Reinforcing patient safety in Europe
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HALMED
Agency for Medicinal Products and Medical Devices of Croatia

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Perspectives from a new Member State

Accession preparation I
Reinforcing patient safety in Europe

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State Medicines Control Agency

VALSTYBINĖ VAISTŲ KONTROLĖS TARNYBA
PRIE LIETUVOS RESPUBLIKOS SVEIKATOS APSAUGOS MINISTERIJOS

Topics

- Phasing-in Lithuanian national competent authority (SMCA) to EU network
- Main safety activities
- Lessons learned

Lithuanian NCA: Small Agency in a Small Country

Population (in millions):

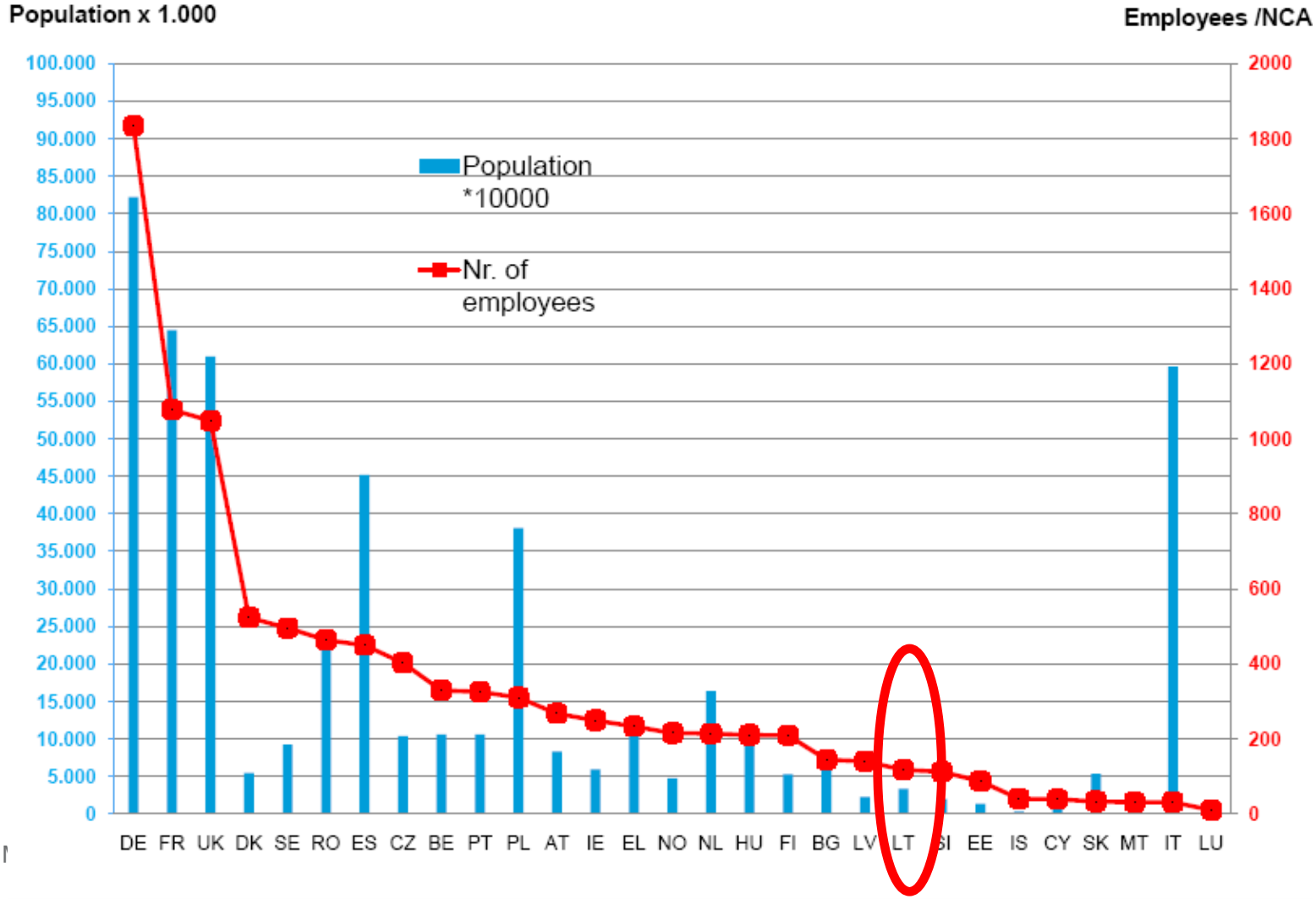
~3.0 (in 2011) from
~3.7 in 1990)

Experts' monthly **salaries** (netto)

