




Mister chair, Ladies and gentlemen,

Thank you for inviting me today. It is a great pleasure to speak about medicinal products and medical devices. Health care would not be possible without them.

To speak about medical devices to an audience that consists mainly of ‘pharma people’ is a challenge. Because you are familiar with medicinal products, I will emphasize medical devices

The medical device world does not have a very distinct image. Unlike pharma, where industry claims that the main driver is to benefit public health, of which the general public is very sceptical.



medicinal product	medical device
<p>a. Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or</p> <p>b. Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.</p>	<p>... means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:</p> <ol style="list-style-type: none"> 1. diagnosis, prevention, monitoring, treatment or alleviation of disease, 2. diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, 3. investigation, replacement or modification of the anatomy or of a physiological process, 4. control of conception, <p>and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.</p>

http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_cons2009/2001_83_cons2009_en.pdf

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1993:169:0001:0043:EN:PDF>

2

Medicinal products and medical devices | 8 June 2011

To demonstrate commonalities and differences of medicinal products and medical devices I would like to show you their respective definitions.

The purpose of both is to treat, prevent, diagnose disease.

For medical devices a large group of products aims at alleviating functioning problems as well.

The difference between the groups, when it comes to definition, is their mode of action: for medical devices their mode of action is non pharmacological, non immunological and non metabolic.



Medicinal product or medical device?



- Condom
- Pregnancy test
- Artificial tears
- Surgical gloves
- Alcohol
- A steriliser
- Glucose 5%
- Dialysis solution
- Drug eluting stents
- Deep brain stimulators
- Nanotechnology based products

I would like to challenge you with regard to some products: are we talking about medical devices or medicinal products. I will not ask for a show of hands; I will just give you a second to make up your mind.

Condom: yes

Pregnancy test: yes, an IVD

Artificial tears: can be both, according to the manual on borderline and classification for medical devices, although the mode of action is not pharmacological

Surgical gloves: yes

Alcohol: depends on its use; to disinfect the skin, a medicinal product; to disinfect a surface, a pesticide. In conjunction with a medical device, a medical device.

Steriliser: yes, if its purpose is to sterilize medical devices or as an accessory to a medical device



	medicinal product	medical device
diversity	4,000	250,000-300,000
innovation	"revolution"	incremental improvement
durability	< 1 day	from instantaneous to life time
responsibility	pharmacist	biomedical engineer?
nomenclature	International Non-proprietary Name	GMDN UMDNS ISO 9999
EU-regulatory framework	1965	1993
number of public officials NL	300	30 (60)

Before talking legislation I would like to mention some differences between medical devices and medicinal products.

The diversity in medical devices is enormous. We estimate that in Europe alone there are hundreds of thousands of medical devices on the market. Most people think of medical devices as the ones used in hospital care like the imaging equipment, the implants, the diagnostics. But in the world of disability the amount of different assistive medical devices probably outnumbers the amount of devices used in the treatment of patients.

In pharma innovation happens through creating NCE's and we hope for breakthroughs like the TNF alpha blockers, the antipsychotics, the PPI's. In medical devices we speak of an ongoing improvement, which shortens the commercial life



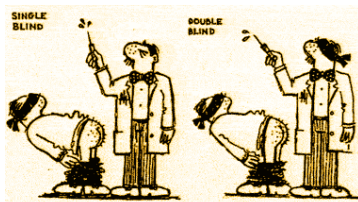
In this presentation I further would like to guide you according to the following steps.

Clinical trials, market approval, use and PMS

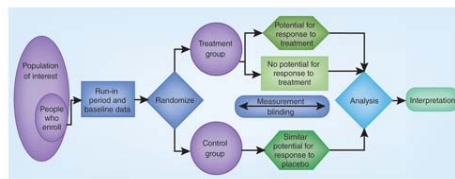


Clinical trials

medicinal products	medical devices
efficacy	safety and performance
interaction with the human body	compatibility
placebo controlled and comparative studies	clinical investigation
large numbers of patients included	clinical evaluation
	data not published
doctors	engineers
	incremental improvements



<http://www.thejabberwock.org/blog/2/blind.gif>



http://www.nature.com/nm/journal/v16/n11/fig_tab/nm.2249_F1.html

The aim of clinical trials is to know how a medical product performs. For medicinal product this concerns efficacy balanced with the risk. The golden standard for medicinal products to prove that is the placebo controlled randomised trials.

