compliance, PMDA recommends approval to MHLW.

Source: Ministry of Health, Labour and Welfare, 2006.

Box 6-3 Important Japanese terms for regulated medical devices

Exempt Medical Devices: Medical devices that pose minimal risk to the human body, such as class I devices that have been designated by MHLW as exempt from the approval regulations.

New Medical Devices: New medical devices whose structure, intended use, indications, effects or performance differ significantly from previously approved devices. Similar to products requiring premarket approval, by the FDA in the United States, new medical devices are the most stringently regulated devices, and companies applying for approval of such devices are often required to submit extensive clinical testing data and other evidence demonstrating the safety of such devices.

Generic Medical Devices: Devices that are comparable to already approved medical devices, or predicate devices. The devices are evaluated for equivalence in terms of structure, intended use, indications, effects and performance similar to FDA's 510 (k) process. In most instances, the process for gaining approval of a generic medical device is much less lengthy than that for new medical devices. It usually only requires a manufacturer to provide information demonstrating the device is comparable to the other approved devices so as to pose no special safety concerns. Generic medical devices in Japan are commonly referred to as "me-too" medical devices. The use of the term "generic" in the Japanese regulatory process has no relationship to the meaning of the term "generic" in the case of drugs.

Improved Medical Devices: Improved medical devices are defined as devices whose structure, effects, or performance are improvements on previously approved products.

Source: PMDA 2005 Annual Report.

Box 6-4 New market authorization holder (MAH) requirement in Japan

Under Japan's amended Pharmaceutical Affairs Law, medical device companies doing business in Japan are now required to have a market authorization holder (MAH), who is responsible for the safety of the company's products. The MAH requirement significantly affects medical device producers entering the Japanese market or already established there. Previously, an in-country caretaker system (ICC) allowed foreign firms without local Japanese offices to register their products in Japan. That system required a producer to obtain a license (kyoka) and approval (shonin) for each product. The manufacturer produced the medical devices and also placed them onto the market. The MAH system replaces the ICC system by separating the two responsibilities. Now the manufacturer will be responsible for producing the product and "the MAH will act as an enhanced regulatory control mechanism to give final permission for product release." Japan's purpose in separating the two responsibilities was to "better regulate the quality and safety of medical devices."

The MAH must be located in Japan and be able to purchase or import medical devices from a manufacturer, sell products to sales organizations, and temporarily store products in a licensed establishment. Firms have the option of (1) using a distributor or importer, (2) a third party, or (3) designating themselves as the MAH. In the last case, a firm may name a subsidiary, branch, or representative in Japan, as long as the MAH meets the requirements specified above.

All ICCs were given the option to go through a more simplified application process to become an MAH. An MAH is required to name up to three people as controllers, who are responsible for overseeing product manufacturing and distribution, and placing medical devices on the market. The first controller is a General Manager responsible for overseeing overall product marketing quality and safety. The second, the quality assurance controller, is in charge of good quality practice. It is responsible for ensuring that the manufacturer abides by the appropriate shipping and receiving methods, notifying MHLW of any changes in manufacturing or in-process controls. The third, the postmarketing safety controller, is accountable for good vigilance practice (GVP). This controller monitors the safety of products released onto the market and reports to appropriate health authorities any adverse incidents or recalls of its products.

For class I products, only one controller is required to perform all of the functions. An MAH for class II products requires two people to carry out all of the functions. Class III and IV products require three people, designated for each of the responsibilities.

Source: Much of the information excerpted or adapted by Commission staff in part or whole from information provided in Gross and Weintraub, "Regulatory Updates for Drugs, Devices & IVDs in Asia;" and Whitacre, "What Manufacturers Need to Know."

reviewed for approval by Japan's reviewing agencies, of which some 90 percent qualify as me-too devices.[47] PMDA is also responsible for postmarketing surveillance activities. While prefecture governments previously were responsible for inspecting Japanese producers of class II, III, and IV devices, under the new PAL they will now be limited to inspecting class III domestic device manufacturers. Meanwhile, PMDA will perform the inspections of foreign manufacturers of class III and IV devices, as well as inspections of class IV devices of Japanese manufacturers.[48] The amended law also requires companies conducting business in Japan to physically separate manufacturing operations from marketing and safety operations and to utilize an entity called a market authorization holder (MAH) (box 6-4) to assume responsibility for safety of their medical devices.[49]

[47] Nakai and Yahiro, "Japan's New Organization and Review Process," 1–4; and *Guide to Medical Device Registration in Japan*, 1.

[48] Nakai and Yahiro, "Japan's New Organization and Review Process," 1–4.

[49] Ludwig, hearing transcript, 13–14.

Qualitative Assessment of the Effects of the Japanese Medical Device Regulatory System

Previous research on the topic of regulation and its economic effects was reviewed prior to conducting the qualitative assessment of the possible effects of Japan's regulatory approval system on the medical device industry. Economists have noted the impact of regulatory decisions on the amount and cost of innovation for both firms and consumers. For example, differences in regulatory decision times directly affect the time to market, which, in turn, affects the return on investment in product development.[50] Additionally, differences in national product standards and regulatory procedures can create impediments to both domestic and foreign production (by requiring production runs to service different markets or by diminishing the ability to promote products, secure investment, or service niche markets) and the ability to export.[51] Industry sources also indicated that differences in regulatory approval times can raise costs of servicing a market by requiring companies to maintain dedicated service lines for older generations of products still being produced for Japan that are no longer being sold to other major markets (which are being supplied with the latest generations of the products).[52]

The estimated length of the approval process for medical devices averages 3-10 months in the United States, 6 months in the EU, and anywhere from 1-3 years for Japan.[53] For each market, the length of time for product approval depends on the classification of the device; lower risk products similar to other products on the market take less time to approve than higher risk, newer devices.[54]

Almost all U.S. medical device firms interviewed by Commission staff, including U.S. subsidiaries of EU and Japanese firms, suggest that their sales and exports are negatively affected by the more demanding and lengthier Japanese product approval process.[55] U.S. industry officials acknowledge that Japanese and EU firms also are adversely affected by the longer average review times in Japan.[56] However, they indicate that given the competitive advantage U.S. firms have in innovative, higher-risk products relative to their foreign rivals, they are more affected given the lengthier period of time required to gain approval and the relatively shorter product life cycles of innovative devices.[57] For example, it took 3 years to obtain approval for a drug-eluting stent in Japan, although it had already been approved in the United States in one year.[58]

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[50] Blair, Downs, and Ndayisenga, "The Potential Gains of Deeper Canada-U.S. Regulatory Cooperation," 230.

[51] Ibid.

[52] Comments by industry official, AdvaMed conference on Globalization of Medical Devices Policies, October 31, 2006.

[53] FDA, ODE, *2005 Annual Report*; JETRO, *Japanese Market Report: Medical Equipment*, 6–40; and U.S., Japanese, and EU industry officials, interviews by Commission staff, United States, June 5–16, 2006; Japan, July 31–August 9, 2006; and EU, September 18–29, 2006.

[54] U.S. industry officials, interviews by Commission staff, June 5–16, 2006, and officials of Japanese affiliates of U.S.-based firms, Japan, July 31–August 9, 2006.

[55] U.S. industry officials, interviews by Commission staff, June 5–16, 2006.

[56] U.S. industry officials, interviews by Commission staff, June 5–16, 2006, and officials of Japanese affiliates of U.S.-based firms, Japan, July 31-August 9, 2006.

[57] Ludwig, hearing transcript, 6–14; Agress, hearing transcript, 15–23; Hanawa, "Medical Equipment," 1–10; and Diller, "Healthcare Products & Supplies," 1–6 and 25–26.

[58] Ibid.

