REPUBLIC OF SLOVENIA
MINISTRY OF HEALTH
AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES

SERVING PATIENT NEEDS:
Marketing Authorization Procedures
Pharmacovigilance
And
Labelling

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REPUBLIC OF SLOVENIA
MINISTRY OF HEALTH
AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES

Assoc.Prof. **Stanislav Primožič**, Ph.D., M.Pharm.
DIRECTOR

With tributes to:

Dr. **Vesna Koblar, Barbara Razinger-Mihovec**
Regulatory Sector – Medicinal Products
and Medical devices for Human Use

Four steps

of entry of a medicinal product to a national market

DRA

Q,E,S

pricing

controlled /
free market

reimbursement

3rd party
payor / user

procurement

public /
institutional

Systemic players:

Transnational

EU/EC-DGs/EUDRA/G10
EMEA
WTO
WHO
Professional Organizations
Pharmaceutical Companies

National

Gatekeepers
Ministries

Local Rep's
Ibid.

HMA

AIMS of EU DRA

- HIGH LEVEL OF PUBLIC HEALTH
- HIGH LEVEL OF COMPETITIVENESS OF PHARMACEUTICAL INDUSTRY
- ENLARGEMENT REQUIREMENTS

DRUG REGULATORY AUTHORITIES IN THE EU

- CORE STRUCTURES:
  - CENTRAL AGENCY:
    - EMEA: European Medicines Agency
  - NATIONAL DRAs
    - MHRA (UK), AFSSAPS (F), BfArM (D), ARSZMP (SLO), …
  - Functional connections:
    - HMA, CMD(h), CMD(v), TIGs…
- SUPPORTIVE STRUCTURES
  - EDQM / European Pharmacopoeia
  - OMCL Network
  - PIC

NETWORKING
Why work-share is the future?

- Regulation of medicines in Europe is a shared task between EU bodies and NCAs
- NCAs knowledge and resources are pivotal in this process
- Resources are limited – co-operation is key to progress
- ”Best excellence” – NCAs and EMEA in united front
- Benchmarking

Perspectives of the

Heads of Agencies (HMA) Process

Safeguard of Public Health and animal welfare

- Cornerstones: Informal co-operation built on mutual understanding, trust and voluntary active participation

- **Members: EEA – 41 NCAs**
  - National competent agencies (NCAs) – united in working for quality, safety and efficacy – we built on our similarities and make mutual advantages of our differences
  - Provide a mechanism for communicating the views of Member States competent authorities with the Commission and with the EMEA.
  - Focus for leadership, channel for co-ordinated action and a mechanism for communication

HMA Vision

- Challenges of the European Medicines Regulatory Network (EMRN)
- Develop and support relevant scientific resources
- Avoid closed/monopolised scientific areas
- Open network based on principles that all can join
- Management of conflict of interests
- Avoid unnecessary duplication of work
- The chain is stronger than the weakest link

HMA Strategy Paper

(http://heads.medagencies.org/heads/hoa_docs.html)

6 Drafting Groups Reports:

- Communication and Information
- Scientific Assessment Process
- Inspection, Laboratory Control and Enforcement
- Scientific Resources
- Pharmacovigilance
- IT Information Systems

NATIONAL IMPLICATIONS
LEGAL ARCHITECTURE

- Medicinal Products legislation
  - (based on EU Acquis, i.e. SI Medicinal Products Act and bylaws)
  - Act entered into force on April 8th, 2006
- Pharmacy Legislation
- Health Care and Health Insurance Legislation
  - Pricing & Reimbursement pf MPs
- National Guidelines (for use of medicines)
- Borderline Legislation (veterinary, food safety...)
- Horizontal Legislation (administrative procedure, inspection procedure)

Legislation: ZZdr-1 (SI)

Specific modifications linked to EU requirements:

- European reference product by balancing of rewarding innovations and assuring quick access to cheaper generic medicinal products.
- Better regulation of herbal and homeopathic medicinal products
- Better transparency of the system for stakeholders
- Other specific provisions aimed to improve the existing system and to transpose EU concept of regulation of medicinal products

