STANFORD biodesign

CHAPTER: EUROPE-OV01
DATE: 04/02/13

BIODESIGN GLOBAL SOURCEBOOK: EUROPEAN UNION OVERVIEW

KEY INDICATORS

TOPICS

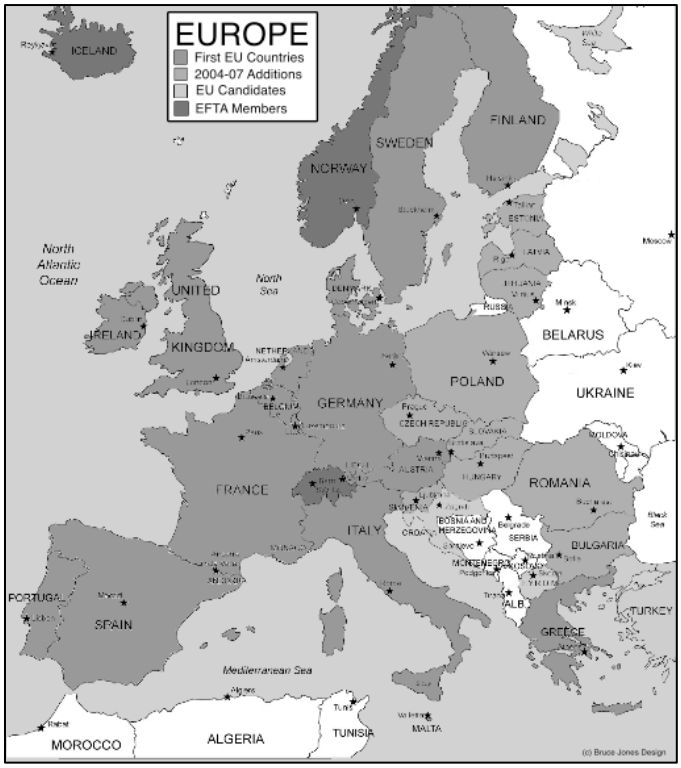
Europe, in geographic terms, is the westernmost peninsula of Eurasia and forms one of the seven global continents. It comprises 47 independent countries and currently is the largest economy on earth. The European Union (EU) as an economically and politically highly integrated group of member states comprises 27 countries. In terms of medical devices, the EU is commonly referred to as the "European market" because of its common device regulation under the CE mark. However, it should be appreciated that the European market goes beyond the EU, and includes such non-member states as Switzerland and Norway. Yet another layer of definition is the 16 EU countries that share the Euro as a common currency.

In 2011, Europe had a total population size of 739.2 million, approximately one ninth of the global population, with the 27 EU member states contributing 503.7 million towards the total. Within the EU, the five largest countries are Germany (82M), France (64M), the United Kingdom (63M), Italy (61M), and Spain (46M). Compared to other parts of the world, population growth in Europe is rather slow and median age comparatively high. Nine of the top

This chapter was prepared by Jan B. Pietzsch and Ritu Kamal as part of a multi-chapter global series for use in Stanford University's Program in Biodesign. These papers can be used individually or as a set. References to other related chapters may refer to the Biodesign Textbook or others in this series.

ten countries with highest median age, worldwide, are European countries, with only Japan having an older population[1].

Figure 1 Map of Europe[2]



In 2008, the 27 EU member states had a total GDP of $ 17.6 trillion, compared to the US' $14.46 trillion. In 2011, the per capita GDP was - about $35,200 in the EU-27 countries, compared to -$48,300 in the United States. Per-capita GDP in EU countries varies substantially, ranging from such high values as $57,600in Sweden to such low values as -$13,600 in Latvia. When considering all 47 countries in Europe, this variation is even higher. Four EU countries rank in the top ten of the world's largest national economies in terms of GDP (at purchasing power parity). The CIA Fact Book ranks them as follows: Germany (5), the UK (6), France (8), and Italy (10). In 2010, the EU27 was the largest exporter globally at 14.6% of global exports, closely followed by China (14.0%) and the US (11.3%). At 16.4%, it ranked second in terms of global imports after the US (16.8%)[3].