Manufacturers of other types of products, such as MRI, CT, X-ray, and electrosurgical devices, report that they also face more difficult and lengthier regulatory product approval processes in Japan than in the United States and the EU.[59] However, because most of their products can be demonstrated to be similar to medical devices already on the market, they experience relatively short regulatory approval processes in all of their principal markets, including Japan, and are less likely to be required to conduct costly clinical trials required of high-technology, newer products.[60] Such mature products also have longer product life cycles than most innovative, higher-risk products entering the market today. Thus, such products, even when they face relatively longer regulatory approval processes in Japan than in the United States or the EU, may be affected less adversely in terms of profitability and sales, and exports to the Japanese market than higher technology, innovative devices.[61]

The following two sections review and compare medical device review costs and approval times, as published annually by the FDA and PMDA. These comparisons will focus on the United States and Japan because official regulatory approval and cost information is unavailable for the EU due to a greater dependence on third-party testing laboratories whose data on costs and approval performance are proprietary.

Medical Device Approval Costs in the United States and Japan

Medical device approval costs consist of (1) user fees paid by applicants to help fund regulatory agencies' product approval activities, (2) opportunity costs if product approval in a particular market takes significantly longer than in other global markets, (3) costs of conducting clinical trials, and (4) capital restructuring costs that firms may incur to meet new regulatory requirements. Both the U.S. FDA and Japanese PMDA have been authorized by legislation to require user fees from medical device product approval applicants to supplement the agency budget to improve the efficiency of their product approval operations.[62] Ostensibly, new user fees are meant to make the regulatory approval systems less dependent on the vagaries of annual national budget decisions and improve the efficiencies of the medical device review process. Medical device firms generally have accepted and supported increases in user fees as a means of increasing regulatory agency resources to meet more rigid targets.[63]

Tables 6-5 and 6-6 show FDA 510(k) and PMA application user fees for fiscal years 2006 and 2007. PMDA has not published user fees in connection with its generic medical device reviews (most comparable to FDA 510(k) reviews), reportedly because it expects most generic class II device evaluations to be conducted by third-party bodies, for which fees will be determined in the marketplace. However, PMDA fees have been established for reviews of approvals of highly controlled class III and IV "new" medical devices" (most comparable to FDA PMA reviews) (table 6-7). According to data presented in tables 6-6 and 6-7

[59] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and Japan, July 31–August 9, 2006.

[60] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006.

[61] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006.

[62] The Medical Device User Fee and Modernization Act (21 U.S.C. § 379j), enacted in October 2002, amended the U.S. Federal Food, Drug, and Cosmetic Act of 1938, and established user fees to fund the process for the review of medical device applications by FDA. The 2002 amendments to the PAL, effective April 2005, similarly provided for the implementation of user fees to fund the review of medical device applications in the Japanese regulatory approval process. Such fees are a major source of funding for the new PMDA in Japan.

[63] U.S. and Japanese industry officials, interviews by Commission staff, United States, June 5–16, 2006 and Japan, July 31–August 9, 2006.

outlining user fees for FDA PMA and comparable PMDA "new medical device" applications, it appears that the costs of FDA approval are substantially more than those for PMDA.[64]

Table 6-5 FDA 510(k) user fees, fiscal years 2006 and 2007

Fiscal year	Standard fee	Small business fee
FY 2006 (Oct. 1, 2005–Sept. 30, 2006)	$3,833	$3,066
FY 2007 (Oct. 1, 2006–Sept. 30, 2007)	$4,158	$3,326
Third-party 510(k)	Exempt from FDA fee, but liable for third-party market-based fee for review.	Exempt from FDA fee, but liable for third-party market-based fee for review.

Source: U.S. Food and Drug Administration, Center for Devices and Radiological Health, 2006.

Table 6-6 FDA PMA user fees, fiscal years 2006 and 2007

Type of application	Standard fee 2006	Standard fee 2007	Small business fee 2006[a]	Small business fee 2007[a]
Premarket application (PMA, PDP, BLA, PMR)[b]	$259,600	$281,600	$98,648 (One time-waiver for first PMA by firm with less than $30 million in sales)	$107,008
Premarket reporting	$259,600	$281,600	$98,648	$107,008
Panel-track supplement	$259,600	$281,600	$98,648	$107,008
Efficacy supplement	$259,600	$281,600	$98,648	$107,008
180-day supplement	$55,814	$60,544	$21,209	$23,007
Real-time supplement	$18,691	$20,275	$7,103	$7,705

Source: U.S. Food and Drug Administration, Center for Devices and Radiological Health, 2006.

[a] Small business=Less than $100 million in sales.
[b] PMA=Premarket approval
PDP=Product development protocol
BLA=Biologics license application
PMR=Premarket report (for a reprocessed device)

Table 6-7 PMDA estimated approval costs for "new medical device" reviews, 2005

Review activities	PMDA user fees	
	Japanese yen	*U.S. dollars*
New medical device review	3,077,000	26,800
Compliance	664,500	5,800
Good clinical practice	918,400	8,000
Good laboratory practice audit	2,282,600	20,000
Quality systems audit	933,500	8,100
Total fees	7,876,000	68,700

Source: PMDA.

[64] However, PMDA does charge fees for other services, including face-to-face consultations, that, if requested, can cost as much as 1,594,700 Japanese yen ($14,000) for complex applications involving clinical trials. PMDA also charges medical device firms about $2,000 each for on-site manufacturing licenses and foreign manufacture accreditation reviews.

Medical Device Approval Times in the United States and Japan

Many U.S. industry officials report that the most significant costs imposed by the Japanese regulatory approval system are not in its user fees and costs associated with meeting clinical trial or business restructuring requirements but in regulatory delays of 1-3 years and associated opportunity costs in gaining market approval for the most innovative medical devices.[65] To help it assess U.S. and foreign industry claims related to the efficiency of the Japanese system, the Commission examined and compared approval time data published in the annual reports of the U.S. and Japanese regulatory agencies. The Commission also conducted a literature review to identify previous attempts to measure the efficiency of regulatory approval systems in Japan and other countries (box 6-5).[66]

In reviewing FDA and PMDA approval data it appears that while FDA has made progress in reducing its approval times in the past five years, Japanese regulatory approval times increased over the same period before declining moderately in 2005. As figures 6-3 through 6-6 indicate, U.S. FDA average approval times declined fairly significantly over the past five years for both PMA application reviews and 510(k) reviews. In contrast, MHLW and PMDA average review times[67] for "new medical device" applications in Japan increased substantially from 2002-4 (table 6-8).[68] According to official Japanese government data, MHLW and PMDA review times of applications for new medical devices in Japan were fairly comparable to those for FDA PMAs in 2001 (figure 6-7). However, average total [69] Japanese review times of new medical device applications began rising significantly over those of total FDA PMA reviews between 2002 and 2003, when they more than tripled from 88 to 285 days. Review times continued to move upward in 2004, when the median[70] time of review reached almost 3 years (1083 work days).[71]

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[65] U.S., Japanese, and European industry officials, interviews by Commission staff, United States, June 5–16, 2006; Japan, July 31–August 9, 2006; and the EU, September 18–29, 2006.

[66] The literature review only identified three research studies of potential relevance to examining performance of countries' regulatory approval systems and none of them specifically pertained to the Japanese system. Two of them included attempts to evaluate the performance of the EU and U.S. approval systems and the third tried to evaluate the performance of the U.S. FDA system alone. Further description of these studies and their findings is contained in box 6-5. Chai, "Medical Device Regulation in the United States and the European Union," 74-80; GAO, "Medical Device Regulation," 1–10; and GAO, "Food and Drug Administration," 16.

[67] PMDA took over medical device application reviews from MHLW in 2004.

[68] PMDA does not publish average review times for generic medical devices in its annual reports.

[69] Both U.S. FDA and Japan's MHLW and PMDA differentiate between "reviewer time" and "total review time" for approval of medical device review applications. Reviewer times represent the time an application is officially under review by the regulatory agency. Total time includes both reviewer time and applicant time from when an application for review is accepted by the regulatory agency to when the final determination on the application is made. Applicant time represents the time attributed to an applicant and is off of the reviewer's "time clock." For instance, it includes time taken by the applicant to respond to reviewers' questions or requests to submit additional data related to an application. U.S. and Japanese government officials, interviews by Commission staff, United States, May 31 and June 5–16, 2006, and Japan, July 31–August 9, 2006.

