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Access to the European Common Market for Medical Devices: A Regulatory Approach

Industry, Science and Technology Canada
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ANNEXES

1.0 EXECUTIVE SUMMARY

Our approach in this work has been to consider the market and the regulatory position of the major countries in the European Community. We have included Sweden due to its long history of socio-economic approach to the needs of its population.

Europe is undoubtedly in a state of flux as the "community" develops. Nevertheless from a trading aspect a North American exporter can anticipate dealing with the regulations inherent to each country for several years. The medical device directives are not totally resolved, and individual country regulations on certain products such as in-vitro diagnostics may continue to be applicable well into the late 1990's.

This work has been written therefore with the individual country and its specific requirements in mind. We must reinforce the need, now and for several years to come, to be cognizant of the local regulatory issues when considering trade in Europe.

A section has also been devoted to the developing EC regulatory format: the medical device directives, the horizontal and vertical standard structure and the quality systems evolving from the ISO 9000 international standards for quality management.

We are particularly in debt to the experts of Biometric Research Institute for their in-depth reporting of local requirements and idiosyncrasies of the various countries included in this study.

Table 1

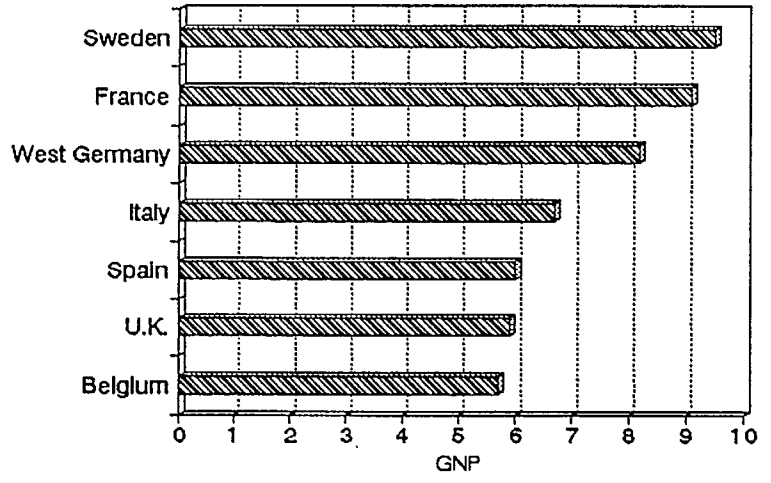
Major Health Care Markets in Europe

	West Germany	France	UK	Spain	Italy
Population (1985)	61M	55M	56.5M	39.2M	57.6M
GDP per capita (1984) in U.S. dollars	$13,265	$12,643	$11,068	$7,240	$12,955
% of GDP spent on health care (1984)	8.1%	9.1%	5.9%	6.0% (1985)	6.7% (1984/85)
Hospital beds per 000 population (1985/86)	11	10.5	7.4	4.6	8.3
Doctors per 000 population (1985/86)	2.7	2.4	1.4	3.3	4.0

Sources: Financing and Health Care, OECD WMI Publications Ltd. "Medical Market in the EEC", The 1990 Almanac, Houghton Mifflin Company, 1990, 1987 Census, (1985) (1986)

Spending on health care in the EC countries varies from 5.9% (United Kingdom) to 9.5% (Sweden) of the Gross Domestic Product (GDP) (See Table 2 on the following page). Further, although the EC governments are attempting to control rising health care costs, the aging population (15% of Germany's population is over 60 years of age) and users' rising health care expectations (the mandate to upgrade southern Italy's medical system and facilities up to northern Italy's standards) are cited as some of the factors that will maintain total EC health care expenditures at current or somewhat higher rates.

Table 2
Percent of Gross Domestic Product Spent on Health Care by EC Country



Source: Arthur D. Little. Medical Devices Sector Initiative. Feb. 28, 1991. p.

The indigenous European medical device manufacturing industry is substantial. For example, West Germany has the largest and most diversified medical devices industry in Europe with an annual production of approximately $2.2 billion (Cdn). Despite the EC's substantial internal manufacturing capacities, it has a significant import market as well. For example, the German, French and Swedish import markets stand at $2.2 (Cdn), $1.9 (Cdn) and $.6 billion (Cdn) dollars respectively. These figures represent approximately 45%, 51%, and 80% of their total medical device market demand (See Table 3 and Table 4 on page 5).

Recent political and regulatory events have further enhanced the European market's import potential. The EC 1993 preparations have introduced a certain flux - a "wait and see" in the domestic market; "Glasnost" paved the way for the reunification of Germany and subsequent access to Central Europe.

Table 3

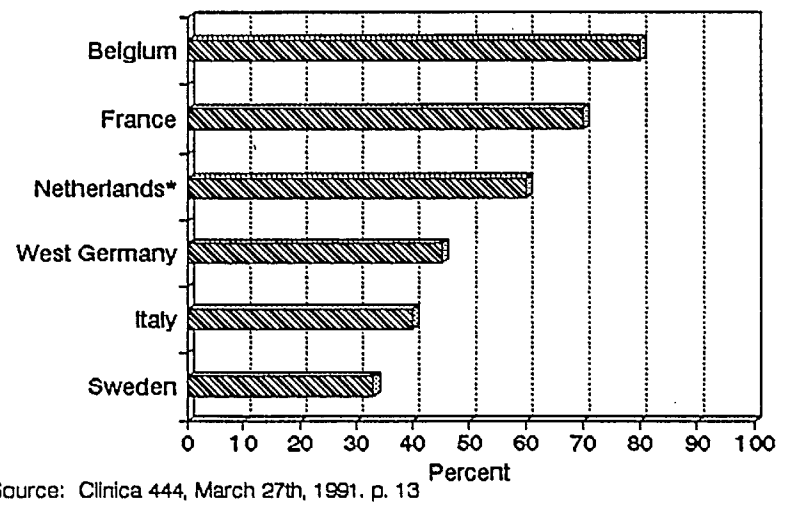
Largest EC Medical Devices Import Markets

EC Country	Canadian Dollars	Statistical Year
West Germany	2.2 billion	1984
France	1.9 billion	1984
United Kingdom	1.4 billion	1988
Sweden	590 million	1987
Netherlands*	122.4 million	1989

Source: Arthur D. Little, Medical Devices Sector Initiatives, Strategic Analysis and Options for the Medical Device Industry. Feb. 28, 1991.

*Source: Clinica 444, March 27th, 1991. p. 13

Table 4
Percent of Medical Devices Market
Served by Imports by EC Country



*Source: Clinica 444, March 27th, 1991. p. 13
Source: Clinica 456, June 26th, 1991. p. 12
Source: Arthur D. Little, Medical Devices Sector Initiative. Feb. 28, 1991. p.

The preceding discussion suggests that the European Community (as represented by the United Kingdom, Germany, France, Spain, Italy, the Benelux Countries, and Sweden) is a tempting market for the Canadian medical device industry.

2.2 European Community Market Access Controls

The EC countries, as all countries throughout the world, attempt to control foreign access to their markets to protect their consumers and their domestic manufacturers. The mechanisms to control access are many, and tend to vary substantially from country to country. Essentially, they may be grouped into three categories, Standards and Regulations, Product (National) Controls, and Legal Requirements.

2.2.1 Standards and Regulations

As stated, market access controls vary substantially by geographic location. For example, Canada has a legislated regulatory system for medical devices which tends to address primarily the efficacy and safety of the products. Devices are evaluated and placed into one of three "degree of risk to consumer" categories, and can be introduced into the market by various means ranging from a simple notification, to pre-market reviews (pre-market approval), to clinical trials.

Although a limited number of mandatory product class performance standards do exist in regulation, individual product assessment is the predominant regulatory mode. This allows for rapid adaptation to changing technology, and supports industry innovation. To date voluntary standards have been very effective, and participation by all agencies is encouraged in both domestic and international standardization efforts.

In Europe, each country has its own government department which controls access to markets for medical devices. Consequently, the European regulatory systems tend to be very complex with mandatory standards and regulations. For example, over 2000 mandatory design specification standards have been delineated and third party testing and type testing of completed products tend to be the preferred regulatory modes. The extension of European access control mechanisms to manufacturing practices has tended to protect the domestic medical device industry.

The complexity of the European regulatory system is compounded by the broad variations in mandatory requirements between countries. Some countries have a strong regulatory tradition - substantial testing, certification or registration, pre-market approval, and so forth. For example, West Germany is regarded as the most stringent, because of the multiplicity of regulatory schemes and the complicated manner in which control of compliance is organized. Other countries are rather flexible in what they will accept as reasonable compliance to their standards and regulations for import purposes. For example, the United Kingdom has relatively few market access controls (See Table 5 below).

Table 5

Pre-market Approval Criteria

	Belgium	France	Germany	Holland	Italy	Spain	UK
Product Registration	X	1	2	3	X	X	5
Local Product Testing	X	X	X		X	X	X
Manufacturer Registration	X	X	X	X	X	X	X
GMP Inspection	X	X	X	X	X		X
Labelling	X	X	X	X	X	X	X
National Standards	X	X	X		X	4	X
National Pharmacopoeia	X	X	X		X		
Registration of Distributor	X	X	X			X	
Pharmacist at Distributor	X	X				X	
Other Import Controls			X			X	

1 Certain electromedical and orthopaedic
2 Haemodialysis and Hemofilters
3 Notification plus dossier available
4 Syringes
5 Limited, voluntary product approval
X Required

As Table 5 indicates, various European countries tend to utilize multiple standards. This approach has stimulated the development of standards, which in turn has resulted in substantial government and industrial funding for the establishment and support of standards bodies. The largest of these bodies is the German Institute for Standardization (DIN), which has published over 1000 health care standards.

In response to the proliferation of the multiple standards, manufacturers demand of each other that evidence of compliance with the standards be provided by independent product testing houses, and that such compliance be identified with a "mark" that is recognized by a legislated regulatory body. (Compliance "marks" are legislated to prevent unfair marketing competition.)

Presently access to the European Common Market can only be achieved by satisfying the medical device standards and certification system requirements of each country for which the product is destined.

2.2.2 National (Product) Controls

It is maintained that the primary objective of national controls is to protect public health by ensuring the safety and quality of devices used in medical treatment. However, in practice, many national product control requirements constitute technical barriers to free trade. An example of this is product risk classification. In many cases there is a conspicuous imbalance in the relationship between the level of control imposed and the nature of the risk presented by the product.

As with Standards and Regulations, National Product Controls also vary by country (See Table 6 on the following page).

Table 6

Regulatory Access Controls by Country and Products

Products	Controls
Belgium	
All sterile devices (and, in future, implants)	Pre-market approval: Local testing of imported product
France	
Sterile devices	Local testing for sterility
Orthopaedic prostheses, haemodialysers, haemofilters, plasma filters	Homologation (pre-market approval scheme) Laboratory and clinical testing in France
Germany	
Sterile single use instruments; dressings and sutures; products introduced into the body.	No registration (except for some implants) but some retesting of imported product.
Holland	
Sterile devices	Notification and product dossier available for inspection; but no pre-market approval.
Italy	
Listed devices	Pre-market approval per product type.
Spain	
Dressings, bandages, sutures Implants Single use sterile devices and instruments	Product registration and testing of imported product.
UK	
Blood and solution sets, surgical gloves, syringes and needles.	"Voluntary" product approval.

Source: Article by M. Reinikainen, Pfizer, UK, M.D.D.I., 2/90

Present national controls comprise the following:

1. With the exception of Ireland and Luxembourg, all EC countries apply specific controls to medical devices.

2. Controls typically involve product approval, the application of labelling requirements, approval of manufacturing premises, and compliance with standards.

3. Most EC countries have, or are considering the introduction of, a system of Good Manufacturing Practices (GMP) for device manufacturers. However, with the exception of the UK, present controls are principally aimed at the product (registration system) rather than the manufacturing facility (GMP inspection).

4. It is common (Belgium, France, Spain and, in future, Germany) for imported products to be subjected to testing prior to release for sale, regardless of what tests were applied by the manufacturer, and whether or not the products originated in the EC.

5. Not infrequently (particularly in Belgium and France) an industrial pharmacist must, in practical reality, be engaged by the distributor to deal with testing of imported products.

There is no reciprocity between EC countries with regard to product registration, product testing or inspection and approval of manufacturing premises. However, most countries recognize the value of GMPs as a basis for device control, and many countries are now enforcing GMP for device manufacturers.

2.2.3 Legal Requirements

There are general legal requirements that may apply (do apply in major countries) to manufactured or imported medical devices. For example:

- Unsafe products are prohibited.

- Misleading information is prohibited.

- A legally responsible resident agent may be required, and may need to be identified on the package.

- Components and containers may have various regulatory compliance requirements.

- Radioactive or irradiated products may be prohibited or may require special authorization.

- Authority notification may be required prior to the commencement of certain activities such as: manufacturing, warehousing, and selling of medical devices.

- Clinical trials having certain key criteria may require authority notification.

- Product trials in market settings may not require authority notification.

- Medical devices to be imported may require an import certificate. The usual criteria for certificate acquisition is proof of GMP compliance. This is obtained from recognized authorities in the country of manufacture.

- Language labelling requirements vary. The acceptability of local, bi-, or multi-lingual labelling depends on location. Label particulars to be considered for language labelling include:

    - Name of company
    - Product
    - Lot number
    - Volume or quantity of contents
    - Expiry date
    - Sample
    - Clinical trial
    - Contra-indications
    - Interactions

2.2.4 The Compliance Process

Prior to committing to product introduction in any European country, it is wise to develop a plan of regulatory action. In that the "compliance process" time factor is frequently unpredictable, such a plan may avoid embarrassment due to missed launch dates or financial losses due to compliance-required product modifications.

In developing such a plan one should consider:

- What is the impact of local regulations on the product?:
  - Implant
  - Electro-medical
  - In-vitro
  - Single use instrument
- Who will you need to deal with?
  - Importer
  - A local agent is essential
  - Local authorities versus federal departments
  - Testing houses experienced in medical devices
- What are the language requirements?
  - Applications must be made in the local language
  - Product labelling will require translation
- Will your product require pre-market approval?
  - Products such a biological implants
  - Electromedical implants
  - Radiation sterilized devices require extensive pre-market submissions and authorization
- How will you maintain regulatory compliance?
  - Good Manufacturing Process (GMP)
  - Other quality control system

2.2.5 EC Developments

The future regulatory schemes of the EC for medical devices will be composed of the following:

➢ Directives which specify the essential requirements.

- Harmonized European technical standards which amplify what the essential requirements mean in practice.

- A system of conformity assessment and certification which governs how regulatory compliance will be controlled.

Achievement of a CE mark will allow a manufacturer to sell a product throughout the European Community. This mark is achieved by some combination of manufacturers' self certification, third party audit of a manufacturer's quality system, third party approval of a product dossier and third party testing of a product. The third party intervention is needed only by one member state in order to obtain a CE mark.

In the field of medical devices, four European directives have been proposed.

Active implantable medical devices received formal adoption by the European council during 1990 and will be implemented on January 1, 1993. The active medical device and non-active medical devices directive apparently will be combined into one with three classes of device. This is still the draft stage.

In-vitro diagnostics directives are still in the discussion stage.

2.3 Summary

In response to world economic and political events, the EC countries have been compelled to focus on their domestic mechanisms for survival in the world market. One outcome of the internal scrutiny is the movement towards a "single market" concept. Implementation of the "single market" concept requires harmonizing of the national standards, and evaluation and reconciliation of differences between various government based medical device approval systems.

The large market represented by the European countries is tempting, but not easy to access. Each country has its own complex regulatory systems. These systems will change as the EC formalizes. However, in the mean time, the novice exporter must be aware of both the export target country's current regulatory system and the impending changes to that regulatory system, in order to assure successful export activities and prevent costly mistakes.

3.0 THE UNITED KINGDOM

3.1 Health Care in the United Kingdom

The public National Health Service (NHS) is over 45 years old, and provides 95% of health care services in the UK. It is made up of the health services of England, Scotland, Wales and Northern Ireland, which are organized on broadly similar lines (See Table 7 on the following page). It is funded through general taxation, insurance contributions from employers and employees, and minimal personal charges. Health spending in the UK is approximately 5.7% of the Gross Domestic Product. This will increase in that the NHS has been allocated an additional £2,700 million in cash funding for the coming year (1992-93) (Clinica #477, Nov. 20, 91, p. 15).

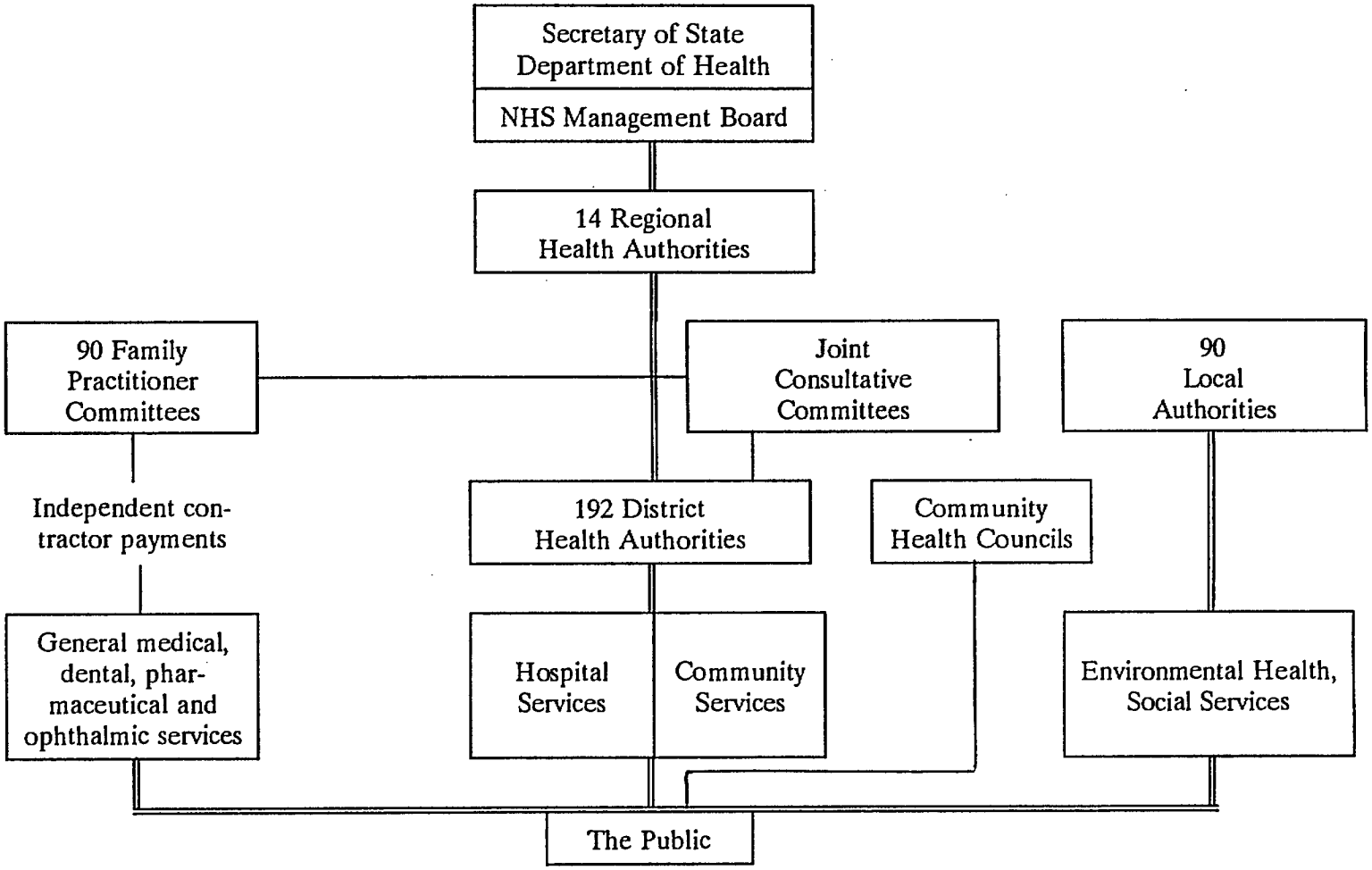
Private health care programs also exist and have been growing. They have increased from 2.0% of the population in the 70's to 6.0% in 1990.

The National Health Service is currently under review as a result of decreasing health care budgets and competition in the health care industry. Proposals have been made:

- To radically alter the structure of hospitals and health care provision so as to impose a free market orientation, and to promote effective and efficient utilization of resources.
- To establish a new NHS supplies authority which will be the central purchasing office.
- To introduce income generating schemes, for example, using hospital stores as a central distribution point.
- To permit physicians to manage their patients and resources under a global budget concept.
- To lower the purchasing decision-making process to the District level.
- The latest restructuring development according to Clinica (#480, Dec., 11, 91, p. 11) is the setting up of a National Supply Authority which will supersede the Procurement Directorate by March 1992, which will have complete managerial responsibility for procurement in the NHS. The new body will incorporate the functions of the existing "Centres of Responsibility". This is established to eliminate the discrepancies in contract requirements between Regional Supply Organizations.

Table 7

The Organization of Health and Social Services in England



Source: G. Higson and A. Howard of Medical Technology Consultants Europe Ltd. Medical Device Approvals in Europe Today - United Kingdom. BRI/MTCE, 1990.

Currently the NHS is highly structured. The structure varies according to geographic location and the existing facilities and bureaucratic bodies. For example, the health care service may consist of a hospital with several clinics or may consist of District and Regional Authorities with a group of hospitals which are associated with a medical school. At present physicians are contracted by NHS and are paid according to the number of patients registered to them.

3.2 Trends in Health Care

The major factors that drive health care trends in the UK appear to be:

- Medical cost curtailment
- Social changes
- Demographics
- Technology

A scan of the 1990 and 1991 issues of Clinica, a UK-based medical devices and diagnostics weekly publication, suggests a number of emerging health trends. Some examples are as follows:

Trends resulting from the UK's government medical cost curtailment efforts:

- Focus on preventative medicine:
  - The Department of Health is circulating a booklet to all households recommending preventative "life-style check-ups for all adults on registering with a GP, or those who have not consulted a GP for quite some time" (Clinica 412, Aug. 1, 1990, p. 9).
  - Target of 30% reduction in number of deaths due to coronary heart disease in those below age 65 by the year 2000 (Clinica 455, June 19, 91, p.10) (coronary heart disease claimed 140,509 deaths in England in 1989 [26% of the total], and takes up 5,000 NHS beds daily [Clinica 455, June 19, 91, p. 10]).
  - Target of 25% reduction in number of deaths due to breast cancer (Clinica 455, June 19, 91, p. 10).
  - NHS invited all women between 20 and 64 years to be screened for cervical cancer, and all women between 50 and 64 years for mammographic screening by March 1993 (Clinica 412, Aug. 1, 1990, p. 9).

- Focus on "day surgery", outpatient, and home care:

  - Demand for instruments which reduce body trauma, hence hospital stay, i.e., instruments to perform laparoscopic cholecystectomies (Clinica 439, Feb. 20, 91, p. 9).

  - Outpatient surveillance of antenatal gynaecology patients.

  - Home care ranging from pregnancy test kits to treatments such as oxygen therapies, haemodialysis, peritoneal dialysis, and various monitoring such as neonate apnoea to enuresis.

Trends resulting from changes in social values and behaviour, and institutions:

- The spread of the AIDS virus has significantly impacted the medical device and diagnostics industry resulting in products ranging from diagnostic tests to single-use needles to "protective suits designed for such purposes (airborne transmission of HIV virus during bone drilling) with a remote air supply" (Clinica 416, Aug. 29, 90, p. 8).

- Personal affluence, social mobility, and women's career independence are creating a demand for home care for the long and short term disabled, terminally ill, and the elderly.

