Doktorandentag

Lehrstuhl für Drug Regulatory Affairs
Pharmazeutisches Institut

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Drug safety monitoring in Poland and the implementation of the new pharmacovigilance legislation – challenges and opportunities

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Poland – country profile

- ≈ 38 mio. inhabitants
- EU member since May 2004
- ≈ 13 500 medicines for human use authorised
- 850 stakeholders who have a marketing authorisation for medicines for human use + 24 parallel distribution companies
- Non-pharmacy availability of OTC products (also drugstores, supermarkets)
- No on-line sale of prescription medicines
- On-line sale of OTC products only via pharmacies (listed in a dedicated register)
- Health care expenditure in Poland: 6.4% of GDP (OECD average of 8.9% of GDP)
- Health care issues are perceived as one of the two most important national problems (40% of respondents, along with the retirement and disability pension system)
- 2,1 medical doctors / 1000 people → one of the lowest numbers in the EU
- 4,87 nurses / 1000 people → 1/3 of the median number in EU

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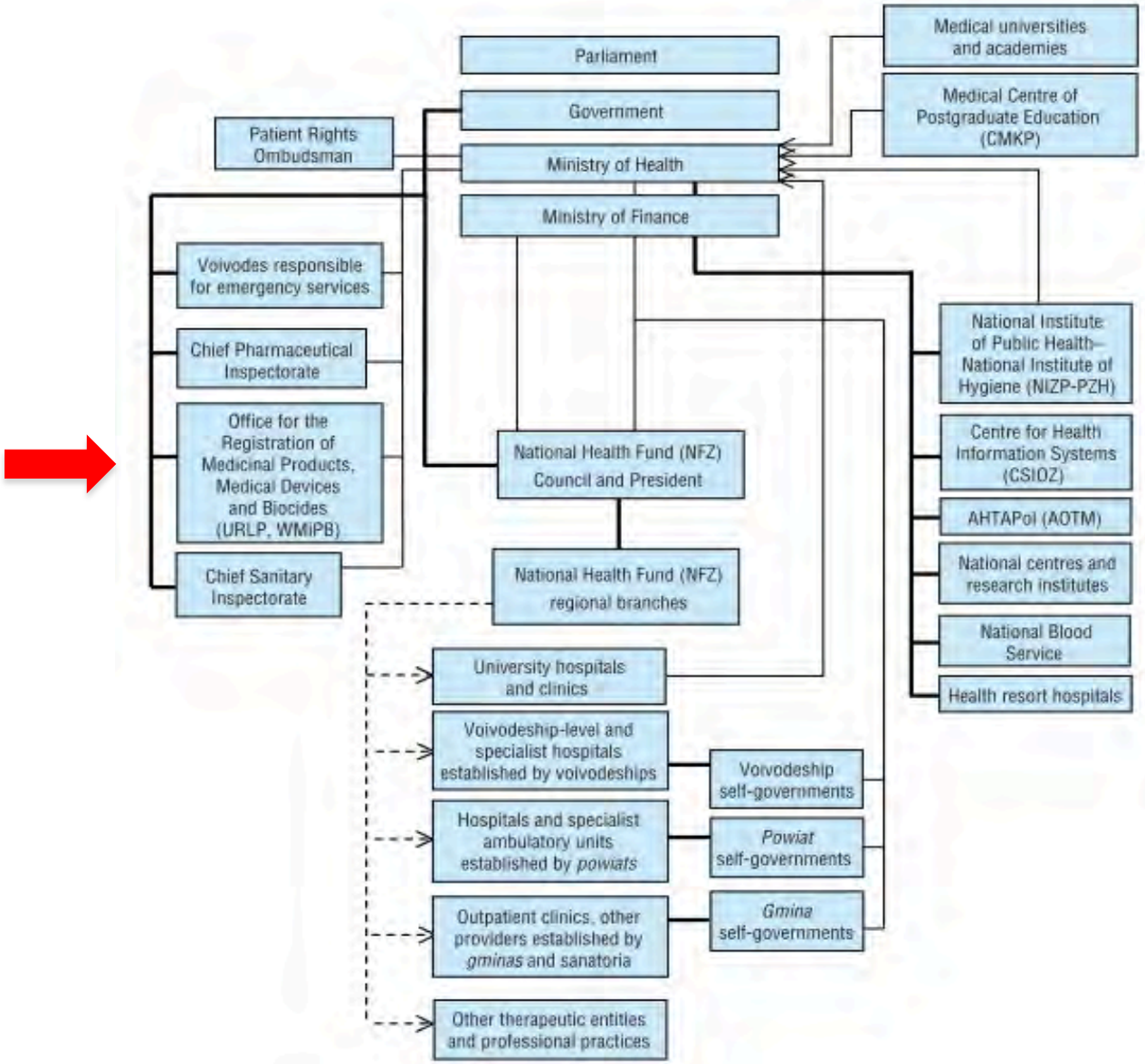
Health care system in Poland