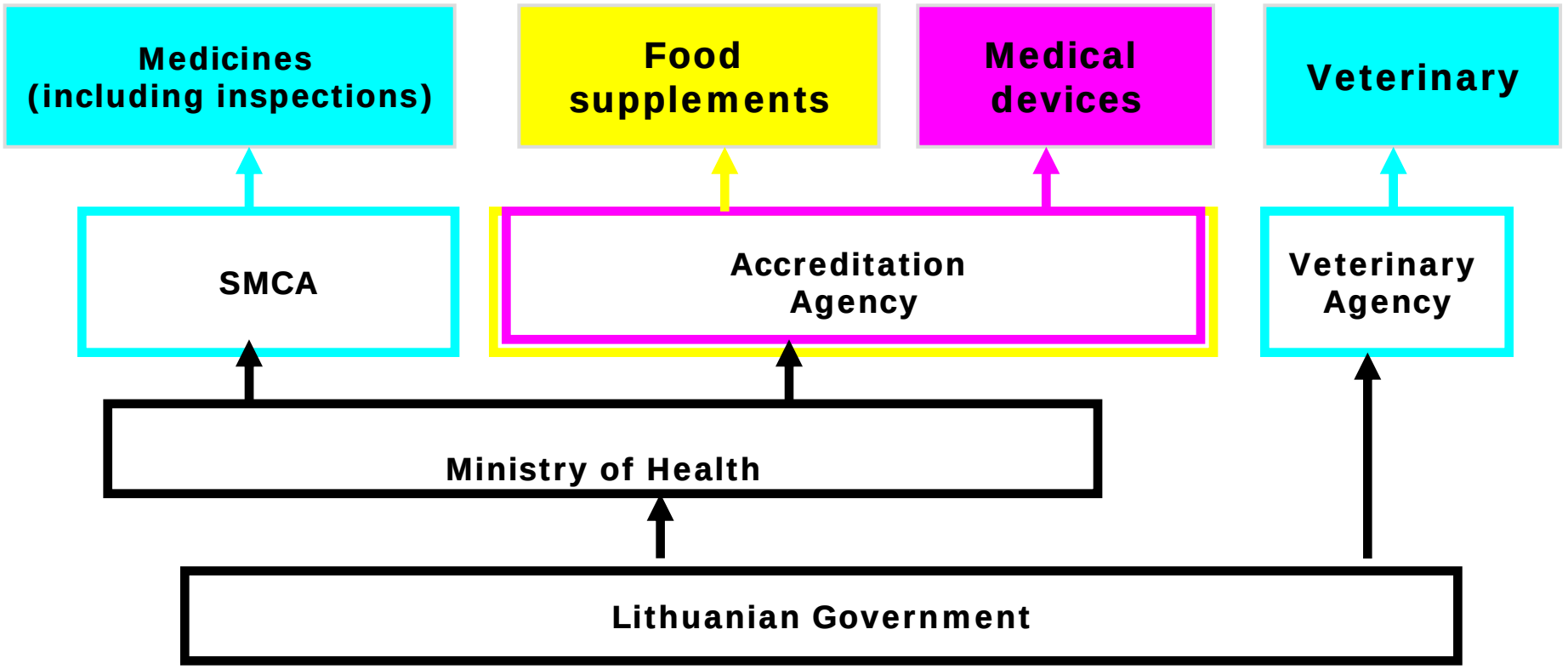
~ $1000 (in 2010) from

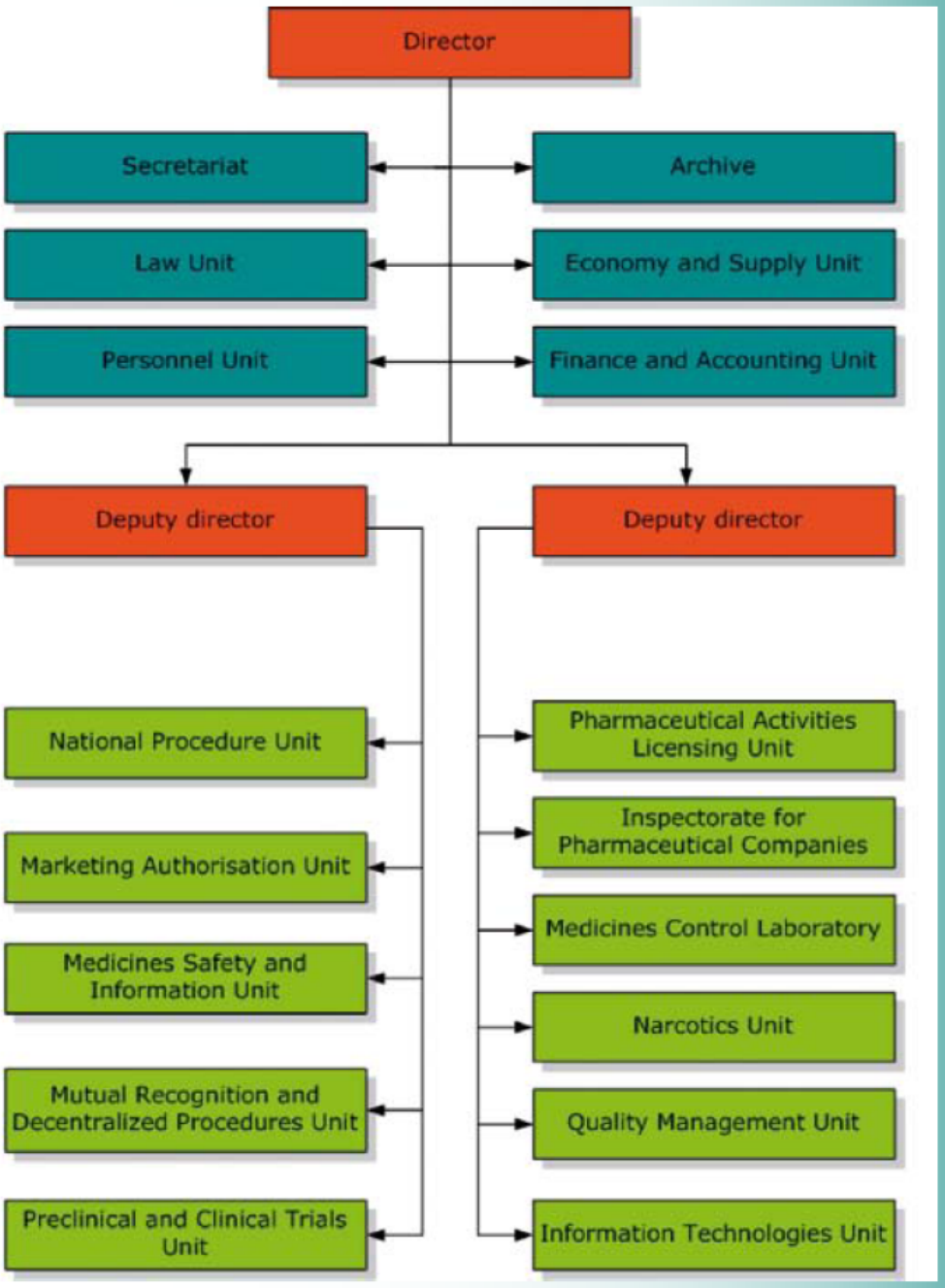
~ $100 (in 1995)

Populations and employees per Agencies



State Medicines Control Agency (SMCA) and regulatory framework





SMCA

~100 internal employees

~130 before crisis

+ 8 external contractors

+ 2 external experts

Challenges during "Phasing-in" and implementing ACQUIS (1/2)

- Continuously changing ACQUIS
  - (2 Pharma laws → 1 Consolidated law + Orders)

- Challenges with SOPs, deadlines, communication with applicants

  => Do not intent to be ideal everywhere from the very beginning

  => Do not just simply copy CRP practices for NRP purposes

- Too limited number of priorities from the activities expected by upper government bodies

Challenges during "Phasing-in" and implementing ACQUIS (2/2)

- Too long time for MA procedures and sometimes just minimal quality in performances

- Too big turnover of experts makes additional burdens to keep constant national competence

- Need for competence development for active participation in EU regulatory framework

Impact on national authorizations

- Conversion of numbers of herbal and "medical purpose" products based on revised benefit/risk assessments
- Not-upgraded dossiers

  => Do not mix regulatory pharma science with economic politics

  => Do not assume that applicants always know what they are doing

  => Learn how to translate scientific judgment into legal language
- Authorization of "ex-concertation" type of products
- Availability problems, including limited consistency in supplies to pharmacies

After 5 years we finally confirmed a status of food supplement for popular MP

Validolis – ne vaistas, o maisto papildas

2009-07-21

Valstybinė visuomenės sveikatos priežiūros tarnyba prie Sveikatos apsaugos ministerijos (VVSPT) informuoja, kad nuo š. m. liepos 1 dienos validoliu prekiaujama kaip maisto papildu. VVSPT atkreipia dėmesį į tai, kad maisto papildas yra ne vaistas, o maisto produktas, neturintis gydomojo poveikio ir nevartotinas jokioms ligoms gydyti.

Lietuvoje validolis nebepriskiriamas vaistams nuo 2003 m. Valstybinė vaistų kontrolės tarnyba atsisakė jį registruoti kaip vaistą, nes nėra įrodyta, kad jis padėtų sergant kokia nors liga. 2004-aisiais validolis buvo įtrauktas į medicininės paskirties produktų sąrašą, kuris š. m. liepos 1 dieną panaikintas.

Ilgą laiką validolis vartotas esant širdies veiklos sutrikimams.

Food supplement

Iron products

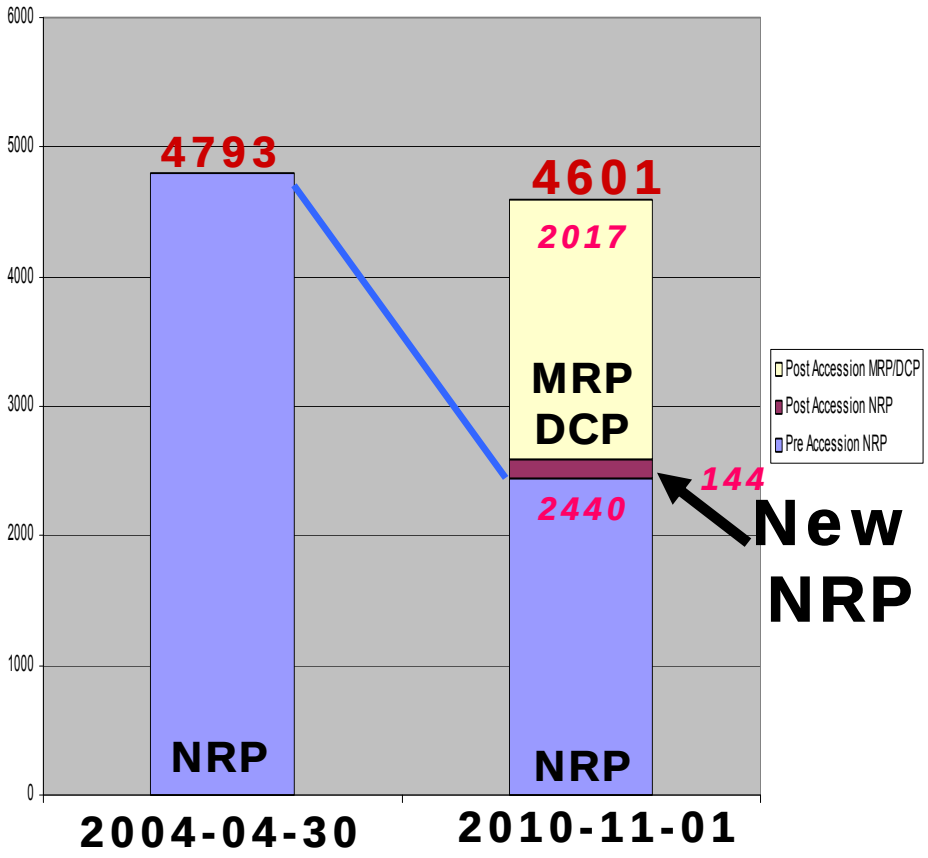
Medicinal product

Impact on National MA procedures

Dramatically changed profile of procedures:

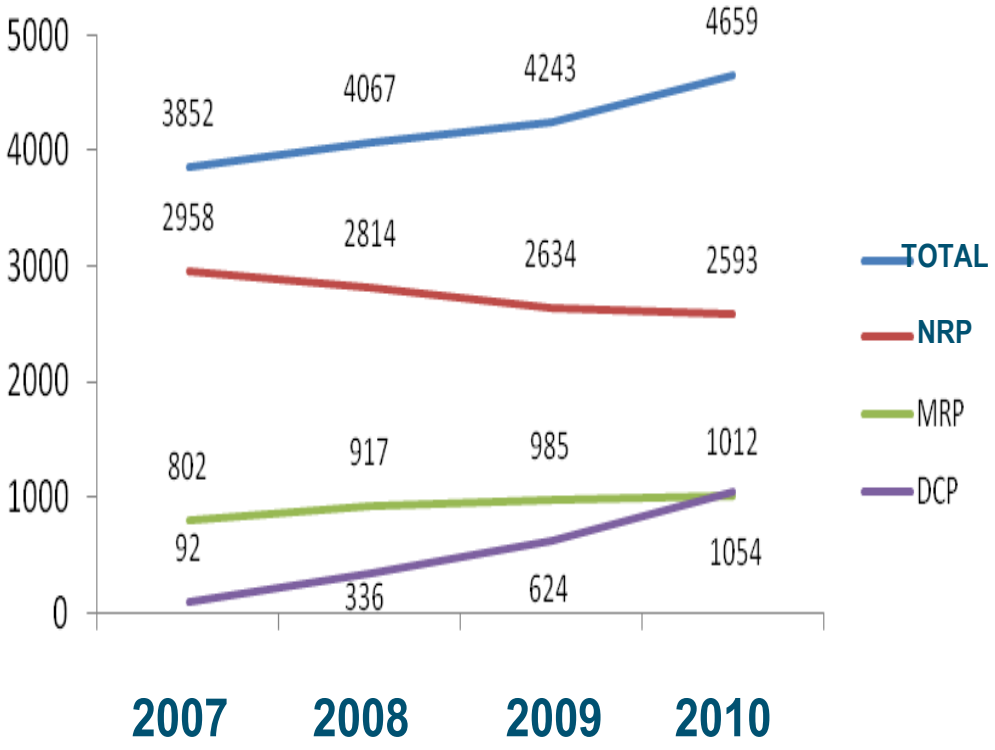
- decrease in NRPs
- constant increase in MRP/DCP
- introduction of CRPs

Evolution of MA in Lithuania (including all strengths and forms)

