Appendix 1: Information sources

**Important notice:** This appendix represents auxiliary content of the HTA Core Model. It is under construction and not fully updated for the HTA Core Model version 2.0. It is not yet a comprehensive presentation of useful information sources for core HTA information producers. It will be updated and amended during Joint Action 2 by September 2015.

**Registers**

Registers may act as an important information source for those involved in the conduct of HTA. Registers are usually managed by medical societies, scientific associations or government institutions; industry-managed registers also exist. Registers collect data for a defined geographical area, usually a single country. However, regional or even European registers also exist.

Registers commonly release periodic reports for disseminating findings and results. The reports are often open-access and downloadable free of charge from the homepage of the registry. Dissemination is also achieved by publishing specific studies or reports in specialised peer-reviewed journals. Registers include technology, procedure and disease registers.

**Technology and procedure registers**

Technology and procedure registers gather information on the use of specific technologies and procedures (e.g., knee arthroplasty register). A new case is registered in the database every time the technology is used (i.e. a procedure is undertaken, an intervention takes place). In some countries, there is an obligation to report the indications and consequences of using a technology before it is approved, for example when there is no high quality evidence to establish effectiveness and, or the safety of the technology.

**Disease registers**

Disease registers gather information on the natural history and/or on the management of single diseases. A new case is registered in the database every time a diagnosis of the target disease is made. Some conditions may occur several times in life (i.e. heart attack), thus a single person might be represented several times in the register. When appropriately designed, disease registers allow assessment of the utilisation and diffusion of different diagnostic strategies or technologies in the care of persons with the condition or even to explore variations in the outcomes of different diagnostic interventions (e.g. differences in the consecutive management).

The Swedish National Board of Health and Welfare maintain a number of registers including the pharmaceutical register, the cause of mortality register and the registers containing the diagnoses of all hospitalised patients in Sweden.

http://www.kvalitetsregister.se/web/Quality_Registries.aspx?pageID=8d07dd0a-4079-4ad7-b47b-58759d7055cb

Quality registers in Sweden

A system of 70 national quality registries has been established in the Swedish health and medical services. It contains individualised data concerning patient problems, medical interventions, and outcomes after treatment. http://www.socialstyrelsen.se/statistics
British Heart Foundation's statistics website is an up-to-date source of statistics on the burden, prevention, treatment and causes of heart disease in the UK http://www.heartstats.org/homepage.asp

**Technology registers**

*Technology registers* gather information on the use of a single technology, for example a register on knee total endoprosthesis, A new case is registered in the database every time the technology is used (i.e. a procedure is done, an intervention takes place). In some countries, there is an obligation of reporting indications and consequences of using a technology before marketing authorisation, and when there is no high quality evidence to establish effectiveness and/or safety of the technology.

**Pharmaceutical registries**

On the other hand, registers on pharmaceuticals are initiated to obtain data on safety and effectiveness, after marketing authorisation. Doubt on the generalisability of study data and volume of consumption are a major drive to set up a pharmaceutical reimbursement registry.

**Utilisation registers**

- Norwegian pharmaceutical prescription database: [http://www.norpd.no/](http://www.norpd.no/)
- Dutch utilisation information: [http://www.gipdatabank.nl/index.asp?scherm=homepage&infoType=g](http://www.gipdatabank.nl/index.asp?scherm=homepage&infoType=g)

**ATC INDEX with DDDs**

- ATC/DDD system is a tool for exchanging and comparing data on pharmaceutical use at international, national or local levels. [http://www.whocc.no/](http://www.whocc.no/)

**Regulatory institutions**

**EMA**

The European Medicines Agency www.ema.europa.eu is responsible for the scientific evaluation of applications for European marketing authorisations for both human and veterinary medicines (centralised procedure).

- All medicines for human and animal use derived from biotechnology and other high-tech processes must be approved via the centralised procedure. The same applies to all advanced-therapy medicines and human medicines intended for the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases, as well as to all designated orphan medicines intended for the treatment of rare diseases.
- EMA becomes involved in the assessment of medicines that do not require centralised procedure, in cases where they have been referred to the Agency due to a disagreement in authorisation or use of the medicine between two or more Member States, or due to some other issue that requires resolution in the interest of protecting public health.

- EMA constantly monitors the safety of medicines through a pharmacovigilance network, and takes appropriate actions if adverse pharmaceutical reaction reports suggest that the benefit-risk balance of a medicine has changed since it was authorised.

- EMA can be considered as the 'hub' of a European medicines network comprising over 40 national competent authorities in 30 EU and EEA-EFTA countries, the European Commission, the European Parliament and a number of other decentralised EU agencies.

- The EMA monitors the safety of authorised medicines through a pharmacovigilance network, and takes appropriate actions if adverse drug reaction reports suggest that the benefit-risk balance of a medicine has changed since it was authorised.

**FDA**

The US Food and Drug Administration (FDA) [http://www.fda.gov/default.htm](http://www.fda.gov/default.htm) is the federal agency responsible for ensuring that human and veterinary drugs, biological products, and medical devices are safe and effective; cosmetics are safe; and electronic products that emit radiation are safe. FDA also ensures that these products are honestly, accurately and informatively represented to the public.

- Drug labeling refers to all of the printed information that accompanies a drug, including the label, the wrapping and the package insert. Food and Drug Administration (FDA) requires that drug labeling be balanced and not misleading. The label must be scientifically accurate and provide clear instruction to health care practitioners for prescription drugs and to consumers for over-the-counter drugs and supplements. Labeling regulations require that the statement of ingredients must include all ingredients, in the order in which they are used in the drug. These ingredients must also be identified by their established name.