Source: WHO, *Health Systems in Transition,* Vol. 13 No. 8, 2011

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Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL)

- Competent authority responsible for marketing authorisation of medicines and for supervision over proper quality, efficacy and safety of medicines (both for human and veterinary use) + medical devices + biocidal products
- Created in October 2002 (merger of the Office for Registration of Pharmaceutical Products and Medical Supplies of the Institute of Medicines and the Main Medical Technologies Center) and subordinated directly to the Minister of Health
- ≈ 350 employees
- Budget: government funding
- Independent governmental agency since March 2011
- Six advisory committees supporting the President of URPL

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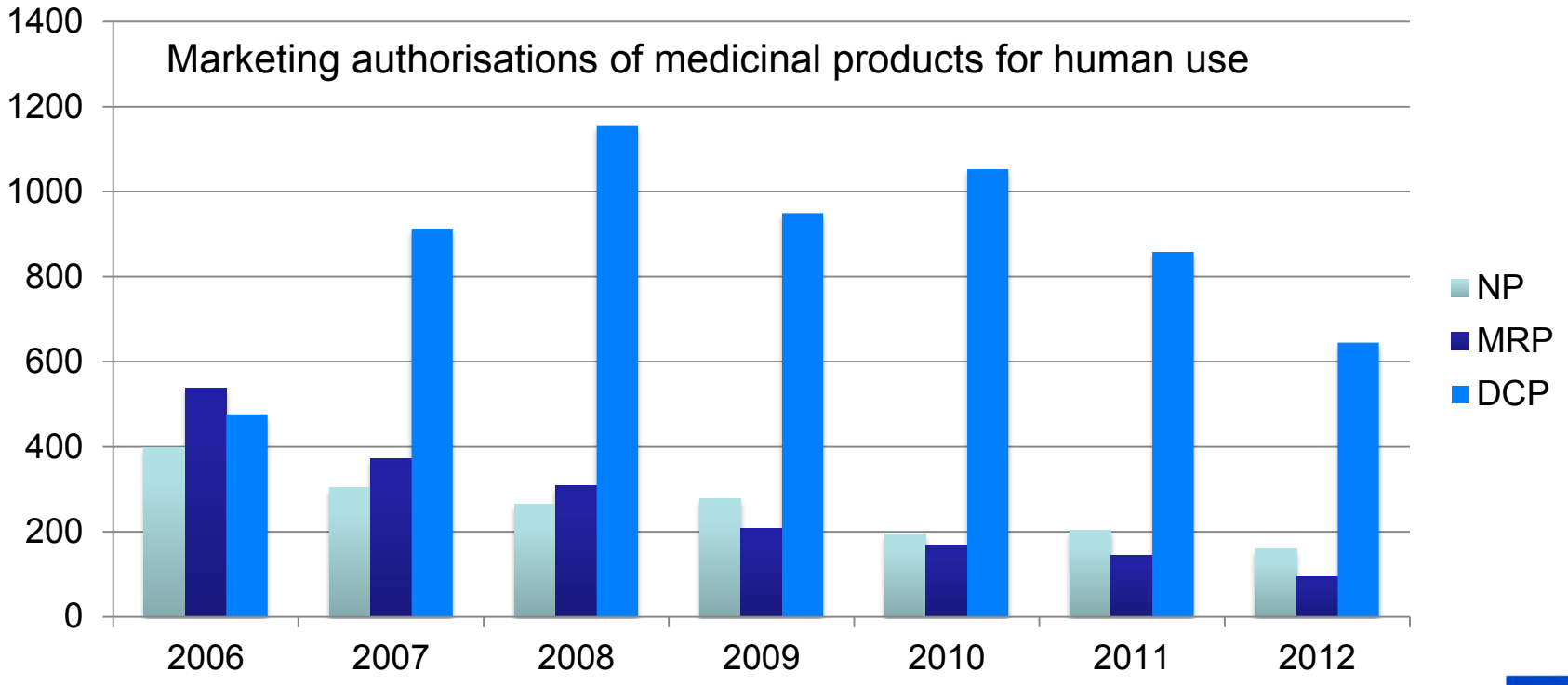
Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL)

Increase in the number of MRP for marketing authorisations shortly after the EU accession, afterwards increase in DCP which has remained the main route of MA. The importance of the NP systematically decreases.