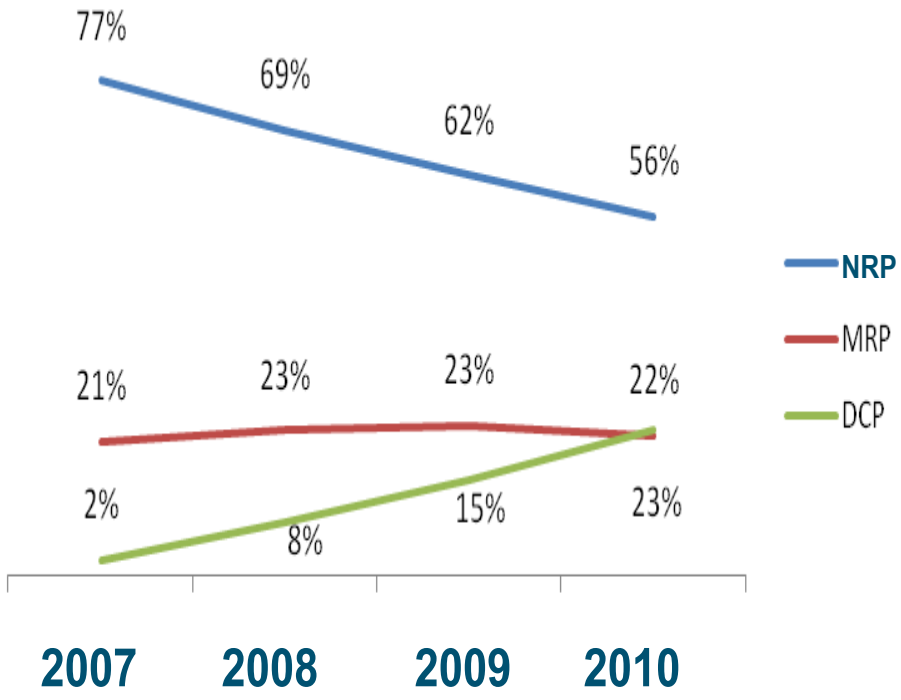


Tendencies in procedures

Medicinal products in national registry

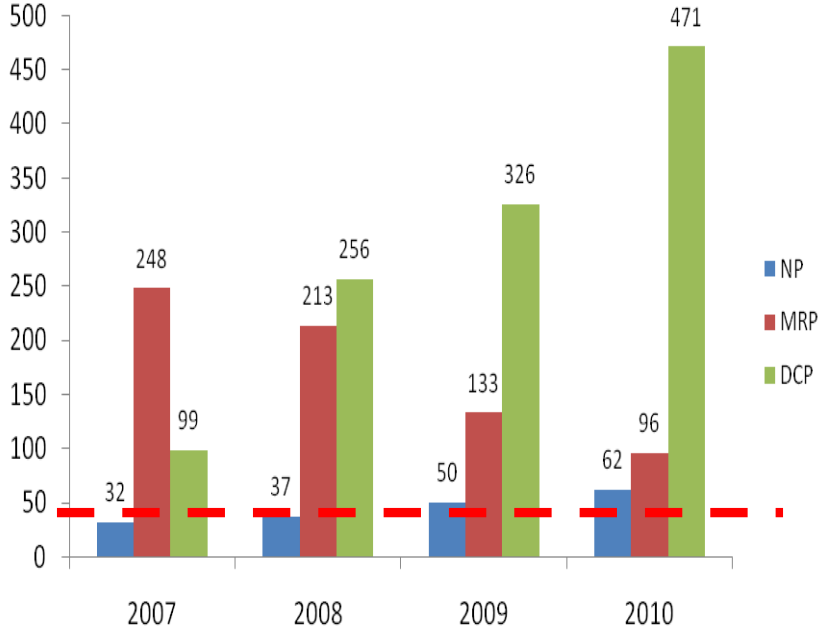


Proportions

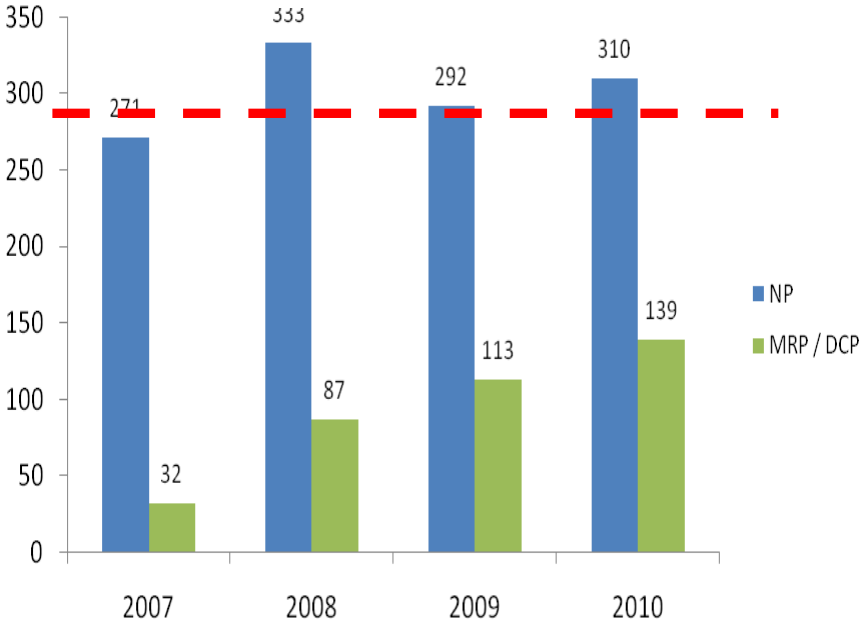


Tendencies in procedures

Authorisations



Renewals



Availability problems used to be observed once upon a time….

As a consequence, medicines availability is not always sufficient: the *absence* of *essential* ones, such as:

- Anticoagulants – *heparinum*
- Hormones – *hydrocortisonum*
- Antibiotics – *izoniazidum*, *amphotericinum*, *tazocinum*
- Cardiovasculars – *nitroglycerinum*, *clonidinum*, *labetololum*, *prazosinum*, *norepinephrinum*, *digoxinum inj.*, *verapamilum inj.*
- Immunosuppressants: *tacrolimus (all formulations)*, *MMF i/v*, *ciclosporinum i/v*
- Other – *40% glucosum*, *calcium i/v*, and various *antidotes*

Employed solutions to availability problems in Lithuania

Different *additional measures* have to be introduced to overcome the shortages putting with an additional burden to all stakeholders:

- *Patient named* supply chains
- Special *hospital supply* arrangements
- *Prioritizations* in MA procedures, including the for variations

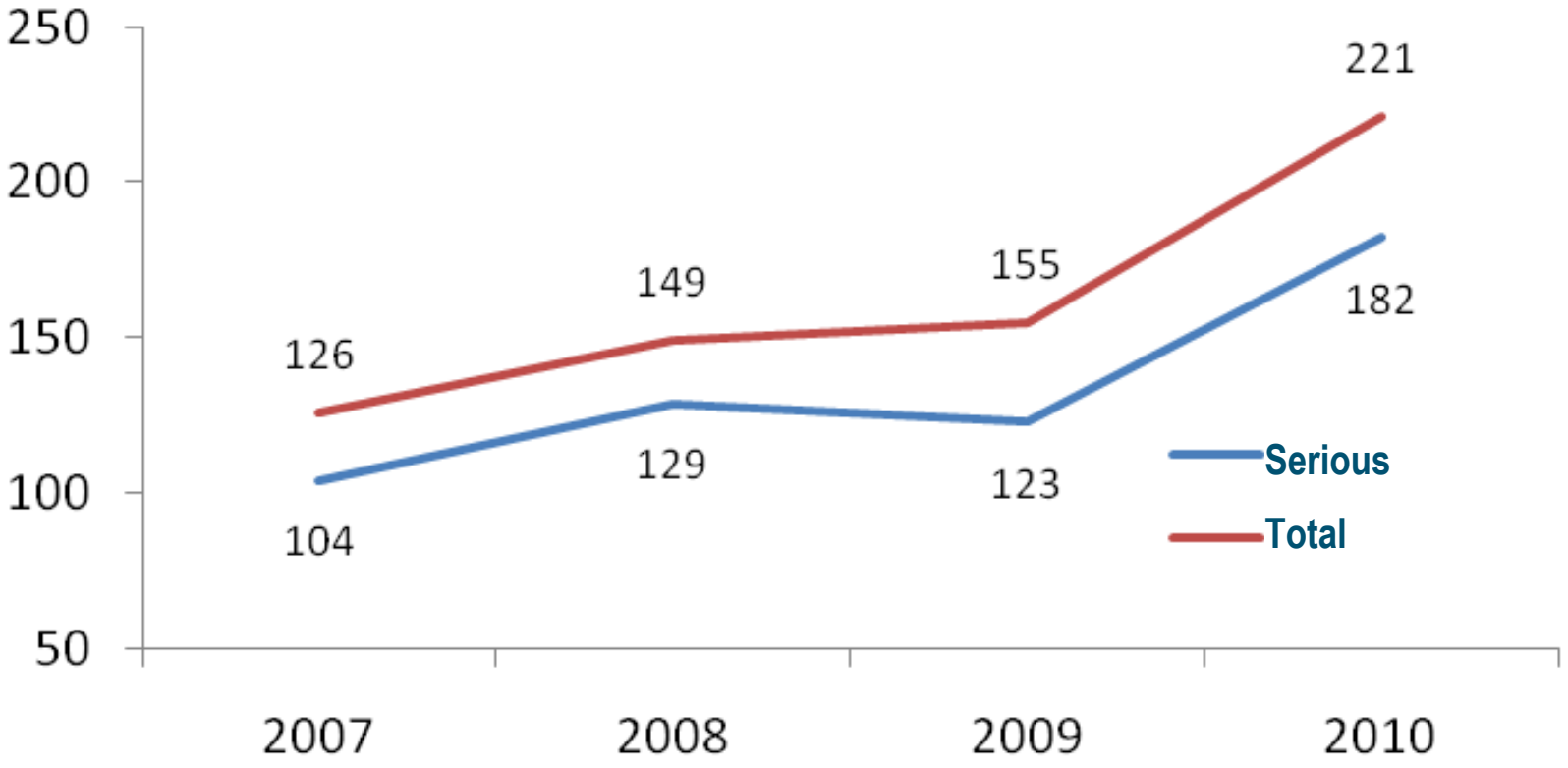
Topics

- Phasing-in Lithuanian national competent authority (SMCA) to EU network
- **Main safety activities**
  - **Safe, or not safe: that is a very relative question… like beauty…**
- Lessons learned

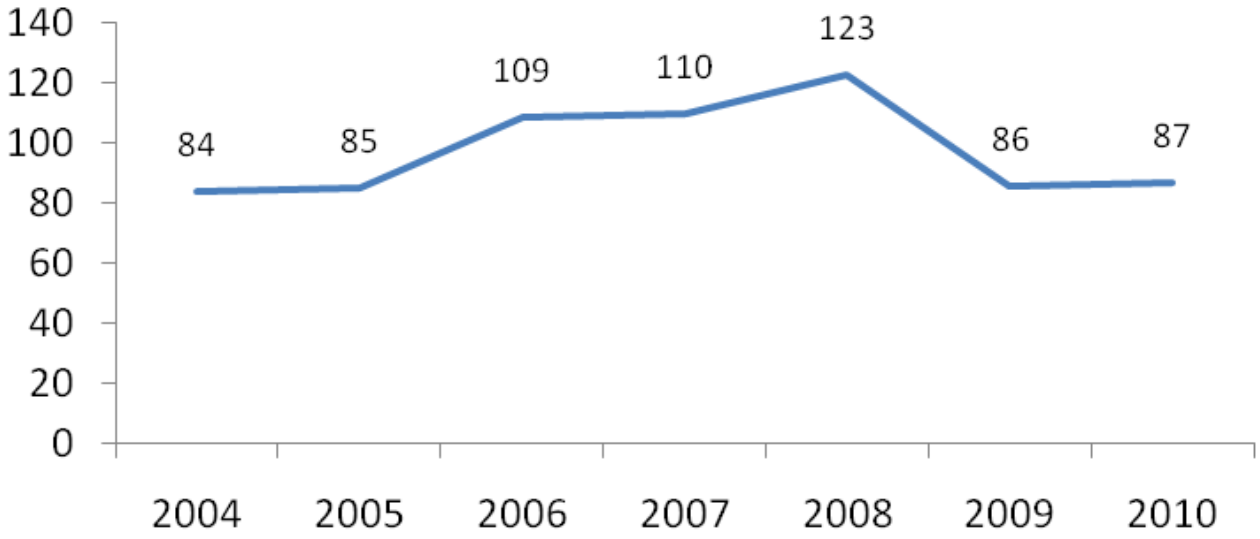
Main regulatory activities for safety

- **Pre-marketing safety evaluations**
  - **NRP**
  - **MRP / DCP**
  - **CRP**
  - **Pre-marketing clinical trials**
- **Post-marketing safety evaluations**
  - **ADR reporting and proceedings**
  - **PSUR, including EU Worksharing**
  - **PhW systems**
  - **DHCP, “Dear Patient” letters, teaching materials**
  - **Post-marketing safety trials**
  - **Quality inspections in pharmacies**