- "Cross-border-shopping", a $400 million high-technology international medical complex to be built in Scotland for patients who do not have access to highly technical tertiary care in their countries (Clinica 466, Sept. 4, 91, p.9)

- Scottish heart transplant centre for 1991-92, capacity of 50 transplants per year (Clinica 455, June 19, 91, p. 10).

Trends resulting from changing demographic statistics:

Fifteen percent of UK's population is over the age of 65, and as a group, are the largest consumers of direct and indirect health care products and services. In light of finite resources and government-backed health care cost reductions, this group has become targeted for home health care. (Clinica 432, Dec. 11, 90, 9. 8-12).

- Approximately 60,000 hip replacements take place each year.

- Some age group specific products and services for the home

  - Remote patient monitoring
  - Data recording and monitoring at-risk patients
  - Medical devices, mobility aids, nutritional support
  - Continence care

- Funding to come for an additional 750 defibrillators for ambulances in England (Clinica 413, Aug. 8, 90, p. 12).

Trends due to changing technology:

- A computer system for Glasgow will increase the number of cancer patients that can be treated each day by radiotherapy staff (Clinica 464, Aug. 21, 91, p. 14).

- UK government to provide funds for software development for computerization of GP surgeries (Clinica 416, Aug. 29, 90, p. 9).

- UK primary care practices indicate need for modem link-up to facilitate communication with health service authorities, hospitals and drug information services - although 80% of survey respondents indicated that they will be computerized by 1992, at present only 9% of practices possess modem links (Clinica 461, July 31, 91, p. 14).

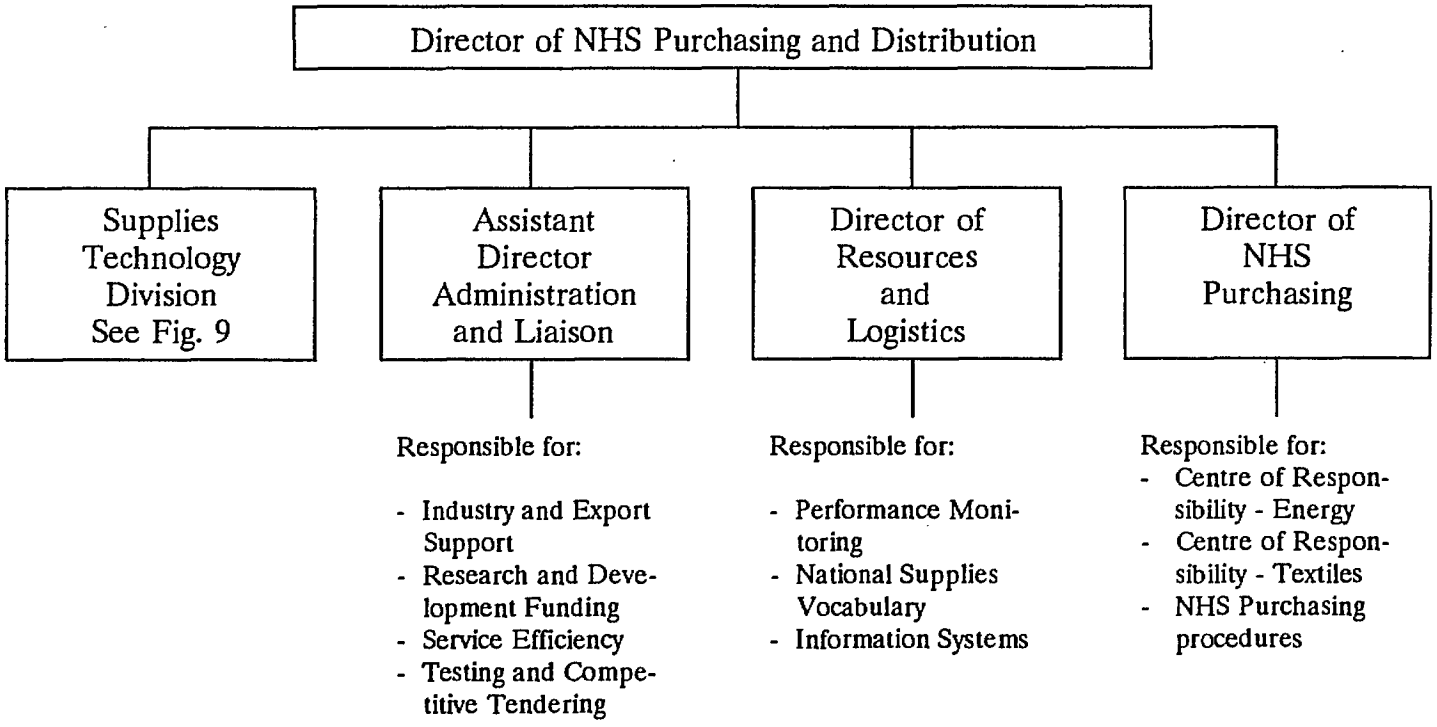
3.3 Regulatory Framework

3.3.1 Regulatory Bodies

Medical device regulation in the UK is unique in that the product and manufacturing process are both controlled, not through legislation, but through the Department of Health Procurement Directorate's buying power (DHPD) (See Table 8 and 9). The DHPD procurement mandate is executed on the basis of a "guarantee of safety principal" which essentially states: the safety of medical devices must be described in published standards, and, the NHS should only buy products which comply with these standards.

Table 8

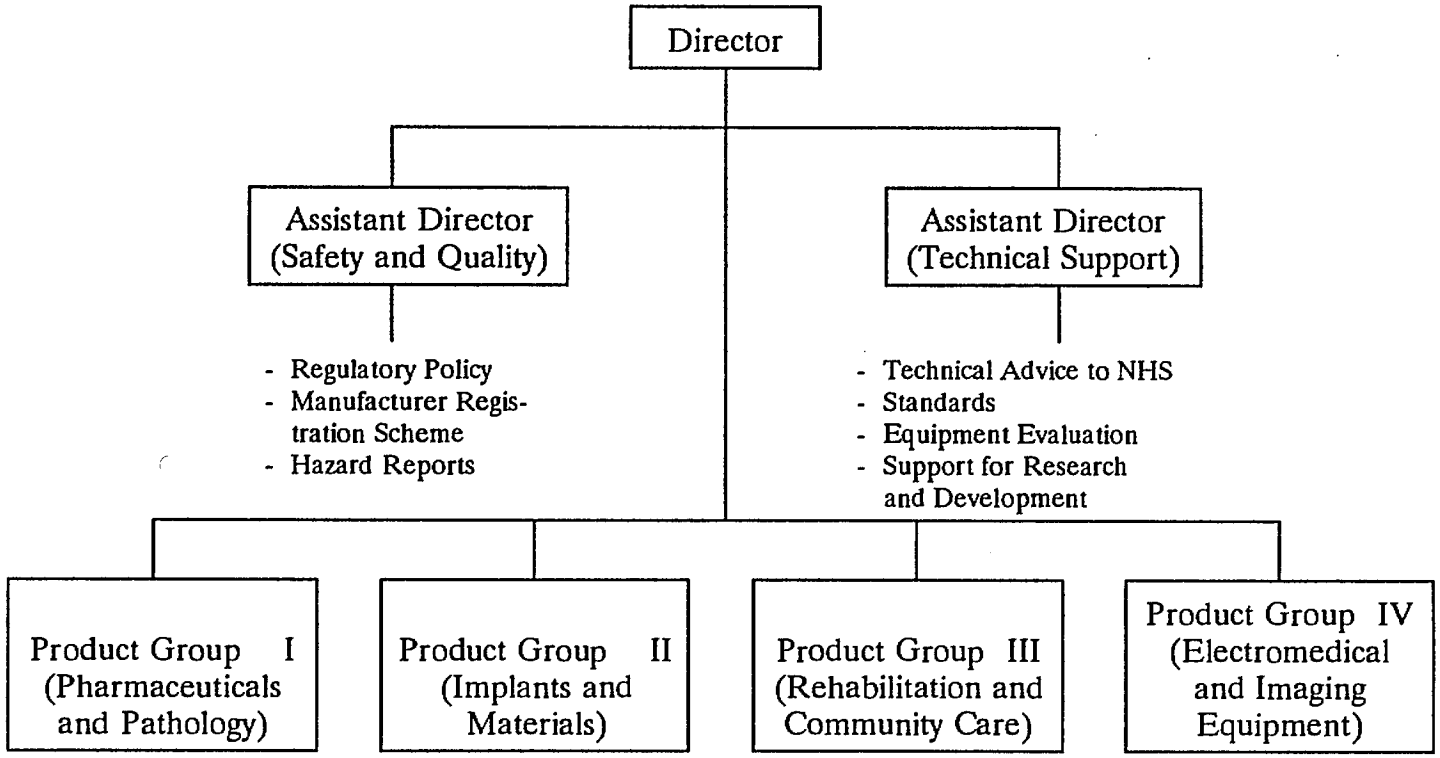
Department of Health - Procurement Directorate



Source: G. Higson and A. Howard of Medical Technology Consultants Europe Ltd. Medical Device Approvals in Europe Today - United Kingdom. BRI/MTCE, 1990.

Table 9

Department of Health - Supplies Technology Division



Source: G. Higson and A. Howard of Medical Technology Consultants Europe Ltd. Medical Device Approvals in Europe Today - United Kingdom. BRI/MTCE, 1990.

Device safety is regulated primarily in two ways, via manufacturing standards, and via medical device standards. Manufacturing standards are described by the Good Manufacturing Practices (GMP) Guides. Each product category has its own colour coded "guide". The guides have been developed from the World Health Organization (WHO) guidelines or the British Standards Institution (BSI) standards, and now approach the ISO 9000 Quality Systems standards. Medical device standards are developed by the BSI.

Medical device manufacturers who have demonstrated compliance with GMP and BSI standards are listed on a Manufacturers Register. The DHPD instructs all purchasing officers to buy only from manufacturers who are listed on said register. (Although this is not legislated, it is "strongly suggested".) The Supplies Technology division of the DHPD acts as the technical and commercial advisor to NHS, maintains the Manufacturers Register, and audits against it.

3.3.2 Regulations

In addition to the GMP and BSI standards, there are a number of other lists/acts/laws that affect medical devices.

1. Health Services Supplies Purchasing Guide - blood and solution administration sets, surgeons gloves, hypodermic needles and syringes

2. Good Practices in the Manufacture and Quality Control of Dental Materials - dental materials

3. Sale of Optical Appliances Order in Council 1984 - specifications for lenses, lens material, frame material

4. The Medicine Act - regulation of any material which is believed to be capable of being absorbed by the body tissue or body fluids comes under this act. (Under this Act anaesthetic gases and sutures require an appropriate license.)

5. BS 5724 and the Electrical Safety Codes - outline requirements for electromedical equipment

   The MLQ2 - a questionnaire to be completed by the manufacturer regarding electromedical equipment and laboratory equipment

   Trade Descriptions Act - labelling re: compliance of electromedical equipment.

6. The TRS 89 (Technical Requirements for the Supply and Installation of Apparatus for Diagnostic Imaging and Radiotherapy - technical conditions for X-ray equipment).

7. British Pharmacopoeia - technical requirements for bandages, dressings, catheters, support hosiery and garments, stoma appliances, etc.

8. Consumer Protection Act - liability for damages.

9. Health and Safety - various laws and regulations directed towards hazardous substances in the workplace.

10. Low voltage electrical equipment is design controlled by safety regulations developed in 1989, requiring construction in accordance with good engineering practice.

In-vitro diagnostics are not controlled.

DOH requires reporting of device defects, and investigations are frequent. A hazard notice issued to NHS can be very serious for a manufacturer.

3.3.3 Standards Bodies

The British Standards Institution has a strong, respected position. It is a member of ISO and IEC and much of the Technical Committee's work is international. The new European standards bodies, CEN and CENELEC are assuming great importance - thus BSI participation in their technical committees is of primary importance.

Approximately seventy technical committees are involved in writing standards in some nineteen categories of medical devices. These are industry standards. Future standards will be written so that they could be used for legislative purposes.

Consistent compliance with BSI standards can result in the awarding of the "Kite" mark, which is a consumer indicator of product safety and specific manufacturing conditions (the manufacturing process consistently produces a product under quality controlled conditions). BSI also awards the Safety mark, which denotes product compliance with particular safety aspects of the relevant product standards.

Testing laboratories for third party testing are available for a variety of products. BSI has established mutual agreements for testing with several testing bodies in other major European countries.

DOH has in recent years included on its audit teams a member from BSI. This move has recently extended to the use of private sector organizations such as BSI, Lloyds, and Bureau Veritas to carry out intermediate surveillance inspections of manufacturing facilities.

In 1986, DOH and the U.S. Food and Drug Administration agreed, by Memorandum of Understanding, to mutual recognition of GMP audits of manufacturing facilities. Attempts have also been undertaken for mutual recognition with West Germany and with Switzerland. With the exception of sterilization processes, the MOU has effectively served its purpose.

3.3.4 Standards

The British Standards Institution has published a complete list of health care and medical devices standards, dated February 1990. The list gives:

- The BSI number of the standards
- Any relevant international equivalent
- A description of the requirements covered
- The BSI committee responsible for producing the standard

The standards are listed by subject and cover the following types of products:

- Anaesthetic and breathing equipment
- Contraception
- Dentistry
- Electromedical equipment
- Equipment for the handicapped
- Hospital equipment, furniture and fittings
- Hypodermic infusion and transfusion equipment
- Laboratory and pharmaceutical equipment
- Medical imaging and radiology equipment
- Medical and surgical supplies
- Ophthalmology

- Prostheses and orthoses
- Sterilisation and disinfection
- Surgical instruments
- Surgical implants
- Textiles and clothing
- Toxicology and microbiology
- Packaging and containers

The complete list, as well as other information on health care standards in the UK, is available from:

BSI
Linford Woods, Milton Keynes
MK14 6LE, UK
Fax: (0908) 320856

3.4 Developments

The following are ISO developments affecting the UK:

- Recent revisions to the UK GMP Guides have followed the text of ISO 9001, including the significant Design Control clause now in place in the Blue Guide.

- Test kits for AIDS will be subject to labelling review in the proposed legislation and be restricted for use by medical professionals.

- Most in-vitro diagnostics are likely to fall into Class I of the forthcoming IVD Directive.

- New Quality Systems Documents have been issued for the Manufacturer Registration Scheme resulting in the audits now being based on the ISO 9000 series of the international standards. This results in the facilitation of obtaining the CE Mark under the EC Medical Devices Directives.

3.5 The Market for Medical Devices

As noted in Table 3, the UK is the third largest market in Europe and is $2.15 billion dollars strong. After years of under-funding, the medical market is experiencing significant growth with an increase of 9%, 18% and 16% for 1987, 1988, and 1989 respectively with projected further increases to exceed a total of $2.15 billion dollars by 1991. The medical equipment industry employs over 20,000 people and is strong in bandages and equipment, with substantial exports.

Despite the domestic manufacturing strength, the industry is particularly under-developed in the fields of imaging, endoscopy, and dental equipment. Although strong on research, the industry has lacked funding for product development, hence products invented in the UK typically are developed and manufactured abroad.

The forthcoming restructuring of the NHS is anticipated to result in new markets for medical devices. Hospitals and clinics may soon be able to procure their own equipment and supplies. If the former GP practice restrictions are eased as anticipated, this may serve to develop another new market serving the physician's office.

Cranial CT scanners are considered as a potential market. According to a group of 25 neurological charities, only half of all hospital accident and emergency units have a head scanner. The impact of this is underscored by population statistics from the average health district which indicate that: 500 people each year suffer strokes, 700 suffer head injuries, and 1,200 are epileptic (Clinica 476, Nov. 13, 91, p. 12)

According to Clinica (474, Oct. 30, 91, p. 16) the world market for transcutaneous electronic nerve and muscle stimulation devices is expected to double to over $800 million by 1996. The 1991 UK market is estimated at $2.6 million.

A Frost and Sullivan report indicates that there may be a bright future for contrast media. The UK market, at $27 million in 1990, is expected to reach $30.6 million by 1996 (Clinica 472, Act. 16, 91, p. 12).

3.6 Market Access

Procurement is made on the basis of call to tender. The 14 regional health authorities, as well as other publicly funded organizations issue tenders. All major supply contracts are published in the Official Journal of the European Communities. Under the NHS reforms, the purchasing procedures will change, and individual hospitals (NHS trusts) will be able to procure their individual equipment requirements.

At present, all purchases of equipment and supplies for the National Health Service (NHS) hospitals are made at the Regional, District and hospital levels by Supply Officers, who operate under policies decided by the National Procurement Group (NPG). This group consists of fourteen Regional Supplies Directors and staff from the DHPD.

Besides sitting on the NPG, the Regional Supplies Director heads a "Centre of Responsibility" for a particular product group or grouping. Although it is necessary for equipment manufacturers to maintain contact with the various levels of the procurement/advisory/management structure of the NHS to maintain visibility as a medical equipment source, it is particularly advisable that manufacturers maintain contact with the appropriate "Centre".

Of course, the relevant "GMP Guide" is a must for a manufacturer entering a specific market. The registration process is as follows:

1. A detailed registration application is completed and submitted with a £750 registration fee.

2. An audit of the manufacturing facility follows in due course, once the application is accepted.

3. The term of registration is three years.

Registration, while not mandatory, is all but essential in marketing products to NHS, and lately to the growing private sector as well. GMP adherence is absolutely essential, and DOH insists on confirmation of the sterilization process.

Import/Distribution channels:

Medical Device manufacturers seeking to sell their products in the UK have five major import/distribution channels. In order of importance they are:

1. Specialist importers - are highly experienced and familiar with the intricacies of their particular market

2. Collaboration with UK manufacturers making non-conflicting products - one advantage of this route is being listed in UK manufacturers' product catalogues (caution must be exercised to maintain control of your product description)

3. Sales subsidiaries

4. Agents - caution in choosing agents must be exercised, also agents hold a limited quantity of products and are paid commission on sale to third parties

5. Manufacturing subsidiaries - advantage of this route is the ready access to NHS contracts

3.7 Import Status

Imports represent approximately 60% of UK's total market. This ranges from 45% of medical disposable and supplies to 80% for electromedical and X-ray apparatus. The import market has been growing and is predicted to continue, particularly in the following categories:

- Dental equipment and supplies
- ECG equipment
- Endoscopes
- Medical furniture
- Adhesive dressings
- X-ray apparatus and contrast media
- Ultrasonic diathermy
- Ophthalmic instruments
- Syringes
- Sutures

The Association of British Health Care Industries annual report (1990) indicates that imports have risen by 7% to £785.0 million, with the following countries as import sources:

Country	Imports
U.S.	£211.8
Germany	£145.3
Netherlands	£ 54.3
Irish Republic	£ 48.6
Switzerland	£ 32.5
Denmark	£ 29.1
Austria	£ 11.4
Taiwan	£ 7.2

According to a MDIS/McGraw-Hill joint publication*, the import market is expected to continue to grow at an annual rate of approximately 5% over the next five years, with the hospital market as the largest consumer. This prediction is based on the following:

- Hospitals are expected to invest in modernizing their facilities and equipment in order to compete for patients with the more modern private hospitals.
- Private hospitals and clinics are also expected to increase in number and scale, so as to maintain their share of the patient market.
- NHS reforms in management and reduction in duplication of service are expected to release funding for needed equipment and products.

The following market sectors have been identified as undergoing development:

- Diagnostic imaging
- Intensive care
- Endoscopy
- Ophthalmic surgery
- Radiotherapy
- Laser surgery
- Orthopaedics and prosthetics
- Rehabilitation and elderly care

According to Clinica (481, Dec., 18, 91, p. 9), the UK Health Secretary has announced the availability of £15 million for body scanners in 1992.

3.8 Medical Device Associations

As an industry voice, the Association of British Health Care Industries (ABHI) has rapport with DOH and meets regularly on issues with the Purchasing Directorate. It actually is a confederation of eight medical device trade associations. The ABHI address is:

*Source: H.I.M.A.

- ABHI — Association of British Health Care Industries
  Consort House
  26/28 Queensway
  London, W2 3RX
  UK

Other important trade associations which are not ABHI are:

- ABPI — The Association of the British Pharmaceutical Industry
  12, Whitehall
  London, SW1A 2DY
  UK

(Although this is the trade association for the pharmaceutical manufacturers, it has a small section for manufacturers of in-vitro diagnostic products.)

- ABSM — The Association of British Steriliser Manufacturers
  c/o MDH Ltd.
  Walworth Road
  Andover
  Hants SP10 5AA
  UK

- AXrEM — The Association of X-ray Equipment Manufacturers
  Leicester House
  Leicester Street
  London WC2H 7BN
  UK

- BDTA — The British Dental Trade Association
  65, Wimpole Street
  London W1M 8AL
  UK

4.0 GERMANY

4.1 Health Care in Germany

Health care in Germany is decentralized. The individual states organize the health care system and regulate the marketing of drugs and devices. Health insurance has been in place for many years and over 85% of the population is covered by a compulsory program. Private insurance is utilized by 9%, and 3% are provided for by welfare programs. Doctors and hospitals are compensated directly by the insurance companies. However, individuals may contribute a small fee on a per diem basis.

Hospitals are half public and half private. The private are run by religious and charitable organizations. Most outpatient care is provided by physicians rather than hospitals.

The recent health reform law was introduced to control the reimbursement process. This will introduce less costly treatment and product pricing will be lowered relatively. Certain products are no longer reimbursed such as compression bandages and minor devices.

4.2 Trends in Health Care

A scan of the 1990 and 1991 weekly issues of Clinica, suggests a number of health care trends resulting from government medical cost curtailment, social changes, demographics, and technology.

Trends due to the German government's attempt to curtail the rising cost of health care:

- According to a researcher at the German Primate Centre in Gottingen, "the German government funding of AIDS research is laughable and compares badly with other industrialised nations". (Clinica 476, Nov. 13, 91, p. 13).

Trends due to changes in demographics:

- About 15% of the German population is over the age of 65, and as a group are the largest consumers of direct and indirect health care products and services.

Trends due to changing technology:

- Clinica 445 (April 10, 91, p. 13) reported that German dentists are using lasers for a wide range of treatment. It is predicted that once the benefits of lasers are widely understood and accepted, this dental tool will come into common use in dentist offices.

Trends due to social behaviour:

- The Federal Ministry for Youth, Family, Women and Health reported that two working groups called on the German Government to end the uncontrolled sales of solaria or other tanning devices and to increase whole-body examinations for skin carcinomas. In 1988, 170,000 Germans died of cancer.

Trends resulting from unification:

- It is suggested that patients from the five new Länder (states) will be streaming west to obtain the quality of health care that is not available back home. The Federal Association of German Private Health Care Institutions stated that, if the health care facilities, equipment, and supplies in the new Länder remain far below the western standards for any prolonged period of time, the new Länder patients will seek medical care in the west, thus causing overcrowding and long delays in treatment for westerners and leave the facilities in the east under used.

4.3 Regulatory Framework

The Federal Republic of Germany prior to reunification consisted of eleven states. The powers to legislate and regulate are shared by the federation and the states in a very complex manner. Customs controls, importation and free movement of products are under federal jurisdiction. Health care products and financing of products are under state jurisdiction.

Each State has its own particular government structure with a Health and Labour Ministry, each dealing with drugs and medical equipment respectively. The Ministries exercise control over all manufacturers and importers residing within their territorial jurisdiction. However, decisions taken by the local state apply to that company's activities in the whole of Germany.

The regulatory process is supported by product certification. This activity is carried out by test houses, commonly known as TüV (Technische Uberwachungsverein = Technical Control Association). TüV offices are found in every Länd, as well as in the UK, USA, and Canada.