ZZdr-1 (SI) Specific modifications linked to EU requirements:

- Introducing of new and updated definitions (generic medicines, biological medicines...)
- Consolidation of procedures (quick, transparent...)
- Improvement of legal basis for co-operation between EU Member States
- Strengthening of pharmacovigilance
- Introducing specific incentives for industry (new data exclusivity period - 8+2+1,

Legislation: ZZdr-1 (SI)

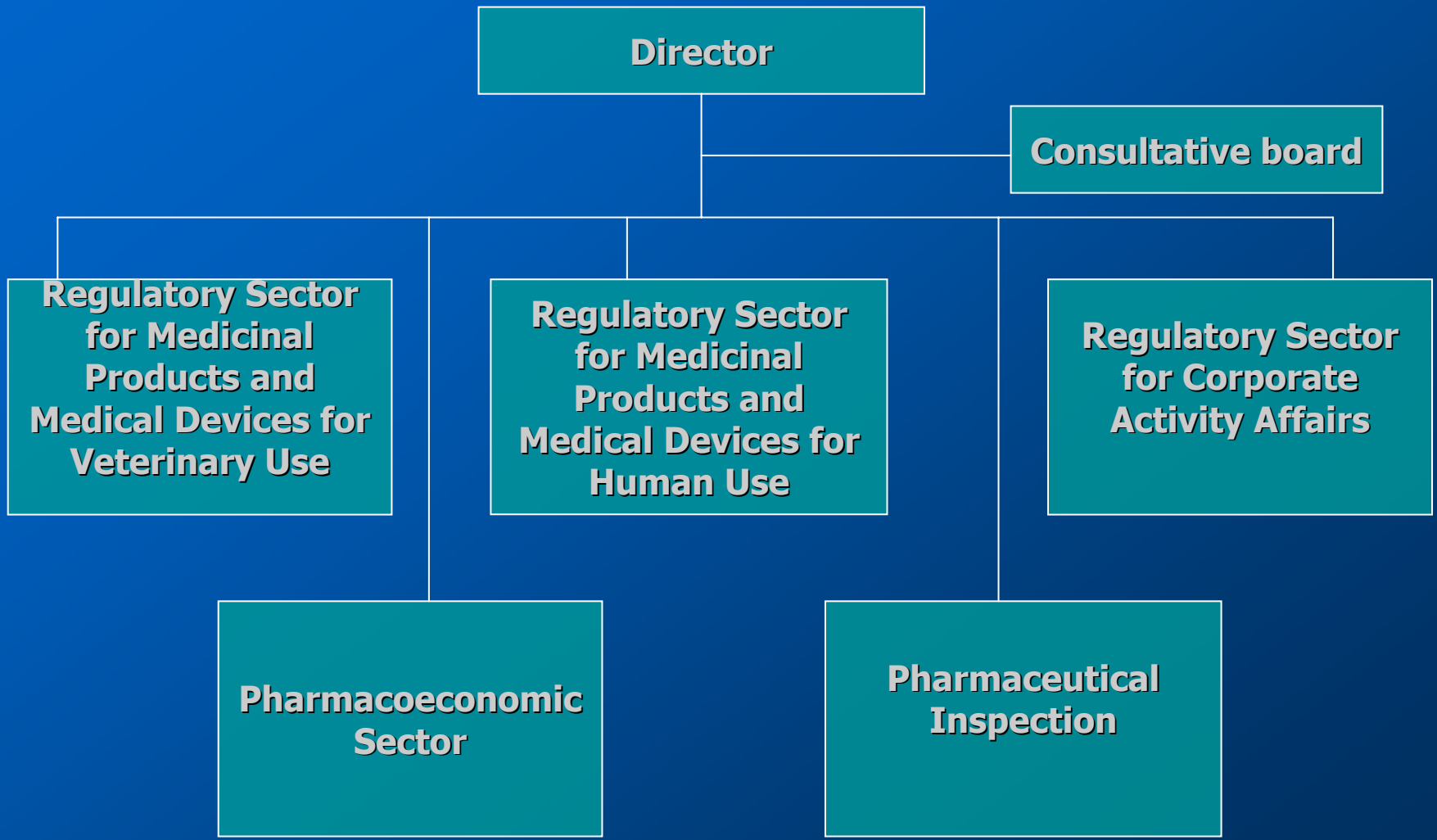
Specific modifications linked to national requirements:

- Better inclusion of provisions on drug pricing, that include the concept of interchangeability of medicinal product
- Retail sale of medicinal products through internet
- Retail sale of OTC medicinal products in pharmacies and specialized shops

ZZdr-1 (SI) Specific modifications linked to national requirements:

- Required professional background of persons responsible for advertising of medicinal products to health care professionals
- Establishing the *Public Agency for Medicinal Products and Medical Devices* that will bring together resources from the existing Agency for Medicinal Products and Medical Devices (as an integral part of the MoH) and Official Medical Control Laboratory
- Other specific provisions aimed to improve the existing system and to improve national concept of regulation of medicinal products

Agency for Medicinal Products and Medical Devices of the Republic of Slovenia
A R S Z M P



Internal organization and systemization decree
(February 2004)

SLOVENIA

ZZdr-1 Medicinal Products Act
establishes
the Public Agency for Medicinal Products and Medical Devices

- Legal person under public law
- Established by the Government
- Merger of the resources of the Current Agency and the national OMCL
- Pharmaceutical Supervision
- HUM/VET
- Medical Devices
- Pricing
- Staff 80+
- Mixed financing: fees + state budget
- Deadline: 1 yr

OBLIGATORY CENTRALISED PROCEDURE

FROM 20.MAY.08, NAS: AUTOIMMUNE, IMMUNE D.

FROM 20.NOV.05, NAS:

DIABETES

HIV

BY 20.NOV.05
LIST A: CR 2309/93/EEC

CANCER

NEURODEGENERATIVE D.

VIRAL D.