ADR reporting



Applications for Clinical trials

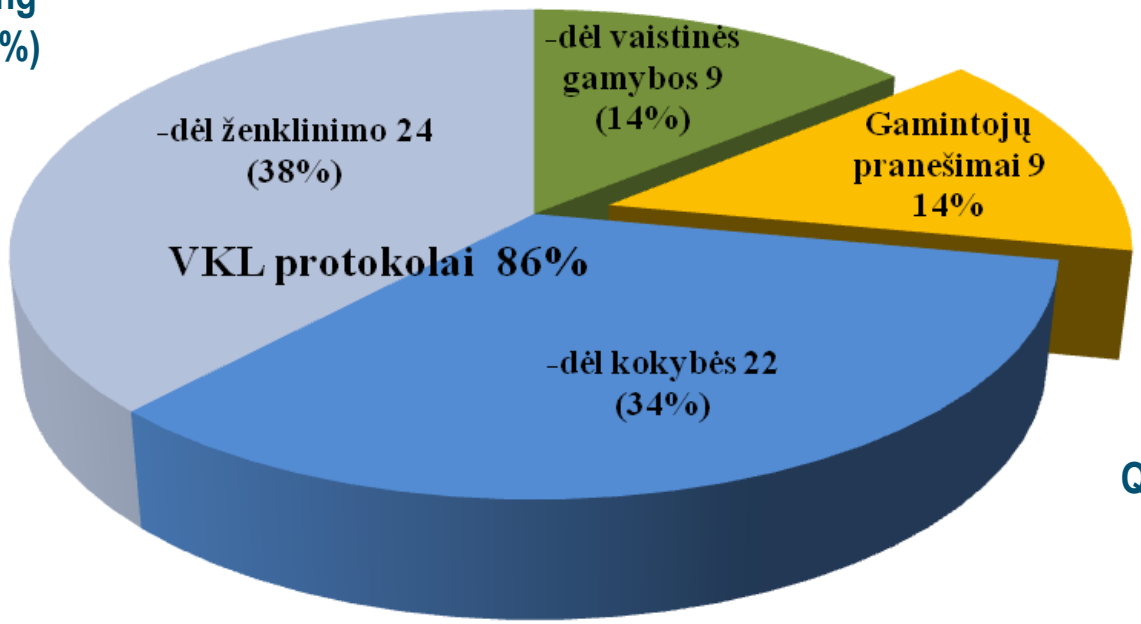


Reports about quality defects (in 2010) n=64

Productions in pharmacy
9 (14%)

Labeling
24 (38%)

Reports from manufacturers
9 (14%)



SMCA laboratory reports
55 (86%)

Quality defects
22 (34%)

Quality inspections and defects

	Medicines		Extemporal production		Pure/Water for injection		Active substances	
	n	%	n	%	n	%	n	%
2007	12	17,1	15	29,4	4	20,0	-	-
2008	-	-	4	22,2		16,7	-	
2009	2	3,4	-	-	-	-	-	-
2010	3	4,6	9	36,0	-	-	19	70,4

	Labeling	
	n	Non-compliant
2007	91	49 (53,8 %)
2008	41	21 (51,2 %)
2009	66	34 (51,5 %)
2010	59	33 (55,9 %)

Topics

- Phasing-in Lithuanian national competent authority (SMCA) to EU network
- Main safety activities
- **Lessons learned**

Lessons learned: 10 “DOs”

(1)Strategic positioning of NCA in Big EU

=> Do not limit NCA to national competences only

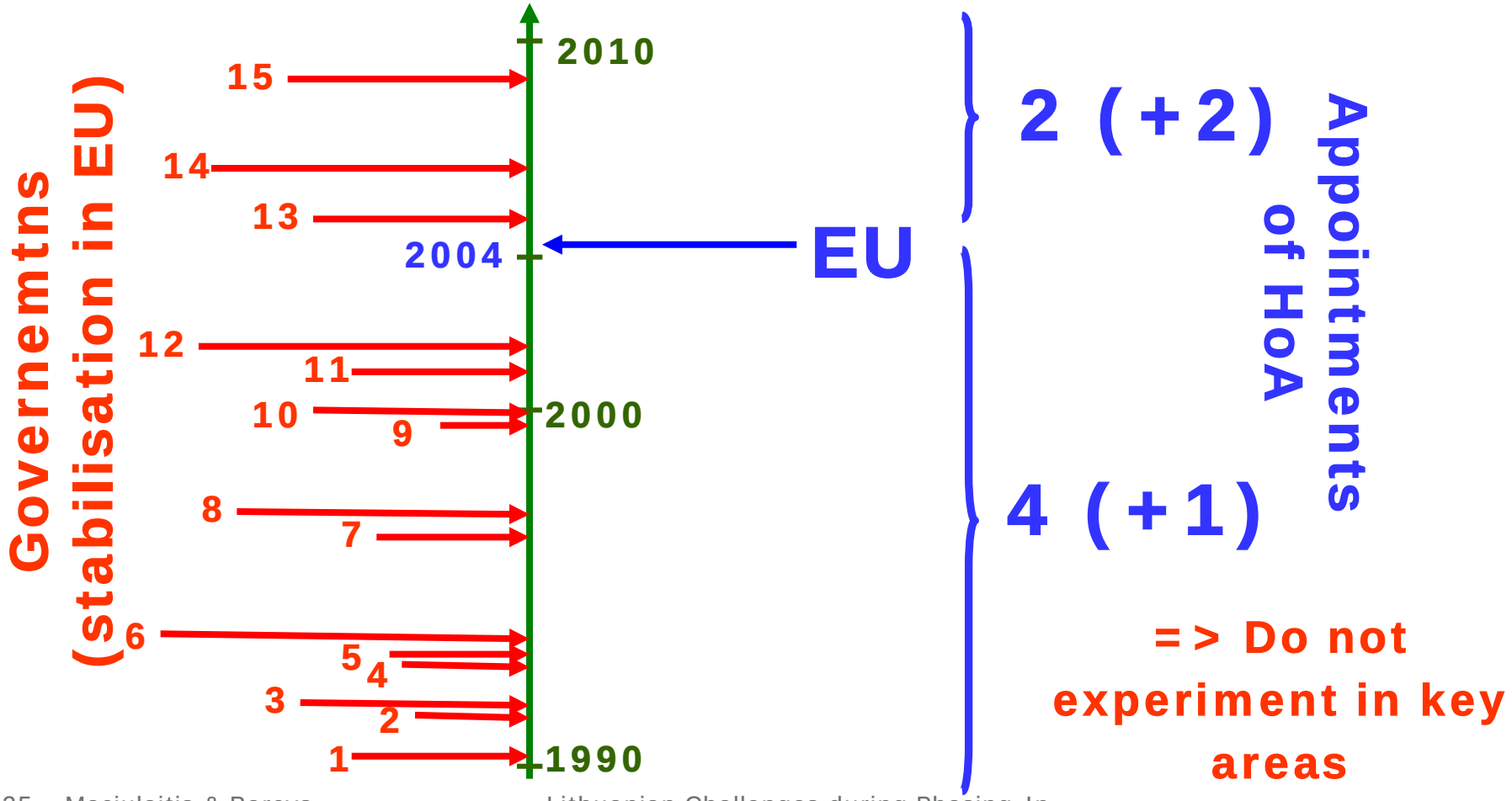
(2) Follow examples of those NCAs that do control flow of their budgets