4.3.1 Regulatory Bodies

Germany's regulatory bodies exist on two levels, federal and state. The two regulatory levels have both agency-specific functions and inter-agency consultative functions.

At the federal level there are the legislative, governmental, and administrative agencies who formulate, interpret, implement, and control medical device laws and regulations. (See Table 10 on the following page).

At the state level there are the health and labour ministries and the semi-public test houses. The state agencies are responsible for the application of the Drug Laws, approval of electromedical devices and product certification. (See Table 11 on page 34).

4.3.2 Regulations

Normal business activities, such as product design, testing, manufacture, packaging, storing, marketing, and selling of medical devices, must be reported to the proper authorities. This is not product specific information, such as would be included in a clinical trial; it is simply the reporting of business activities in conjunction with the sale of medical devices.

Four distinct regulatory activities form the regulatory system in Germany:

1. The Drug Law addresses drug-device combinations, plus implants, sterile instruments, sutures, dressings, and in-vitro diagnostics. Its principle aim is safety.

2. The Law on Safety of Appliances covers mainly electromedical devices. It aims to secure the technical safety of these products.

3. The Nuclear Law addresses products related to irradiation such as x-ray equipment and radioactive devices.

4. The Verification Law addresses calibration of laboratory equipment and medical measuring instruments.

In addition, other laws address advertising, distribution, health and safety, product liability and high frequency equipment.

Table 10

Federal Institutions

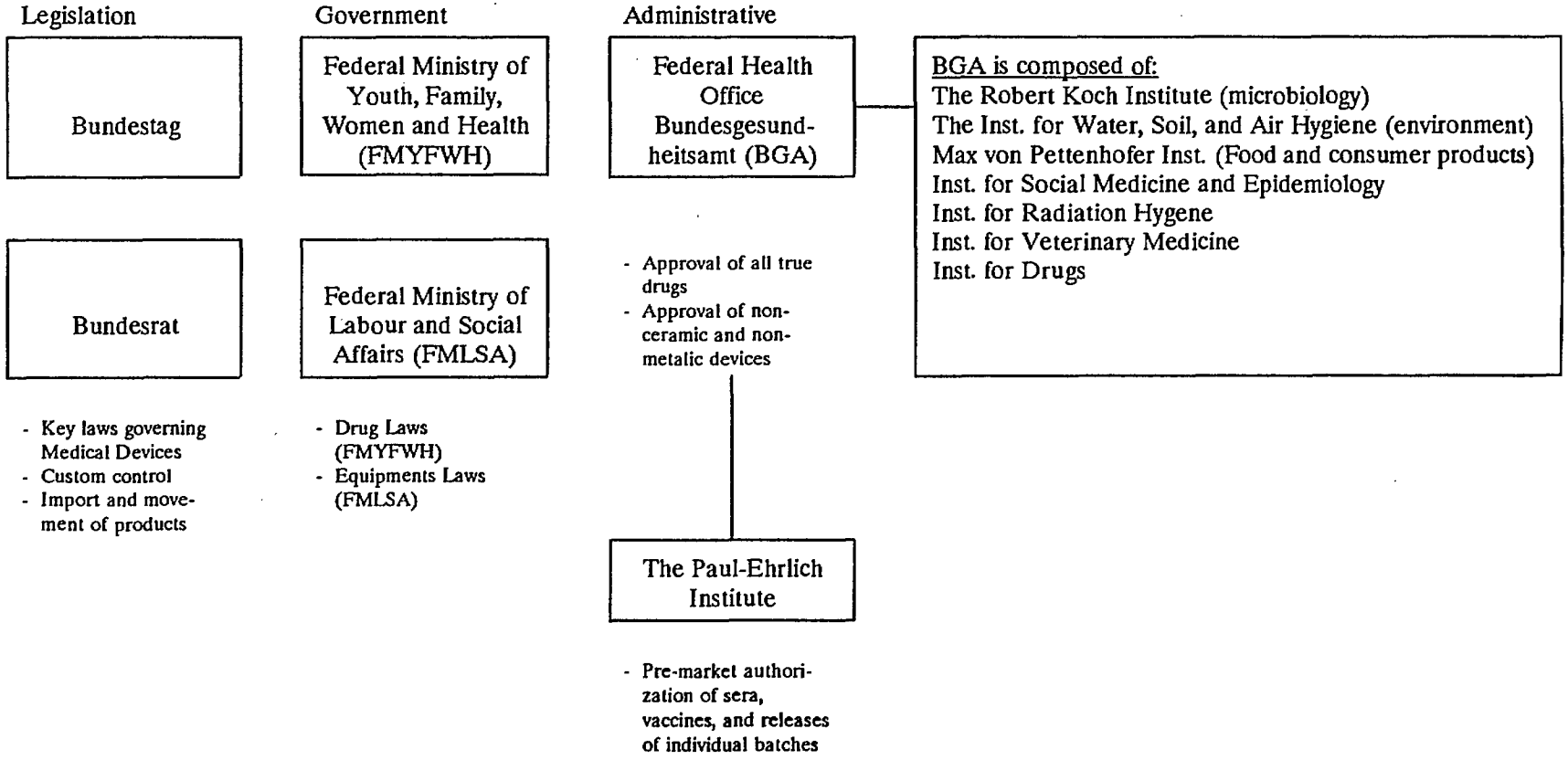


Table 11

Länder (State) Institutions

Ministry of Health (MH)	Ministry of Labour
- Control the application of the Drug Law - Interpretation of Drug Law - Manufacturer inspections - Advise companies on practical matters	- Approve electromedical devices - Consult with the MH re: their functions

Test Houses (Semi-public institutions)
- Product certification

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1. The Drug Law

The Drug Law is applied to:

➢ The definition of "true drugs" and "fictitious drugs"

As a general rule, if the device contains a pharmaceutical, chemical or biological substance, it is highly probable that the German authorities will consider it a "true drug". Examples of these would be:

1. Biological heart valves
2. Catheters containing drugs
3. Medicated dressings
4. Dental filling materials

Examples of "fictitious drugs" are:

1. Sterile single-use instruments such as syringes, electrodes, catheters, intended for single use and sold sterile.

2. Implants such as mechanical heart valves and joint replacements but also including contact lenses, extracorporeal circulation of blood products.

3. Surgical sutures and dressings.

4. In-vitro diagnostics and disinfecting products.

However, many devices such as incontinence products and fever thermometers are left outside of the scope of the drug laws.

- Clinical trial (there is a vague legal distinction between clinical trials and market acceptance trials) requirements:

    1. Require notification
    2. Toxicological information
    3. Informed patient consent
    4. Work conducted by qualified physicians
    5. Insurance coverage

- Product labelling (must be in German, can be multilingual) which includes:

    1. Labelling on both inner and outer packages
    2. Name of the seller
    3. Name of the product
    4. Batch code
    5. Quantity of content
    6. Expiry date
    7. Intended use
    8. Contra indications
    9. Interactions

- Import authorization

    1. Import certificate, or

    2. Proof of GMP compliance which is issued by the company of manufacture.

- Facility inspections (generally performed once every two years)

Certain regulatory requirements for medical devices have specific application such as:

1. Regulations covering pharmaceutical enterprises (importer or manufacturer) chiefly focus on manufacturing quality assurance.

2. Documentation of product testing carried out in the country of manufacture.

3. Maintenance of samples for one year after expiry date.

4. A record of product complaint handling.

Regulations exist on drugs that are radioactive or that have been treated with ionizing regulation. Sterilization of medical devices by radiation is permitted but special approval must be maintained.

Specific regulations regarding sterilization by ethylene oxide do not exist but concerns have been expressed regarding EtO residue.

Currently Germany applies the World Health Organization (WHO) requirements for GMP to all drugs, this also includes fictitious drugs. It can be expected that application of the European standard EN 29000 Quality Systems will be accepted in the near future.

Pre-market approval exists for certain in-vitro diagnostic products related to:

1. Notifiable diseases
2. Venereal diseases
3. Blood group characteristics
4. AIDS or hepatitis
5. Determination of immunoglobulins
6. Epilepsy drugs

2. *The Law on Safety of Appliances (Medical and Technical Equipment)*

The Law, referred to as MedGV (Verordnung über die Sicherheit medizinish - technischer geräte [Medizingerätever ordnung = MedGV]), places requirements on manufacturers, importers and operators of medical equipment. These requirements concern the following:

1. Safe construction
2. Safe installation
3. Instruction and training of users
4. Regular and careful maintenance

The purpose of the 1986 law was to guarantee the safety of equipment used in doctors' and dentists' offices, in hospitals and other health care establishments, and to ensure that medical/technical equipment satisfied certain conditions.

For certain types of equipment, pre-market approval in the form of type certification is required.

This regulation addressed all "medical and technical equipment (including laboratory and combinations thereof) used in medical or dental diagnosis, or for therapeutic purposes". The equipment is classified into four groups:

Group I

Specified energized medical technical equipment such as defibrillators, high frequency surgical equipment, infusion pumps, respirators, incubators, dialysis equipment and NMR scanners.

Group II

Energized medical technical implants such as pacemakers.

Group III

Energized medical technical equipment not specified in Group II and Group IV.

Group IV

All other medical technical equipment.

The most stringent regulatory provisions apply to Group I. Combinations of other groups with Group I are also classified as Group I.

The MedGV stipulated that all four classification groups must meet or comply with generally accepted industry standards thus ensuring a minimal level of safety. For example, general requirements specify the parameters for such items as: equipment controls, product labelling, instruction manuals, and, in certain instances, a warning device. Implants require a card identifying the date of implantation, the individual responsible for implants, and dates of follow up examinations.

The MedGV also stipulates that type certification is obligatory for Groups I and II. The certification process includes type testing by a recognized testing agency and type certification by an appropriate state authority. Type testing refers to the initial assessment of a new product for patient and operator electrical safety and software assurance. The type certificate must be supplied with each piece of equipment on delivery, and may be revoked if the type of equipment no longer complies with the general accepted standards.

Many of the MedGV requirements are addressed to the user of the equipment. There are requirements for the upkeep and handling of equipment to prevent malfunctions due to improper operation or inadequate maintenance.

3. *The Nuclear Law (Regulations Related to Radiation)*

The Nuclear Law and its regulations of 1987 covering x-ray installations address the manufacturer and the operator of the equipment. Operation and use of x-ray equipment must be certified. The regulations specify operator responsibilities and qualifications, x-ray equipment quality control, the equipment housing, and the x-ray personnel's qualifications.

4. ***The Verification Law (Regulation of Measuring Instruments)***

The so called Calibration Regulation of 1988 essentially states that: If the device measures something, the manufacturer should check if the regulations apply and which set of regulations. For example, electro-cardiographs and syringes, cannot be used unless they have been approved. However, all types of measuring instruments used in all areas are covered.

The regulations cover two groups of equipment - medical measuring instruments and medical laboratory equipment. There are three types of approvals for the four product groups.

1. Declaration of conformity - manufacturers can be accredited to test and certify their own equipment using standards which are traceable to national standards.

2. Pattern approval - granted on the basis of the product's compliance with the general requirements of the regulation.

3. Verification - consists of technical testing carried out by a competent authority.

4.3.3 Standards Bodies

The DIN is the dominant standards body in Germany. It represents Germany in ISO while the DKE of DIN represents Germany in IEC. These German organizations are very prominent in international standards organizations. They hold the secretariat from many technical committees in IEC, ISO, CEN, and CENELEC. Many of the most important international standards have been adopted as DIN standards, for example the IEC 601-1.

This has led to mutual recognition agreements between the TüV test house in Bayern and the British Standards Institution testing in the UK. Under this arrangement tests can be undertaken jointly for the German and UK markets at either location, and the BSI test certificate and the GS proven safety mark awarded.

Germany was one of the first countries to base its regulations on the principle of "reference to standards"; that is, legislation lays down the general requirements and states that compliance with one or more identified standards satisfies the legislative requirement. The DIN has published more than 25,000 standards, of which approximately 1,500 are in the health care field. This approach to regulation has stimulated the production of standards, and, has also resulted in massive industrial and government financial support for standards bodies.

The legislative backing for standards has resulted in a demand for manufacturers' independent evidence of compliance with standards. The legislative backing also has resulted in the development of a network of test houses. These test houses may be recognized by the authority for legislative purposes, and frequently their unique mark is applied to the satisfactory product.

The TüVs dominate the testing services. The main aim of the association is to protect health, life, and environment from any dangers which may arise from industrial development. They offer a broad scientific and technically qualified staff of specialists who perform: quality assurance, testing of design materials, manufacturers, processors, site inspection and accident analyses.

This emphasis on standards testing, marks, and the freedom of the test houses to decide on their own testing requirements is an obstacle to obtaining approval in Germany, and therefore makes Germany a difficult export market.

4.3.4 Standards

The German pharmacopoeia contains several provisions with regard to medical products such as sterilization methods, sterility control, plastics and silicon materials, and sutures.

Most of the electromedical equipment testing is based on the DIN adoption of the IEC 601-1 standard. National standards are also utilized. TüV has set up their own study group on computer safety and their work is applied to software controlled medical devices.

The TüV "GS" mark of proven safety is a requirement under the MedGV Law for certain types of equipment but is frequently applied voluntarily to other equipment such as laboratory or non-electrical medical devices as a means of satisfying requests from hospitals for proof of product safety.

Pre-market Approval Process

The pre-market approval process varies according to the type of medical device to be marketed. Three types of medical devices that require pre-market approval are:

- Devices considered as true drugs
- Non-ceramic and non metallic implants sterilized by irradiation
- Electromedical devices that are implants.

The pre-market approval process for true drugs and certain medical devices, such as dental filling materials and biological heart valves, is governed by the Drug Law. Specific types of information must be provided in German on the application form. The results of physical, chemical, and biological or micro biological testing must also be included. For example, irradiated implants must be tested for possible changes in the materials' integrity. Medical technical equipment requires type testing, certification by a test house, and formal approval by a state authority.

Acceptance of the marketing application usually takes four months. A request for additional information may extend this time frame. The marketing authorization is granted for five years.

4.4 Developments

In response to pressure from the medical devices industry in general and the trade association BVM (German Dressings and Medical Products Association) the Federal Health Council passed a vote in 1986 recognising the need to create a medical products law. Broadly the aim is to separate out from the Drug Law those products which are not absorbed by the body.

In August 1988 a 12-point set of draft guidelines for a Medical Devices Act ("Leitsätze zu einem Medicalproduktengesetz") was published by the Federal Health Ministry.

The basis of these guidelines is to separate objects having physical effects from substances having pharmacological effects. The applied controls should be based on risk, broadly along the following lines:

Class I products	-	notification
Class II products	-	GMP
Class III products (critical devices)	-	PMA

Quality of the products would be based on a list of standards, similar to the procedure of the MedGV. Clinical trials requirements would be based on the risk class. With regard to products manufactured outside Germany and the EEC, attempts would be made to achieve mutual recognition of authorisation and supervision measures. Other requirements involve labelling and the notification of any post-marketing problems to the authorities.

4.5 The Market For Medical Devices

Prior to unification, West Germany was the largest single market for health care supplies and equipment in the EC. With unification, the German market is expected to grow rapidly as the former East German health services are brought up to western standards.

The German medical manufacturing industry satisfies 55% of the requirements of the market. The industry is dominated by large companies. Several of them are U.S. owned. Further, certain pharmaceutical companies are also providing medical devices.

4.6 Market Access

Everyone agrees that Germany has the most difficult regulatory scheme in western Europe. Therefore, prior to considering a market launch a plan of "regulatory compliance" should be developed. Such a plan would address the following elements:

1. Identify a distributor and local authorities.
2. If clinical trials are planned, in addition to the standard protocols, compile a preclinical dossier, consisting mainly of toxicological information.
3. If measuring devices are under consideration refer to the 1985 Verification Act.
4. Develop labelling for the product package in German.
5. Obtain an import certificate.
6. Consider GMP and Quality Control requirements.
7. Depending on the sterilization method, consider the issue of residuals.
8. Verify compliance with relevant standards.
9. Certain products will require additional consideration such as pre-market approval for biological source materials.

In addition to the above general requirements, there are product specific requirements.

1. Identify the regulatory nature of the product. For example, electromedical implants are subject to both the Drug Law and the regulation on medical/ technical equipment. Products accepted in other countries as medical devices may be identified as drugs in Germany. Products containing substances which may be modified as a result of implantation should be treated with concern.

2. Identify the impact of regulatory requirements on a product. Many requirements are new and their implementation is confusing. Interpretation varies substantially from one German state to another. Further, many of these requirements will change because of the harmonization process evolving toward EC 93.

   - ➤ Drugs and irradiated implants may require a longer approval time and more complete data than one might anticipate.

   - ➤ Electromedical devices may require design modification before they can be approved, especially if they are software driven.

   - ➤ Identify the organizations and the people responsible. A manufacturer using an importer to access the German market must assure himself that the importer is competent in dealing with regulations. Additionally, if the importer is carrying out the regulatory compliance requirements he will need to be thoroughly versed with the product design and manufacturing process. This may require access to proprietary documents; therefore it may be necessary to use a third party consultant to preserve proprietary information.

   - ➤ The authorities should be known personally because practical recommendations may be exchanged in conversation rather than formally on paper.

   - ➤ It is frequently advantageous to have personal contacts among the federal office administrative personnel.

   - ➤ Familiarity with personnel in the test house (TüV) where substantial experience in medical devices is available is essential, especially for the first time approval.

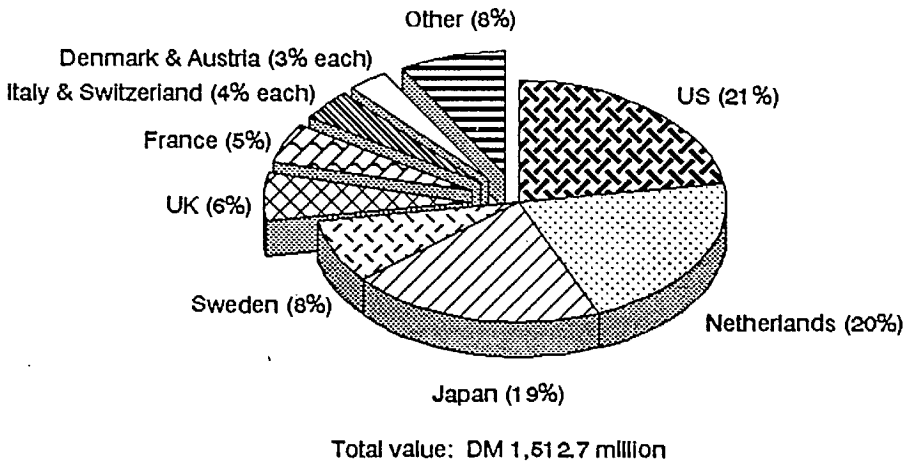
- Identify any communication problems. While most Germans speak English, the official language of communication, especially in writing, is German. German is required on product labelling, instructions, controls, and video screens. Applications must be submitted in German; therefore translation can be a major cost and introduce a new time factor. A competent, experienced translator and quality proof reading is essential at all stages of the printing process.

4.7 Import Status

Despite Germany's strong indigenous medical device industry, the importation of medical devices has risen consistently over the past four years, from DM 1,251.7 million in 1988, to DM 1,420.0 million in 1989, to DM 1,512.7 million in 1990.

Sources of medical device imports are as depicted in Table 12.

Table 12
Sources of Medical Devices Imports



Total value: DM 1,512.7 million

Source: Clinica 453, June 5, 1991

The German optical instruments industry is experiencing an upswing. Along with this upswing is an increase in the import market, which rose 3.7% to DM 305 million, in the first six months of this year (Clinica 433, January 9, 1991, p. 16.)

- A recent report issued by the Bundesgesundheitsamt (BGA) stated that it is BGA's intent to "bring about a level of parity in equipment provisions between east and west by 2000. This may prove to be quite a challenge, in that the BGA estimates that equipment provision must be doubled, and 50% of the existing equipment replaced due to safety or other defects" (Clinica 472, Oct. 16, 91, p. 11).

- The average number of users per large medical device per location (FRG or GDR), together with estimated costs for the upgrading the eastern to the western standards were sited by Clinica (#433, Jan. 9, 1991, p.16) and appears in Table 13.

Table 13

Cost and Number of Medical Devices Required to Upgrade Eastern Facilities

	No. of inhabitants per device ('000)		No. of Devices required	
	(FRG)	(GDR)	Number	Price (DM million)
Cardiac catheterisation laboratories	380	2,285	35	140
CT scanners	110	515	114	171
Gamma cameras	55	275	233	163.1
Digital angiography systems	185	1,335	74	111
Magnetic resonance imaging systems	1,070	16,000	14	35
Linear and circular accelerators	475	695	11	22
Cobalt units	320	1,065	35	52.5
Kidney lithotripters	20[1]	2,665	10	20
Other devices, technologies, surgical and analytical devices				714.6
Total			526	1,492.2

Source: Clinica 433, January 9, 1991, p. 16 (1989 figures).

- A report by Frost and Sullivan indicates that the contrast media market is expected to grow significantly (Clinica 472, Oct. 16, 91, p. 11). Specifically:

  - The nonionic (low osmolar) agent market is expected to reach an annual sale of $154.1 million by 1996 (ionic media is expected to fall to $38.9 million by 1996)

  - MRI enhancement agents are expected to enjoy the fastest growth, going from $1.7 million in 1990 to $4.5 million in 1996.

- "Over 33,000 pacemakers were implanted in over 700 hospitals across the Federal Republic in 1990. With 421 new pacemakers per million inhabitants implanted every year, Germany is the number one market for these devices." (Clinica 463, Aug. 14, 91, p. 10).

4.8 Medical Device Associations

The key trade associations are as follows:

- BVM — The Association for Dressings and Medical Products
  BVM
  Viktoriastr. 45
  6200 Wiesbaden 1
  West Germany

  This association represents manufacturers and distributors of single-use, sterile devices.

- VFOI — The Association of the German Precision mechanical and Optical Industry
  VFOI
  Pipinstr. 16,
  D-5000 Koln 1
  West Germany

  This association represents manufacturers and distributors of electromedical devices.

➤ ZVEI The Central Association of the Electrical Industry
ZVEI
Postfach 70 12 61
Stresemannallee 19
6000 Frankfurt am Main 70
West Germany

This association represents manufacturers of medical instrumentation and some manufacturers of implants.

➤ VHCH The Association of Manufacturers of Surgical Sutures
VHCH
Karlsstrabe 21
6000 Frankfurt am Main
West Germany

This association represents suture manufacturers.

5.0 FRANCE

5.1 Health Care in France

France provides its citizens with national health insurance coverage which relies on a reimbursement scheme of 80% for physician and drug costs. Hospital care, both private and public, is fully and directly paid by the insurance authorities. Indigent patients are completely covered under a separate health insurance scheme.

France has 21 health care regions and 90 districts to administer health care needs. Twenty-nine large hospitals, approximately 3000 beds each, provide 70% of all hospital bed capacity. These hospitals are also the centres for research, teaching and all specialist services. Two hundred district hospitals cater to general medicine and surgery. Three hundred and forty community hospitals offer limited services concentrating on medicine and maternity.

The private sector plays an important role in health care. Of the total health care budget for 1990, approximately 3/4 of the funds were used for public health care costs, and 25% for private health care costs. However, in terms of the system's rate of growth, the public system increased by 5.4% whereas the private system increased by 10%.

5.2 Trends In Health Care

All health care systems in the EC countries are similarly impacted by economic, social, technological, and demographic factors. The economic factors have been particularly significant in that virtually every country has attempted to either curb or reduce health care spending by various methods and schemes. For example the UK has begun a cost containment program by reorganizing its medical device and supplies systems, thereby hoping to reduce the bureaucracy and duplication of effort. The French government's cost containment schemes appear to target medical services costs.

