Pharmaceuticals in the framework of EU Health Policy

Fernand Sauer, Parma, April 2013

Pharma policies in Europe

National health, social and industrial policies

An over-regulated sector, but for good reasons:

Quality, safety, efficacy and cost effectiveness

(Benfluorex/Mediator crisis in France)

Progressive integration of marketing authorizations

National/EU inter-actions, EU hub + national enforcement

Open and transparent regulatory dialogue

Convergence of economic and social regulations?

Partnership for innovation and intellectual property rights

Pricing transparency, health technology assessment

How to reconcile health, social protection and innovation?

Pharmaceutical life cycle

Early discovery; Patents

Basic research; physico-chemical & biological methods

Toxicology & pharmacology (in animals), GLPs

Clinical studies approval (in Man), ethics, GCPs

Manufacturing/import authorisation, GMPs

Marketing authorisation, Summary (SPC) & leaflet

Legal status: on prescription or not (OTC)

Health technology assessment (price and reimbursement)

Post-marketing surveillance (pharmacovigilance)

PRESENTATION OUTLINE

- EU HEALTH & HEALTH PRODUCTS
- INTEGRATION: EU HARMONISATION
- EU COOPERATION ON SOCIO-ECONOMICS
- INTERNATIONAL ASPECTS
- THE FUTURE

I) EU HEALTH & HEALTH PRODUCTS

EU health mandate and activities

Capacity building by EU bodies

Role of industry & civil society

Health products

EU HEALTH IN PERSPECTIVE

PHARMACEUTICALS (since 1965):

- slow EU harmonisation over half a century,
- 18 years of joint EU marketing decisions

PUBLIC HEALTH (since 1993):

- previously, health was an exception to EU rules
- now it is a limited EU policy under Treaty Art 168
- Health Ministers and EU Health Commissioner

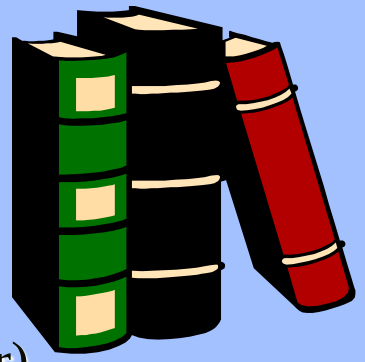
Public Health in the European Union

General Treaty Obligation

- attainment of a high level of health protection

Article 168, Lisbon Treaty (ex 152)

- improving health
- preventing diseases
- obviating sources of danger to health
- **quality & safety of health products**
- **reinforced cooperation** (pandemics, cross-border)
- ensuring that all EC policies protect health
- international co-operation, WHO



EU Health Measures

Tobacco control

Communicable diseases and ECDC

Health services and patient mobility

Regulation of Health Products:

- Medical devices
- Human therapeutic substances
- Pharmaceuticals and EMA
- Cooperation on socio-economics

International aspects

DG SANCO/ PUBLIC HEALTH

Luxembourg:

Progr. Management
Health Information
Health Threats
Health Determinants

PHEA Executive Agency

Brussels:

Health Strategy
Health Measures
Health Products
Risk Assessment

Interservice Health Cttee

Health agencies related to SANCO:

London: EMA
Parma: EFSA
Stockholm: ECDC

EU « Health » Agencies

1990: European Environment Agency (EEA), Copenhagen

1993: European Monitoring Centre for Drugs and Drug Addiction, Lisbon

1994: European Agency for Safety and Health at Work (EU-OSHA), Bilbao

1995: **European Medicines Agency (EMA), London**

2002: European Food Safety Authority (EFSA), Parma

2005: **European Centre for Disease Prevention and Control (ECDC), Stockholm**

2006: **Executive Agency for Health & Consumers (EAHC), Luxembourg**

2007: European Chemicals Agency (ECHA), Helsinki

EU HEALTH AGENCIES

- No polical interference on scientific issues
- MS would not delegate to Commission alone
- Commission cannot cope with such technicalities
- Manage interfaces between national agencies
- Create and develop wide expert networks
- Establish joint ownership national + EU
- Pool best expertise available throughout EU
- Reduce/contain overall expertise costs