(3) Invest into key national scientific competences

(4) Make use of administrative support available from EU, including IT developments

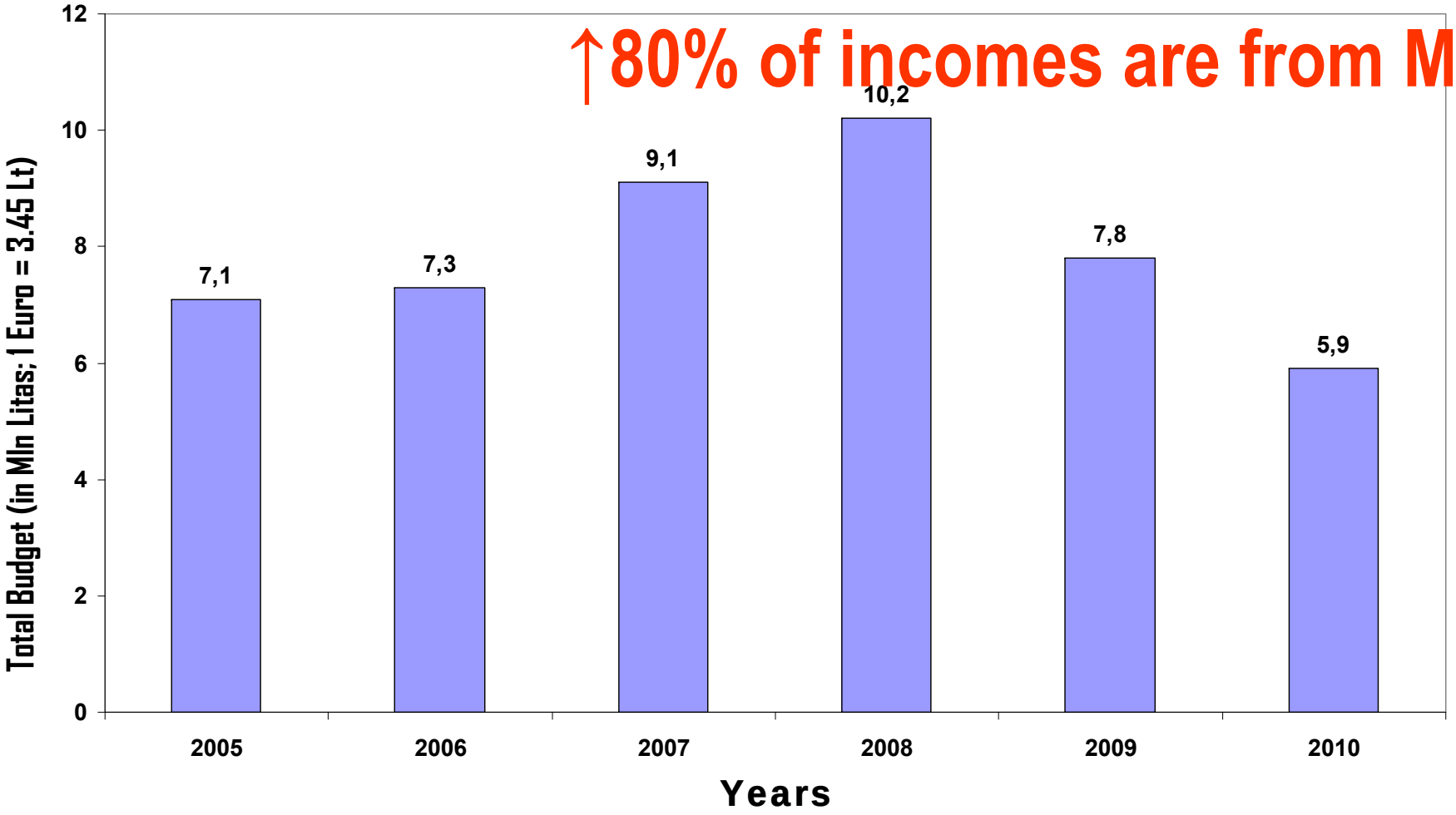
(5) Utilize worksharing opportunities of EU regulatory framework