Trends due to government cost containment efforts:

- The French health care bill for 1990 was a total of FFr 538,100 million (of which Social Security paid 74%), a 7.4% increase over the previous year's total. The governments response to this has been the introduction of cost-containment measures such as:

- The introduction of fixed prices for clinical analyses per patient rather than per analysis (a saving of approximately FFr 3000 million for this year).

- A freeze on any increases in the amount reimbursed to private hospitals for operating theatre expenses (a saving of approximately FFr 800-900 million).

- The introduction of contracts between private hospitals and the state insurance bodies for given periods of time rather that open-ended contracts (Clinica 434, Jan. 16, 91, p. 14).

- The association for the French medical equipment industry, SNITEM, reports that as a result of government cost-containment measures, the medical device industry is reporting drops of up to 40% in product turnover. Further, they are also reporting that hospitals are averaging payment delays between 60 and 90 days (Clinica 478, Feb. 5, 92, p. 12).

Trends due to social/behavioral factors:

➤ Between 1 and 1.5 million tests for HIV are carried out each year in public and private laboratories in France.

- Of the approximately 60% of the tests ordered by G.P.s, 6% are seropositive.

- Forty percent of all ordered tests are for at-risk-group individuals, and of these 94% are seropositive.

- There are approximately 119 centres for anonymous and free AIDS testing (Clinica 401, May 16, 90, p. 12).

➤ New French legislation has made HIV testing mandatory for all sperm donations (Clinica 481, Dec. 18, 91, p. 10).

Trends due to changing technology:

➤ Due to recent advances in implant technology, it is estimated that approximately 1,500 defibrillators will be implanted annually in France (Clinica 411, July 25, 90, p. 9).

➤ The number and sophistication of medical devices is predicted to grow at about 10% per year, and will reach FFr 21,000 million by the end of 1992 (Clinica 481, Dec. 18, 91, p. 12).

- An obstetric ultrasound examination at term is being defined as necessary to insure patient welfare. As are the first and second examination, this third examination will be totally reimbursed by the French Social Security system of health care coverage (Clinica 484, Jan. 15, 92, p. 16).

Trends due to changing demographic factors:

- The French market for orthopaedics and prostheses is presently worth approximately FFr 2,000 million. This market is expected to grow with the aging population and as new fields of application open resulting from advances in technology (Clinica 480, Dec. 11, 91, p. 9).

5.3 Regulatory Framework

The various directorates and sub-directorates of the Ministry of Solidarity, Health and Social Protection (commonly referred to as the Ministry of Health) are responsible for medical device regulation. The regulatory activities can be grouped into four distinct systems: homologation, the pharmacopoeia scheme, clinical experimentation, and specific product regimes. Presently, the implementation and enforcement of regulatory activities are subject to regional and individual interpretation. However, the "interpretive" implementation and enforcement of regulatory activities is not to be confused with regulatory laxity, regulatory activities are vigorously pursued and enforced.

5.3.1 Regulatory Bodies

Table 14 depicts the regulatory framework in terms of responsibility for specific medical device categories and their respective regulatory schemes. The umbrella organization is the French Ministry of Health, which is divided into a number of Directorates, which consists of a number of "Bureaux", as indicated in Table 14.

- Bureau 5D of the Directorate of Hospitals acts as the Secretariat for the National Homologation Commission. This organization is responsible for the homologation scheme.

- Bureau 7 of the Directorate of Technical Affairs is responsible for the Pharmacopoeia regime.

- Bureau 6 of the Directorate for Economic and Industrial Affairs controls advertising for medical devices which claim a "therapeutic" effect.

Table 14

Ministry of Solidarity, Health and Social Protection

Directorate of Hospitals	Directorate of Technical Affairs	Directorate Economic and Industrial Affairs	Division for the Registration of Drugs	Directorate of Professional Affairs and Litigation
Bureau 5D	Bureau 7	Bureau 6	- Drug authorization	- Authorization for pharmaceutical establishments
- Control of medical device homologation	- Control of Pharmacopia regime	- Control of advertising for "therapeutic" medical devices		- Matters relating to pharmacists

24 Regional Directorates for Health and Social Affairs

- Interpret Pharmacopia requirements in their regional territory

- The Directorate of Professional Affairs and Litigation is responsible for the authorization of pharmaceutical establishments and of matters related to pharmacists.

- The Division for the Registration of Drugs is responsible for drug authorization.

- The 24 Regional Directorates for Health and Social Affairs are responsible for the interpretation of the Pharmacopoeia requirements in their respective regional territory.

5.3.2 Regulations

Four distinct regulatory activities form the regulatory system in France. (There is no specific "Good Manufacturing Practices" (GMP) certification requirement for medical devices. However, the French Pharmacopoeia GMP for drugs [2nd. edition, October 1985] is sometimes used in part).

1. Homologation (Pre-market Approval Certification)

Homologation is a pre-market approval scheme which involves a process of testing and evaluation (see Annex I). Until recently, homologation was a mandatory process for public hospitals which purchased devices subject to homologation (sales to private hospitals were not subject to this approval process). As of January 1991, the purchaser's identity is no longer a homologation application criterion.

Initially homologation only covered certain electromedical devices. However, recent amendments to the process have extended homologation requirements to non electromedical devices in sectors such as:

- Imaging
- Surgery and therapy
- Functional assistance
- Anaesthesia, resuscitation, and emergency procedures
- Acquisition and processing of physiological data

Each of the named sectors has a review board, which is staffed by relevant specialists. These specialists examine the manufacturers application and may require that the product be submitted for testing by a certified test house. Testing protocol includes procedures which examine the product for performance, effective environmental conditions, electrical safety, mechanical characteristics, measuring controls, materials, etc.

Depending on the product, clinical trials may also be required. Clinical trials, involving independent participating clinicians, evaluate the device in situations of actual use, employing a protocol established by the Ministry of Health.

On successful review, a report is made to the Ministry of Health for final approval. Approval carries a three to five year term with a simple review and renewal process. The entire homologation approval process takes six to twelve months or longer in the case of certain implants. There is a post market surveillance system which is empowered to recall questionable products.

2. Pharmacopoeia Regime

The National Pharmacopoeia Commission, under the auspices of the Ministry of Health, publishes the French Pharmacopoeia. This regime is an aberrant regulatory scheme in that it:

- Only applies to devices which are referenced in its monographs, for example:
  - Specific products such as syringes, infusion and blood sets
  - Composite materials and packaging
  - Biological safety tests
  - Principles and methods of sterilization, and testing for sterility
- Applies to products which claim pharmacopoeia compliance.

- Applies to pharmacists' execution of professional responsibilities (in France pharmacists have a vital role in the purchasing of medical devices).
- Evaluations of compliance vary according to the individual inspector's interpretation.
- Includes specific instructions for packaging and extensive labelling requirements.

Note: A French law of 1975 requires the use of the French language on all labelling and information provided on products. The foreign language translation may appear with the French text. A violation of this requirement may constitute fraud. According to a Canadian manufacturer who exports into the French market, the penalties for being found guilty of fraud include the loss of one's importing license for one year, or a restraint of sale of the product in question.

3. Clinical Experimentation

A law concerning the protection of subjects involved in biomedical research (clinical experimentation) was passed in 1988 but continues to suffer delays in implementation. This law imposes standardized requirements for:

- Informed consent
- Liability insurance
- Risk/benefit evaluation
- Safety measures

These requirements are enforced regardless of the purpose of the clinical trial.

A pre-trial consultation with the Regional Consultative Committee for the protection of "persons undergoing biomedical research" is required. Unfavourable pre-trial evaluations are reported immediately to the Ministry of Health. Final experimentation results and evaluation thereof are also communicated to the Ministry of Health. The Ministry of Health is authorized to discontinue investigation at any time.

4. Specific Product Regulations

Certain devices have, in addition to the previous stated regulatory requirements, additional laws, regulations and requirements as follows:

- The purchase of heavy equipment such as: CAT and NMR scanners, dialysis equipment, etc., requires Health Ministry approval. The approval depends on meeting the specific government established economic ratio of population per equipment coverage.

- Contraceptives (condoms excepted) require pre-market approval. Public advertising is prohibited and sales restricted to pharmacies or family planning centres. Certain medical devices, which may be employed in abortions, are prohibited for public sale.

- Medical (mercury-in-glass) thermometers require pre-market approval with labelling and post market controls. Electronic thermometers cannot be called medical thermometers. Mercury thermometers require type testing and approval.

- Use and installation of equipment emitting ionizing radiation for medical purposes carries a complex set of regulation.

- Contact lenses and cleaning solutions require pre-market approval and specific labelling.

- Syringes and needles are subject to special requirements related to drug addiction. Sale is restricted and import requires special authorization and specific labelling.

- In-vitro diagnostics.

  France is one of the few European countries which has a specific regulatory scheme for in-vitro diagnostics. This scheme sets down two sets of rules; one concerning a notification to be submitted and the second concerning batch certification.

  The notification deposited with the National Health Laboratory by the manufacturer or the importer must include:

- Name and address of the manufacturer/importer.

- Product information - including all pertinent information such as constituents, mode of action, reactions, specificity, shelf life, false-positive/false-negative results, and result interpretation.

- Handling instructions - the inner container and shelf package must include general information, statement-of-use, storage instructions and, if applicable, warning statements.

- Labelling and specific information must be in French but other languages may be included.

- Research report and bibliography.

In addition to the above, the National Health Laboratory must have access to product batch control files showing the dates, type of controls and results, and control methodology. Approximately six weeks after the dossier is submitted, the National Health Laboratory will issue a registration number, which is the authorization for product launching.

Finally, radioimmunoassy products are subject to a true pre-market approval procedure which involves medical and analytic evaluation. Blood products and reagents for HIV testing also have additional specific requirements.

5.3.3 Standards Bodies

France rates with Germany and the United Kingdom in producing a high number of medical device standards in the European medical device industry.

There are two standards organizations, Association française de normalisation (AFNOR), which deals with non-electrical issues, and Union technique de l'électricité (UTE). In total these organizations have published approximately 13,000 standards, 300 of which relate to medical devices. These standards are used in homologation and in voluntary certification.

Groupment des laboratoires d'essais des matériels de technique médicale (GLEM) is an independent organization carrying out certification in the context of granting NF marks. Testing is done in a variety of laboratories within France, similar to the German Technische Uberwachungsverein (TüV) system. GLEM also has reciprocal testing agreements with British Standards Institution (BSI) and TüV with further agreements being established in the near future. These reciprocal agreements would permit GLEM or another test house to test against standards such as IEC 601-1, with the results be acceptable in France.

5.3.4 Standards

There are approximately 300 medical devices standards pertaining to devices such as:

- Aids for the handicapped
- Dental material
- Disposable single-use devices
- Implants
- Orthopaedic devices
- Surgical instruments

The standards are applied as elements of the homologation process and voluntary certification.

The homologation procedure may require products to be tested by a certified laboratory such as GLEM. The laboratory will verify conformity of the devices to the appropriate standards. The Health Ministry relies heavily on testing to appropriate standards when placing a new device on the list of products.

Voluntary certification to standards, inspection of the manufacturer, and continuing testing of samples will qualify the manufacturer to place the NF mark on their products.

Quality systems certification is not yet highly developed in France as it is in the UK. Nevertheless, there is increasing awareness of the need to develop expertise in the area. The French association for quality assurance, a private organization, is also offering quality systems certification based on ISO 9000.

5.4 Developments

It is anticipated that France will continue to develop regulatory requirements prior to the formal development of the European Community. These will be in the aid of consolidation and preparation for the EC common market, and to develop better regulatory control of the market. New measures will enable France to gain experience, and prepare to be in the forefront of the EC regulatory scheme.

Homologation, originally applying only to electromedical devices, will gradually extend to non-electrical implants. Other products will follow, particularly in the assessment of bio materials. Homologation will also extend to the private hospitals and thereby cover the whole marketplace from a purchasing aspect.

A new biomedical experimentation law covering all products will introduce concepts such as informed consent, ethical review board approval, and insurance protection for patients. This national system of review will reduce variability of approval criteria for clinical trials.

To date, product approval has been the French medical device industry's control system. GMPs for drugs have only recently been introduced. The homologation system for hip joints began the introduction of quality assessment of manufacturing. Subsequent submissions based on quality system certification will undoubtedly enjoy overall acceptance.

5.5 The Market For Medical Devices

As noted in Table 1 the French market for medical devices is the second largest after West Germany at approximately 21% of the EC market. Spending on medical technologies is growing by approximately 10% per year, and is predicted to reach FFr21,000 million in 1992, or around 3% of the total health care budget.

Domestic production of medical devices is primarily made up of medium to small companies concentrating on x-ray, EEG and OR equipment and furniture. High-tech manufacturing of NMR, lasers, and ultra-sound is being encouraged. Consequently imports are very important and account for 70% of all purchases. These are sourced from the U.S., Japan, West Germany, Italy and the UK. Increasing investment from these countries is anticipated as the EC market develops.

Although the major segments of the medical markets are already being supplied by the large multinationals, such as Siemens, Phillips, General Electric and Toshiba, there are a number of new niche markets which have no true leader or major player. These niche markets are in the "functional assistance" field and include items such as dialysis equipment, biomaterials, informatics, and prostheses (Clinica 436, Jan. 30, 91, p. 12).

Another market which is predicted to grow rapidly is the MIR enhancement agents. The French market stood at $62 million in 1990, and is expected to triple by 1996 (Clinica 472, Oct. 16, 1991, p.12).

5.6 Market Access

There are a number of voluntary and mandatory guidelines a manufacturer must seriously consider prior to attempting to enter the French medical devices market. The following are some examples:

- Purchasing requirements and tariff reimbursements are outlined in monographs which deal specifically with conditions and regimes that affect sales of products in France.

- Public tenders may require conformity with French standards as a condition of purchase.

- French language capability is critical. Official correspondence is always in French. Working through a local distributor may seem to be a logical solution but they in turn may not understand the more complex circumstances of a specific product.

- Although there is no legal requirement to have local representation, or to sell through a registered pharmaceutical establishment, this is advisable, particularly with sterile, implantable, or disposable products.

- The pharmacopoeia again plays a significant role for products subject to its authority. The utilization of a pharmacist at the distributor level opens many doors at the hospital purchasing facility.

5.7 Import Status

As noted earlier, the French import 70% of their medical supplies and equipment, hence are a significant import market.

French medical imports have shown steady growth over the past five years. Between 1986 and 1988, French medical imports grew in value by 11% - 12% per annum. In 1989, the rate of increase accelerated to 18% with imports reaching FFr 9.2 billion. The increase in activity reflects expanding market share for foreign manufactured products which now account for 65% of the market compared to 50% in early 1980s. (See Table 15 on the following page).

The French market is expected to continue to achieve annual real growth in excess of 5% over the next three years. The 4% per annum increase in hospital activity and the move by major public hospitals to invest in the latest medical technology are both growth factors, but activity in the private sector is also fuelling the market, as hospital groups restructure and modernize newly acquired facilities. The level of investment needed for this process is estimated at up to FFr 40 billion over the next five years with as many as a half of France's 1,000 private commercial hospitals set to change ownership over the next decade.

Consolidation will also be a feature of the medical manufacturing industry, as the presence of multinational groups grows in importance. The influx of foreign companies whilst providing support for the local manufacturing industry is also opening up new distribution channels for foreign-manufactured equipment, and imported products are likely to continue their advance in the market.

The growing presence of multinational groups and the rising level of imports, particularly at the high technology end of the market, is partly a reflection of the weakness of the domestic manufacturing industry. Many small firms are without the resources to develop new technology necessary to remain competitive in a fast-changing market. This factor has been recognized by the French Ministry for Industry and National Development which has launched a number of initiatives aimed at encouraging French companies to diversify into fast-growing high technology sectors identified as biomedical materials such as artificial membranes, orthopaedic, cardiovascular, ocular and dental implants.

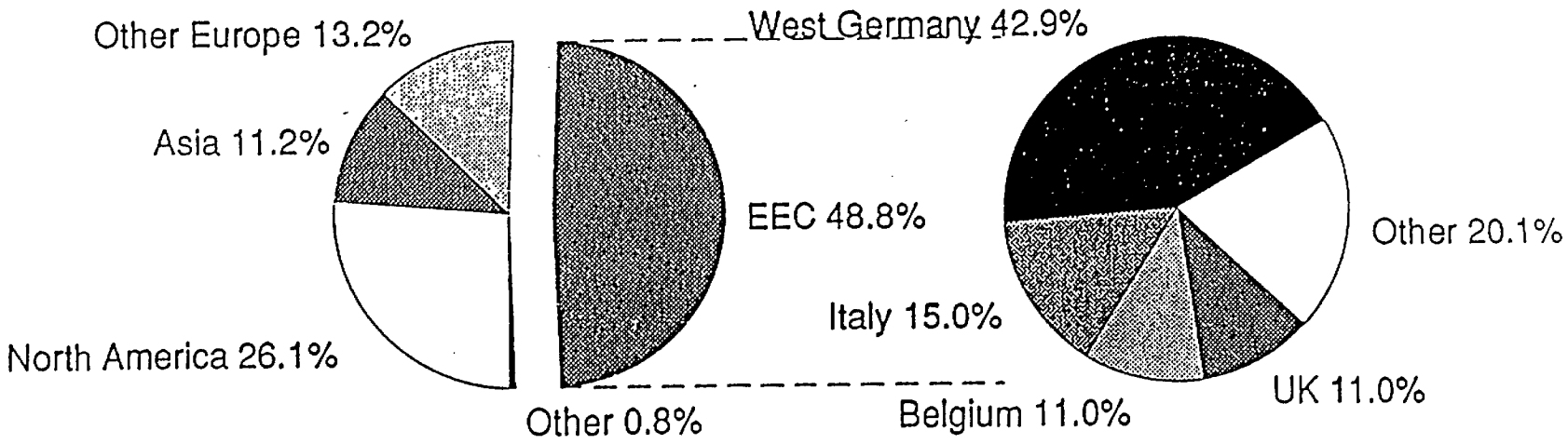
5.8 Medical Device Associations

Syndicat national de l'industrie des technologies médicales (SNITEM) is the primary French medical device trade association. It consists of 140 member companies which cover approximately 80% of the total industry. Their products range from radiology equipment to implants to disposable devices.

- SNITEM — Syndicat national de l'industrie des technologies médicales
  10 Avenue Hoche
  75382 Paris, Cedex 08
  France

Table 15

French Medical Imports 1988



Includes imports of non-medical x-ray

Source: United Nations Statistics

Another association, Syndicat général des ouates et pansements addresses the dressings and cotton aspects of the industry.

➤ SGOP Syndicat général des ouates et pansements
37-39 Rue de Neuilly
BP 249
92113 Clichy Cedex
France

6.0 ITALY

6.1 Health Care in Italy

Italy's economy in the 1980's enjoyed a period of significant growth and stability. However, this development was unequal as strong regional diversity continues to exist. There are significant economic differences between the prosperous industrial north and the poor agricultural south. The south with 35% of Italy's population only produces 24% of the GDP and affords significantly lower incomes (59% that of the northern population). Nevertheless, Italy has a national health care system and a well developed medical device industry.

The National Health Service in Italy is organized in a four-tier structure with all services organized by the Ministry of Health and the National Health Council. There are 20 health care regions responsible for planning and coordination of health services. These in turn are divided into local health areas responsible for the supervision of hospitals and family practitioners - 670 in total. The population of Italy is covered by a national health insurance scheme which provides all services free of charge.

Italy has approximately 60 regional general hospitals which offer full specialized services. Smaller hospitals provide more general services. The use of private services has been increasing over the last few years as the public sector has proved to be inadequate. Health care system changes similar to those proposed for the U.K. have been put forward. To date the changes are not totally implemented.

6.2 Trends in Health Care

All health care systems in the EC countries are similarly impacted by economic, social, technological, and demographic factors. In Italy the political/economic factor is another consideration.

- There are more hospitals in northern Italy than can be justified by a needs analysis. The disproportionate number of hospitals is particularly apparent in some clinical specialty areas where the doctors outnumber the patients (Clinica 469, Sept. 25, 91, p. 10).

- Clinica 481 (Dec. 18, 91, p. 8) reports that the lack of skilled technicians, under-use of equipment, and inflexible x-ray department opening hours and protocols are resulting in some 75% to 90% of women in northern Italy not receiving the mammographies that they should receive.

- 1991 - 1992 health care budgetary increases under the 1992 Finance Law were less than 3%.

Trends due to government cost-containment efforts:

- Clinica 484 (Jan. 15, 92, p. 16) notes that the patient part-payment towards diagnostic procedures is due to increase from 30% to 50%, once a 1992 Finance Law is approved.

- A decree has been signed by the Health Minister which changes the percentage of diagnostic test fees billable to the patient. As of now, a patient who does not "bother to find out what his/her diagnostic tests indicated, will be fully billed for said tests" (Clinica 480, Dec. 11, 91, p. 11).

- A recent Treasury and Health Care Ministry decree allows treasury departments at the local health authorities to pay debts owed to suppliers of medical devices, products and services to avoid further interest payments. Some suppliers have been waiting for as long as three years to be paid (Clinica 479, Dec. 4, 91, p. 16).

Trends due to social/behavioral factors:

- Of all the EC markets, Italy is predicted to become the largest contraceptive and home diagnostics market by 1995 at $300 million. Presently its condom market is four times that of France (Clinica 486, Jan. 29, 92, p. 11).

- Declarations by the Catholic Church that pharmacists should not sell contraceptives and other "anti-life" products have left pharmacists in a legal/moral/ethical quandary in that by law, pharmacists are required to dispense products authorised by prescription. Decisions to sell or not to sell prescription contraceptives, based on their own moral beliefs, raise the issue of the legitimacy of the Italian Pharmacopoeia (Clinica 431, Dec. 12, 90, p. 10)

- Non-reusable self-blocking syringes are now being marketed for sale through pharmacies (Clinica 484, Jan. 15, 92, p. 16).

Trends due to changing technology:

- The Italian Commission for Industrial Policy (CIPI) has approved funding for two areas of medical technology research. The telemedicine research project will receive Lir 94,400 million ($75 million) and the neurobiological system research will receive Lir 107,700 million.

The telemedicine research project proposes to investigate:

- The creation of integrated hospital information systems.
- A new method for educating medical personnel and the general public regarding health matters.
- Diagnostic systems for digital image processing.
- New technologies for hospital department management.
- Development of an auxiliary system to aid communications between disabled persons.

The neurobiological systems research project proposes:

- To study neuroreceptors' mechanics of transmission in the peripheral and central nervous system.
- The production of new molecules capable of identifying particular pathological states in the brain (Clinica 484, Jan. 15, 92, p. 16).

➢ The first European artificial heart transplant was performed in Naples on a 55-year-old man who was waiting for a suitable donor heart (Clinica 481, Dec. 18, 91, p. 10).

Trends due to changing demographic factors:

➢ The Health Ministry has plans to submit a proposal for an elders' home care project. The objective is to encourage home care, hospitalization-at-home, and home-rehabilitation of the chronically and terminally ill (Clinica 436, Jan. 30, 91, p. 12).

6.3 Regulatory Framework

6.3.1 Regulatory Bodies

The Ministry of Health (MoH) is the prime governmental body that issues health regulations and approves registration authorizations (See Table 16). The Ministry is divided into eight Directorates, of which the Directorate General of Pharmaceuticals is responsible for the regulation of pharmaceutical and medico-surgical products. The Higher Council of Health, a non-governmental advisory body, councils the MoH on health issues. Its Section Five is responsible for issues related to medico-surgical product issues. The Higher Institute of Health is comprised of 20 laboratories and carries out product testing and the principal technical reviews related to product registration.