[70] An important caveat in comparing MHLW to FDA average review times is PMDA's use of "median" in contrast to FDA's use of "mean" in reporting average review times in comparisons such as in figure 6-7. Thus, PMDA review times could potentially be significantly higher on "average" than FDA average times for all years being compared if values of PMDA review times above the mean time are biased upward.

[71] While total Japanese "new medical device" review times declined in 2005, according to official MHLW data, they cannot yet be compared to FDA PMA review times, as FDA PMA data are not available for 2005, reportedly because a significant number of PMA submissions are still under review. PMDA *Annual Report FY 2005*; and FDA, ODE, *2005 Annual Report.*

Box 6-5 Research studies concerning medical device regulatory performance

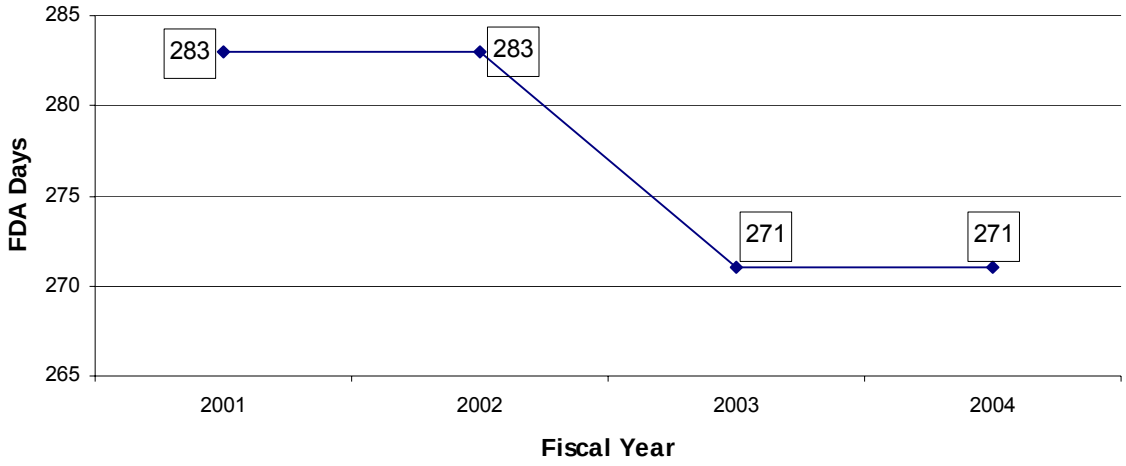
In one of the studies, the U.S. Government Accountability Office (GAO) investigated the EU medical device approval system (including its significant use of third-party review) in 1995-6 as a potential model for the United States after U.S. manufacturers had complained about the inefficiency and unfairness of the FDA's review processes. The GAO concluded that it was too soon to evaluate the performance of the EU system. Chai also compared medical device regulations in the EU and the United States. Although, as previously noted, Japan has provisions for third-party evaluation, which were authorized in 2005 when the 2002 amendments to its PAL took effect, these registration bodies are a recent phenomenon. Therefore, information to assess their performance is limited, although they have evaluated some medical devices.

Another study evaluated the performance of the FDA in meeting new requirements of the Food and Drug Modernization Act that added other objectives for the FDA, such as promptly reviewing product applications and consulting with stakeholders and the public. Meanwhile, an EU report looked at EU efforts to streamline its regulatory processes. Chai found that approval times for the FDA's 510(k) and PMA reviews both decreased between 1997 and 1999, and the EU report suggests that its device approval times may be shorter than those of the United States, although the comparison is not totally clear because different data gathering and analysis tasks were performed.

More recently, the GAO conducted a study to assess the FDA's progress towards meeting the 2003 and 2004 performance goals required by the Medical Device User Fee and Modernization Act (MDUFMA) of 2002 (21 U.S.C. § 301 note, et seq.). The MDUFMA increased incentives for the FDA to improve its performance in evaluating medical devices by authorizing the FDA to collect user fees from manufacturers that submit applications. The MDUFMA directs the FDA to review product applications promptly and efficiently, to collaborate with other countries to harmonize regulatory requirements and achieve reciprocal agreements, and to consult with stakeholders and the public in accomplishing its mission. MDUFMA also required the GAO to report on the FDA's progress towards meeting the 2003 and 2004 performance goals and whether the FDA would likely meet the 2005 goals. Although the GAO stated that it lacked the data to evaluate the FDA's performance completely, it found that the FDA had hired additional staff, consulted more frequently with outside experts, and made some progress in evaluating applications more efficiently.

Source: Chai, “Medical Device Regulation in the United States and the European Union,” 74-80; GAO, “Medical Device Regulation,” 1-10; and GAO, “Food and Drug Administration,” 16.

Figure 6-3 Average total FDA review time[a] for all original PMAs and PMA supplements, 2001–4

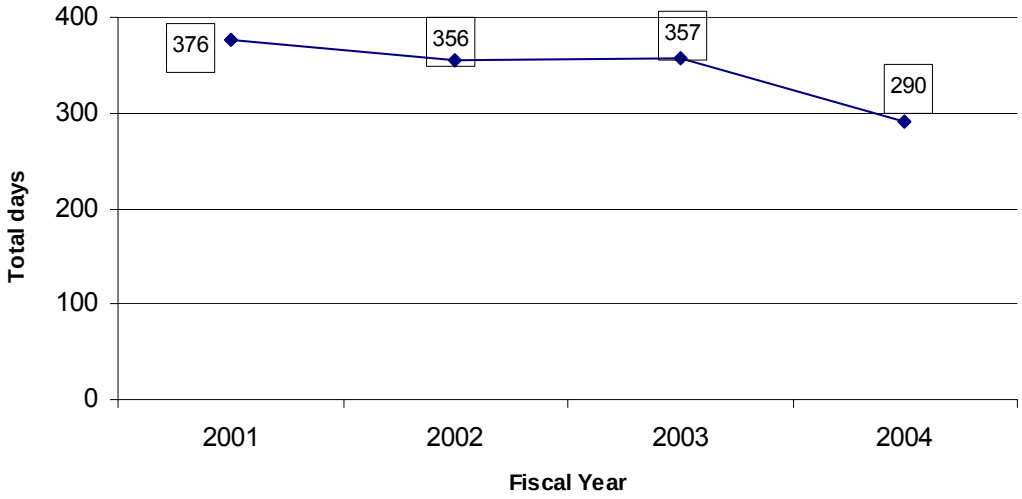


Source: U.S. Food and Drug Administration, Office of Device Evaluation, *2005 Annual Report* (extracted by Commission staff).

Note.—FDA data for 2005 are not available because a significant number of PMA submissions are still under review.

[a] FDA time includes only time that can be attributed to FDA. Does not include applicant time such as responding to requests for additional information from FDA.

Figure 6-4 Average total[a] elapsed days from filing to FDA approval for all original PMAs and PMA supplements, 2001–4

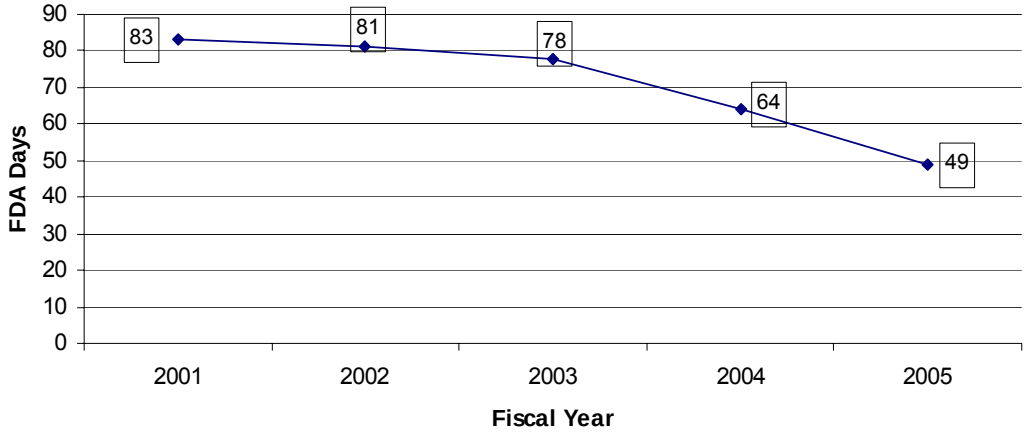


Source: U.S. Food and Drug Administration, Office of Device Evaluation, *2005 Annual Report*.