.. Firstly, negotiate the strategic balance between national and EU priorities



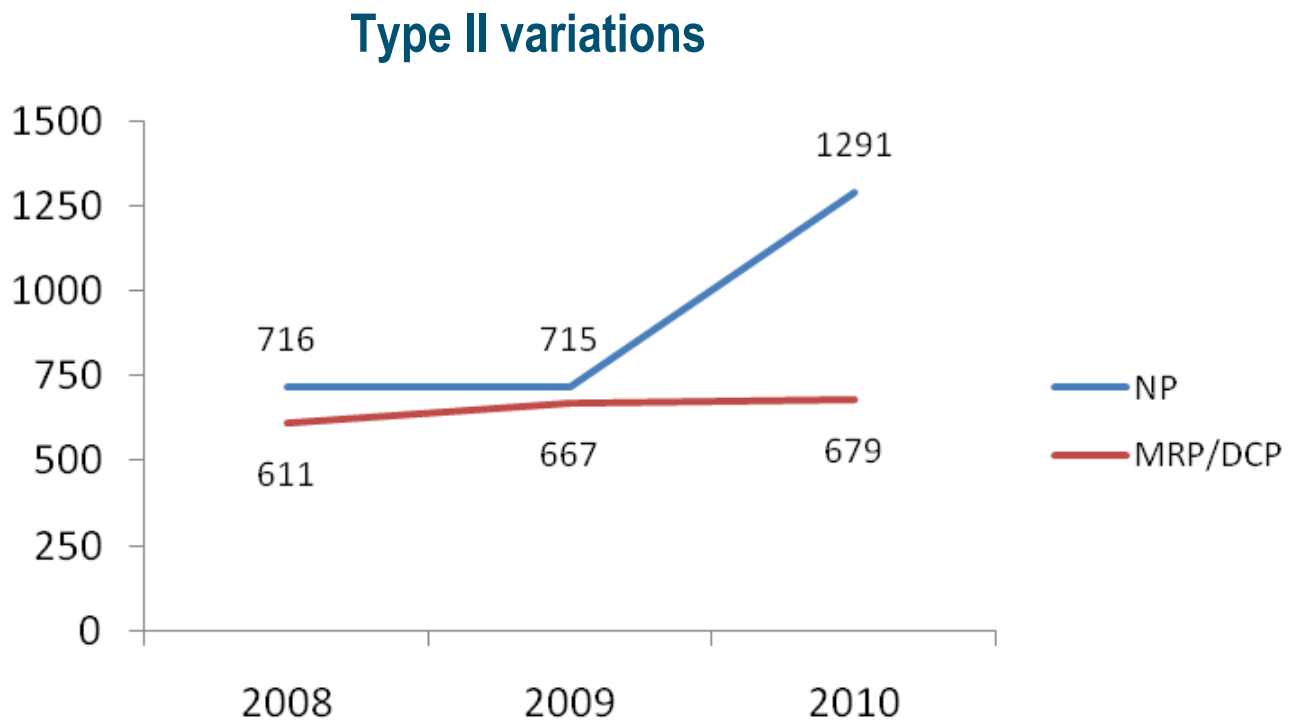
Budgetary Conditions of the Agency

↑80% of incomes are from MA



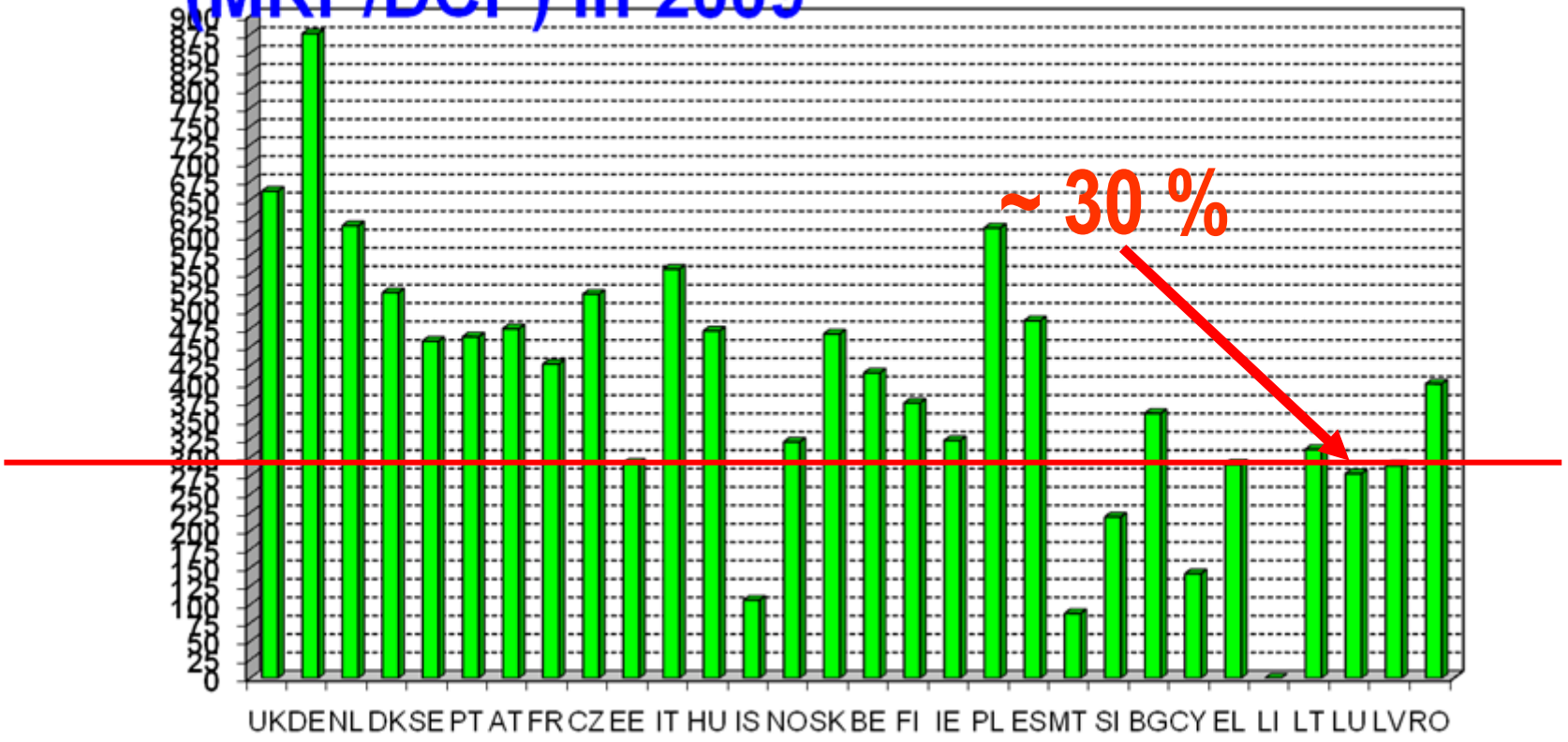
.. E.g., by avoiding unnecessary work

.. Breakthrough implementing fast-track procedures



=> Do not spend too much effort on not essential activities

CMS for MA-Applications (MRP/DCP) in 2009



Lessons learned: 10 "DOs"

(6) Start contributing to EU network asap

(7) Employ regional initiatives (multilingual packages, GMP inspections)

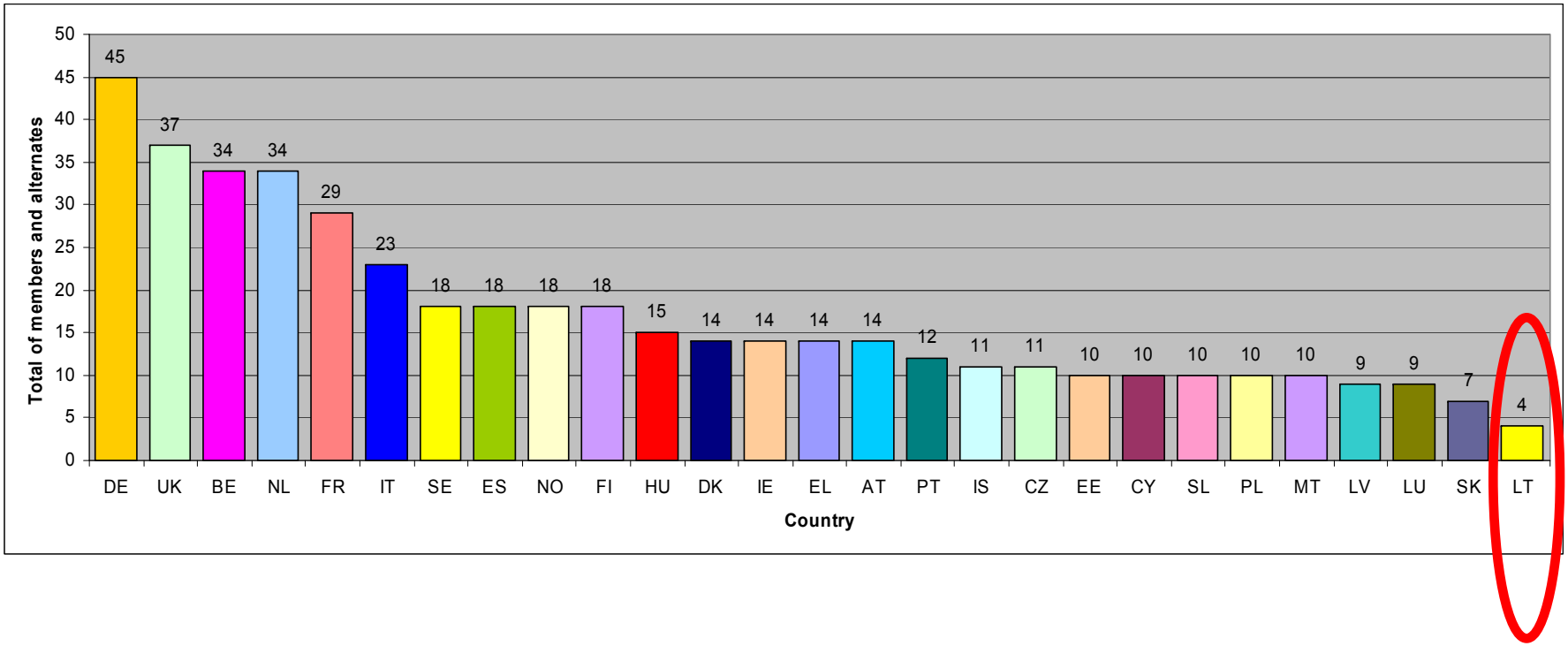
(8) Initiate pro-active agreements with other stakeholders, including the applicants