HEALTH SYSTEM OVERVIEW

The organization of healthcare systems varies substantially among European countries. This is because of a variety of reasons that include historical, political, and socio-economic factors, as well as the fact that the national laws, which also govern healthcare system design, are explicitly excluded from harmonization, per the statutes of the EU Treaty[4].

Healthcare Delivery

Healthcare delivery is partly driven by the mechanism of funding, described further below. Two extremes exist. Countries with national health service systems, such as the UK, provide all care for its citizens through government-run programs. The UK's National Health Service (NHS), through its trusts, owns hospitals, doctor's offices and other related services. Doctors, nurses, and other personnel are employed by the NHS. In other countries, such as Germany, a strict separation exists between payers (insurances/sickness funds) and healthcare service providers, with many hospitals and all doctors' offices privately owned and operated; however, with service

fees determined by bargaining processes between the major healthcare institutions[5]. Compared to the U.S., European countries tend to provide a higher number of services in classic in-patient hospital settings, as opposed to the outpatient setting.

Healthcare Financing

While considerable differences in capital and human resource allocation exist, two main financing models of healthcare exist:

- Social insurance systems, in which insurance funds may be independent of the government (e.g., Germany)
- National health service systems that are tax-financed (e.g., the UK)

Independent from these general system differences, variation exists in individual countries' per capita healthcare spending: differing willingness and ability to pay, with implications for spending on medical technology). Figure 2 provides further detail on the sources of healthcare financing.

Figure 2: Methods of Financing Health Care in selected EU Member states[6]

Countries	Predominant System of Finance	Supplementary System of Finance
Finland, Greece, Ireland, Italy, Sweden, Spain, United Kingdom	Public: Taxation	Private voluntary insurance; direct payments
Denmark, Portugal	Public: Taxation	Direct payments
Austria, Belgium, France, Germany, Luxembourg	Public: Compulsory social insurance	Private voluntary insurance; direct payments; public taxation
Netherlands	Mixed compulsory social insurance and private voluntary insurance	Public taxation; direct payments

Coverage of new medical technologies differs across countries. While a centralized regulatory system exists in the EU, coverage needs to be negotiated separately with payers in each country. Structured and centralized processes exist in a number of countries, such as the UK, France, and Germany. In other countries, coverage is often decided at the regional level (e.g., in Italy) or is handled through less formalized negotiation processes between manufacturers and payers.

Recent History and Trends

In recent years, new member states in the European Union (such as Poland, Romania) have shown significant progress in modernizing their healthcare and delivery systems. However, substantive differences continue to exist between healthcare states of western European countries and newer member states, partly because of GDP-related differences, which limit the amount of available per-capita healthcare spending.

Similar to the US, continued growth in health care spending is a substantial concern of policy makers, and can be expected to be even more so with the current EU economic crisis. One of the resulting trends is an increased focus on health technology assessments (HTA) to estimate the value contribution of new therapies.

DISEASE BURDEN

Life expectancy at birth in the EU-27 is on average 78.1 years, with lowest country value of 73.5 years (Lithuania) and highest value of 82.3years (Spain)[7]. While part of these differences stem from differences in healthcare systems, lifestyle and other factors can be expected to have a substantial impact. The disease burden is widely comparable with the burden in other parts of the developed world, with non-communicable diseases and chronic conditions presenting the majority of health issues. [See WHO Burden of Disease statistics for global comparison[8]]. Cardiovascular diseases and neoplasms continue to be main clinical challenges. In addition, the comparatively old and further aging population will present future challenges not only in these two groups of conditions, but also in areas such as dementia that require substantial levels of care, with associated resource use.

MEDICAL DEVICE INDUSTRY

The medical technology industry in Europe is an important part of the economy providing quality employment and a sizable contribution to Europe's balance of trade. According to Eucomed, the European medical device industry association, the medical technology industry currently employs nearly 500,000 people and generates sales of €95 billion ($120 billion). There are almost 22,500 medical technology companies in Europe; of these nearly 18,000 – around 80% - are small to medium-sized enterprises[9]. Europe accounts for approx. 34% of total global sales in medical technology. Close to 70% of total EU medical technology sales come from the four largest countries (Germany 31%, France 16%, Italy 11%, UK 11%). Germany, Ireland, the UK, Sweden, and Finland have a positive trade balance, exporting more medical technology than they import. The two major exporters are Germany (~$18 billion in 2007 exports) and Ireland (~$8.6 billion)[10].