6.3.2 Regulations

The Pharmaceutical Department of the Ministry of Health lists of medical and surgical products into one of three categories:

1. For personal use (eye washes, insect repellents)

2. For environmental use (insecticides, rodent poisons).

3. For various uses (pacemakers, catheters, sutures, dialysis components, syringes, hearing aids).

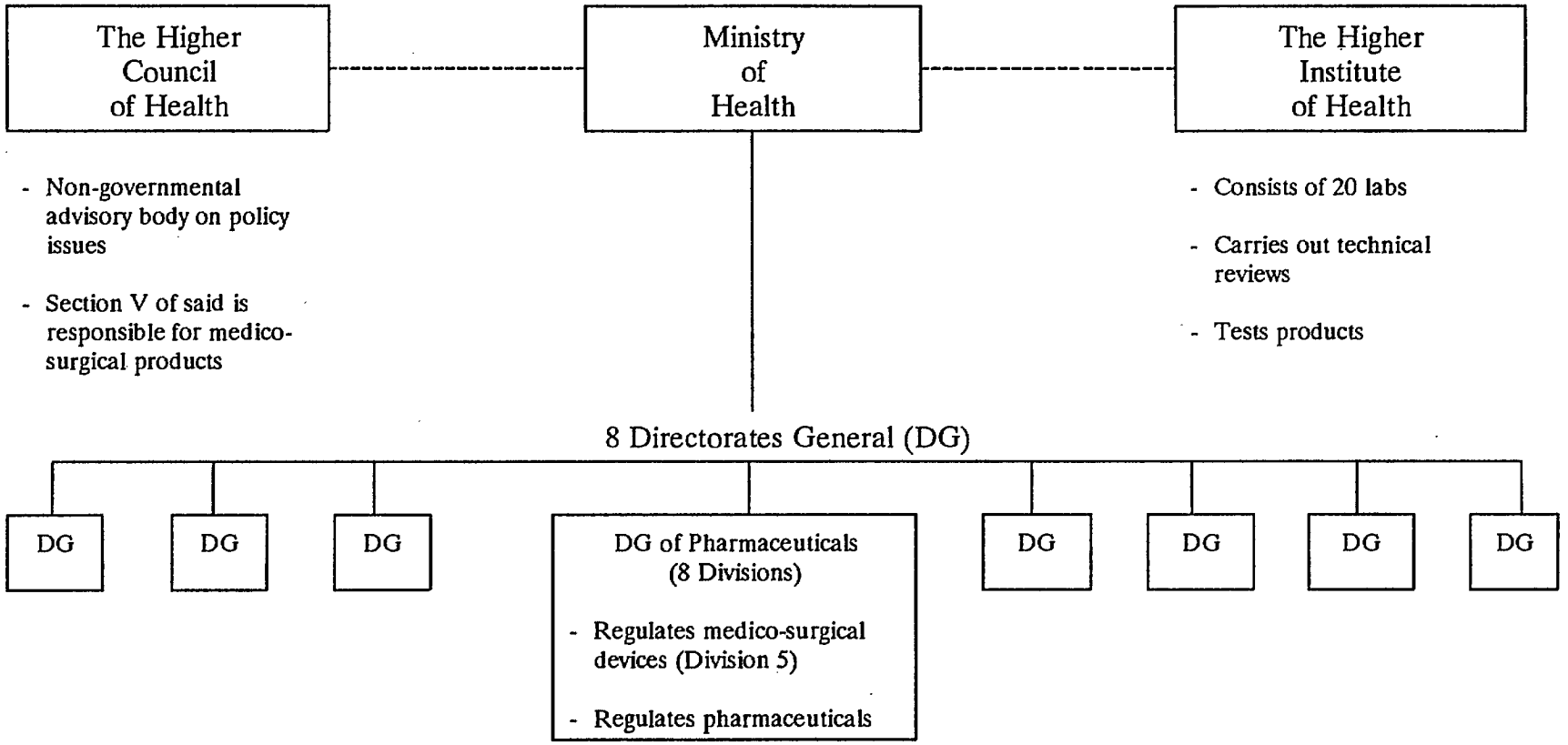
4. HIV antibody detection kits.

Medical devices not listed in any of these categories can be marketed without registration by the MoH. One would be advised to contact the Ministry to verify whether or not the product in question is interpreted as being included in one of the above categories. Occasionally products that were not on the list were nonetheless required to be registered.

All medical devices listed by the Ministry must be registered before being marketed in Italy. This includes approval for the production plant, the production of the product, and the marketing of the product. It can take up to two years to receive approval. Clinical trials must now be conducted in Italy.

Table 16

Ministry of Health



Multilingual labelling, as long as Italian is included, is acceptable. Labelling must include:

- Product name
- Instructions for use
- The amount and name of chemicals/compounds
- Name and address of the manufacturer
- Warnings regarding the key chemicals/compounds
- The Ministry registration number

In addition, certain products, especially sterile products, must include the lot number, date of production, and expiration date.

The Ministry uses the Italian drug GMP as a guide to inspect medical device facilities. Difficulties have been acknowledged in these inspections due to the drug requirements. In future the application of the EN29001 Quality Systems Standards will undoubtedly be introduced.

Imported products in finished form that are listed as medical devices must have prior approval of the Ministry before sale.

If the manufacturer does not have an Italian distributor, a legal Italian representative must be appointed. Applications for approval must be made in Italian, but supportive documentation can be in another language.

All advertising copy of medical devices needs to be approved by the MoH. If more than one mode, format, or script is to be use for the product, each mode, format, etc. must be approved.

Modification of any medical device already registered must also be authorized by the Ministry.

Laboratory equipment must meet the requirements of several standards relating to the needs of general manufacturing and electrical equipment and installation such as safety, vibration, speed, loading, guards, etc. Testing is carried out by the Italian Institute of the Mark of Quality (IMQ).

6.3.3 Standards Bodies

There are two national standards bodies: UNI, the Italian Body of Unification, and CEI, the Italian Electro-Technical Committee. Both have an extensive history of developing technical standards - UNI for non-electrical and CEI for electrical products. Both have approximately 30 standards relating to medical products. Both of these organizations receive funds from the Italian National Council of Research to develop national standards.

The only government recognized medical device testing house in Italy is IMQ. It is a non-profit organization sponsored by the Italian National Research Council.

6.3.4 Standards

The Ministry of Health requires that medical devices in the various use categories undergo testing in the laboratories of the Ministry. Some manufacturers will attempt to obtain the "IMQ" mark for electrical products as a marketing advantage. Italian laws do not specify which standards should be used to test medical devices, but more recently there has been an increased effort to use Italian standards that are based on international standards.

Medical equipment is tested according to the IEC 62 series which is based on IEC 601 -1 and -2. In addition, IMQ participates in testing agreements with European countries under CENELEC with mutual recognition of national marks of conformity. IMQ also has a mutual recognition agreement with BSI.

6.4 Developments

Italy published new medical device regulations in 1986. However, only one product has been regulated under this new law - HIV test kits. In 1988 a standard for hearing aids was published based on a IEC standard which was similar to a Harmonized CENELEC Standard.

6.5 The Market For Medical Devices

Italy is ranked as one of the top four medical markets of Western Europe, on a par with the United Kingdom. Consumption of medical products has reached 2,250 billion lire (US$1.95 billion). 1988 saw exceptionally strong growth in imported products which now account for 75% - 80% of the medical market.

The medical manufacturing industry is fairly extensive with around 700 manufacturers of medical, surgical and dental equipment, and several thousand involved in the production of orthopaedic and prosthetic aids. A large number of these companies are very small business concerns. There are around 50 major manufacturers of medical equipment with a workforce of some 3,500. The majority are situated in the industrial north.

An increasing number of multinational groups are setting up manufacturing bases in Italy, with the majority headquartered in Lombardy.

Total output by Italian manufacturers is estimated at around US$1,000 million.

Italian companies are strongest in the areas of x-ray diagnostic equipment, implantable pacemakers, cardiology equipment, dialysis apparatus, operating theatre equipment, anaesthesia equipment and respiratory apparatus, dental chairs and other medical furniture.

6.6 Market Access

In order to access the Italian market there are a number of "things to do" if the device needs to be registered.

Registration of medical devices in Italy is achieved through the Ministry of Health; however, the bureaucratic system consists of many different levels, and registration often becomes onerous and time consuming. Processing of applications takes from one to three years.

In preparing an application for registration one must determine whether or not the product is considered to be a "device" in Italy. There is the possibility that it would fit into a "drug category". Secondly, is registration a requirement under the Ministry of Health regulations? If not, no further action is required. Be aware that the MoH has a tendency to scrutinize compliance to regulations for products made of plastic.

It is advisable to utilize an Italian legal representative who may also be a manufacturer's distributor. However, consultants can be used and are often beneficial in identifying the path through the maze of local authorities. The legal representative or consultant should be a native Italian speaker, and should be on friendly terms with the government officials in charge of product registration.

It is advisable to meet the registration authorities in person. They can be invaluable in explaining issues that are less well defined. These authorities may also provide verbal practical advice on the application procedure or on regulation compliance, advice which is not readily translatable into writing.

Review the registration application for:

- Applicable standards
- The need to use an electrical test house (or is there a reciprocal agreement)

If there is a need to use a test house, it is advisable to meet with the test house personnel before any testing is done.

The application should include the following:

- Identification of the legal representative and of the manufacturer.
- A complete description of the product and its intended use.
- A brief description of the manufacturing procedures including sterilization.
- Copies of all labelling.

A note on communication:

It behooves the importer to be acutely aware of communication problems due to variations in language fluency or usage from one region to another within the importing country. The caution extends to translations and proof reading of product dossier, compliance materials, and procedural communications.

For companies without offices in Italy, the market is best approached through the appointment of an exclusive agent. Due to significant regionalization of the market (north, south, islands) it is important to ensure agents have adequate national coverage.

Since most agents are based in the industrialized north, national coverage is normally achieved through branch offices/sub-agents in southern Italy and Sicily/Sardinia.

The Italian medical market is distributed as follows:

+ Public hospitals: 70%
+ Private hospitals: 20%
+ Doctors: 10%

Within the public sector, procurement is decentralized to the local level. Equipment purchases are made on the basis of invitations to tender issued by the regional and local health authorities. The procedure incorporates a pre-selection phase. Payment is generally slow (6 - 9 months). Excessive bureaucracy is a problem in selling to the public sector. Procurement in the private sector is generally much less complicated and payment is faster.

6.7 Import Status

Imports have exhibited strong growth in recent years and now cover 75% - 80% of the Italian market. In 1988, Italian imports of medical equipment and supplies exceeded US$1 billion, representing a rise of 22% over 1987. Germany is the leading foreign supplier, contributing 25% - 30% of all Italian medical imports. German manufacturers are prominent in all sectors with a strong showing in the market for radiology equipment, dental equipment and supplies, surgical instruments, respiratory apparatus, medical furniture, bandages and dressings and suture materials.

The United States is the number two supplier with a 19% share of imports. U.S. manufacturers are particulary strong in the market for orthopaedic and prosthetic equipment, and in the market for catheters and cannulae.

France and the Netherlands are the other main contenders in the Italian medical market. The Netherlands is an important supplier of electro-diagnostic equipment, pacemakers, portable aids and implants, whilst France supplies mainly x-ray and dialysis equipment.

Generally speaking, companies with a significant share of the Italian market are those which have established manufacturing operations within the country e.g. Siemens, Hospal.

6.8 Medical Device Associations

There are two main trade associations:

- Assobiomedica which represents a large variety of medical products and is a member of the European Confederation of Medical Suppliers Association and European Diagnostic Manufacturers Association.

  Assobiomedica
  Via Accademia, 33
  20131 Milan
  Italy

7.0 SPAIN

7.1 Health Care In Spain

The Spanish constitution (1978) defines coordination of health care as an exclusive responsibility of the State. Although Spain is a unitary State, the responsibility for executing medical device control measures has been delegated to the six regions of Spain, known as the Autonomous Communities. The degree of autonomy granted each individual community, to execute the control measures, varies with the Community in question; hence, business arrangements are managed accordingly.

Most of the population is covered by the national insurance scheme. Social security contributions fund 80% of these programs and the balance comes from general taxation. The scheme covers only hospital and doctor treatments; for example, dental and ophthalmic procedures are excluded.

The National Health Institute is the administrative body of the health care system (including purchasing for the Health Ministry). Approximately one half of the hospitals in Spain are government owned or controlled; 45% are operated by profit making organizations and 15% are church operated. The government hospitals tend to be the larger, accounting for approximately 70% of the beds, and are mostly located in major cities.

As noted in Table 1 there is a relatively high number of doctors per thousand population. However, health care services such as primary and outpatient care are poorly organized and insufficient. The Ministry of Social Security health clinics and the Ministry of Health clinics are mandated to provide primary diagnosis, treatment and basic health care; however, they have been unable to meet these health care requirements and therefore the government hospitals have been pressed into service. This has resulted in demands for government funding to update and expand the smaller hospitals.

7.2 Trends In Health Care

All health care systems in the EC countries are similarly impacted by economic, social, technological, and demographic factors. In addition to these factors, Spain's health care system has been affected by the inequalities in health care facilities across geopolitical boundaries. Aware of these inequalities, the Health Ministry has commissioned a committee of health care experts to do an in-depth study of the health services, with the intent of proposing a new model for a health care system which will be more in line with the country's health care requirements as of 1991 (Clinica 415, Aug. 22, 90, p. 13).

Trends due to government cost-containment efforts:

- The Spanish health care system is under review in order to assess financial and technical requirements and resources, budgetary restrictions, and pharmaceutical spending, with the objective of rationalising health care spending in light of the aging population and high number of chronically ill patients (Clinica 415, Aug. 22, 90, p. 13).

Trends due to social/behavioral factors:

- By 1995, Spain is predicted to be the smallest contraceptive and home diagnostic market of all the EC, total approximately $120 million (Clinica 486, Jan. 29, 92, p. 11) as compared to Italy $300 million, France $150 million and Germany $180 million.

- A recent $8 million government campaign to encourage teenagers to use condoms has come under fire from the Catholic Church as well as from mothers' groups (Clinica 431, Dec. 12, 90, p. 10).

- In Spain some 200,000 women have had breast implants for cosmetic purposes (Clinica 487, Feb. 5, 92, p. 12).

7.3 Regulatory Framework

7.3.1 Regulatory Bodies

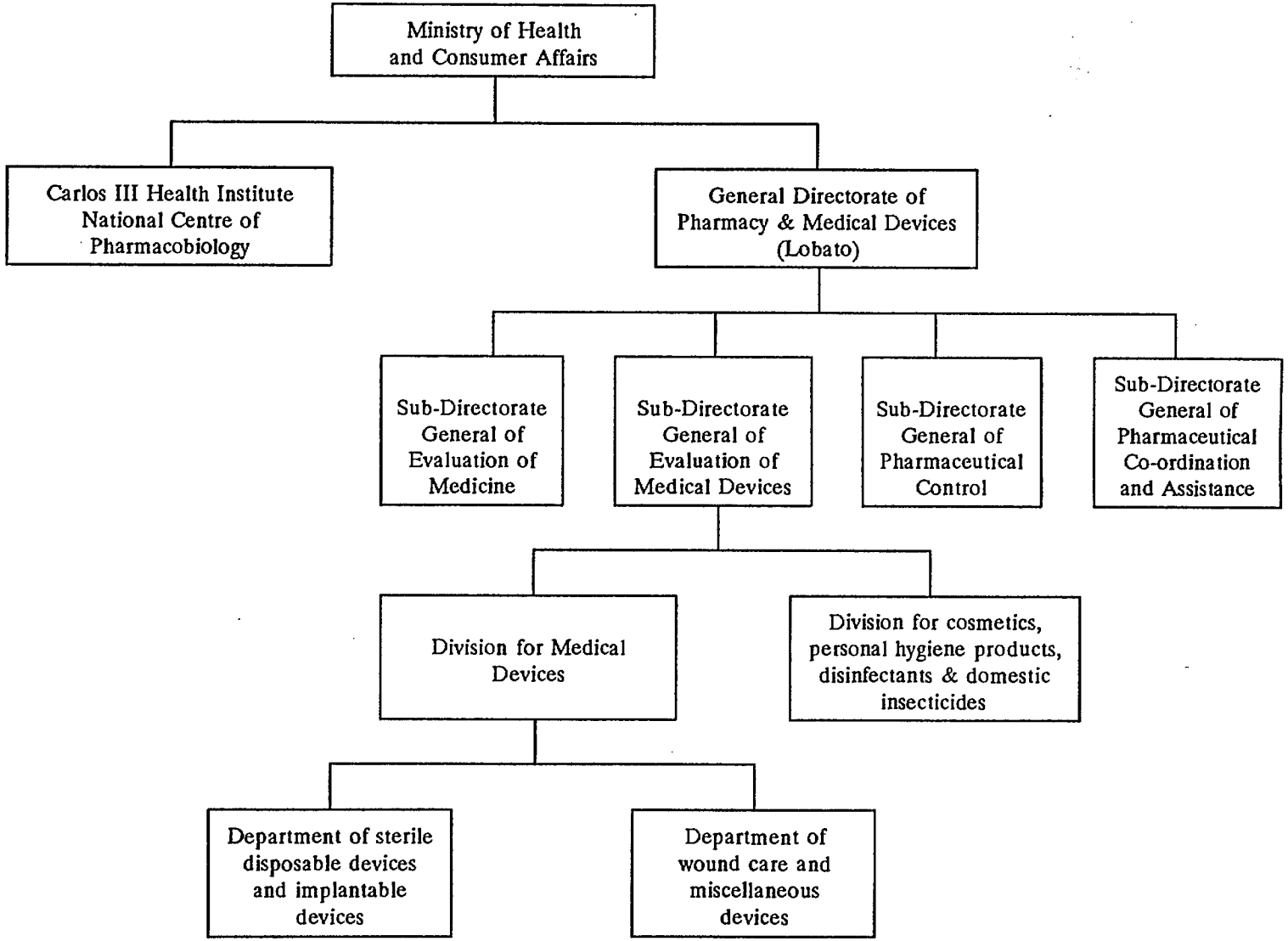
The Ministry of Health and Consumer Affairs executes its mandate to regulate and control all aspects of the medical device industry, (except the homologation of electromedical devices) via the General Directorate of Pharmaceutical and Medical Devices (Lobato), and the Carols III Health Institute National Centre of Pharmacobiology. Lobato is divided into four sub-directorates with each responsible for some particular aspect of medical device control (See Table 17 on the following page). For example:

Sub-Directorate General of Evaluation of Medical Devices

- Accept and select products for NHS
- Manage the product register
- Authorize manufacturers and importers
- Manage application process for scientific product evaluation

Table 17

Ministry of Health and Consumer Affairs



Source: Medical Device Approvals in Europe Today - Spain. G. Higson and A. Howard, Medical Technology Consultants Ltd., 1990, BRI/MTCE

Sub-Directorate General of Pharmaceutical Control

- ➢ Inspect manufacturers
- ➢ Control product market entry
- ➢ Control customs

The Centre of Pharmacobiology

- ➢ Responsible for the actual scientific evaluations of medical devices.

The Ministry of Industry and Energy

- ➢ Homologation (certification) of electromedical devices.

7.3.2 Regulations

Medical devices are included under Section V of the General Health Law of 1986, which in actuality deals with pharmaceutical products. Due to this peculiar method of referencing medical devices, the controls delineated under Section V may or may not be applied to medical devices, depending on the circumstances at the time of the interpretation of said section. Controls which may be affected in this manner are as follows:

- Pre-market approval
- Licensing of distributors and manufacturers
- Inspection of facilities
- Employment of a qualified technical director
- Reporting of adverse experiences
- Approval of advertising

Clinical trial requirements on the other hand have their own legislation and therefore have very specific requirements which include:

- Sufficient preclinical data prior to beginning the trials.
- Statement of ethical standards and patient rights.
- Experimenters' academic and professional qualifications.
- Ethical review of the trial protocols.

The regulatory framework identifies six categories of medical device schemes as follows:

- Sterile disposable devices
- Implants
- In-vitro diagnostics
- Contraceptive devices
- Dressings
- Homologation (certification) procedures

Sterile Disposable Devices

The regulation applying to sterile disposable devices does not include implants, dressings, IUDs etc. It requires the manufacturer to submit to inspection prior to being authorized; to employ a technical director, and to limit sterilization methods to radiation, EtO, steam and dry heat.

Importers must fulfil these same requirements. In addition, imported products must meet the requirements of the exporting country.

Pre-market approval of sterile disposable devices is required. The approval applies to all materials, sterilization methods, and product packaging. Companies are closely supervised, products inspected, and the five year approval may be cancelled at any time, with just cause.

Labelling is specific; it must be only in Spanish and indicate at least the product description, the batch number and the expiry date. The protective container must carry the preceding information, as well as instructions for use, risk factors, conditions for storage, and a warning not to use the product if the container appears to be damaged.

There are separate and specific control requirements for non-reusable devices such as needles and syringes. Any agent who does re-use a non-reusable device does so at his/her risk and assumes the responsibility for any adverse consequences. There are also specific requirements addressing technical specifications and labelling.

Implants

There are requirements for the testing of the physical, chemical and biological properties of implants. There are also testing requirements for such processes as oxidation, corrosion, toxicity, irritation, and dimensional calibration. However, none of these are implementable because of the lack of specific scientific criteria or reference monographs. Therefore no implants have been authorized in Spain except on an "exception" basis. Often the physician who proposes using the implant is required to justify its clinical necessity in order to buy or import said implant.

In-Vitro Diagnostics

In-vitro diagnostics require an authorization process for any reagents used in the detection of the HIV virus. Pre-market approval must be obtained under certain documentation requirements. Samples to carry out several hundred tests are required. Finally, positive test responses may not guarantee authorization; final authorization is dependent on whether the tests have been approved in the country of export.

Contraceptive Devices

The sale and advertising of intrauterine contraceptive devices are regulated as implants, or as drugs, depending on whether they contain active ingredients such as spermicides. Non-implantable contraceptive devices are also subject to control and inspection. All types of such devices have regulations controlling the content of the product information inserts.

Dressings and Similar Material

The manufacturer of cotton, gauze and dressings is subject to three regulation authorities: the Ministry of Health, the Ministry of Industry, and the Spanish Pharmacopoeia. If sold sterile, the materials must be registered with the Ministry of Health. Registration with the Ministry of Health also applies to sterile sutures.

Homologation

There are two homologation regimes, one for electrically powered devices and one for non-electrical devices.

Homologation of Non-Electrical Devices

Homologation is the certification process carried out by the authorities of the Ministry of Health, to test that the products meet the specifications issued in ministerial regulations. Unless certified, such products are not covered by Social Security, and are prohibited for "commercialisation". Products such as dressings, catheters, ostomy devices, elastic hosiery, and various external braces and trusses are subject to certification and price controls.

The Certificate of Authorization is granted for five years. It contains product information, regulations as to labelling, and a code of therapeutic classification for Social Security coverage. The Authorization also informs the manufacturer that random product inspections in the market place will by carried out periodically by the authorities.

Homologation of Electrical Devices

Electromedical devices, including: monitoring, x-ray, tubes, parts, tables, and mobile radiosurgical devices, cannot be sold or installed without homologation by the Ministry of Industry. Each type of electromedical device has its own specific and self-contained regulation.

All instructions for maintenance and use of the equipment, technical characteristics, and specifications, must be supplied in a dossier signed by a competent practical expert. The Ministry in turn will conduct testing and provide certification on a type approval basis dealing with electrical and radiological safety.