Note.—FDA data for 2005 are not available as a significant number of PMA submissions are still under review.

[a] Includes both time attributed to FDA and time attributed to applicant (not on FDA's time clock).

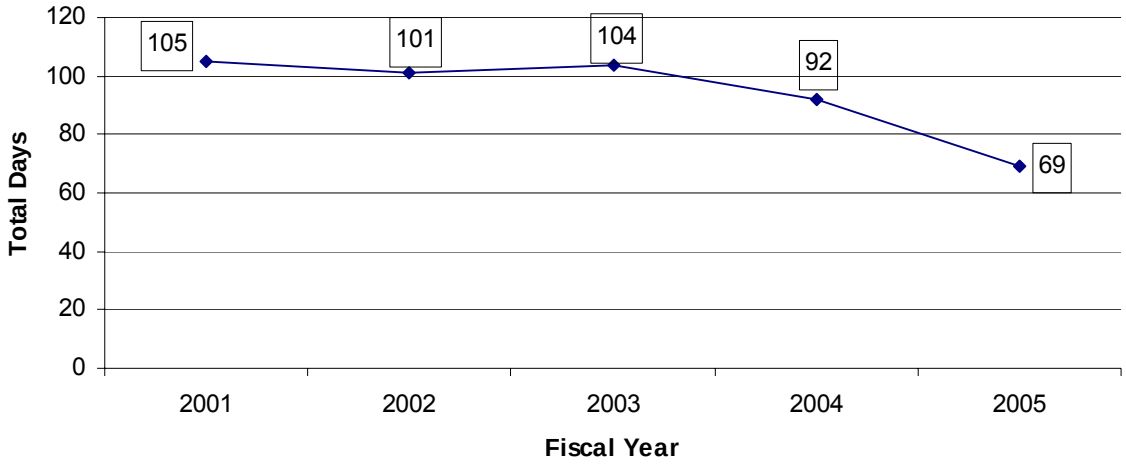
Figure 6-5 Average FDA[a] time from receipt of 510(k) to final decision, 2001–5



Source: U.S. Food and Drug Administration, Office of Device Evaluation, *2005 Annual Report*.

[a] FDA time includes only time that can be attributed to FDA. Does not include applicant time such as responding to requests for additional information from FDA.

Figure 6-6 Average total[a] time from receipt of FDA 510(k) to final decision, 2001–5



Source: U.S. Food and Drug Administration, Office of Device Evaluation, *2005 Annual Report*.

[a] Includes both time attributed to FDA and time attributed to applicant (not on FDA's time clock).

Table 6-8 PMDA new medical device approvals and median PMDA review [a] processing time, 2002–5

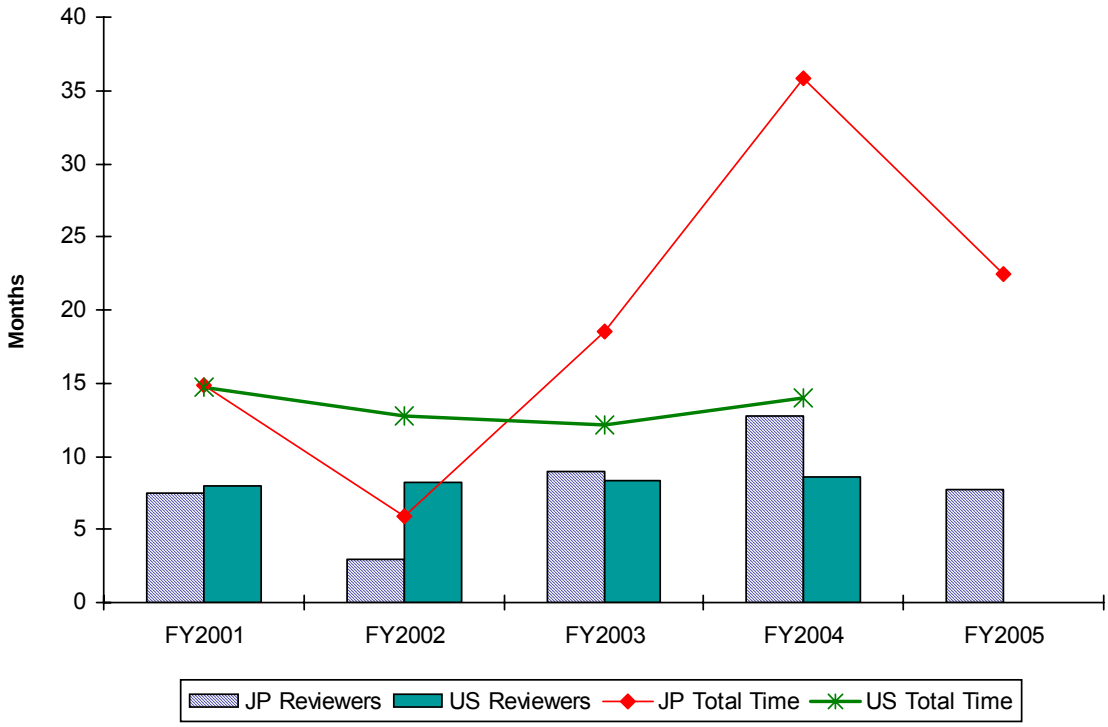
Fiscal Year	2002	2003	2004	2005	Filed in and after FY 2004, but approved in FY 2005 [b]
Median PMDA review time[a]	88 days	284.5 days	386 days	232 days	55 days
Total review process time	176 days	564.5 days	1,083 days	678 days	308 days

Source: Japan Pharmaceuticals and Medical Devices Agency (PMDA), *Annual Report FY2005*.

[a] PMDA review processing time includes only time that can be attributed to PMDA. Does not include applicant time, such as time taken to respond to requests for additional information from PMDA.

[b] Does not include PMDA backlog cases.

Figure 6-7 Comparison of reviewer times and total review times for new medical device applications between Japan (median) and U.S. (mean), 2001–5



Source: Japan Ministry of Health, Labour and Welfare, 2006.

Note: Both PMDA and FDA differentiate between "review time" and "total time" for the review of medical device applications for approval. Reviewer time represents the time an application is officially under review by either PMDA or FDA. Total time represents both reviewer and applicant time from when an application is accepted by PMDA or FDA and when the final determination on the application is made. Applicant time represents time attributed to the applicant, such as responding to reviewer's questions or requests to submit additional information. FDA has not yet reported review times for FY2005.

An important caveat in comparing MHLW to FDA average review times is PMDA's use of "median" in contrast to FDA's use of "mean" in reporting average review times.

U.S. industry officials expressed disappointment in Commisson hearing testimony that PMDA had not yet met its own performance goal of completing and processing 90 percent of the applications within 12 months.[72] However, Japanese regulatory officials point out that progress has been made toward this goal, with PMDA's figure improving to 82 percent in 2005.[73] The Japanese government also reported that 100 percent of applications filed in or after 2004 were approved within the 12 month target time; however, this figure does not include those applications filed before the reform that are part of the backlog. The officials report that full achievement of PMDA processing goals has been hampered by a large number of unworked applications submitted prior to creation of the new agency in 2004.[74] Thus, it has had to review these simultaneously with new applications submitted after 2004. PMDA reports that as it has been able to make progress on eliminating the backlog over the past two years, it has been able to reduce its approval times for new applications.[75] This is reflected in its annual report data showing that review times came down by more than 60 percent in 2005, a year after PMDA replaced MHLW as the reviewer of medical devices.