CIVIL SOCIETY & HEALTH

- The EU Health Forum disseminates information, launches ideas for debate and policy building
- The EU health policy forum brings together 50 pan-European stakeholder organizations to ensure that the EU responds to public concerns
- The Open Forum extends the work to a broader set of stakeholders in an annual flagship event, for networking and exchanging ideas

http://ec.europa.eu/health/interest_groups/eu_health_forum/policy_forum/index_en.htm

PATIENTS' INVOLVEMENT

Early involvement of various patient groups in EMA and SANCO activities

Representation of patients with Health Ministers in EU Groups (Pharma Forum, Patient Mobility)

Representation within EMA and ECDC Boards

EU logistical support to patient groups

Working with EURORDIS

Emergence of the European patient's Platform /2003

http://www.eu-patient.eu/

Medical Devices

Based on the so-called “New Approach” normalisation.

Directive 90/385/EEC on active implantable devices

Directive 93/42/EEC on medical devices

Directive 98/79/EC on in vitro diagnostics

Last technical revision Directive 2007/47/EC

CEN/MEDDEV guidelines for manufacturers and Notified Bodies involved in the conformity assessment procedures

Following the breast implants scandal, fundamental revision underway to simplify and strengthen the EU legal framework.

Blood,Tissues, Organs (I)

Risks of HIV, hepatitis, TSEs, etc..:

- assessment of donor suitability
- prevention of (cross) contamination
- agents removal or inactivation

Ethics: informed and free consent of donors and recipients, confidentiality and anonymity, non-remuneration of donation

Council of Europe principles/precursor activities

Blood,Tissues, Organs (II)

Framework Directive 2002/98/EC on the quality and safety of blood

Framework Directive 2004/23/EC on the quality and safety of tissues and cells

Various **Commission Technical Directives** on: donors, storage, distribution, traceability, adverse events, coding, establishments

Directive 2010/45/EU on the quality and safety of human organs intended for transplantation

Various Commission status reports

II) PHARMACEUTICAL HARMONISATION

Pharmaceuticals and the European Medicines Agency (EMA)

Initiation of EU Pharmaceutical Legislation

- 1965 - First Directive on principles of Marketing Authorization
- 1975 - First Quality/Safety/Efficacy testing requirements
- 1978 - Start of CPMP activities and guidelines
- 1981 - Specific veterinary legislation & CVMP
- 1985 – “White Paper on Single Market for 1992”:

  13 pharma measures among 300 proposals

Harmonisation of EU Pharma Legislation

- 1986 - “Biotech/High Tech Package” Incentives
- 1988 - Transparency of Pricing and reimbursement
- 1989 - Extension to plasma, vaccines and radiopharma
- 1990 - Future Market Authorization System proposals
- 1991 - ICH harmonisation starting (EU/US/Japan)
- 1992 - Patent term extension up to 5 years; advertising control; legal status; pack leaflets; wholesale distribution; homeopathics.
- 1994 - EU accession to European Pharmacopoeia; EEA treaty

Start of the EU marketing authorization system

- 1993 - Formal adoption of system, choice of London for EMEA
- 1994 - First recruitments, search/refurbishment of Canary Wharf
- 1995 - EMEA operational, EU-wide authorisations, EPARs
- 1996 - Quality management, SOPs
- 1997 - Performance indicators, benchmarking, audits
- 1998 - Mutual Recognition reinforced
- 1999 - Recognition by EFTA; PERF activities for enlargement
- 2000 - Orphan drug policy
- 2001 - Formal codification of EU Pharma legislation

INITIAL EM(E)A FEATURES

- Protection/promotion of human and animal health
- Rapid EU-wide access for innovative medicines
- Reliable regulators and experts (EU & national)
- Early dialogue on R&D (scientific advice)
- Science based auditable evaluation process
- Transparency: EPARs, hearings, Infodays
- Risk assessment and most of risk management
- Strong stakeholders involvement (patients)
- Significant international input and output
- No support from host country, outside EURO zone
- Important fee revenue (75%)

Consolidation of EU marketing authorisations

- 2001 - Council Directive on Clinical Trials
- 2004 - Reform of the European authorization system
- 2006 - Incentives for SMEs and Paediatric Medicines
- 2007 - Advanced Therapies Regulation
- 2008 - Innovative Medicines Initiative
- 2009 - Lisbon Treaty incorporates pharma into health (Art 168)
- 2010 - Major reinforcement of Pharmacovigilance
- 2011 - Authenticity feature; reinforced controls of active subst.