OPTIONAL CENTRALISED PROCEDURE

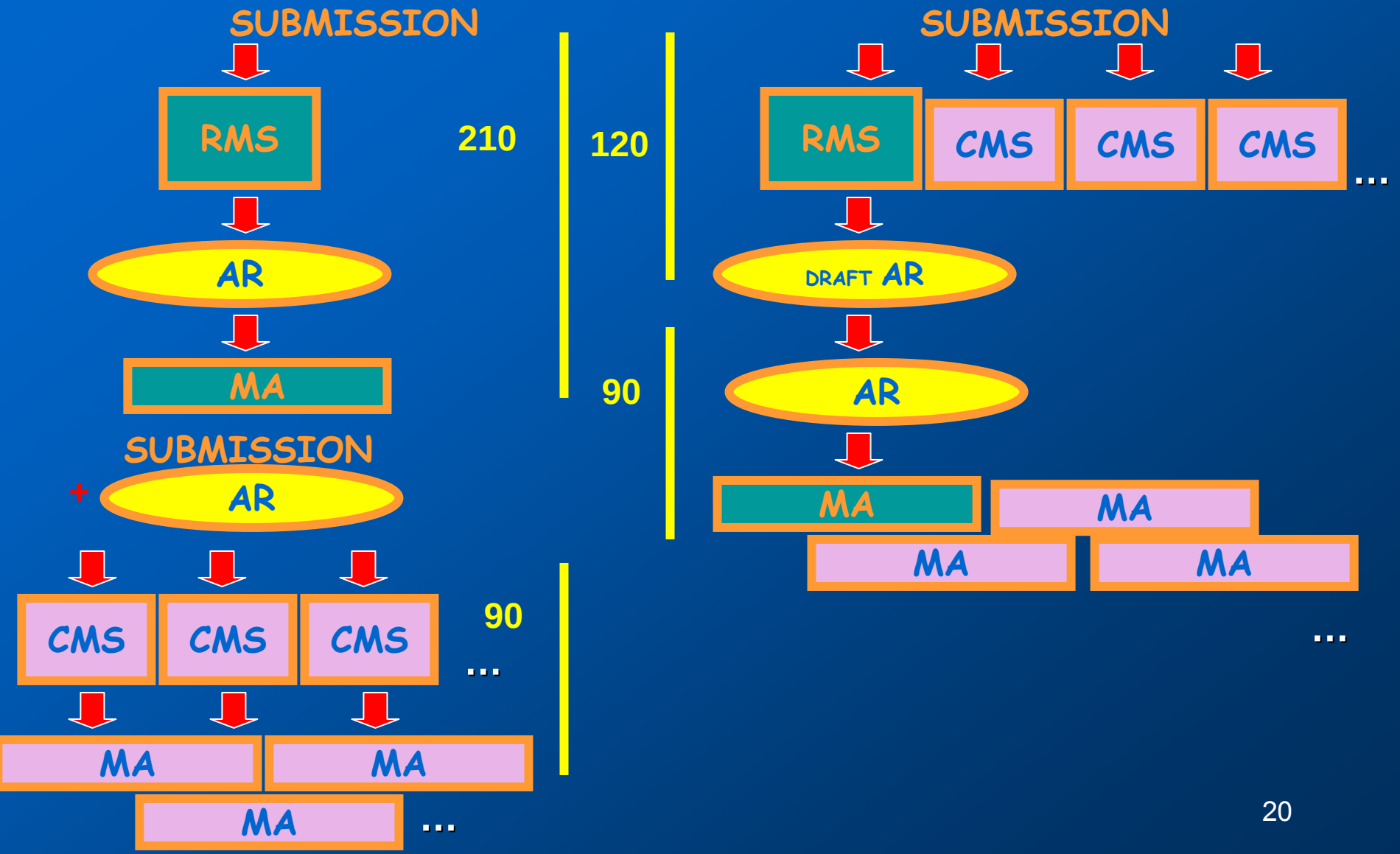
FROM 20.NOV.05, NAS:

- NOT AUTHORISED IN THE EU
- COMMUNITY INTEREST

BY 20.NOV.05
LIST B: CR 2309/93/EEC

-GENERICS OF CENTRALLY
-AUTHORISED PRODUCTS

MRP vs DP


SUBMISSION
RMS
210
AR
MA
SUBMISSION
+
AR
CMS
CMS
CMS
90
...
MA
MA
MA
...
120
90
SUBMISSION
RMS
CMS
CMS
CMS
...
DRAFT AR
AR
MA
MA
MA
MA
...

LABELLING AND PIL

- SECTIONS DEFINED BY DIRECTIVE 2001/83/EC:
- PIL AND OUTER PACKAGING SHALL REFLECT THE RESULTS OF CONSULTATIONS WITH TARGET PATIENT GROUPS THAT IT IS LEGIBLE, CLEAR AND EASY TO USE
- BRAILLE

PharmacoVigilance

- STRENGTHENING OF PhV
- ASSESSMENT OF SAFETY
- POSITIVE ASSESSMENT OF THE RISK/BENEFIT RATIO
- RISK MANAGEMENT SYSTEM

PhV IN THE NEW EU PHARMA LEGISLATION

- RISK MANAGEMENT SYSTEM
- COMMUNICATION BETWEEN MSs
- MAH OPBLIGATIONS: REPORTING THE DATA REFLECTED IN SmPC AND OTHER DATA AND ADR
- QUALIFIED PERSON
- ACTIONS TO BE TAKEN IN CRISES
- PhV INSPECTION
- REPORTING FROM PATIENTS

PSUR

- 2X/Yr AFTER GRANTING THE MA AND UNTIL THE PLACING ON THE MARKET
- 2X/Yr, FIRST 2Yrs AFTER GRANTING MA
- 1X/Yr, NEXT 2Yrs
- 1X/3 Yrs, WITHIN THE PERIOD OF VALIDITY OF MA
- UPON ON REQUEST OF CA