PMDA officials indicated that when the review backlog is eliminated in late 2006 or early 2007, as expected, it will begin to more consistently achieve its performance goals.[76] However, U.S. industry officials counter that, notwithstanding the 2005 decline in PMDA average total review time for new medical devices, it still represents more than triple the average review times for such devices in Japan in 2002.[77]

Impact of Japanese Regulatory Approval on U.S. Firms

The Commission was unable to identify any quantitative analyses that empirically measured the impact of regulatory approval systems on sales and exports of medical devices. Although studies were identified that have used quantitative means to estimate foregone sales due to regulatory impacts on pharmaceuticals, the medical device industry, characterized by incremental innovation and shorter product life cycles than the drug industry, is much more difficult to quantify. Consequently, Commission staff determined that a quantitative analysis measuring the impacts of foreign regulatory approval systems on U.S. sales and exports could not be adequately and reliably completed for purposes of this report.

However, U.S. industry officials estimate that complying with changes in Japan's regulatory system since 2005 has cost U.S. companies $350 million[78] and that U.S. firms will incur an additional $1.2 billion in compliance costs over the next five years.[79] Specifically, innovative U.S. firms incur three types of unique costs in Japan: forgone opportunity costs associated with much longer product approval times; requirements for conducting additional clinical trials to acquire safety data equivalent to that obtained in previous trials and accepted by regulators in other markets; and new requirements for firms to separate marketing and safety

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[72] Ludwig, hearing transcript, 12; and U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006; and Japan, July 31–August 8, 2006.

[73] MHLW officials, posthearing statement, 5; and PMDA, *Annual Report FY 2005*.

[74] Ibid.

[75] Japanese government officials, interviews by Commission staff, Japan, July 31–August 8, 2006.

[76] Ibid.

[77] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[78] Agress, hearing transcript, 17; and AdvaMed/ACCJ, *Japan Medical Technology Issues*, 15.

[79] Based on a survey of U.S. companies in a study sponsored by AdvaMed and the American Chamber of Commerce in Japan. For further information on the survey methodology, see AdvaMed/ACCJ, *Japan Medical Technology Issues*, 15.

operations from production functions, thereby requiring expensive organizational changes and associated ongoing maintenance costs not required in other countries.

U.S. industry officials contend that the Japanese regulatory approval system adversely affects the ability of U.S. firms to export or sell their medical devices into the Japanese market in several ways.[80] As demonstrated in the previous section, although regulatory approval fees are higher in the United States, Japan's regulatory approval times still are demonstrably slower than in the United States despite some improvement in 2005. The delay in regulatory approvals is associated with significant opportunity costs to medical device firms of not having products on the market while they are undergoing review.[81] Thus, companies lose sales that otherwise would have been made if the regulatory system had been more timely in approving the product. Product approval denials, of course, have an even more significant impact on companies' revenues in that companies receive no return in revenues for costs incurred in developing and trying to market their products. When regulatory approval delays or denials result in forgone or lost sales, companies are also deprived of an important source of funding for reinvestment in R&D to develop even better products.[82]

As a result of the large costs and delays associated with placing medical devices on the Japanese market, medical technology experts report that some firms may withdraw from the Japanese market.[83] Further, firms that continue to sell in Japan could withhold certain, newer, more innovative medical devices that they sell in the rest of the world from the Japanese market due to the difficulty and expense in obtaining approvals in Japan. There is evidence that companies are submitting fewer applications for new medical device approvals in Japan. In fiscal year 2003, manufacturers submitted 132 applications for new medical devices.[84] In 2004, the number was down to 56, and only 8 such applications were submitted in 2005.[85] Continuation of this trend in Japan could lead to fewer U.S. exports and sales to that market.

U.S. medical device firms reportedly incur additional costs as they must retain separate manufacturing lines "for products that are obsolete throughout the rest of the world, but are being supplied to Japan, while later generations of the product await approval by Japanese regulators."[86] For example, according to a U.S. industry leader, "an advanced pacemaker for cardiac resynchronization therapy available in the United States in 2003 will only become available to patients in Japan [in August 2006]."[87] Another problem for companies having to keep production lines open for older products is that some components are more difficult to source from their suppliers, or are no longer made.[88]

Finally, U.S. company officials report they have incurred significant reorganizational costs to comply with the new requirement for firms marketing products in Japan to separate their

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[80] U.S. industry officials, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[81] Ibid.

[82] Ibid.

[83] Ludwig, hearing transcript, 13–14.

[84] Agress, hearing transcript, 22; and PMDA,*Annual Report FY2005*, 17.

[85] The number of comparable applications submitted by manufacturers to the FDA was 54 in 2003, 41 in 2004, and 49 in 2005. FDA, ODE *2005 Annual Report*, 26; and OIVD, *2005 Annual Report*, 49.

[86] Ludwig, hearing transcript, 10; and U.S. industry official, e-mail message to Commission staff, November 22, 2006.

[87] Lugwig, hearing transcript, 9-10.

[88] Ludwig, hearing transcript, 10; and U.S. industry official, e-mail communication to Commission staff, November 22, 2006.

production from their marketing and safety operations in Japan. The president of a prominent U.S. medical device company testified that it took about two years and cost millions of dollars to comply with this new requirement.[89] Smaller companies without a direct market presence or who cannot afford to set up an MAH must hire, appoint, or designate an expert in Japan. Neither the United States nor the EU require such separation of medical device companies' manufacturing and marketing operations.

Outlook

Many U.S. and foreign industry officials and analysts attribute the difficulties of the Japanese regulatory system to several problems they believe need to be addressed before further progress may be made (table 6-9).[90] Among these are overly detailed administrative requirements that industry officials contend are unrelated to the safety and efficacy of medical devices; insufficient resources and manpower for PMDA to ensure timely approval of new medical devices; lack of transparency in the process (limiting the ability of companies to interact with regulatory officials to resolve product approval problems and delays); and redundancy in clinical trial requirements by requiring companies to conduct additional studies to produce equivalent safety data to those obtained in clinical trials in other countries. While the United States and EU commonly use foreign clinical trial data for use in their reviews of new medical devices,[91] additional clinical trial requirements significantly extend regulatory approval times and costs in Japan.[92]

In response, MHLW officials state that the PAL reforms include more rigorous premarket and postmarket surveillance measures to ensure safety and quality of medical devices and are similar to premarket and postmarket measures advocated by the Global Harmonization Task Force[93] and used in the United States and the EU. Moreover, they point out that PMDA 2005 annual report data demonstrate the significant use of foreign clinical data by Japanese regulatory authorities (table 6-10).

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[89] Ludwig, hearing transcript, 13–14.

[90] Agress, hearing transcript, 15–23; and U.S. and Japanese industry officials, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[91] Agress, hearing transcript, 20; JETRO, *Japanese Market Report No. 69: Medical Equipment*, March 2004, 1–40; and U.S. industry official, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[92] U.S. government and industry officials have encouraged Japan to improve its transparancy by clarifying when it will accept foreign clinical data from clinical trials. They also encouraged PMDA to accept clinical data from outside Japan according to international standards, specifically to the requirements of ISO 14155 (Good Clinical Practices) and not requiring conformance with ICH guidance. U.S. Department of Commerce, *2006-7 Annual Reform Recommendations*, Annex 15–16; and JETRO, *Japanese Market Report No. 69: Medical Equipment*, 1–40.

[93] For more information on the Global Harmonization Task Force (GHTF), see chapter 5.