Marketing authorisations in the EU: 4 types

Strictly national authorisations (mainly old products)

Decentralised national authorisations or mutual recognition

EU Centralised: biotech products, cancer, neurology, AIDS, diabetes, orphan drugs; optional for other new drugs

EU MEDICINES AGENCY IN 2013 (EMA)

- Evaluation of novel human and veterinary medicines
- Hub for 42 national agencies & over 4.500 experts
- Staff: around 600
- Budget: 230 Mio € (75% from fees)
- Management Board: MS/EP/++
- 7 Scientific Committees + numerous working parties
- 3rd Director: Guido Rasi

http://www.ema.europa.eu

EMA POSITIVE TRENDS

- EMA + Heads of Agencies Cooperation for a sound EU regulatory environment
- Reliable regulators (EMA & national)
- Early dialogue on R&D
- Science based evaluation process
- Quick and auditable decision making
- Increasing public confidence
- International benchmarking: ICH, FDA

EMA MAIN ACHIEVEMENTS

Central approval of **Medicines for human use** (since 1995):

- Around 800 EU marketing authorizations granted
- More than 3000 EMA scientific advices

Orphan medicines (since April 2000):

- Around 1100 orphan designations and 78 marketing authorizations

Central approval of **Veterinary Medicines** (since 1995):

- EU marketing authorizations granted: 147
- Maximum residues limits for ‘new’ substances : 170
- EMA Scientific advice: 90

EMA MAIN CHALLENGES

- Maintain high quality and performances
- Improve transparency of evaluation/EPARs
- Access to EMA safety & clinical data
- Effective pharmacovigilance
- Better information to health professionals
- Improved patient information
- EMA 2015 Road Map

III) EU COOPERATION:

Pharma socio-economics

EU PHARMACEUTICAL SECTOR (*Key figures, EFPIA, 2012)*

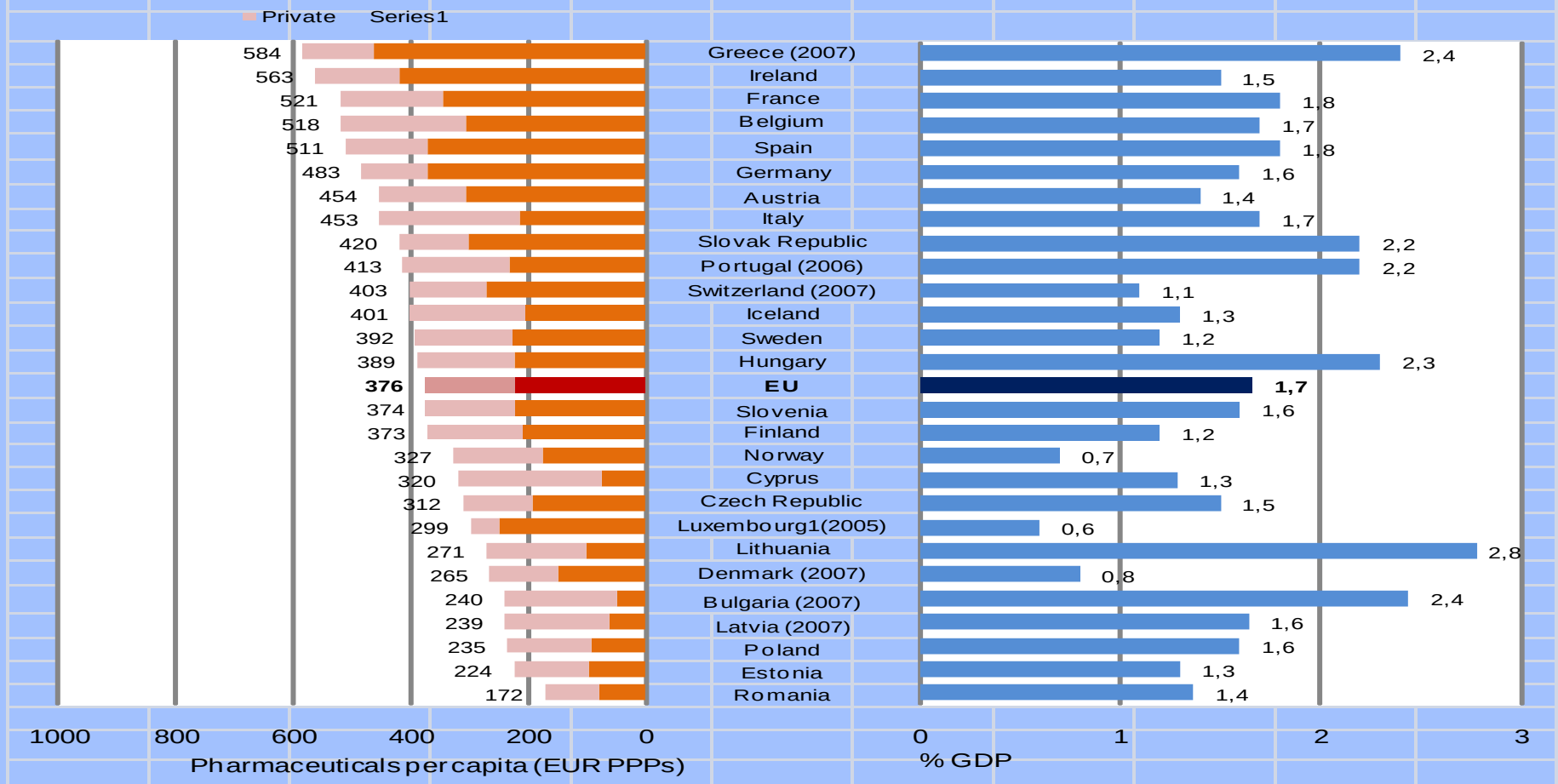
Employment	660 000
Production	205 Billion €
Trade balance	80 Billion €
R&D	28 Billion €
Social coverage (ambulatory)	122 Billion €

Innovative Medicines Initiative
IMI (2008/2013)

- Research done by academia, clinics, industry, SMEs, patient organizations, following open calls and peer evaluation.
- New “toolbox” for **better prediction of safety and efficacy** (toxicology tests, biomarkers, clinical trials...) to reduce the risk of failure during development.
- IMI provides the infrastructure for **validation** of the new tools for rapid uptake into regulatory and industry practice.
- IMI sets up **‘knowledge platform’** pooling data from toxicology testing and biomarker validation - available to all researchers.
- With 1 billion from EU and 1 billion from Industry– it aims at reducing the attrition rate during development of new medicines.
- Run by Commission/EFPIA joint body (based in Brussels)

http://www.imi.europa.eu/

PHARMA EXPENDITURE per Capita & GDP



1. Prescribed medicines only.

Source: *OECD Health Data 2010* ; Eurostat Statistics Database; WHO National Health Accounts.

NATIONAL ECONOMIC & SOCIAL REGULATIONS

Diversity of national pricing and reimbursement schemes, based on national solidarity and social cohesion

National socio-economic agencies: NICE, HAS….

Directive 89/105: Transparency of pricing and reimbursement

EU Court of Justice rulings

“G10 / Pharma” process and 14 recommendations (2001/2003)

“EU Pharmaceutical Forum” (2005/2008) on:

pricing, information and relative effectiveness

EU cooperation on health technology assessments

Diversity of National Pharmaceutical Pricing & Reimbursement Systems

Control of prices in most countries (profits in UK), reference prices, generics, parallel import, wholesale/retail margins, VAT.