The European medical technology industry benefits from substantive investment into research and development. Of the $120 billion in annual sales, approximately 8% ($9.6 billion) are directly reinvested into R&D[11]. A highly skilled labor force makes Europe an attractive place for medical technology development and manufacturing. Compared to the United States, venture funding for medical technology companies, at least historically, has been more limited, presenting a challenge for early-stage companies.

REGULATORY ENVIRONMENT

Within the EU-27, medical device regulation is governed by common directives of the European Union (leading to granting of the "CE" mark, which indicates a product's compliance with these directives). Countries outside the EU-27 continue to have country-specific regulations, which, in principle, tend to follow the general requirements applied in the EU. The following section describes the EU-specific regulatory pathways.

Three directives apply to medical device regulation, depending on the type of the technology[12]:

1. MDD – Medical Devices Directive
2. AIMDD – Active Implantable Medical Devices Directive
3. IVDD – In Vitro Diagnostic Medical Devices Directive

CE Marking demonstrates that the manufacturer has declared and, where applicable, demonstrated that they meet the requirements of all applicable directives. The criteria applied in the evaluation of devices are safety and performance, as opposed to safety and effectiveness, which are the two criteria applied by the US FDA. This generally leads to a comparably lower regulatory hurdle in the EU, because clinical effectiveness does not need to be demonstrated.

Figure 3: EU Medical Device Classification and CE Mark Requirements Summary[13]

<table>
<tr><th>EU Class</th><th>Device Risk</th><th>Type of Device</th><th>Technical File Required</th><th>Requires Full Quality System</th><th>Requires NB Audit</th><th>Requires Authorized Representative</th><th>Form of Clinical Evaluation</th><th>Requires Device Registration</th></tr>
<tr><td>Class I (non-sterile / non-measuring</td><td>Low</td><td>Examination Gloves</td><td rowspan="4">Yes</td><td>No</td><td>No, self-declaration of conformity by manufacturer is acceptable</td><td rowspan="5">Yes</td><td>Possible scientific literature review</td><td>Yes</td></tr>
<tr><td>Class I (sterile / measuring</td><td>Low</td><td>Surgical Gloves, patient scales</td><td rowspan="4">Yes</td><td rowspan="4">Yes</td><td rowspan="3">Possible scientific literature review; Pre-clinical work; Possible clinical trial</td><td rowspan="4">No; Notified Body conducts annual audits</td></tr>
<tr><td>Class IIa</td><td>Medium</td><td>Natural orifice access, wound management, hearing aids</td></tr>
<tr><td>Class IIb</td><td>Medium</td><td>Partial/total implantable, surgical lasers, ventilator</td></tr>
<tr><td>Class III</td><td>High</td><td>Heart valves, life-support</td><td>Yes, in the form of Design Dossier</td><td>Highly likely that clinical trial is required</td></tr>
</table>

Instead of a central government regulatory body (like the US FDA), the EU has set up a system of private entities, so-called "notified bodies" (NBs), which are private organizations accredited by the national governments that evaluate conformance of a product with the directives (see List of Notified Bodies[14] for current listing). For most classes of devices, the declaration of conformance needs to be demonstrated to or established by the Notified Body. Exceptions exist for low risk devices, in which the manufacturer can "self-certify" its product and keep records for inspection demonstrating they are in compliance with all applicable directives (see Figure 3 for a summary overview of classes and requirements). Comprehensive guidance documents with useful information for innovators are available on the European Commission's website[15].

REIMBURSEMENT

As opposed to regulatory requirements, the mechanisms for medical device reimbursement vary widely between European countries. While the majority of European healthcare systems have adopted diagnosis-related group (DRG) payment systems for in-hospital care, the extent to which medical devices are paid for under these DRG systems, and how quickly the technologies can be adopted, differs. Some countries have implemented formal technology assessment procedures (such as those implemented by the UK's NICE), in other countries, reimbursement is decided at a regional level (e.g. in Italy) and may be subject to certain budgets set aside to pay for new technologies. Several healthcare systems have implemented payment schemes to facilitate add-on payments for new technologies (e.g., the NUB reimbursement system in Germany). These payments are intended for technologies that otherwise would not be sufficiently covered under the existing DRG scheme. Applications for these payments commonly need to come from hospitals that intend to use the technology. In general, the willingness and ability to pay for innovative new healthcare technologies correlates with the respective country's per-capita healthcare spending. A useful overview of country-specific reimbursement processes is given on the International Society for Pharmaco-economics and Reimbursement's (ISPOR) global healthcare systems roadmap website[16].