**Standardisation and regulatory concerns of medical devices**

The government of each European Member State is required to appoint a **Competent Authority** responsible for medical devices. The Competent Authority (CA) is a body with authority to act on behalf of the government of the Member State to ensure that the requirements of the Medical Device Directives are transposed into National Law and are applied. The CA reports to the Minister of Health in the Member State. The CA in one Member State does not have jurisdiction in any other Member State, but they do exchange information and try to reach common positions.

- In UK the **Medicines and Healthcare products Regulatory Agency** (MHRA) acts as a CA, in Italy it is the Ministero Salute (Ministry of Health).

In the EU, all medical devices must be identified with the **CE mark**.

The ISO standards for medical devices are covered by
• ICS 11.100.20 standard for biological evaluation of medical devices
  http://www.iso.org/iso/products/standards/catalogue_ics_browse.htm?ICS1=11&ICS2=100 &ICS3=20&
  and

• ICS 11.040.01 standard for medical equipment

The quality and risk management regarding the topic for regulatory purposes is convened by ISO 13485 and ISO 14971. Further standards are IEC 60601-1, for electrical devices (mains-powered as well as battery powered) and IEC 62304 for medical software. The US FDA also published a series of guidances for industry regarding this topic.

**Packaging standards**

Medical device packaging is highly regulated. Often medical devices and products are sterilised in the package. The sterility must be maintained throughout distribution to allow immediate use by physicians. A series of special packaging tests is used to measure the ability of the package to maintain sterility. Relevant standards include: ASTM D1585- Guide for Integrity Testing of Porous Medical Packages, ASTM F2097- Standard Guide for Design and Evaluation of Primary Flexible Packaging for Medical Products, EN 868 Packaging materials and systems for medical devices which are to be sterilised, General requirements and test methods, ISO 11607 Packaging for terminally sterilised medical devices, and others.

**Medical Device Directive**


The Medical Device Directive (Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ No L 169/1 of 1993-07-12) is intended to harmonise the laws relating to medical devices within the European Union. The MD Directive is a 'New Approach' Directive and consequently in order for a manufacturer to legally place a medical device on the European market the requirements of the MD Directive have to be met. Manufacturers' products meeting 'harmonised standards'[2] have a presumption of conformity to the Directive. Products conforming with the MD Directive must have a CE mark applied. The Directive was most recently reviewed and amended by the 2007/47/EC and a number of changes were made. Compliance with the revised directive became mandatory on March 21, 2010.

## Other sources

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<tr>
<th>Name</th>
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<tbody>
<tr>
<td>CADTH – Canadian Agency for Drugs and Technologies in Health</td>
<td><a href="http://www.cadth.ca/en">http://www.cadth.ca/en</a></td>
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<tr>
<td>MSAC – Medical Services Advisory Committee (Australia)</td>
<td><a href="http://www.msac.gov.au/">http://www.msac.gov.au/</a></td>
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<td>SIGN</td>
<td><a href="http://www.sign.ac.uk/guidelines/">http://www.sign.ac.uk/guidelines/</a></td>
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<td>NICE</td>
<td><a href="http://guidance.nice.org.uk/CG/Published">http://guidance.nice.org.uk/CG/Published</a></td>
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<td>Cochrane collaboration</td>
<td><a href="http://www.cochrane.org">http://www.cochrane.org</a></td>
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<td>Guideline producer</td>
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<td>American College of Occupational and Environmental Medicine’s (ACOEM) Occupational Medicine Practice Guidelines</td>
<td><a href="http://www.disabilitydurations.com/pr_acoem.htm">http://www.disabilitydurations.com/pr_acoem.htm</a></td>
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<tr>
<td>Guidelines International network (GIN)</td>
<td><a href="http://www.g-i-n.net/">http://www.g-i-n.net/</a></td>
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<tr>
<td>Current care guidelines (Käypähoito)</td>
<td><a href="http://www.kaypahoito.fi">http://www.kaypahoito.fi</a></td>
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<tr>
<td>NICE guidance, National Institute for Health and Clinical Excellence (NHS)</td>
<td><a href="http://guidance.nice.org.uk/CG">http://guidance.nice.org.uk/CG</a></td>
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<tr>
<td>Scottish Intercollegiate Guidelines Network (SIGN)</td>
<td><a href="http://www.sign.ac.uk/index.html">http://www.sign.ac.uk/index.html</a></td>
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<tr>
<td>See many more guideline producers in the list of Open Clinical</td>
<td><a href="http://www.openclinical.org/guidelines.html">http://www.openclinical.org/guidelines.html</a></td>
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National or international safety monitoring systems (databases)
(which may be managed by a national statutory body or by a supra-national body)


IAEA: Radiological protection of patients http://rpop.iaea.org/RPoP/RPoP/Content/index.htm


US Food and Drug Administration, MedWatch safety alert system http://www.fda.gov/medwatch/safety.htm

The Medical Devices section of the UK Medicines and Healthcare Products Regulatory Agency (http://devices.mhra.gov.uk/)

National Prescription Database for pharmaceuticals.

A0021 List of websites of national agencies with information on reimbursement

AIFA: http://www.aifa.gov.it/


Canada: http://www.cadth.ca/en/products/cdr or http://www.pcodr.ca

Czech Republic: http://www.sukl.eu

Finland: http://www.kela.fi/in/internet/english.nsf


The Netherlands: http://www.medicijnkosten.nl/

Norway: http://www.legemiddelverket.no/

Poland: http://www.aotm.gov.pl/

Portugal: http://www.infarmed.pt/portal/page/portal/INFARMED

Scotland: http://www.scottishmedicines.org.uk/
Spain: http://www.msc.es/profesionales/farmacia/

Sweden: http://www.tlv.se/beslut/sok/lakemedel/

UK: http://www.nice.org.uk/