Table 6-9 Industry views on sources of Japanese regulatory delays and difficulties and Japanese government responses

U.S. industry views	PMDA Response
The Japanese regulatory approval system has not been effective enough in ensuring that leading innovations approved and used safely in other advanced countries, such as the United States and Europe, are available in Japan. Thus, they are depriving the Japanese public of the most recent medical technologies, as well as preventing innovative medical device companies from being rewarded sufficiently for medical innovations.	In the amended PAL, the Japanese government reformed the system to ensure that (1) the Japanese public and healthcare professionals swiftly enjoy the maximum benefits of leading-edge, yet safe, pharmaceuticals and medical devices that answer their needs; and (2) pharmaceutical and medical device companies are ensured the benefits "brought forth by such swiftness."
The PAL reforms, which went into effect in 2005, and creation of an independent medical device agency (PMDA), have not improved the efficiency of the medical device approval process. In fact, many U.S. companies report that it now takes up to twice as long to gain approvals than before.	The reforms only went into effect in 2005, and the reorganization has not been completed. The current increased delays are principally due to the backlog of applications inherited by the new PMDA, which have almost been completed.
There are too few PMDA medical device reviewers (28 with target of 35). This is about 10 percent of the number of the U.S. FDA reveiws. Lack of sufficient manpower by PMDA slows the regulatory approval process considerably.	The number of reviewers required is based on the level of medical device applications received.[a] The appointment of a large independent advisory panel of experts will greatly leverage PMDA's review staff. Further, the new provisions establishing an independent third-party certification system allowed to review a large portion of class II devices will enable PMDA reviewers to focus more of their efforts on more complex new medical device reviews, adding efficiency and speed to the entire approval process.
Reviewers at PMDA do not have requisite experience in medical device technology. Because of the historical importance of pharmaceutical reviews in MHLW, most reviewers transferred over to PMDA are too narrowly specialized in pharmaceuticals.	PMDA criteria for recruitment of medical device reviewers have broadened. PMDA is now recruiting employees with backgrounds and expertise in mechanical, electronic, and bioengineering, statistics, quality management, and other areas relevant to medical device evaluation and appraisal.
Required job rotations of MHLW reviewers every two years has reduced retention of institutional knowledge in the Japanese regulatory approval system. Such rotations also interrupt completion of reviews of specific device applications when reviewers working on them depart in middle of the process.	As an independent agency, PMDA is not required to rotate its examiner staff and, in fact, PMDA employee retention is an important objective of the revised regulatory approval system in Japan.
Transparency has been lacking in the Japanese medical device regulatory approval process. Unlike in the United States and the EU, companies have had a difficult time providing input to the Japanese regulatory approval process.	PAL reforms provide PMDA with more opportunities and resources for reviewers and other staff to dialogue with industry.
In the past, MHLW has not had clear regulatory performance goals or deadlines for processing and approving medical device applications.	PMDA is required to set clear targets for approval of medical devices within specified deadlines and publish them in their annual report. While PMDA may not reach all of the targets, such targets give PMDA goals to move toward, measure progress against, and be held accountable to.

Source: Compiled by Commission staff based on interviews with U.S. and Japanese industry and government officials, June-August 2006.

[a] Commission staff were unable to obtain sufficient data to allow them to compute the average number of applications handled per number of FDA and PMDA reviewers, respectively.

Table 6-10 Number of cases approved in Japan by using foreign and domestic clinical data, FY 2001-FY 2005

Year	Foreign clinical data only	Foreign and domestic clinical data	Total	Domestic clinical data only
2001	21	4	25	24
2002	9	0	9	11
2003	14	3	17	12
2004	11	1	12	8
2005	33	1	34	16

Source: Japan Pharmaceuticals and Medical Devices Agency (PMDA), *Annual Report FY 2005*.

U.S. and Japanese industry officials assert that a significant portion of the medical device approval delays results from too few and inadequately trained medical device reviewers to handle the increasing number of medical device applications received, and the backlog inherited from the previous system.[94] With a current review staff of 28[95] compared to about 300 at the FDA, and a cap of 35, the staffing level in Japan is well below that in the United States, even when taking into account the relative differences in size of the two economies.[96]

The United States recently recommended that PMDA review staff be doubled to 56 by March 2008.[97] However, Japanese healthcare economists, market analysts, and consultants concur with industry officials that PMDA will be especially challenged in recruiting new staff with requisite experience and expertise in competition with much higher paying major U.S. and Japanese manufacturers who are also actively recruiting such expertise to help them navigate the new regulatory landscape in Japan.[98] To address this and the other challenges PMDA faces in meeting the objectives envisioned by the PAL amendments to deliver more advanced technologies and safer medical devices to the Japanese people more quickly, they believe that PMDA will need to be funded at substantially higher levels than it currently is.[99]

Responding to these criticisms, MHLW and PMDA note that the regulatory reforms appear to be working. PMDA officials state that they have several priority issues that need to be addressed before they can fully achieve the PAL objectives. These include enhancing the timeliness of reviews (including the authorization of 12 certified bodies to review class II medical devices), eliminating the inherited backlog of applications,[100] hiring an additional seven reviewers with non-pharmaceutical specialized training (e.g., bioengineering), relying on team-based reviews to enhance reviewer skills, providing customized consultation services for individual firms, and participating in training and medical device conferences with such groups as the JFMDA, AdvaMed, ACCJ, academics, and policy makers.[101] To help

[94] PMDA still appears to U.S. and foreign industry officials, including Japanese healthcare analysts and economists, to be significantly understaffed. U.S. and Japanese industry officials and healthcare analysts, interviews by Commission staff, United States, June 5–16, 2006, and Japan, July 31–August 9, 2006.

[95] MHLW officials, posthearing statement, 5.

[96] U.S. and Japanese government officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

[97] "USTR Schwab Calls on Japan to Accelerate Economic Reform," 1; and U.S. Department of Commerce, *2006–7 Annual Reform Recommendations,* Annex 15.

[98] U.S. and Japanese industry officials, analysts, and consultants, interviews by Commission staff, Japan, July 31–August 9, 2006.

[99] Ibid.

[100] The United States has recommended that the PMDA application backlog be eliminated by March 2007. U.S. Department of Commerce, *2006–7 Annual Reform Recommendations,* Annex 15.

[101] MHLW, posthearing statement, 6–7; and U.S. and Japanese industry and government officials, interviews by Commission staff, Japan, July 31–August 9, 2006.

ensure that it achieves its goals to make advanced products available to the Japanese public sooner and to reward innovation, PMDA is required to measure and report on progress made against previously agreed upon and published targets. This makes the agency publicly accountable to both Japan's legislators and public, as well as to U.S. industry and government officials in the high-level U.S.-Japan Regulatory Reform meetings.

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APPENDIX A
REQUEST LETTER FROM THE HOUSE COMMITTEE ON WAYS AND MEANS

Congress of the United States

U.S. House of Representatives

COMMITTEE ON WAYS AND MEANS
1102 LONGWORTH HOUSE OFFICE BUILDING
(202) 225-3625
Washington, DC 20515-6348
http://waysandmeans.house.gov

March 7, 2006

received @ ER on 3/9/06
#023

The Honorable Stephen Koplan
Chairman
United States International Trade Commission
500 E Street, S.W.
Washington, D.C. 20436

Dear Chairman Koplan:

On behalf of the Committee on Ways and Means, and under authority of section 332(g) of the Tariff Act of 1930, 19 U.S.C. § 1332(g), I am requesting that the U.S. International Trade Commission institute a fact-finding investigation on competitive conditions affecting U.S. trade of medical devices and equipment in principal foreign markets. A number of important trade issues were raised at the September 28, 2005, hearing held by our Committee on United States-Japan Economic and Trade Relations, including regulatory and reimbursement policies affecting the U.S. medical device and equipment industry in Japan. Members of the Committee have a long-standing interest in this matter as they expressed at the hearing.

In order to gain a greater understanding of these issues, we ask that, in its investigation, the Commission closely examine the regulatory conditions of competition affecting U.S. sales and trade of medical devices and equipment in Japan, and other principal foreign markets, for the most recent five-year period. The investigation should focus on the main U.S. exports of medical devices and equipment to these markets during this period, and compare Japan's regulatory conditions to those of the other major foreign markets for U.S.-made medical devices and equipment. To the extent possible, we ask that the report also include for the most recent five-year period:

- an overview of the global market for medical devices and equipment, including production, consumption, and trade;
- profiles of the medical device and equipment industries in the United States and principal foreign producer countries;
- an analysis of U.S. trade in medical devices and equipment with major competitor

countries, including a description of trade practices, regulatory measures such as product approvals, and government and private expenditures on medical research; and

- an examination of bilateral and multilateral trade agreements that have addressed regulatory issues in major foreign markets, including Japan's, and the implications for the U.S. medical device and equipment industry.

The Committee requests that the Commission transmit its report no later than 12 months following receipt of this request. It is the Committee's intent to make the Commission's report available to the public in its entirety. Therefore, the report should not contain any confidential business or national security confidential information. Thank you for your consideration in this matter.