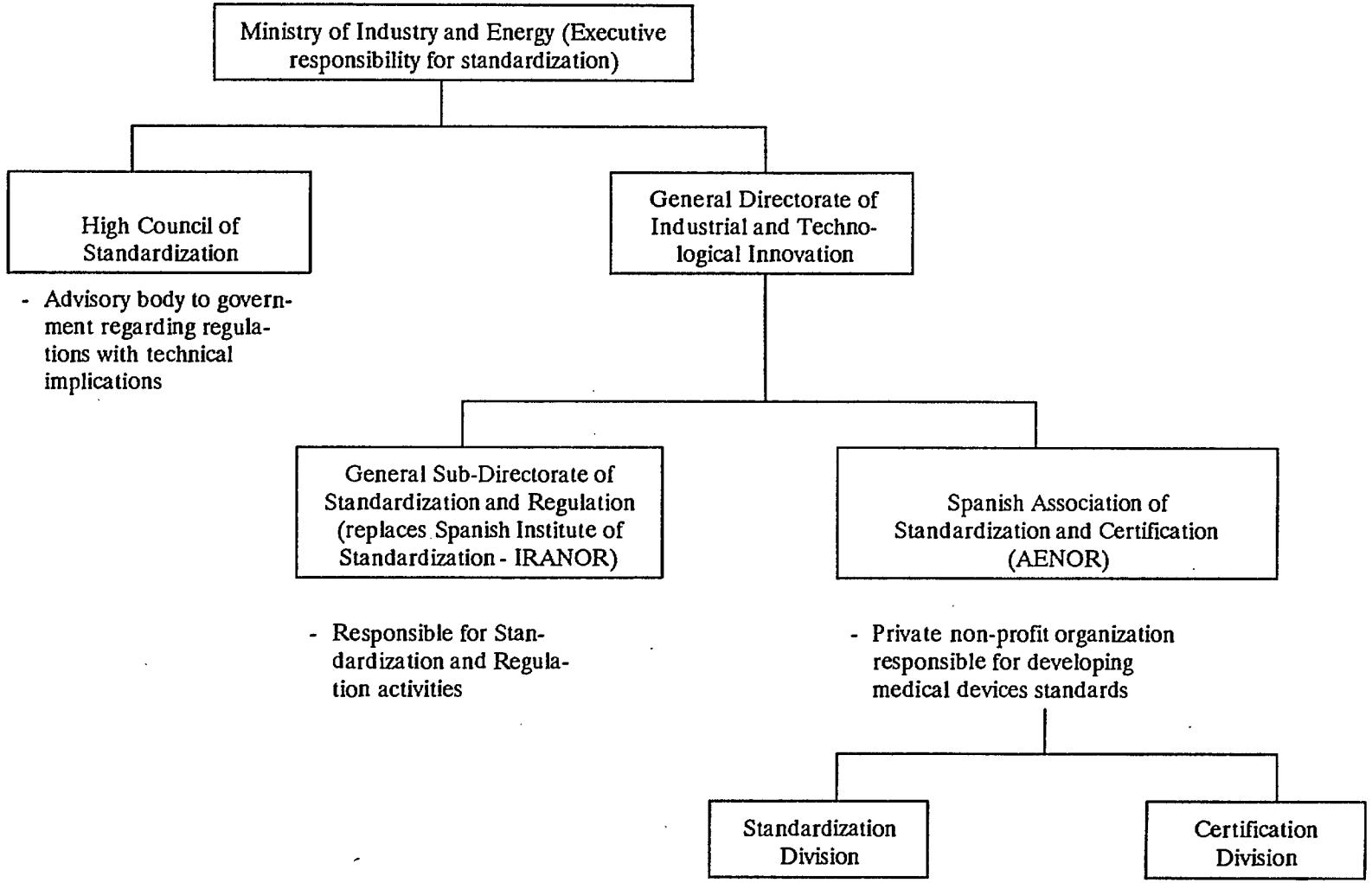
Homologation is required for each batch of devices that is imported into the country.

7.3.3 Standard Bodies

The Ministry of Industry and Energy has the executive responsibility for standardization. It receives advice and technical recommendations from the High Council of Standardization. The General Sub-Directorate of Standardization and Regulation, which now replaces the Spanish Institute of Standardization (IRANOR), has the responsibility for standardization and regulation activities, under the direction of the General Directorate of Industrial and Technological Innovation. Finally, the Spanish Association of Standardization and Certification (AENOR), a non-profit organization, is responsible for the development of medical device standards (See Table 18 on the following page).

Table 18

Spanish Standardization Bodies



7.3.4 Standards

The medical device standardization efforts in Spain are a recent development; in fact, only eight standards have been issued to date. However, with the coming EC standardization, many more standards are under way. At present standardization occurs at two levels, a general approach (standardization) and a specific approach (metrology).

Standardization

The health care section of the standardization division of AENOR is comprised of four technical committees: medical and surgical equipment and devices, dentistry, surgical implants, and laboratory medicine. As stated above their work is just getting under way.

Metrology

A similar requirement for units of measurement was introduced in 1985. This establishes the Metric System (SI) as legal measurement in Spain, particularly on all instruments and appliances that measure or weigh or count, which cannot be sold without prior approval. The type approval is given for a maximum of ten years and can be renewed. It does limit the number of units installed and where they are located.

7.4 Developments

Recently Spain has developed a program to introduce new regulations: a new medical device law, pre-market approval requirements for specific implants, certification and standards for various types of dressings, requirements for orthopaedic and incontinence aids, dental materials, and in-vitro diagnostic reagents. However, draft regulations for intraocular lenses and cardiovascular implants have not been implemented. The most recent regulations have dealt with HIV diagnostic reagents in an emergency situation. It appears that the lack of progress may be in anticipation of EC 92.

7.5 The Market For Medical Devices

Spain is able to provide itself with approximately 15% of its medical device needs. The growth of exports is slow; however, imports are increasing quite rapidly. Spain has a positive balance of payment in the area of syringes, needles, and related parts. Their second most important export product is x-ray and radiotherapy equipment. Imports of orthopaedic supplies, prostheses, and respiratory products are substantial.

The Spanish medical market is expected to continue to register above average growth for Europe as a whole. Much of the equipment in Spanish hospitals is obsolete and this is reflected in the large capital investment budget of the National Health Institute. Demand is centring on diagnostic technology including capital intensive scanning equipment. However, it should be noted that the recent boom in purchases of expensive technology has already drawn a reaction from the government which is establishing a body to control the use of advanced technology. Despite this development, substantial investment in new equipment is expected to continue to clear the backlog of equipment requirements. Another trend impacting the medical market is the shift in emphasis towards smaller, specialized hospitals with a corresponding expansion of out-patient services. This means a greater demand for more flexible, mobile equipment, as well as equipment associated with non-invasive techniques (medical lasers, endoscopy, etc.).

Foreign manufacturers, particularly German and American, will continue to dominate the market for advanced technology equipment.

7.6 Market Access

In order to access the Spanish medical device market, the importer must be aware of a number of critical factors:

1. It is a legal requirement to have Spanish representation. Devices can only be sold through a registered importer and in most instances must be technically approved.

2. A knowledge of Spanish is absolutely necessary as English is used very little, and poorly used in the regulatory area.

3. Experienced representation and personal contacts with the authorities is essential. The success of obtaining various authorizations frequently depends on the local representative's expertise and personal connections. Further, in that customs has the power to hold products, often the eventual release of said products is dependent on the personal intervention of a local representative.

4. It behooves the importer to verify precisely what information is actually "required" for the product dossier (to avoid releasing requested but not required proprietary information). The accuracy of the translated dossier about to be submitted should also be verified.

5. Spanish law requires that hospitals or other establishments which purchase medical devices and products must have the proper storage facilities. Failure to have the required storage facilities may result in the establishment being closed down.

6. In Spain customs officials play a significant role in the regulation of medical products that enter the country. Some of the roles of customs are:

   - ➤ Verification of all required authorization and importer license documentation.
   - ➤ Verification of pre-market authorization for:
     - Single use sterile medical devices
     - Implants
     - Sterile and adhesive dressings
     - Elastic hosiery
     - Ostomy products
   - ➤ Control and health inspection of products such as optical instruments, medical surgical instruments, and devices.
   - ➤ Testing of certain products.
   - ➤ Sending out samples of batch products to the applicable authorities for control purposes.
   - ➤ Inspection of labelling and packaging.

7. Device registrations in Spain may take four or five years. Implants frequently will not be approved at all. However, once the product pre-market approval application has been made, temporary import approvals can be obtained for individual shipments.

8. Product approval dossier contents, for most devices, are contained in the resolution of 17 June 1983. Dossier contents for products that require homologation are compiled on a by product basis.

9. Purchasing is often accomplished through calls for tender. Many exporters find that, by working through local agents, the details of the tender may be available before general publication; a bid can be placed through the agent.

10. Private health care suppliers tend to purchase directly through contact with local suppliers. National hospitals tend to purchase through local firms that offer sales service, technical training, and product support.

7.7 Import Status

Spain's import market of electromedical equipment is worth around U.S. $450 million, with growth rates around the 40% according to the Spanish Association of Electronic Industries. The majority of this growth is in high-tech, high-cost equipment such as CT scanners, NMR imaging equipment, and lithotripsy devices. Other equipment is as follows:

- X-ray equipment and accessories are worth about $100 million.
- Medical furniture about $12 million.
- Mechano-therapy apparatus, respiratory and massage equipment at about $35 million.
- Orthopaedic appliances at about $120 million.

Clinica 469 (Sept. 25, 91, p. 10) reports that previously prohibitively high import duties are being phased out over a seven year period, making the Spanish import market somewhat more accessible.

7.8 Medical Device Associations

The primary medical devices trade association is the National Federation of Scientific, Medical, Technical and Dental Instrumentation Companies.

- FENIN — Federacion Nacional de Empresas de Instrumentacion Cientifica Medica Tecnico y Dental
  Zurbano 92 - 6 izqda
  28003 Madrid
  Spain

8.0 SWEDEN

8.1 Health Care In Sweden

Health care in Sweden is the responsibility of the National Board of Health and Welfare, a subordinate government body. Under this body's auspices are 26 County Councils and 284 Primary Communes. The Councils are responsible for all of the hospitals, including the six premier regional hospitals. The Communes provide health care that is associated with schools and social services.

In Sweden 96% of the health care is public. The Swedish population enjoys a high level of health care which is funded through local taxes (approximately 66%), with the remainder funded through patient fees and State transfer payments.

8.2 Trends In Health Care

Sweden's above average life expectancy of 77 years has resulted in a considerable expansion of the elderly population. Nearly 18% of the population is aged 65 and over, and by 2000 9% of the population will be over 75 and 5% over 80.

Until recently health care in Sweden was heavily concentrated in hospital services and the country had one of the highest bed/population ratios in the world. Current development is aiming to shift the balance of resources away from hospital care to the primary health service.

Key features of the development program include:

- An 11% reduction in the number of hospital beds, particulary for acute care.
- Concentration of hospital services in larger facilities with a wider range of specialties.
- Replacement of older methods of treatment with newer methods leading to higher quality, and a continuing improvement in the productivity and effectiveness of care.
- Reduction of in-patient care through a speedier discharge of patients and an increase in treatment in out-patient facilities. The number of doctor visits to increase by 14% to an average of 3.7 visits per inhabitant per year.
- A more equal distribution of medical practitioners.

- Development of alternative long-term care facilities including expansion of the local nursing home network, and expansion of home care facilities.

- Other initiatives to improve elderly care include specific programs to treat cardiovascular disease, diseases of the locomotive organs and mental illness. Since 1987, more money has been made available to cut patient waiting lists by increasing the number of cataract, hip joint and coronary vessel operations.

8.3 Regulatory Framework

8.3.1 Regulatory Bodies

Although in many respects Sweden is considered a highly regulated country that focuses on safety, medical devices are subject to relatively few regulations. In fact, some medical device categories, for example implants, are not regulated at all. At present the principle medical device categories that are regulated are single-use devices and certain electromedical equipment.

Although the Ministry of Health and Social Affairs is responsible for public health, the National Board of Health and Welfare is the administrative arm for medical devices. Under this administration are several boards and agencies that have responsibility for certain product groupings and aspects of medical device regulation. They are as follows:

- The Advisory Board for the Safety of Single-use Sterilised Disposables - handles single-use devices (It is expected that the newly created Medical Products Agency will in the future take over this function.)

- Advisory Board for Medical Technical Safety - key agency for medical device technical safety.

- National Energy Administration (STEV) - key agency for electrical safety; the administration branch of this agency is the Electrical Equipment Registrar

- National Institute for Radiation Protection - issues dealing with radiation.

8.3.2 Regulations

Sterile Single-use Medical Devices

Sterile single-use medical devices are regulated according to the Act Governing the Control of Industrially Sterilized Single-use Medical Devices (SFS 1975:187). The law and regulations primarily apply to the manufacturers of the product; if the product is manufactured out-of-country, the importer is responsible for all legal and regulatory compliance. Implantable devices are excluded under these regulations.

Notification Process

The manufacturer or importer notifies the National Board of Health and Welfare of their intent to sell the sterile single-use product by completing the Nordic Product Notification (NPN) Form. Submitting the notification completes the regulatory process. (No review or pre-market approval is required.) The notification is used as a means of tracing the product should there be an incident associated with it.

The NPN Form requires the following information:

- Identity of the importer of manufacturer's representative in Sweden
- Product manufacturer
- Basic information on the product
- Listing of components and materials that come in contact with body fluids, tissue, or drugs
- Packaging and labelling
- Sterilization method and assurance data
- GMP and Quality Assurance
- Testing data, particularly biological safety

Unless all the information is provided in detail, the authorities will request additional information or clarification of the form's content.

Labelling

Mandatory labelling requirements identify four possible scenarios: direct labelling on product, individual product packs, ward packs (multiple or shelf packs), and transport packs. Although labelling in Swedish is preferable, especially instructions, English is tolerable in many instances.

1. Direct labelling on product pack requirements

   - Name of manufacturer
   - Name of the product, model number or size, number of items
   - Directions for use
   - Statement of sterility and single-use
   - Batch number and expiry date
   - Storage instructions

2. If the product pack is transparent, the above information may be applied directly to the product.

3. Ward pack labelling requirements

   - Name and address of manufacturer or Swedish importer
   - Date of manufacture/sterilization
   - Name of the product, type, model number or size, number of items
   - Directions for use
   - Statement of sterility and single-use
   - Batch number and expiry date
   - Storage instructions

4. The transport pack for ward packs with the same contents have the same labelling requirements as the ward pack labelling requirements. On transport packs the method of sterilization and single-use statement may be omitted.

Manufacturing

The Swedish authorities do inspect manufacturing facilities and importers; however, they do not carry out foreign inspections. For such inspections the guidance documents contain the following sections:

- Definitions
- General principles
- Personnel

- Premises, fixtures, fittings, equipment, etc.
- Documentation
- Raw material and packaging material
- Manufacturing process
- Recycling of materials, components, and products
- Quality control
- Handling during distribution and sales
- Complaints and product recalls

The objective of the inspections is to assure sterility as outlined in the National Board of Health Document, "Microbiological Purity of Industrially Sterilized Medical Devices for Single Use". This document contains several important requirements:

- ➤ Sterility level of 10^{-6}
- ➤ Sterility testing as outlined in the European Pharmacopoeia
- ➤ Routine sterilization preceded by qualification of equipment used, and validation of sterilization process
- ➤ Low bioburden prior to sterilization
- ➤ Recommended biological indicators
- ➤ Sterilization methods:
  - Autoclaving
  - Dry heat sterilization
  - Ethylene oxide
  - Formaldehyde in steam at 78°C to 80°C
  - Ionizing radiation

<u>Electromedical Equipment</u>

The National Energy Administration (STEV) has recently introduced legislation for registration and type approval of certain categories of electromedical equipment. Requests for information regarding the application of these regulations and an English translation should be addressed to:

Statens Energiverk (STEV)
Division for Electrical Products
S-11787 Stockholm

The STEV regulations outline the following categories of equipment which must be registered:

- General domestic electrical equipment
- Installation equipment
- Heated mattresses for operating room
- Home-use electromedical equipment such as:
  - Haemodialysis equipment
  - Recorders
  - Apnoea monitors

Generally, equipment supplied to hospitals does not require registration. However, if said equipment is not designed and built according to Swedish standards, or equivalent harmonized international standards, but otherwise incorporates similar safety features, it must be approved. The Swedish Institute of Testing and Approval of Electrical Equipment (SEMKO) does type testing for electromedical devices. Information on testing procedures, standards, and costs can be obtained from SEMKO at the following address:

SEMKO AB
S-164 22 Kista
Stockholm

The Laboratory of the Planning and Rationalization Institute of the Health and Social Services (SPIRMA), carries out safety conformity assessments on most of the electromedical devices used by hospitals. This is a voluntary regulatory scheme run by hospitals for hospitals. Using SPIRMA findings, they publish lists of recommended and non-recommended equipment. It is prudent to be listed as recommended.

SPIRMA
Novum
S-14152
Huddinge

Medical Laboratory Equipment

Currently there are no specific regulations for medical laboratory equipment other than the electrical wiring rules (STEV=-FS 1988:1).

Ionizing and Non-Ionizing Radiation Equipment

This type of equipment is regulated via regulations issued by the National Institute of Radiation Protection. The regulations concern the radiation limits of lasers and certain types of x-ray equipment. All laser products require pre-market approval. Testing is to insure safety and the prevention of accidental exposure. The National Testing Institute or SEMKO do the testing.

The National Testing Institute
Box 857
S-501 15
Boras

8.3.3 Standard Bodies

The two national standards bodies in Sweden are the Swedish Electrotechnical Commission (SEK) and the Swedish Standardization Commission (SIS).

8.3.4 Standards

SEMKO AB is a testing house that carries out mandatory and voluntary type testing in accordance with Swedish standards (which are transpositions of IEC 601-1 standards) or Nordic deviations.

The official Nordic deviations from IEC 601-1 are generally in line with the revision of IEC 601-1, 1977, which have been largely adopted in the latest edition, IEC 601-1: 1988.

The advantage of using SEMKO is that they are an independent body and are primarily standards oriented; they offer a certification mark (S-mark), and are members of several international certification schemes. This facilitates obtaining certification in other countries with reduced testing and time scales.

The applicant for compulsory registration must be a resident of Sweden and may be the manufacturer, importer, or distributor.

Registration does not entitle the applicant to affix the SEMKO S-mark to the equipment; for this the applicant must apply separately to SEMKO. A small administration fee is charged for the registration which may be extended annually up to the 10th year or until the product is altered.

SEMKO, like most other European test houses, is often perceived to be idiosyncratic in its interpretation and application of standards such as IEC 601-1. In part this reflects the absence of IEC 601-1 Part 2 standards for all types of electromedical equipment. Since the S-mark attests to the electrical safety and construction of the product, SEMKO reserves the right to draw on collateral safety standards to supplement the IEC 601-1 test requirements that they judge incomplete. For example, they may draw on standards such as, IEC 335 for Safety of Household and Similar Domestic Electrical Products and Components, or similar IEC specifications.

8.4 Developments

In 1985 the Swedish government appointed a commission to investigate the safety of medical devices and called for recommendations for regulatory control. The outcome of said commission was recommendations for:

- Improved training of users
- Quality assurance systems and product controls
- A proposal for a complete overhaul of the regulatory control system to include:
  - All medical devices to be manufactured under a GMP system
  - A proportionate control system by product class
  - Class III (high risk) to have mandatory testing and pre-market approval
  - All Class II products should be registered

Sweden intends to implement all of the above recommendations, but is waiting for the EC proposals to be finalized, so as to adhere to the EC system. Sweden has also indicated that it has intentions of applying for membership in the European Community.

8.5 The Market For Medical Devices

The high level of Swedish health care demands a corresponding high level of medical devices. Domestic medical device producers (approximately 100 manufacturers) provide approximately 2/3 of Sweden's medical device requirements.

The Swedish market for medical equipment and supplies is currently valued at SK 2.2 billion (US$400 million).

Swedish production of medical equipment and supplies is in the region of SK 3 billion. Electromedical equipment accounts for around 35% of output. Sweden maintains a sizeable balance of trade surplus in the medical equipment field. Deficits do, however, occur in a number of sectors, most notably syringes and needles, dental instruments, ophthalmic instruments, orthopaedic apparatus, hearing aids, bandages and surgical gloves.

The Swedish medical market is expected to continue to achieve substantial real growth over the next five years. Swedish hospitals are generally equipped to a high standard and are committed to remaining at the forefront of technology. The aging population will be the main impetus for demand with growth focused on orthopaedic and prosthetic equipment. Advanced diagnostic equipment and non-invasive surgical apparatus should also show strong growth. Best prospects for foreign suppliers include implants, advanced handicapped aids, cardiology equipment, medical lasers, medical imaging equipment and patient monitoring.

8.6 Market Access

The major end-users of medical equipment and supplies in Sweden are the county council and municipal heath care authorities. These organizations handle their own purchasing. In addition, there are a number of public organizations which handle equipment purchases on a national scale. The most important are:

- The Purchasing Company of the Federation of County Councils (SUB), which handles all purchases of handicap aids used privately by individuals outside of hospitals.
- The National Corporation of Swedish Pharmacies (Apoteksbolaget) which handles purchasing and distribution of ostomy and incontinence aids via a network of 760 pharmacies.
- The County Council Purchasing Centre (LIC) which controls over 65% of the market for orthopaedic and prosthetic equipment.

The Swedish Institute for the Handicapped sets standards for handicapped aids. A special unit with SPRI also carries out product testing for medical manufacturers. Whilst not mandatory, these test evaluations are closely followed by central purchasing authorities.

Although there is limited direct import of medical equipment from abroad, most foreign medical equipment is handled by agents and joint-venture companies.

8.7 Import Status

Imported products supply around 70% of the Swedish medical market. Imports have grown strongly with rises in excess of 20% over the past three years. (See Table 19). Particularly strong growth has been registered for orthopaedic and prosthetic equipment, with imports more than doubling between 1986 and 1988.

The EEC supplies over 50% of Swedish medical imports. The major suppliers are Germany (23%), United Kingdom (8%), and Denmark (7%). The United States is another important supplier accounting for around 27% of medical imports. Japan supplies around 6%.

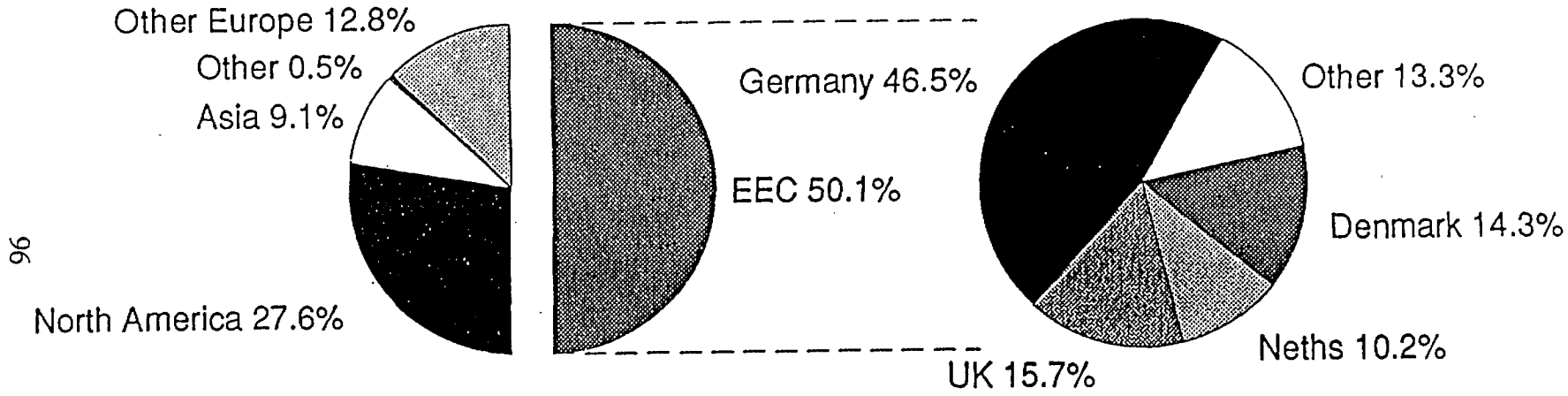
8.8 Medical Device Associations

The key Swedish trade association is the Swedish Association of Suppliers of Hospital Equipment (Svenska Sjukvards Leverantorere Forening) (SLF). The members are manufacturers, wholesalers and importers of medical devices, both active and non-active.