TRANSPARENCY

- **PUBLICLY ACCESSIBLE INFORMATION**

  (NO COMMERCIALLY SENSITIVE INFORMATION SHOULD BE INCLUDED):

  - DECLARATION ON NO CONFLICT OF INTEREST FOR CA STAFF AND EXPERTS
  - AR
  - RULES OF PROCEDURES, AGENDAS OF MEETINGS, RECORDS, DECISION TAKEN
  - JUSTIFICATIONS FOR REFUSAL OF MA
  - PhV DATA THAT CONCERN PUBLIC HEALTH
  - EUROPHARM DATABASE – PARTIALLY AVAILABLE TO THE PUBLIC

Labelling

- In accordance with the Title V of the Directive 2001/83/EC, which provides for also some national requirements “blue box” (price, reimbursement conditions, legal status, identification)
- transposed in the Rules on labelling of MP and package leaflet (OGRS, No. 54/06)
- Particulars for the identification and for proper, safe use of medicinal products

Labelling – particulars for identification

- **(Invented) name + strength + pharmaceutical form + common (INN) name**
  E.g.: (Invented) name 60 mg tablets
  venlafaxine
- **Active substances expressed qualitatively and quantitatively**
  E.g.: 1 tablet contain x mg venlafaxine in the form of y mg venlafaxine hydrochloride
- **Important excipients** (in parenteral, opthalmic and topical medicinal products **all** excipients, for all other MPs only those excipients known to have a recognised action or effect, included in the Commision's guideline)
  - ***<"Information and other excipients are stated in PIL.">***
  - ***<"Excipients are listed in PIL.">***
- **Pharmaceutical form and contents** (by weight, V or No. of doses)
  E.g.:10 g, 30 tablets, 50 ml
- **Marketing authorisation holder**
  E.g.: Dola d.d., Bergantova 1, Ljubljana
- **Manufacturer's batch number**
- **Number of authorisation for placing MP on the market**

Labelling – particulars for proper, safe use

- **Method and if necessary the route of administration:**
  E.g.: *»Do not chew!«, »Capsule to be swallowed with a glass of water!«*
  Always: ***"Read the package leaflet before use!"***
  E.g.: *»Intravenous use« , »Intramuscular use«*
  In the case of non-prescription MP, instructions for use
- **Warning:** ***"Medicinal product to be stored out of the reach and sight of children!"***
- **Other special warnings, if necessary**
- E.g.: *»For external use only!«*
- **Expiry date** (month and year)
- Special **storage precautions** – in accordance with stability guidelines:
  - *<Do not store above <25 °C.> <30 °C.>*
  - *<Store in a refrigerator.>*
  - *<Store and transport frozen.>*
  - *<Keep the container tightly closed.>…*
- Specific **precautions for the disposal of unused MPs or waste derived from MPs**, e.g. *radiopharmaceuticals, cytotoxic,…*


10 mg/1 ml
Metadon Krka
peroralna raztopina
10 mg/1 ml
methadonum
100 ml raztopine
KRKA


MST 100 mg
Continus® tablete
Morphinum
filmsko obložena tableta s podaljšanim sproščanjem
obložene tablete s postupnim osvobajanjem
60 tablet / tableta
mundipharma

Blue box – Slo national requirements

- Marks of warnings for narcotic and psychotropic MPs: (Δ,  , §,!)
  - Δ - empty triangle in the text colour – relative prohibition of driving and using machines
  -  - full triangle in red colour - absolute prohibition of driving and using machines
  - § - paragraph in the text colour – narcotic
  - **! – exclamation mark** in the text colour – limited amount of a single delivery of the medicinal product on the prescription
- Classification (legal status of MP)
  - *Rx – MP subject to medical prescription: H/Rp, Rp/Spec., ZZ*
  - *OTC – MP not subject to medical prescription, pharmacy retail*
  - *OTC – MP not subject to medical prescription, pharmacy and special shops retail*
- Slovenian bar code EAN 13 – denotation that MP has a MA in RS