INTELLECTUAL PROPERTY PRACTICES

The European Commission describes intellectual property as comprising of two categories: industrial property, including inventions, trademarks and industrial design; and copyright, including literary and artistic works[17]. In certain countries such as France and Germany, utility models can be registered to protect technical innovations that might not qualify for a patent[18]. Currently, technical inventions in Europe can be protected by national patents, granted by national patent bodies or by European patents, granted by the European Patent Office. European patents are a bundle of national patents, singular from a patent granting perspective but can only be enforced at the national level[19]. Patent reform is currently underway in Europe to create a system of unitary patent protection in the EU, whereby the entire region will be under a single

patent jurisdiction[20]. Similar to other developed patent regimes, European country patents are protected for the standard 20-year term. The European Patent Office maintains an updated website with information on intellectual property basics, filing, examination, patent search and other pertinent information[21].

ENDNOTES

[1] "EuroStat: Total Population," European Commission, http://epp.eurostat.ec.europa.eu/portal/page/portal/eurostat/home (April 2, 2013)
[2] Interactive Map of European States, *Nationsonline.org*, http://www.nationsonline.org/oneworld/europe_map.htm (Apr. 1, 2013)

[3] "Statistics," European Commission Trade Statistics, http://ec.europa.eu/trade/creating-opportunities/bilateral-relations/statistics/ (Jan. 17, 2013)
[4] Elke Jakubowski and Reinhard Busse, "Healthcare Systems in the EU – A Comparative Study," Working Paper, European Parliament, Directorate General for Research, May 1998, p.5 http://www.europarl.europa.eu/workingpapers/saco/pdf/101_en.pdf (Jan. 17, 2013)
[5] Ibid, p.19
[6] Ibid, p.18
[7] "Health Status Indicators," HEIDI Data Tool, European Commission, http://ec.europa.eu/health/indicators/echi/list/echi_34.html#main?KeepThis=true&TB_iframe=true&height=650&width=920 (January 16, 2013)
[8] "Globla Burden of Disease," World Health Organization, http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html (January 16, 2013)
[9] "What Medical Technology Exactly Is," Eucomed, http://www.eucomed.org/medical-technology (January 16, 2013)
[10] "Medical Technology: Key Facts and Figures," Eucomed, http://www.eucomed.org/medical-technology/facts-figures (January 16, 2013)
[11] Ibid.
[12] "Council Directive Concerning Medical Devices," European Parliament, June 14, 1993, pp. 2-5, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:en:PDF (April 1, 2013)
[13] Ellis Garai and R Miri,"CE Marking Process and Notified Bodies", Stanford BIOE 371 class Project Report, Spring 2011
[14] "List of Notified Bodies," European Commission, February 4, 2013, http://ec.europa.eu/enterprise/newapproach/nando/index.cfm?fuseaction=directive.pdf&drc_refe_id=13&type_dir=cmp&refe_cd=93/42/EEC&drc_desc_v2=93/42/EEC%20Medical%20devices&requesttimeout=900 (April 2, 2013)
[15] "Guidance: Medical Devices," European Commission, http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm (April 1, 2013)
[16] "Global Healthcare Systems Roadmap," ISPOR, http://www.ispor.org/htaroadmaps/ (April 1, 2013)
[17] "Intellectual Property," European Commission, http://ec.europa.eu/internal_market/top_layer/intellectual-property/index_en.htm (April 1, 2013)
[18] "Where can Utility Models be Acquired," World Intellectual Property Organization, http://www.wipo.int/sme/en/ip_business/utility_models/where.htm (April 1, 2013)
[19] "Applying for a Patent," European Patent Office, http://www.epo.org/applying.html (April 1, 2013)
[20] "Patents," European Commission, http://ec.europa.eu/internal_market/indprop/patent/index_en.htm (April 1, 2013)
[21] European Patent Office, http://www.epo.org/index.html, (April 1, 2013)