Reimbursement: positive or negative lists, co-payment, generic substitution .

Publications:

Pharmaceutical Pricing and Reimbursement Information, Gesundheit Österreich GmbH (GÖG-ÖBIG), June 2008. http//ppri.goeg.at

Analysis of differences and commonalities in pricing and reimbursement systems in Europe, Andalusian School of Public Health, June 2007.

Tender systems for outpatient pharmaceuticals in the European Union: Evidence from NL, DE and BE, London School of Economics, Oct 2009.

DIRECTIVE 89/105 ON PRICING TRANSPARENCY

1. Unanimously adopted in 1988 by Council of Ministers
2. Ensure transparency of national pricing and reimbursement
3. Prevent discrimination and market distorsions
4. Time limits for decisions: 90/180 days
5. National decisions must be properly motivated
6. Objective and verifiable criteria for decision making
7. Rights of appeal to national courts
8. EU transparency Committee

Commission proposal on revision of Directive (2012)

HEALTH TECHNOLOGY ASSESSMENT

Health technology assessment (HTA) is a multidisciplinary process to inform the formulation of safe, effective, health policies that are patient focused

Rooted in research for diagnostic and treatment methods, medical equipment, pharmaceuticals, rehabilitation and prevention, organizational health care systems

The Commission aims at enhancing the cooperation between the Member States in evidence-based health decision-making.

Joint Action under the Health Programme to avoid duplication between national agencies and spread expertise

http://www.eunethta.eu/Public/Home/

IV) INTERNATIONAL

International health organizations

Multilateral and bilateral initiatives

INTERNATIONAL HEALTH ORGANIZATIONS

WHO *Copenhagen & Geneva*:

Joint Health Conferences:
Stockholm, Budapest, Luxembourg, Helsinki, Copenhagen, etc..

Tobacco Convention (FCTC)

International Health Regulations (IHR)

International Agency for Research on Cancer (IARC)

Council of Europe *Strasbourg*:

Health Promotion in schools

Therapeutic Substances of Human origin

European Pharmacopoeia

http://www.edqm.eu/

OECD, *Paris*:

Health economics and health care statistics

International Pharma

ICH & VICH (harmonisation EU/Japan/US)

EEA: Norway+Iceland; extension to Switzerland

European Pharmacopoeia (36 countries+observers)

Future enlargements (Croatia…)

Bilateral contacts with Russia, China, etc...

Mutual recognition agreements:

(US, Canada, Japan, Austral./N-Zealand)

WHO Certification Scheme, Counterfeiting

ICH: EC/EMEA, Japan and USA

- International Conference on Harmonisation
- Initiative launched by Commission in 1990
- Regulators and industry from EU - Japan - USA
- Observers include WHO, Canada and EFTA
- ICH partners represent 90 % of world R&D
- VICH initiative in veterinary sector
- Maintainance and dissemination since 2000

EU versus US AGENCIES

- **US FOOD AND DRUG AGENCY (FDA)**

  Rockville (Maryland) 1906

- **CENTER FOR DISEASE CONTROL (CDC)**

  Atlanta (Georgia) 1946

NIH National Institute for Health

- **EMA: EUROPEAN MEDICINES AGENCY**

  London 1995

- **EFSA: EUROPEAN FOOD SAFETY AUTHORITY**

  Parma 2002

- **ECDC: EUROPEAN CENTRE FOR PREVENTION AND CONTROL OF DISEASES**

  Stockholm 2005

[Innovative Medicines Initiative]

V) THE FUTURE:

Personalised medicines?

- ***Prediction and precision (biomarkers)***
- ***Better targeted drugs, less side-effects***
- ***Effective patients' participation***
- ***Implies major regulatory changes***

First targets: Cancer, Asthma, Diabetes, Rheumatic diseases, Alzheimer, Parkinson, Chronic obstructive pulmonary disease

EU Health & Pharma on the Internet

http://ec.europa.eu/health

http://www.ema.europa.eu

http://ec.europa.eu/research/health

http://www.ecdc.europa.eu