=> e.g., do not employ WEU to replace generic application or MRP/DCP

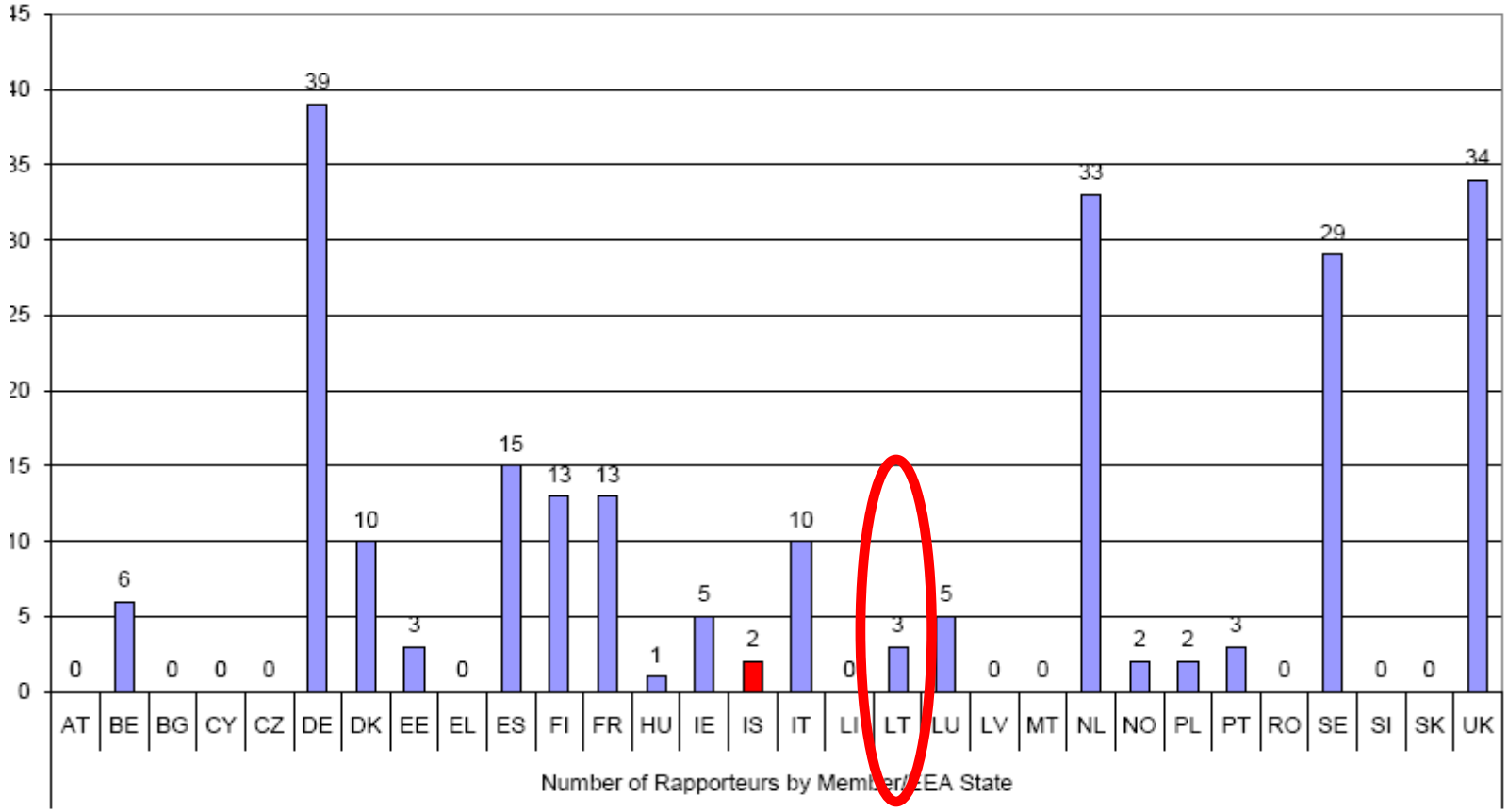
=> e.g., consolidate non-essential SmPC changes during renewal

(9) Select 4 – 5 persons for key areas and motivate them to do long-term commitments

Count of members and alternates in the CHMP and WPs

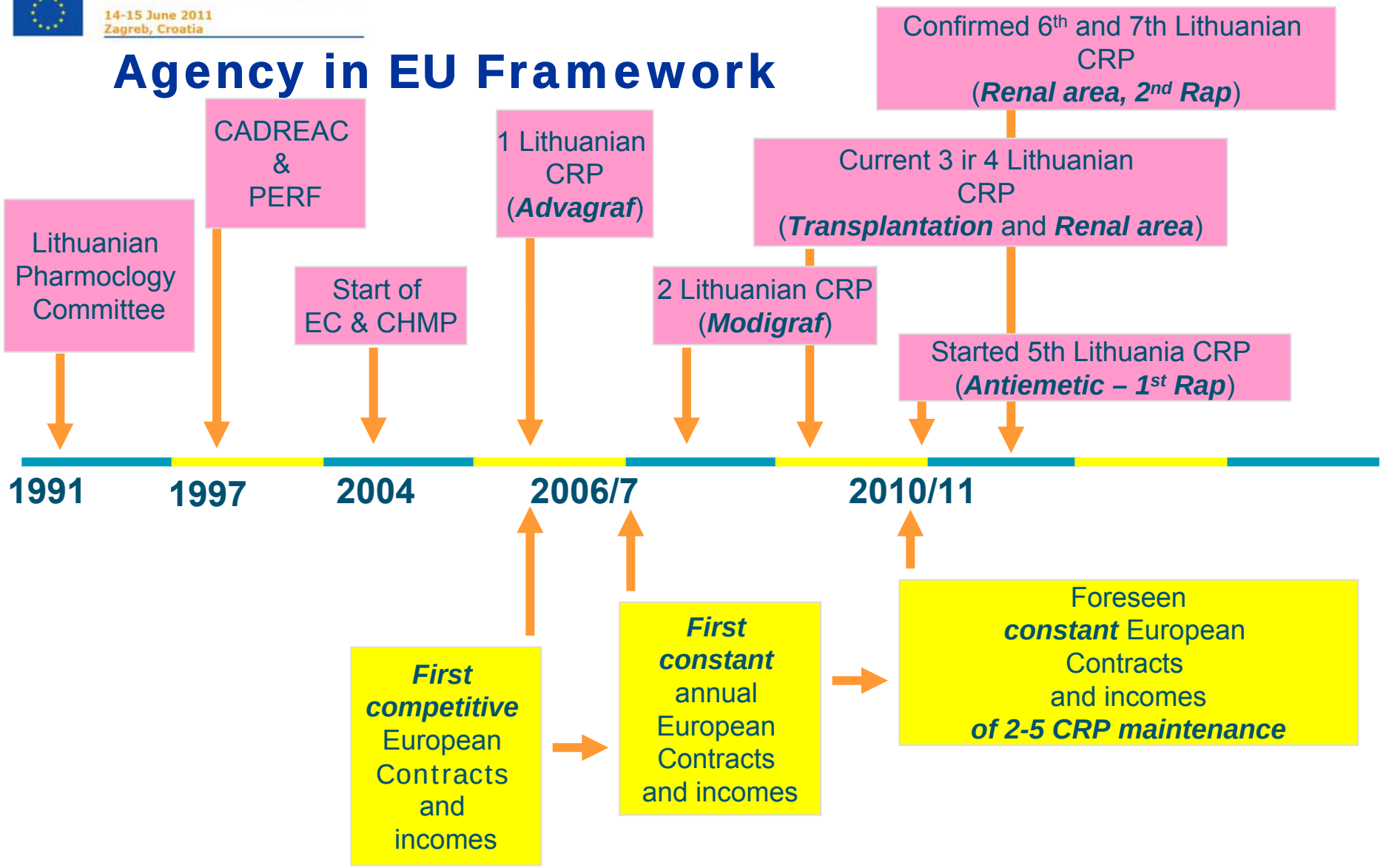


Concept papers / Guidelines developed by the CHMP in 2007



=> Do not delegate national expert(s) to EMA without clear objectives

Agency in EU Framework



… just manage the risks to keep experts motivated

10. Arrange consultations within a EU regulatory framework

Thus, You are welcome to meet
the experts of
The State Medicines Control Agency

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Conclusions

- Phasing-in to EU regulatory system harmonize the ***principles*** of evaluations and activities
- Safety evaluation remains one of key national ***duties***
- Invest into local competences and explore EU ***commitments*** and ***opportunities***

Special thanks to:

- Dr *Sif Ormarsdóttir*, Islandic MCA, CHMP London
- Dr *Truus (G.M.) Janse-de Hoog*, Chair CMD (h), London
- Dr *Daniel Brasseur*, Former Chair of CHMP, London

Croatia, let's contribute to the development of EU regulatory competence

Thank you