Best regards,

Bill Thomas
Chairman

APPENDIX B
FEDERAL REGISTER NOTICE

INTERNATIONAL TRADE COMMISSION

[Investigation No. 332–474]

Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets

AGENCY: United States International Trade Commission.

ACTION: Institution of investigation and scheduling of hearing.

EFFECTIVE DATE: April 3, 2006.

SUMMARY: Following receipt on March 9, 2006, of a request from the Committee on Ways and Means of the U.S. House of Representatives (Committee) under section 332(g) of the Tariff Act of 1930 (19 U.S.C. (332(g)), the Commission instituted investigation No. 332–474, Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets.

Background: As requested by the Committee, the Commission will conduct an investigation under section 332(g) and prepare a report assessing competitive conditions affecting U.S. trade of medical devices and equipment in principal foreign markets.

In preparing its report, the Commission will, as requested, closely examine the regulatory conditions of competition affecting U.S. sales and trade of medical devices and equipment in Japan, and other principal foreign markets, for the most recent 5-year period. The Commission will focus on the main U.S. exports of medical devices and equipment to these markets during this period, and compare Japan's regulatory conditions to those of the other major foreign markets for U.S.-made medical devices and equipment. This report will also include, to the extent possible, for the most recent 5-year period: (1) An overview of the global market for medical devices and equipment, including production, consumption, and trade; (2) profiles of the medical device and equipment industries in the United States and principal foreign producer countries; (3) an analysis of U.S. trade in medical devices and equipment with major competitor countries including a description of trade practices, regulatory measures such as product approvals, and government and private expenditures on medical research; and (4) an examination of bilateral and multilateral trade agreements that have addressed regulatory issues in major foreign markets, including Japan's, and the implications for the U.S. medical device and equipment industry.

The Commission will provide its report to the Committee by March 9, 2007.

FOR FURTHER INFORMATION CONTACT: Co-Project Leader, Christopher Johnson (202–205–3488 or *christopher.johnson@usitc.gov*). Co-Project Leader, Heather Sykes (202–205–3436 or *heather.sykes@usitc.gov*). Industry specific information may be obtained from the above persons. For more information on legal aspects of the investigation, contact William Gearhart of the Commission's Office of the General Counsel at 202–205–3091 or *william.gearhart@usitc.gov*. The media should contact Margaret O'Laughlin, Office of External Relations at 202–205–1819 or *margaret.olaughlin@usitc.gov*. Hearing impaired individuals are advised that information on this matter can be obtained by contacting the TDD terminal on 202–205–1810. General information concerning the Commission may also be obtained by accessing its Internet server (*http://www.usitc.gov*). The public record for these investigations may be viewed on the Commission's electronic docket (EDIS–ONLINE) at *http://edis.usitc.gov/hvwebex*.

Public Hearing: A public hearing in connection with this investigation will be held beginning at 9:30 a.m. on July 11, 2006, at the United States International Trade Commission Building, 500 E Street, SW., Washington, DC. All persons have the right to appear by counsel or in person, to present information, and to be heard. Persons wishing to appear at the public hearing should file a letter with the Secretary, United States International Trade Commission, 500 E St., SW., Washington, DC 20436, not later than the close of business (5:15 p.m. e.s.t.) on June 27, 2006, in accordance with the requirements in the ''Submissions'' section below.

Written Submissions: In lieu of or in addition to participating in the hearing, interested parties are invited to submit written statements or briefs concerning this investigation. All written submissions, including requests to appear at the hearing, statements, and briefs, should be addressed to the Secretary, United States International Trade Commission, 500 E Street, SW., Washington, DC 20436. Any prehearing statements or briefs should be filed not later than close of business, June 29, 2006; the deadline for filing posthearing statements or briefs is close of business, July 25, 2006. All written submissions must conform with the provisions of section 201.8 of the Commission's Rules of Practice and Procedure (19 C.F.R. 201.8). Section 201.8 of the rules requires that a signed original (or a copy designated as an original) and fourteen (14) copies of each document be filed.

In the event that confidential treatment of the document is requested, at least four (4) additional copies must be filed, in which the confidential information must be deleted (see the following paragraph for further information regarding confidential business information). The Commission's rules do not authorize filing submissions with the Secretary by facsimile or electronic means, except to the extent permitted by section 201.8 of the rules (see Handbook for Electronic Filing Procedures, *ftp://ftp.usitc.gov/pub/reports/electronic_filing_handbook*.

Any submissions that contain confidential business information must also conform with the requirements of section 201.6 of the Commission's Rules of Practice and Procedure (19 C.F.R. 201.6). Section 201.6 of the rules requires that the cover of the document and the individual pages be clearly marked as to whether they are the ''confidential'' or ''nonconfidential'' version, and that the confidential business information be clearly identified by means of brackets. All written submissions, except for confidential business information, will be made available in the Office of the Secretary to the Commission for inspection by interested parties.

In its request letter, the Committee stated that it intends to make the Commission's report available to the public in its entirety, and asked that the Commission not include any confidential business or national security confidential information in the report it sends to the Committee. The report that the Commission sends to the Committee will not contain any such information. Any confidential business information received by the Commission in this investigation and used in preparing the report will not be published in a manner that would reveal the operations of the firm supplying the information.

Persons with mobility impairments who will need special assistance in gaining access to the Commission should contact the Secretary at 202–205–2000.

By order of the Commission.

Issued: April 3, 2006.

Marilyn R. Abbott,

Secretary to the Commission.

[FR Doc. E6–5021 Filed 4–5–06; 8:45 am]

BILLING CODE 7020–02–P

APPENDIX C
CALENDAR OF PUBLIC HEARING

CALENDAR OF PUBLIC HEARING

Those listed below appeared as witnesses at the United States International Trade Commission's hearing:

Subject: Medical Devices and Equipment: Competitive Conditions Affecting U.S. Trade in Japan and Other Principal Foreign Markets

Inv. No.: 332-474

Date and Time: July 11, 2006 - 9:30 a.m.

Sessions were held in connection with this investigation in the Main Hearing Room (room 101), 500 E Street, S.W., Washington, D.C.

ORGANIZATION AND WITNESS:

Advanced Medical Technology Association ("AdvaMed")
Washington, D.C.

Edward J. Ludwig, Chairman of the Board, AdvaMed;
and Chairman of the Board, President, and CEO,
Becton Dickinson (a member of AdvaMed)

Philip R. Agress, Vice President, Global Strategy and Analysis, AdvaMed

Pharmanet Inc.
Washington, D.C.

Joyce L. Frey-Vasconcells, Executive Director,
Pharmanet Inc.

-END-

APPENDIX D
GLOSSARY

GLOSSARY

Angioplasty - procedure to treat damaged or diseased arteries (or coronary artery disease) in which a catheter with an inflatable tip is inserted into an artery, guided to the site of the disease, inflated to redistribute plaque, deflated, and removed.

Adverse event - a negative event experienced by a patient attributable to medical devices or drugs.

Ambulatory surgical center - a place performing outpatient surgery where patient stay is limited to a few hours or one night.

Biologic - a preparation, such as a drug or vaccine, derived from living organisms or their products and used to diagnose, prevent, or treat disease.

Biophenomena - vital signs such as blood pressure, respiratory rate, and temperature.

Bio-research - the investigation of the nature of living organisms.

Cardiac rhythm devices - devices used to treat cardiac rhythm disorders, including cardiac pacemakers, implantable cardioverter defibrillators, and antiarrhythmic agents (drugs).

Cardiovascular catheter - small tubing system with an attached deflated balloon used in angioplasty procedures (related terms: angioplasty catheters, balloon catheters, PCTA (percutaneous transluminal coronary angioplasty), catheters).

Cash flow model - a method for financial evaluation of long-term, R&D-intensive projects; term is used (secondarily) in this report to indicate the economic benefits of reduced regulatory delays in product approval.

Catheter - a small tubing system used to conduct the flow of bodily fluids such as blood and urine.