A clinical investigation is required for the highest risk medical devices, like implants. However, a RCT, the device against placebo, is not fit to trial a medical device: could you imagine a placebo hip implant. An additional reason would be that in a number of cases the body does not interact with the device: like the infusion pump or imaging equipment. Of course we need scientific data and therefore an effort to develop 'golden standards for clinical investigations' which targets the safety and clinical outcome data, would help to bridge the gap the two



medicinal products	medical devices
one single system	concept of risk class: essential requirements applicable to all risk classes
competent authority determines prescription status	risk assessment by manufacturer
assessment of clinical trials	bibliographic data
benefit / risk	safe at the intended purpose; risk / benefit
Competent Authority, experts	Notified Body, according to their expertise, and Competent Authority
national licences and centralised procedure	single market in EU
high threshold	low threshold



Medicinal products are very carefully assessed by a competent authority on the benefit risk of the product. After a positive benefit risk balance, the marketing authorisation is issued.

For medical devices, the manufacturer is responsible for the risk assessment.

Depending on the risk class the medical devices are assessed according to a quality system, the **type** of medical devices or the **individual** medical device by a Notified Body.

Key is the performance of the device. The medical device is assessed to be safe at the intended use. Provided that any risk is weighed against the benefits.



Use

medicinal products	medical devices
prescribing and dispensing strictly regulated	prescribing and dispensing not regulated, linked to professional skills
responsibility assigned	no single responsibility assigned
efficacy is not dependent on context: skills and physical environment	efficacy and effectiveness are context dependent
treatment guidelines available	medical devices included in a treatment guideline to a limited extent
effectiveness studies performed	limited benefit / cost data
comparative studies; systematic reviews	very limited data publicly available



Medicinal products are among the most regulated products worldwide. Every step needs licensing and prescribing and dispensing is limited to the doctors and pharmacists.

This is unlike the use of medical devices: this is not restricted by the Medical Devices directive and a doctor would not need a license prior to using a medical device. On the other hand, a doctor is responsible for delivering appropriate care and society holds the doctor responsible if he performs outside his skills and competences. In other words: a GP would never implant artificial heart valves. Unlike medicinal products, the effectiveness of a medical device depends more on the context, including the skills of the user, whether this is the patient, the doctor or the nurse. Most medical devices are used in conjunction or combination with



Post Market Surveillance

medicinal products	medical devices
pharmacovigilance legislation: new and detailed	PMS system in legislation
responsibility of Marketing Authorisation Holder	responsibility of manufacturer
reporting system regulated and well established	not properly implemented by manufacturers and monitored by authorities
effective?	very few data



To know the effectiveness in day to day use, we need post market data. To secure safety and collecting input to make products safer, the feed back loop of both medicinal products and medical devices has to improve.

Pharma is a structured and well-established sector. Reporting systems are usually in place. Still, we know that due to medication errors as well as – and like a recent publication in the UK suggested – off label use of antipsychotics in frail elderly, there is a high rate of harm caused by medicinal products.

About medical devices: we simply do not know. A survey we performed a few years ago among medical devices manufacturers showed that a large proportion of manufacturers do not have a PMS-



Best of both worlds

'A public health approach recognises that the potential good of a new medical product or policy must be balanced against the potential harm.'*

How to balance risk and availability?

How to concentrate on high risk?

How to detect unknown risk?

Who is responsible?

Would we design the regulatory system differently if we were to start now?

*Margaret Hamburg: NEJM 360: 24, June 11, 2009

Dr Hamburg, FDA-commissioner, wrote an article in the NEJM in 2009: FDA has two speeds of approval: too fast and too slow. Too fast because of potential harm, too slow because people with life threatening diseases have no time to wait.

The question is: who can balance and who is responsible?

If we would be able to develop regulatory system to enable this balance, how would it look like? Would a single regulatory system for all medical products be an option?

The aim would be to contain public health risks and to provide for the availability of medical products.

I would opt for a modular, risk based system, in which the manufacturer indicates the risk. The



Courtesy of the University of Amsterdam





Medicinal products & medical devices: differences

- Diversity
- Innovation
- Durability
- Mode of action
- Regulation
- Supply
- Usage



Risk analysis