- SLF
  Sveavagen 17
  S-11157
  Stockholm

Table 19

Swedish Medical Imports 1988



Includes imports of non-medical x-ray

Source: United Nations Statistics

9.0 THE BENELUX COUNTRIES

The Benelux union of countries originated with Belgium and Luxembourg with the agreement of 1921, which entailed establishing common customs and balance of payments. The Netherlands joined the union after World War II. By 1948 the three states adopted a common external tariff; and by 1949 a harmonization process of internal tariffs was begun. The Benelux union is considered a harbinger of the European Community.

Headquartered in Brussels, the Benelux countries are constitutional monarchies, economically linked, with currency and exchange rates within 1% of the Deutsch mark. (Belgium's and Luxembourg's currencies are interchangeable.)

Statistics	Belgium	The Netherlands	Luxembourg
Population (1988/89)	10 Million	15 Million	372,100
GDP per capital (1987/88)	US$15,310	US$15,160	Added to Belgium
Hospital beds per 000 population (1986/87)	9	11	12.5
Doctors per 000 population (1986/87)	2.6	2.1	1.4

Source: Europa World Directory, 1990
Economist Intelligence Unit, 1990

BELGIUM

9.1A Health Care in Belgium

The health care system in Belgium is under the auspices of the Ministry of Health and integrated into the regional and national health service. All 500 hospital establishments, of which 50% are private and 50% are public, are licensed by the Ministry.

Belgium has a national health insurance scheme which covers all hospital care, including ophthalmic and dental. Ambulatory care is provided in health centres or in private practitioners' offices. Patients are reimbursed 75% of the cost of care that is received outside of hospital.

9.2A Trends in Health Care

Belgium is one of the most densely populated countries in the world, and like the rest of the EC is attempting to cope with the demands placed on its health care system by an aging population. Belgium's response to the spiralling health care costs has been to severely restrict:

- Laboratory and ambulatory diagnostic testing
- X-ray examinations
- Pharmaceutical products

The government has also halted installations of large devices and instituted a neighbouring hospital sharing arrangements (Clinica 470, Oct. 2, 91, p.11; Clinica 474, Oct. 30, 91, p.16).

Attempting to cope with its own aging population's demands for cardiac surgery and organ transplants, Belgium's response to the pressure on its hospitals from EC patients, particularly from Germany and Italy requiring these procedures, was to ask the European Commission and the Council of Europe to come to its aid. These two bodies are considering setting up registries of such services to co-ordinate and better utilize available resources (Clinica 476, Nov. 13, 91, p.13).

According to 1988 statistics mortality by major cause was distributed as follows:

- Circulatory System Diseases 41%
- Malignant Neoplasms 24%
- Respiratory Diseases 8%
- Violent Deaths 6%
- Other 20%

A comparison of the total surgical to total geriatric and long stay admissions to hospital (1982) and number of patient days in hospital (1982) indicates the following:

	Admissions	Hospital Days
Total surgical	240,235	2,401,192
Total geriatric and long stay	30,366	2,653,725

In view of Belgium's population density and age statistics (14.5 % over the age of 65), it can be predicted that a large proportion of health care resources will be devoted to the treatment and care of circulatory diseases and malignant tumours.

An extensive hospital construction program in the 1970's resulted in an over supply of beds by the middle 1980's. Although the government has cut back beds to rectify the excess, it is committed to maintain the high standards for hospital medical equipment. This commitment is exemplified by the annual capital investment of about US$200 million.

9.3A Regulatory Framework

9.3.1A Regulatory Bodies

Medical device regulatory control is organized under the Ministry of Public Health. Within its jurisdiction is the Pharmaceutical Inspectorate which is the specific authority in charge of regulating the manufacture and importation of sterile medical devices. In that it also controls pharmaceuticals, this can at time create difficulties.

Ethical review of experimental protocols are the Provincial Council's responsibility; while the Public Health Council is responsible for irradiated product approvals. Finally, the Institution of Hygiene and Epidermiology supervises the inspection of materials of biological origin.

9.3.2A Regulations

Non-Active Devices and Active Implants

The devices are covered by the Royal Decree of June 6, 1960. These require pre-market approval. The regulation addresses products, such as:

- Surgical sutures
- Sterile bandages
- Sterile injection, infusion, transfusion or drainage material as well as probes and catheters
- Internal surgically placed permanent prostheses and prosthetic material

The regulation covers the following controls:

- Licensing medical device manufacturers
- Product pre-market approval
- Product release by an authorised industrial pharmacist
- Labelling of medical devices

➢ Licensing of medical device manufacturers' includes:

  - Manufacture
  - Supply
  - Import
  - Wholesale

➢ Facility inspection includes:

  - Staff
  - Equipment
  - GMP (WHO standards)

➢ Pre-market approval includes

  - Identification of the device and the materials used
  - Documentation of sterilization process
  - Results of pyrogenicity and toxicity testing
  - If radiation sterilized the Public Health Council must also review the file.

➢ Market release by industrial pharmacist or authorized lab

  - Supervises analysis and testing process
  - Keeps samples
  - Insures regulatory and GMP compliance
  - Applies label signifying regulatory compliance

(In practice this has frequently meant that sterile products imported into Belgium have had to be re-sterilized prior to release on the market.)

➢ Labelling should be in one of the national languages, i.e. Dutch (Flemish) or French, and include:

- Health Ministry license number
- The batch number as follows: (manufacturing or sterilization date)
  - Year in digits
  - Months as a letter
  - Day as digits
- Expiration date
- If sterilized by irradiation:
  - Method of sterilization
  - Date of sterilization
  - Dose received
- Use and storage instructions (on the external package)
- For sutures:
  - Dimensions
  - Type
  - Nature of any conservation or antiseptic liquid

➢ Additional Controls

- If a medical device is deemed dangerous or lacking therapeutic efficacy:
  - The manufacturing premises may be entered
  - Its manufacture, importation, distribution or sale can be prohibited and delivery may be suspended

- It can be seized or destroyed
- Various penalties may be imposed including fines and prison sentences
- If the product is altered or damaged, a second pre-market approval may be demanded, even if the product had been approved and commercialized

Electromedical Devices

These devices have no specific regulatory scheme other than the European Community Directive 84/539 on electrical devices used in human and veterinary medicine. The regulation covers a wide range of low risk electromedical equipment such as: electroencephalographs, thermometers, various types of lamps, and so forth. Compliance (self-certification) to regulatory controls is left to the manufacturer or importer.

Medical Laboratory Equipment

Lab equipment has no special regulations; however, this equipment may be subject to the Drug Laws if:

➢ It is sold as having preventative or curative properties

➢ It is used in conjunction with accessories such as diagnostic chemicals, single-use sterile tubes, and sterile syringes.

The only national standards on medical laboratory equipment are two International Electrotechnical Commission (IEC) standards:

➢ IEC 278 "Documentation to be supplied with electronic measuring apparatus"

➢ IEC 348 "Safety requirements for electronic measuring apparatus"

Ionising Radiation

Ionising radiation is extensively regulated in Belgium by the 1963 decree referencing protection of the populous and workers from radiation, accordingly:

- Radiation emitting equipment requires Ministerial approval

- Unsealed radioisotopes cannot be imported, manufactured or sold without Ministry of Health approval, sealed radioisotopes are also strictly regulated and may in addition be subject to the Drug Laws

- Approval applications must contain:

  - Name of the isotope, type of radiation
  - Activity
  - Half-life and shelf-life
  - Physical and chemical state
  - Manufacturer/importer identification
  - Description of quality control procedures
  - The identity of the pharmacist or lab who will follow the product
  - Identity and Ministerial authorization of the customer

- Additional requirements re: mandatory use of accredited pharmacists, periodic reporting on delivered isotopes, labelling, and distribution

- Medical device sterilization by irradiation is restricted and must be authorized (done in conjunction with pre-market approval process) and labelled with the following:

  - Sterilized by irradiation
  - Nature of irradiation
  - Method of irradiation
  - Date of irradiation
  - Absorbed dose

  Information about the irradiation process and its effects on the product must be included.

Medical Mercury-In-Glass-Thermometers

Mercury thermometers are regulated by the Decree of October 31, 1986. The commercialization of thermometers bearing the EC control mark cannot be prohibited or curtailed. These products are controlled by the metrological division of the Ministry of Economic Affairs.

In-Vitro Diagnostics

The Royal Decree of January 9, 1990 on certain Diagnostic Preparations for Human use covers all chemical or biological preparations commercialized for testing of substances originating from the human being for diagnostic purposes. Products that are used in testing laboratories and which require the use of specialized equipment and particular specialist knowledge are excluded from the scope of this regulation. In practice, therefore, this regulation covers basically in-vitro diagnostic products sold to be public. The products covered by this regulation are subject to some of the requirements concerning medicines.

Clinical Trials

Clinical trials are conducted under a voluntary code of practice as outlined in the Code of Medical Ethics instituted by the National Council of the Order of Physicians (1975).

9.3.3A Standard Bodies

The Institute belge de normalization (IBN) holds the secretariat of CENTC 251 - Medical Informatics and is the Belgian member of CEN and ISO. The Comité electrotechnique belge (CME) is the member of CENELEC and IEC.

9.3.4A Standards

Belgium has a limited ability to develop national standards and draws heavily on international and European standards. The basic voluntary technical requirement is conformity with the Belgian standard NBN C 74-101, which is equivalent to IEC601-1. The Belgian standard contains minor variations from the international standards.

9.4A Developments

The Belgian Government passed a law on July 20, 1990 creating a National Accreditation and Certification Council, which will determine the criteria for accreditation and control the accreditation process for test laboratories and related bodies. The Council's longer term objective is to obtain international recognition, reciprocal agreements, and to link into the new European medical device directives system.

9.5A The Market for Medical Devices

Belgium produces 25% of its medical devices, primarily in the x-ray equipment and disposable devices, mainly dressings and syringes. The domestic manufacturers tend to be small organizations; however large multinationals are beginning to set up shop in Belgium in order to establish a central base to serve the rest of the EC market.

Luxembourg forms a part of the Belgo-Luxembourg Economic Union, hence its market assessment and import status have been included as part of Belgium.

The Belgo-Luxembourg market for medical equipment and supplies is currently worth in the region of BFr 17 billion (US $535 million). Its domestic production is currently estimated to be around US$300 million. There is limited manufacture of electro-diagnostic equipment, pacemakers, transfusion apparatus, dental instruments and supplies, sterilization equipment, orthopaedic and prosthetic devices.

The medical equipment and supplies market is projected to grow at approximately 3-5% in real terms over the next three years. Despite budget cutbacks, the government is committed to maintaining the high health care standards, and the introduction of new medical technology will continue. Above average growth is expected in the following equipment categories:

- Cardiology and neurology equipment
- Ophthalmic instruments
- Electro surgical equipment
- Orthopaedic and prosthetic goods

9.6A Market Access

The General Pharmaceutical Inspectorate accepts applications for pre-market approvals. The application form (M1) requires certain specific information about:

- The applicant and origin of the product
- Brand name and catalogue numbers
- Parameters such as: sterilization, cycle parameters, bioburden, validation and use of biological indicators.
- Copies of labelling instructions for use
- The packaging variables
- Diagram and description of the device, including its functions
- List of materials (or medicinal products) that come in contact with human tissue and any testing of said
- Dossier on product's complete testing history including initial research data

Medical devices that are sterilized by ionizing radiation are subject to additional information requirements concerning radiation safety for inhabitants and workers:

- Post-irradiation component materials and toxicological tests
- Hygienic measures incorporated into the manufacturing process
- Pre-sterilization bioburden
- Irradiation plant description, including safety measures and plant authorization
- Reference micro-organism inactivation curve employed at plant commissioning
- Irradiation process controls, including dosimeters
- Shelf-life, packaging and related testing data

The Pharmaceutical Inspectorate reviews the application, whereas the Public Health Council inspects the irradiated device.

The medical device market is served by a network of experienced local distributors (many of whom are involved in re-export activities), and by the manufacturing and sales subsidiaries of multinationals (particularly U.S.). The market is very open as opposed to a "buy-local" procurement policy.

The private sector is an important end-user of medical devices and supplies, accounting for 55-60% of total consumption. Many private hospitals are dependent on government subsidies for equipment funding.

9.7A Import Status

Belgium imports 80% of its medical devices. The most active areas include: electro-medical devices, orthopaedic equipment, dental apparatus, and dressings.

Germany and the Netherlands are Belgium's chief trading partners.

Imports play a dominant role in the supply of medical devices to the Belgo-Luxembourg Economic Union. In 1989 80% of this market was supplied through imports worth approximately BFr 20.7 billion.

Table 20 depicts the source importers by percentage of market share.

9.8A Medical Device Trade Associations

There are two major trade associations for medical device manufacturers:

FABRIMETAL, the Belgian Member of COCIR and EUROM and UNAMEC, the Belgian member of EUCOMED.

➤ FABRIMETAL

FABRIMETAL
Fédération des entreprises de l'industrie
des fabrications métalliques
Lakenweversstraat 21
B-1050 Bruxelles

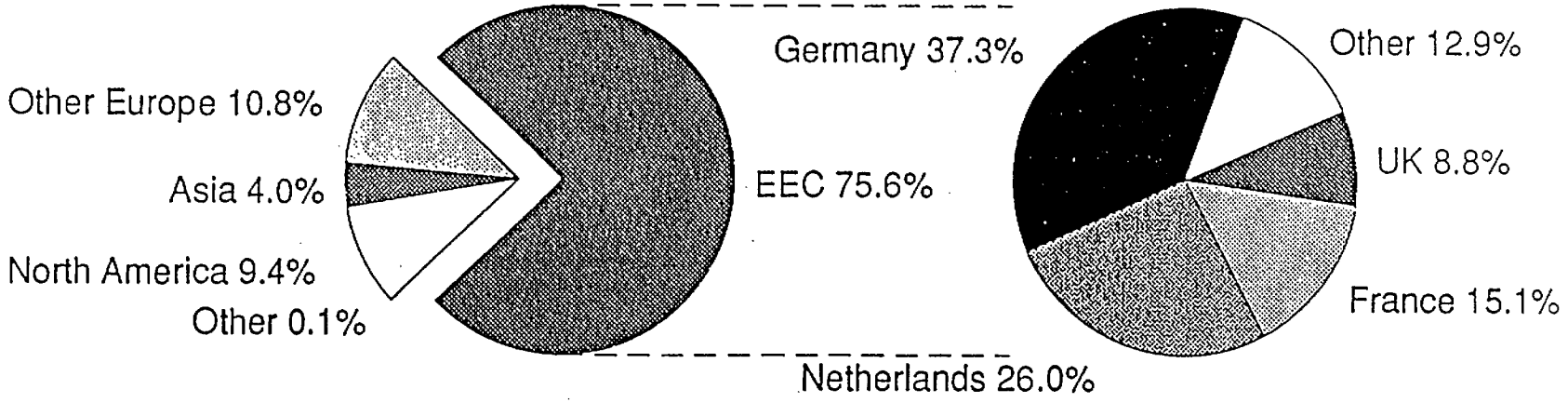
UNAMEC is the Belgian member of EUCOMED.

➤ UNAMED

UNAMED
Union professionelle reconnue des fournisseurs
en equipment médical et para-médical
Leuvensestraat 29
B-1800 Vilvoorde

Table 20

Belgo-Luxembourg Economic Union Medical Imports 1988



Includes imports of non-medical x-ray

Source: United Nations Statistics

NETHERLANDS

9.1B Health Care In The Netherlands

Health care in the Netherlands is organized on a regional basis under the auspices of the Ministry of Health. The national health care insurance scheme (Ziekenfondsverzekering) covers 70% of the population, and is mandatory for individuals below a certain income level (approximately $22,000 per year). The remaining 30% of the population is covered by private health insurance. The state health insurance covers all hospital treatment for a flat fee.

Hospitals in the Netherlands are primarily private (80%) and non-profit. Although there are a few group practices, the majority of physicians work in private practice settings.

9.2B Trends in Health Care

- Elderly facilities have seen a rapid growth in the past 20 years. In 1989 there were 325 nursing homes with 51,000 beds, an increase of 9.4% since 1980. There are approximately 150,000 elderly care beds in old people's homes.

- Cardiovascular diseases represent the largest single cause of admission to hospital, followed by disease of the locomotor system, neoplasms and gastro-intestinal diseases. According to 1987 statistics the mortality rate from circulatory system diseases was 42%, and from malignant neoplasms was 29%.

- The health care system in the Netherlands is scheduled to undergo a major restructuring, with an anticipated finish date of 1992. Part of the changes will be the elimination of the three-tier health insurance system. From that date forward health care will be covered by a comprehensive state insurance system which will include all care other than dental, physiotherapy treatment and medicines, which will be covered by a supplemental insurance scheme. There no longer will be a distinction between state or private insurance schemes; both will have to accept all applicants. The scheme will be financed by income-adjusted levies.

- The restructuring program's objectives included the introduction of market forces into the system in hopes of generating greater efficiency and flexibility. A part of this objective is the recommendation for the reduction of some 12,000 beds, a reduction in the number of medical specialists, and a restriction on the annual increase in the number of new nursing home beds.

9.3B Regulatory Framework

9.3.1B Regulatory Bodies

The medical devices regulatory authorities are organized under the Ministry of Welfare, Public Health and Cultural Affairs. The specific department responsible for medical devices is the Directorate General of Public Health, Head Department for medicines, medical devices and infectious diseases.

The Laboratory for Medicines and Medical Devices (LGM) is responsible for the management and administration of the sterile device regulatory scheme. The Department of Radiation Hygiene controls the regulation of medical devices falling under the Atomic Energy Law. Finally, facilities and procedural inspections are carried out by The Pharmaceutical Inspection.

9.3.2B Regulations

The Dutch medical device control system is considered one of the least bureaucratic of all the EC schemes. In fact, electromedical devices are not regulated in practice and the regime governing non-active sterile devices has been described as uncomplicated, particularly the pre-market authorization process.

Non-Active Medical /Devices

For regulatory purposes, medical devices are defined as appliances and objects intended for human use in diagnosis and the treatment/repair of the human body.

Sterile Products

Sterile product regulations cover all medical devices which are marketed as sterile medical devices. The regulations require:

- Pre-market notification
- Documentation of sterilization process
- Labelling requirements
- Batch certification
- Follow-up inspection of the warehouse, sterilization process, labelling, and sterilization documentation

Pre-market Notification for Sterile Medical Devices

The pre-market notification procedure requires the following type of information:

- Name and address of the local distributor, the accountable local agent and an excerpt of their Dutch Commercial Register
- Intended device application, type, and brand name
- Name and address of the foreign manufacturer and sterilizer
- Sterilization method

The application tends to be confirmed within two or three weeks, after which the product may be sold.

Documentation of the Sterilization Process

The manufacturer is required to compile a sterilization dossier containing the following information:

- Product registration number
- List of the device components and packaging materials
- Documentation on the sterilization equipment, sterilization parameters, and the sterilization equipment's maintenance schedule
- Validation of the sterilization process
- Chemical and physical sterilization effects on the product and product component materials

The regulation parameters on the sterilization of medical devices (particularly those used in drawing human blood) in hospitals are as exacting as those for industry. This may promote the sale of industrially sterilized products and most important, deter the re-use of single-use products.

Labelling

Unit-product containers and the outer container (if applicable) must display the following information:

- Description of contents if the container is not transparent
- Indication of sterility
- Batch code
- If appropriate, expiration date, expressed as a month and a year
- Directions for opening
- If appropriate, indicate single-use
- Storage instructions
- Sterilization method
- Product registration number

Labelling information may be written in Dutch, English, French or German.

Batch Certification

A batch certificate must be issued for each sterilization batch and signed by the sterilization supervisor. The certificate must indicate that the sterilization method is consistent with the designated pre-market approval method. The certificate may be in Dutch, English, French or German and should be kept by the Dutch distributor for five years.

Electromedical Devices

Electromedical devices are not regulated, in that the purchase of reliable and safe devices is considered a part of the medical practitioner's professional responsibility. To that end the major control of electrical devices lies in the reimbursement system as delineated in the Hospitals Provisions Act, Article 18. In practice many hospitals prefer to buy equipment that has been certified by a reputable laboratory such as KEMA or TNO.

Medical Laboratory Equipment

Medical laboratory equipment is regulated by the Low Voltage Directives (73/23/EEC). To comply with this regulation the manufacturer self-certifies the product and provides product identifying documentation. Other than this, there are no national standards for this type of equipment.

Ionising Radiation Regulations

The Ionizing Radiation Safety Decree and the Nuclear Energy Act set out parameters for the protection of personnel working with x-ray equipment and materials emitting radiation. These directives apply to all environments that handle radioactive material, ranging from hospitals to nuclear reactor plants.

Linear accelerators and X-ray apparatus with tube voltages in excess of 100kV are licensed by the Minister of Social Affairs and Public Health. Even though the award of a licence is published in the Governmental Gazette, the end user is required to notify the local authority upon installation or removal of said equipment.

Devices in medical or veterinary practice have restricted radiation emission leakage of not greater than 100 milli-roentgen per hour for diagnostic equipment, or one (1) roentgen per hour for therapeutic equipment. These devices are subject to examination by the regional public health inspector who is in charge of environmental hygiene.

9.3.3B Standards Bodies

There are two standards institutions: Nederlands Normalisatic-Instituut (NNI) is responsible for non-electrical products and is the national member of CEN and ISO. Nederlands Electrotechnisch Comite (NEC) is responsible for electrical products and is the national member of CENELEC and IEC.

The test and certification body for electrical safety is Keuring Van Electrotechnisch Materialen (Electrical Test Authority, KEMA). Until recently, KEMA had not been actively involved in conformity assessments of electromedical equipment. This situation has changed; manufacturers may voluntarily apply for KEMA certification based upon type-tests to the IEC 601 standard series with inspection of the production facility in accordance with EN 29002. Products found to comply are eligible to bear the KEMA-KEUR certification mark.

Electromedical safety testing for electromedical device manufacturers and health care organizations is conducted by the Medical Technology Unit (MTD) of Toegepast Natuurwetenschappelijk Onderzoek (TNO).

9.4B Developments

There are a number of changes occurring in regulations and guidelines for medical devices:

- Medical experiments have to date been reviewed by various hospital and university committees. This will change as soon as the newly drafted medical experimentation laws come into effect.

- New regulations are presently being drafted for in-vitro diagnostics, which for the present will be contained within the pharmaceutical law framework.

- At present Dutch hospitals need to be accredited in order to obtain social health insurance contracts. The accreditation requirements include safety of patients and personnel assurance, and a mechanism for reporting medical device incidents. An upcoming health care delivery Act will modify the current legal responsibility agreements and the control systems involved in accreditation.

- The National Institute of Public Health and Environmental Hygiene (RIVM) is involved with other interested parties in developing new guidelines related to sterilization carried out in hospitals.

- The Toegepast Natuurwetenschappelijk Onderzoek (TNO) has issued a guideline on disposable transfusion and infusion devices.