Competent authority - EU member state health authorities responsible for national level compliance of medical device directives in connection with the EU regulatory approval system and appointment of notified bodies.

Computerized tomography (CT) - type of diagnostic imaging procedure using X-rays enhanced by a computer to generate cross-sectional images of body tissue (related terms: CAT (computerized axial tomography) scanner, CT (computerized tomography) device).

Conformite Europeene mark (CE mark) - an insignia granted by EU member states to indicate conformity to European safety standards, thus allowing marketing on the EU market.

Conformity assessment - the technical term given to the process of medical device evaluation and approval.

Contract research organization (CRO) - in the context of the medical device industry, an organization that contracts with medical device firms to provide a variety of services, including administration of clinical trials, preparation of regulatory materials, etc.

Controlled device - in Japan, class II medical device products posing moderate risk to patients, usually requiring third-party certification.

Coronary - pertaining to the arteries that channel blood to the heart.

Curette - a spoon-shaped surgical instrument used to remove tissue from body cavities or clean diseased surfaces.

Defibrillator - an external paddle device used on the chest to shock the heart out of filibration (ineffective pumping) and bring it back to its normal routine. Also, see implantable cardiac defibrillator.

Derivative devices - medical devices substantially similar to ones already on the market, often referred to as precedent or "me-too" devices.

Diagnostic imaging - various methods, including X-ray, CT, MRI, or ultrasound, used to create images of the body or parts thereof to diagnose disease.

Diagnosis-related groups (DRGs) - a type of hospital procedure classification system developed by U.S. Medicare and Medicaid program, and now increasingly used in other major foreign markets, that is used to determine healthcare insurance reimbursement rates related to severity of the diagnosis.

Dialysis - a treatment to remove harmful materials from blood that has been contaminated due to kidney failure.

Dialyzer - a semipermeable membrane used in dialysis through which small molecules can pass by diffusion and be removed from the body.

Drug-eluting stent (DES) - a tiny, hollow metal or plastic tube inserted into an artery or blood vessel to restore blood flow, which is coated with a drug to preventing scarring of the arterial tissue (related terms: bare-metal stent, stent).

Electrocardiograph - a machine used to generate electrocardiograms (a continuous graph that depicts the electrical voltage in the heart) often used to diagnose cardiovascular diseases.

Electromedical equipment - electronic medical devices, such as diagnostic imaging devices (X-ray, MRI, CT), cardiac pacemakers, and medical lasers.

Electrosurgical device - electronic medical devices for surgical purposes, such as cutting or vaporizing.

Endoscope - a telescope or tube passed through a natural orifice or small skin incision used to directly visualize a diseased area inside the body.

Essential requirements - EU requirements, or technical regulations, that medical device manufacturers are responsible for meeting and documenting. The term is found in several European Council directives for different types of medical devices, including the medical device directive (MDD), the active implantable medical devices directive (AIMDD), and the in vitro diagnostics directive (IVDD).

Gainsharing - incentive-based compensation that ties wages to increased productivity rather than profit increases.

Good manufacturing practices (GMP) - FDA requirements outlining that manufacturers must have a quality system for the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices intended for commercial distribution in the United States.

Group purchasing organization (GPO) - a group of organizations (such as hospitals) that collectively purchases medical devices to obtain discounts from vendors based on the their buying power.

Health technologies assessment - assessments to measure the impact of a new healthcare technology on citizens, patients, and healthcare organizations (measurement of impact generally includes safety, cost, efficacy, effectiveness and efficiency of a new technology, and the social, legal, and ethical consequences of its introduction).

Implantable cardiac defibrillators (ICDs) - small pacemaker-like devices implanted beneath the skin that monitor heart rhythm and correct abnormal heart beats by sending an electrical shock to the heart (related terms: cardiovascular implantable defibrillators).

Implantable pacemakers - miniature electronic devices that provide electrical stimulation of the heart muscle to regulate contractions of the heart muscle, implanted beneath the skin.

In vitro diagnostics (IVDs) - literally "in glass" diagnostics or tests of bodily substances such as blood, urine, and tissues used to detect, diagnose, or monitor disease.

In vivo diagnostics - tests performed on or in a body often using diagnostic imaging techniques.

Informatics - the sciences concerned with gathering, manipulating, storing, retrieving, and classifying recorded information.

Intrauterine devices - widely used form of reversible contraception where the uterine lining is altered such that it becomes unfavorable for sperm implantation.

Lithotripter - an electromedical technology used for disintegrating kidney stones.

Magnetic resonance imaging (MRI) - type of diagnostic imaging procedure using radio waves and short bursts of a powerful magnetic field to provide cross-sectional images of any portion of the body.

Medicaid - a U.S. program providing medical care for low-income patients that is jointly funded by federal and state governments.

Medical device - instruments, tools, machines, implants, diagnostic tests, or software systems used to diagnose, treat, monitor, or prevent diseases and other medical conditions.

Medical Device Directive (MDD) - EU document containing rules and requirements that need to be met for placing medical devices on the market.

Medical imaging diagnostics - expensive systems used to detect, diagnose, and monitor diseases that cannot be characterized by in vitro diagnostics (related terms: imaging devices, diagnostic imaging, diagnostic imaging instruments).

Mutual Recognition Agreement (MRA) - agreement between national governments serving as a vehicle for regulatory cooperation, which may be based on harmonization, equivalence, or external criteria such as the host country's standards or other mutually agreed standards, or international standards. (In an MRA, two or more governments agree to recognize and accept all, or selected aspects, or test to each other's regulations because they are harmonized or judged to be equivalent, or because they satisfy other agreed-upon external criteria).

Nanotechnology - technology development at the atomic, molecular, or macromolecular range of approximately 1-100 nanometers to create and use structures, devices, and systems that have novel properties (1 nanometer = 1^{-9} meters).

Neurostimulation - medical treatment for people suffering from chronic pain that uses an implanted device to deliver small doses of drugs or low levels of electricity directly to nerve fibers.

Notified bodies (NBs) - standards, certification, and testing bodies designated by EU member state health authorities for regulatory review of medical devices.

Orthopedic devices - medical devices such as crutches; splints; and hip, knee, and spinal implants used to compensate for a defect or disability of the body.

Pacemaker - see implantable pacemaker.

Patient monitoring - eletromedical devices and systems used to monitor critical bodily functions, such as temperature, blood pressure, and pulse.

Positron emission tomography (PET) - type of diagnostic imaging procedure using small amounts of radioactive substances to produce images of activities in the body.

Postmarket surveillance - government or manufacturer established system to ensure that feedback from the marketplace provides early warning of medical device quality problems.

Premarket approval (PMA) - type of application submitted to FDA for marketing approval of new class III medical devices.

Premarket notification, 501(k) - type of application submitted by a manufacturer to notify the FDA of intent to produce a medical device substantially equivalent to one already on the market.

Prosthetic - a device, either external or implanted, that substitutes for or supplements a missing or defective part of the body (artificial limbs, breast implants).

Reagent - a substance used in in vitro diagnostics that reacts chemically to detect, measure, examine, or produce other substances for purposes of analysis and diagnosis.

Restenosis - scarring and reblocking of the arterial tissue that occurs in some patients who have had stents implanted in their arteries or other blood vessels to treat coronary artery disease.

Snare - a surgical instrument with a wire noose used to remove tumors and polyps.

Stent - tiny, hollow tubes permanently inserted into clogged arteries to restore blood flow (related terms: bare-metal stent, drug-eluting stent).

Stethoscope - a device with a small bell-shaped end piece coupled to a flexible tube that splits to feed two earpieces used by physicians to amplify the sound of and listen to the heartbeat.

Ultrasound - the use of ultrasonic waves for diagnostic or therapeutic purposes, specifically to visualize an internal body structure, monitor a developing fetus, or generate localized deep heat to the tissues.

Ultraviolet apparatus - electromedical devices using LEDs, fluorescent lamps, dichroic lamps, or very bright, full-spectrum light for a prescribed amount of time to treat skins diseases such as psoriasis, acne, and other medical disorders.

User fees - application and other fees paid to regulatory agencies to help cover the costs of the review and approval of medical devices.