9.5B The Market For Medical Devices

Despite the climate of cost-cutting, Dutch hospitals have been making considerable investment in new technology, such as CT scanning, Magnetic Resonance Imaging and Positron Emission Tomography. These techniques are being used in an increasingly wider range of applications, and further investments are likely, although these will be subject to approval from the Ministry of Health.

Although private commercial enterprise is still effectively excluded from the Dutch health care network, there are signs that private enterprise on a limited scale may gradually be introduced in the 1990s. A number of feasibility studies have been undertaken in this field. Private practice will most likely take the form of independent practitioners setting up in private practice, the creation of diagnostic screening centres and existing hospitals undertaking certain private work, as opposed to the establishment of new commercially oriented private hospitals.

The Dutch medical market will continue to be characterized by low growth. In the capital equipment sector, the market is essentially a replacement one with the only growth arising from the acquisition of more expensive technology. Medical imaging is a market which continues to be active with a substantial government funded research program into new techniques such as MRI and PET. The tight financial situation means that the marketplace is highly competitive. Dutch end-users have a reputation for loyalty to established suppliers. New-to-market equipment is most likely to succeed if it offers clear technological advantages or is labour saving. Dutch end-users are extremely quality-conscious and also expect first class service and after sales backup. The market for disposables and supplies is also feeling the effects of government cutbacks, although to a lesser extent, and certain areas associated with orthopaedic and cardiac surgery and elderly care in general are steadily expanding.

9.6B Market Access

Although there are no regulatory requirements for electromedical devices, it is prudent to check the hospital imposed technical conditions of purchase. These conditions tend to act as a quasi-regulatory filter.

The regulations and pre-market notification on sterile devices should be completed by a "responsible party", usually the distributor. In selecting the "responsible party" some key points should be kept in mind:

- They have adequate warehousing facilities
- They are competent to handle the required documentation
- They understand the required content and are able to store the required files for up to 5 years

The Dutch medical market is primarily serviced by agents and distributors representing manufacturers on an exclusive agency basis. Several of the larger agents maintain sales offices in Belgium to service the Belgian market (particularly the Flemish region). Most agents and local manufacturers are members of the trade association Het Instrument which covers scientific and laboratory instrumentation in addition to medical technology products. There are approximately 500 members of which 100 are active in the medical field.

The most important end-users of medical equipment are the eight university hospitals at Amsterdam(2), Groningent, Leiden, Masstricht, Rotterdam, Utrecht and Nijmegen and the 172 other acute care hospitals.

The market breaks down roughly as follows:

- Teaching Hospitals 15%
- Acute Care Hospitals 65%
- Other Hospitals and Nursing Homes 10%
- Independent Practitioners 10%

An important purchaser of medical equipment is the Rijksinkoopbureau, a government purchasing agency which buys on behalf of university hospitals together with many other hospitals. Smaller orders are purchased through agents and distributors registered with the agency. Larger equipment orders are conducted on the basis of restricted tenders published in the Supplement to the Official Journal of the European Community. The Ministry of Defence also regularly issues tenders for medical equipment.

9.7B Import Status

Imports supply 60% - 70% of demand in the Dutch medical market. This figure rises to 80% when radiology sector (where Philips dominates) is excluded, and in sectors such as orthopaedic implants the market is almost entirely covered by imported products.

Between 1985 and 1986, total imports of medical equipment and supplies rose in value by 6.8%. In 1987, there was an increase of just 2.1%, followed by an increase of 6.6% in 1988 to 1.6 billion guilders.

There has been strong demand for electromedical and x-ray equipment. Imports of medical and dental instruments, mechano-therapy/artificial respiration apparatus and medical furniture have also risen steadily. There has been a downturn in the sectors of orthopaedic and prosthetic equipment and medical supplies.

Above average growth has been recorded for:

Table 21

Medical Device Impact Growth for 1985 - 1988

Medical Device	Percentage
Medical x-ray units	+ 66
ECGs	+ 34
Syringes	+ 95
Needles	+ 68
Optical ophthalmic instruments	+126
Wheelchairs	+ 60
Medical and dental furniture	+ 44
Endoscopes	+ 27
Hearing aids	+146
Fracture appliances	+154
Dental instruments	+ 48
Adhesive dressings	+ 54

9.8B Medical Device Associations

The major Trade Associations for suppliers of medical devices are NEFEMED, the Dutch member of EUCOMED and FME/FARON, the Dutch member of COCIR and EUROM.

- NEFEMED
  NEFEMED
  Postbus 90154
  NL-5000 LG Tilburg

- FME/FARON
  FME/FARON
  PO Box 190
  NL-2700 AD Zoetemeer

LUXEMBOURG

9.1C Health Care in Luxembourg

Luxembourg's health care insurance system is under the auspices of the Ministry of Labour and Social Security. The health care insurance scheme applies to the entire population and is funded by employee and employer contributions. Although all hospital care is free of charge, patients contribute to specialty consultations and dental treatment.

According to 1985 health care statistics, there are 20 general hospitals and 13 specialty hospitals. These health care facilities are considered very adequate and no development was planned at that time. Finally, patients are free to choose their doctor and facility.

9.2C Trends in Health Care

According to 1988 statistics mortality by major cause was distributed as follows:

- Circulatory System Diseases 47%
- Malignant Neoplasms 25%

In view of Luxembourg's population age statistics (13.4% over the age of 65 in 1988), it can be predicted that a large proportion of health care resources will be devoted to the treatment and care of circulatory diseases and malignant tumours.

9.3C Regulatory Framework

9.3.1C Regulatory Bodies

Luxembourg is a small country and thus has very little regulation on medical devices, apart from implementing EC law. A proposal was made in the recent years which would have introduced home-grown regulation of medical devices. This was never implemented because of EC developments.

9.3.2C Regulations

There are no specific regulations on non-active devices; however, the EC Directive 84/539 of September 17, 1984 on electromedical devices used in human and veterinary medicine is implemented by the Decree of August 8, 1985. In accordance with this Directive Member States may not, on grounds of safety relating to the manufacture, refuse, prohibit, or restrict the sale, free movement, or use for its intended purpose of the equipment provided it conforms with the requirements of the basic technical requirements embodied in the CENELEC harmonization document HD 395-1 (=IEC 601-1:1977 with minor amendments). The regulation covers a substantial range of devices, mostly at the lower risk end of electromedical equipment, e.g. electro-encephalographs, thermometers, various types of lamps, etc. The manufacturer or importer must self-certify conformity of the devices with the requirements of the regulation.

No regulations apply to medical laboratory equipment.

9.3.3C Standards Bodies

Luxembourg imports equipment from Germany, France, Holland, or Belgium, and relies on the regulations which apply to manufacture in these source countries.

9.3.4C Standards

Neither certification nor testing of equipment is required as a prerequisite, although naturally there is an expectation that products are safe according to state-of-the-art.

The Department of Radiation Protection requires that approval be obtained before any medical devices which emit ionizing material are installed. The department also carries out periodic safety audits.

The August 8, 1985 regulation of the Grand Duke on electrical equipment using ionizing radiation lays down post-marketing technical requirements.

Luxembourg has no formal regulation governing the control of clinical trials.

9.4C Developments

Luxembourg relies on the regulatory controls and standardization requirements of its source countries. It can be anticipated that any ISO developments that occur within the export countries will by default apply to Luxembourg.

9.5C The Market For Medical Devices

Luxembourg forms a part of the Belgo-Luxembourg Economic Union; hence, its market assessment and import status has been included as part of Belgium. Its health care services are well developed, but the medical market is limited by the small population of less than 400,000.

9.6C Market Access

In the absence of specific regulations for most medical devices, there should be little difficulty in their commercialization in this regard. From a product liability stand-point, observance of the EC directives will serve to meet the suppliers' legal obligations, and compliance with harmonized standards will serve to underwrite the safety and construction of the design.

Please refer to Market Access - Belgium

9.7C Import Status

Please refer to Import Status - Belgium

9.8C Medical Device Associations

Please refer to Medical Devices Associations - Belgium

10.0 STANDARDIZATION EFFORTS FOR 1993

10.1 After 1992 the single market of the European Community will develop a single regulatory scheme, rendering obsolete the unique regimes of the current member states. Introduction of a product in Belgium, for example, will be the same as the UK or France. The procedure will involve achieving the CE mark status by demonstration of conformity to the EC regulatory process.

10.2 Requirements of the EC regulatory process will consist of:

- Legally binding directives which specify the essential requirements for medical devices.
- Voluntary harmonized technical standards, which clarify what the essential requirements mean in actual practice.
- A system of conformity assessment and certification which governs how regulatory compliance will be controlled.

10.3 Conformity with the essential requirements of the directives will be illustrated by the awarding of the CE mark. (See Tables 21 - 23). This will be achieved through one or more of the following options:

- Manufacturer's self certification (declaration of conformity).
- Audit by a third party of a manufacturer's quality system, based on the ISO 9000 series of quality management standards.
- Approval by a third party of a product dossier, and
- Third party testing of a product (type-testing).

Only one member state of the EC will need to provide such third party approval in order to obtain a CE mark. Access to the entire EC is thus achieved.

10.4 The entire population of medical devices will be covered by three harmonising directives.

- Active Implantable Medical Devices (AIMD)

  i.e. pacemakers, implantable drug pumps, neuro-stimulators, cochlear implants, etc.

This Directive was adopted in 1990 and comes into force on the 1st January 1993. This document sets the pattern for the other two Directives.

- In-Vitro Diagnostic Devices (IVDD)

  i.e. laboratory analysers, reagents, kits, etc.

This is at a very early stage.

- Medical Devices

  i.e. any medical device which is not an AIMD or an IVDD.

This Directive is now at an advanced stage and will probably come into effect in mid-1994 or early 1995.

10.5 Implementation/Harmonization

The Directives become EC legislation and require member states to adjust their laws and regulations to the requirements of the Directive within a certain time frame. The AIMD directive has achived this status. The following time tables are not firm (for medical devices and in-vitro diagnostic devices).

10.5.1 Active Implantable Medical Devices

- Adopted 20 June 1990
- Comes into force 1 January 1993
- Tansitional period to 1 January 1995

10.5.2 Medical Devices

- Commission proposal 30 August 1991
- Comes into force 1 July 1994
- Transitional period to 30 June 1997

10.5.3 In-Vitro Diagnostic Devices

- In preparation
- Comes into force 1 January 1996
- Transitional period ? 1 January 2000?

10.6 Essential Requirements

Examine the essential requirements and decide which ones apply to your product.

There are 46 essential requirements in Annex 1 of the proposed Medical Device Directive. Six of these are general requirements and the remaining 40 address particular requirements such as:

- Chemical and physical properties;
- Infection and microbial contamination;
- Construction and environmental properties;
- Devices with a measuring function;
- Protection against radiation;
- Requirements for medical devices connected to or equipped with an energy source;
- Information supplied by the manufacturer.

10.7 Conformity Assessment

Decide on the conformity assessment procedure to be used.

The conformity assessment procedures increase in severity with increase of class number and for all classes except Class 1 there is a choice available to the manufacturer.

Class 1 - Manufacturer's declaration of conformity (plus production control for sterile devices or devices with a measuring function).

Class 2a - Either:

- Manufacturer's full quality assurance; or:
- Manufacturer's declaration of conformity accompanied by production verification or by production quality assurance or by product quality assurance.

Class 2b - Either:

- Manufacturer's full quality assurance; or:
- Type examination followed by production verification or by production quality assurance or by product quality assurance.

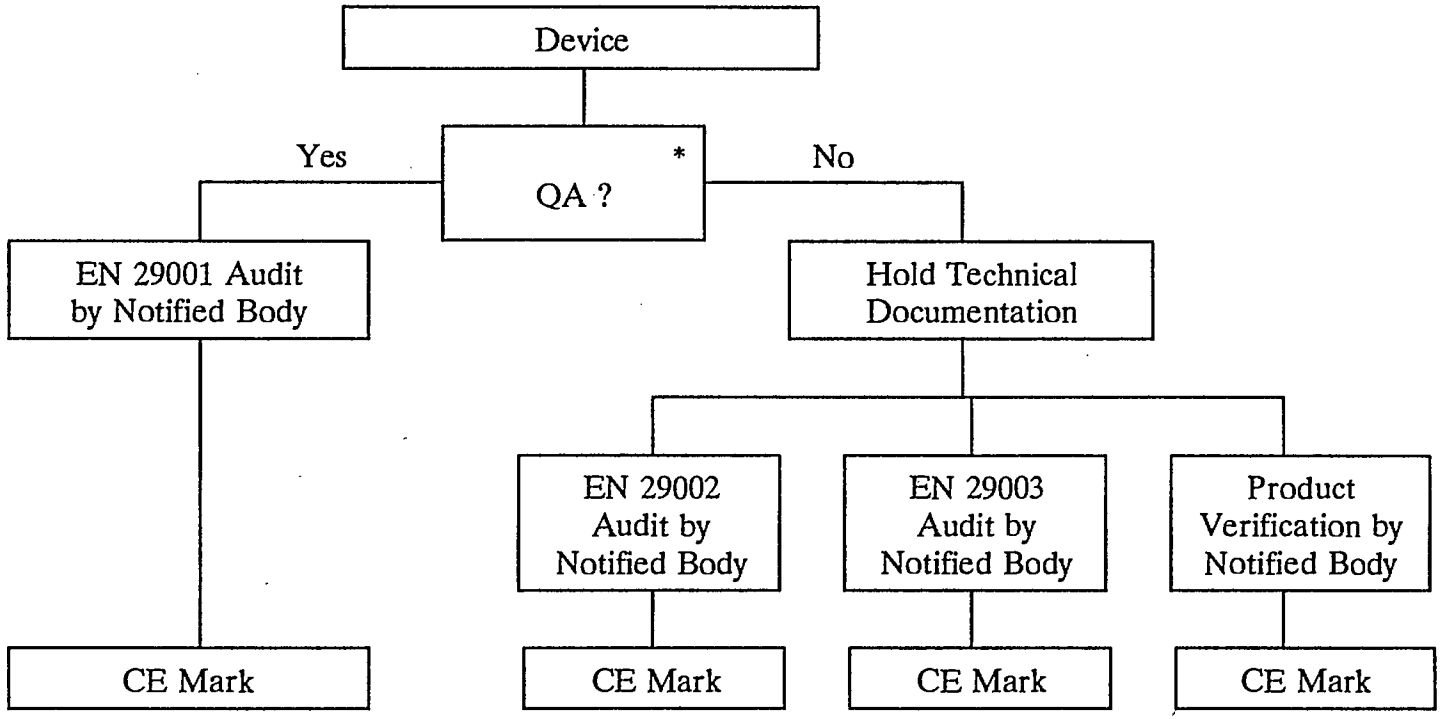
Class 3 - Pre-market approval of each device based on either:

- Manufacturer's full quality assurance plus design examination; or:
- Type examination followed by production verification or by production quality assurance.

Table 22

Process to Attain CE Mark

Class IIA

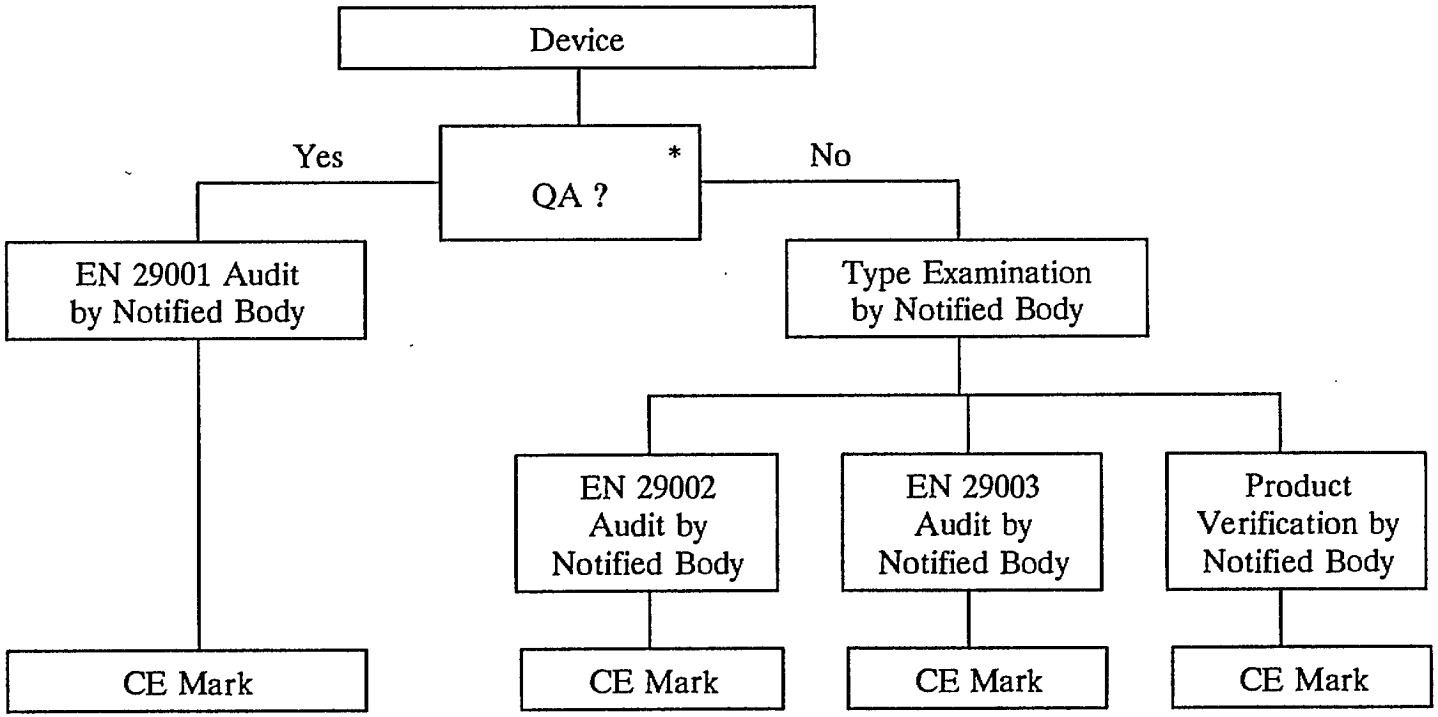


* Is a quality assurance system in place?

Table 23

Process to Attain CE Mark

Class IIB

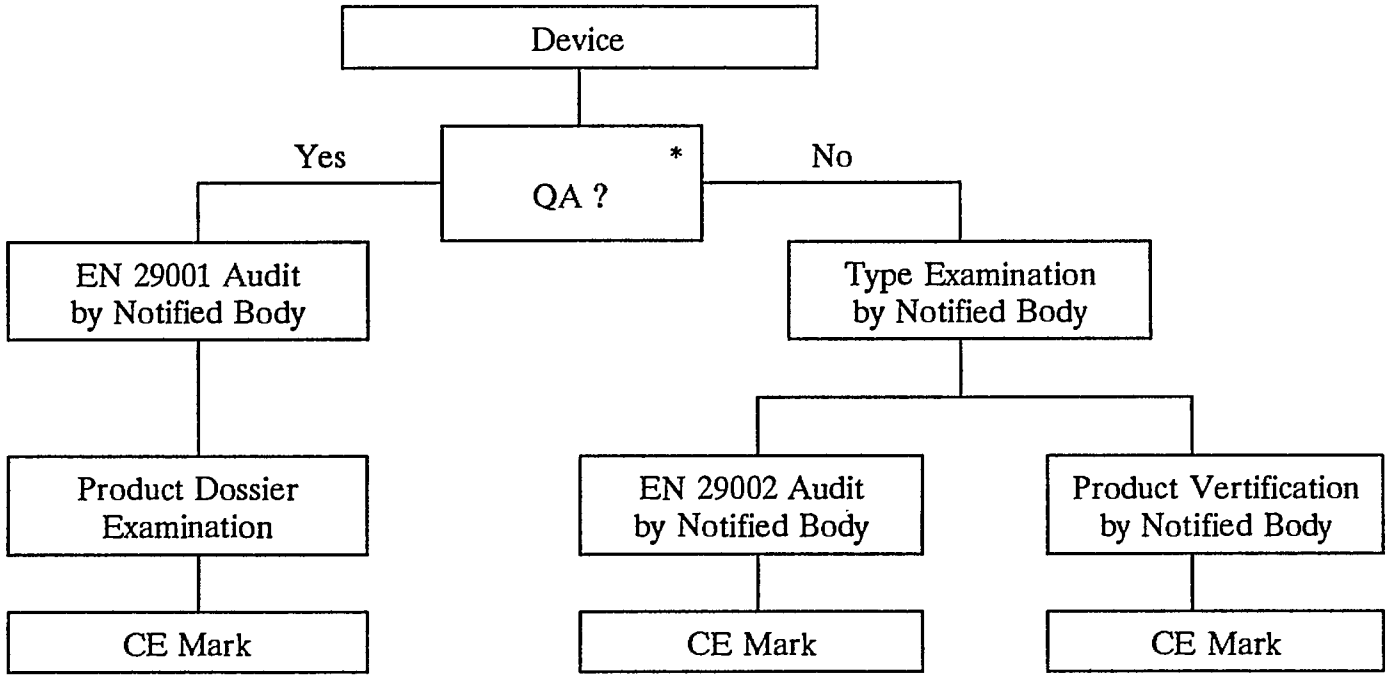


* Is a quality assurance system in place?

Table 24

Process to Attain CE Mark

Class III



* Is a quality assurance system in place?

ANNEX I

HOMOLOGATION PROCESS FOR HIP PROSTHESIS (AN EXAMPLE)

Class I:

- Total hip prosthesis on the market before 85-06-1

Class II:

- Total hip prosthesis on the market after 85-06-1

Class III:

- Innovative total hip prosthesis

I **The Dossier**

A Administrative part

B Produce part

- Manufactured article identification and description
- Materials conformity with NF or ISO standards
- G.M.P.

In addition for the Class III:

- Technical characteristics (materials and prosthesis)
- Biocompatibility evaluation
  - Cytocompatibility
  - Mutagene power
  - Immuno-toxicologic assay
  - Implantations on animals
  - Pyrogenicity
- Biofunctionality

C Clinical Trials (Only for the Class III)

Source: Colloque Franco-Canadien, LYON Sept. 1991

ANNEX I

HOMOLOGATION PROCESS FOR HIP PROSTHESIS (AN EXAMPLE)
(Continued)

Technical Tests

a) Packing and labelling ISO 6018 and NF.S.90-443

b) Dimensions controls NF.S.90-449-444, NF ISO 7206/2

c) Metals controls NF.S.90-401 and 407, ISO 643

d) Mechanical assay NF.S90-448

e) Chemical control

Clinical Trials

➢ *The Goal:*

- To confirm the safety of the devices

➢ *The Means:*

- A minimum of two trials by selected surgeons in hospitals

➢ *The Promoter Chooses:*

- The investigator on an official list of authorized investigators
- The moment

But must comply with some conditions:

- Relevant national regulation
- Pre-requisite conditions
- Protocol
- Report

ANNEX I

HOMOLOGATION PROCESS FOR HIP PROSTHESIS (AN EXAMPLE)
(Continued)

The Protocol

- The promoter and the investigators are responsible for the protocol.
- The main expectations of the sub-committee experts in charge of the final evaluation concerns:

I *Prosthesis valuation before implantation*

- Packaging
- Labelling
- Ancillary
- Tracings

II *Pre-operative Valuation*

III *Post-operative valuation*

- Complications
- Radiological evaluation
- Patient stability, mobility, pain, walk

ANNEX II

CEN/CENELEC MEMBER BODIES

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ANNEX II

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ANNEX II

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ANNEX II

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ANNEX III

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