NP – national procedure; MRP – mutual recognition procedure; DCP – decentralised procedure

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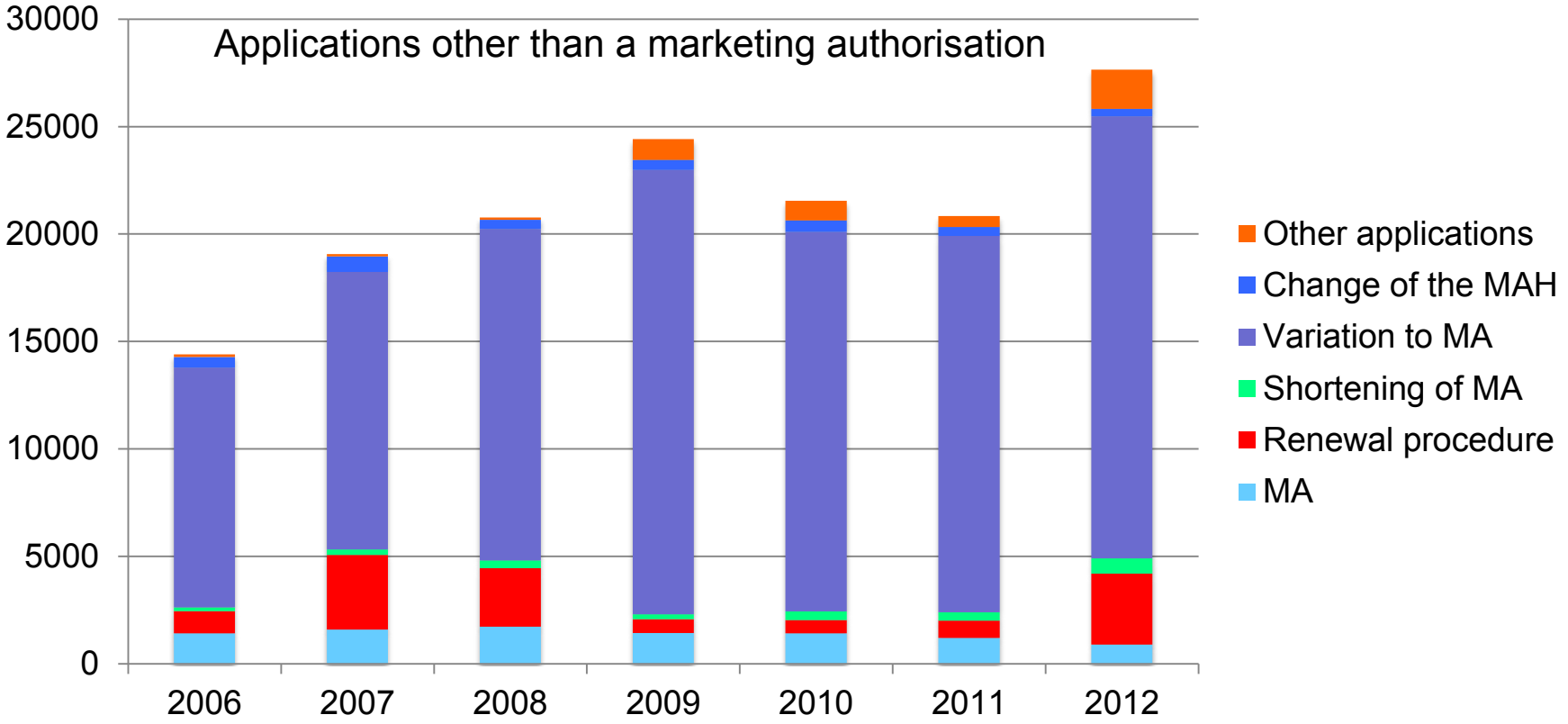
Source: *Annual Reports* on URPL from the years 2006-2012 kindly provided by the URPL

Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL)

The amount of received applications doubled between 2006 and 2012



MA – marketing authorisation; MAH – Marketing authorisation holder

* Other applications, e.g. suspension of the proceedings, reopening of the proceedings, for the correction of an error, applications relating to the sunset clause, for changes in the course of examination of the submitted applications for granting MA, for re-examination of the case.

Source: *Annual Reports* on URPL from the years 2006-2012 kindly provided by the URPL

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Pharmacovigilance Departement

- First PV department established in 1971 as a division of the Institute of Medicines
- WHO member since 1972
- Incorporated into the URPL in 2002
- Responsible for drug safety aspects within the pre-marketing and post-marketing phase of drug development + publishing Drug Bulletin (quarterly)
- 11 employees (incl. 2 administrative staff members)
- Nr of employees has remained constant despite of increasing workload
- High turnover of employees is one of the main problems within the Department
- External experts support the PV department in the fulfilment of its statutory tasks
- ADR reports stored electronically at URPL since 2006
- National ADR database with limited query and tracking capability
- No PV advisory group → cancelled in 2011

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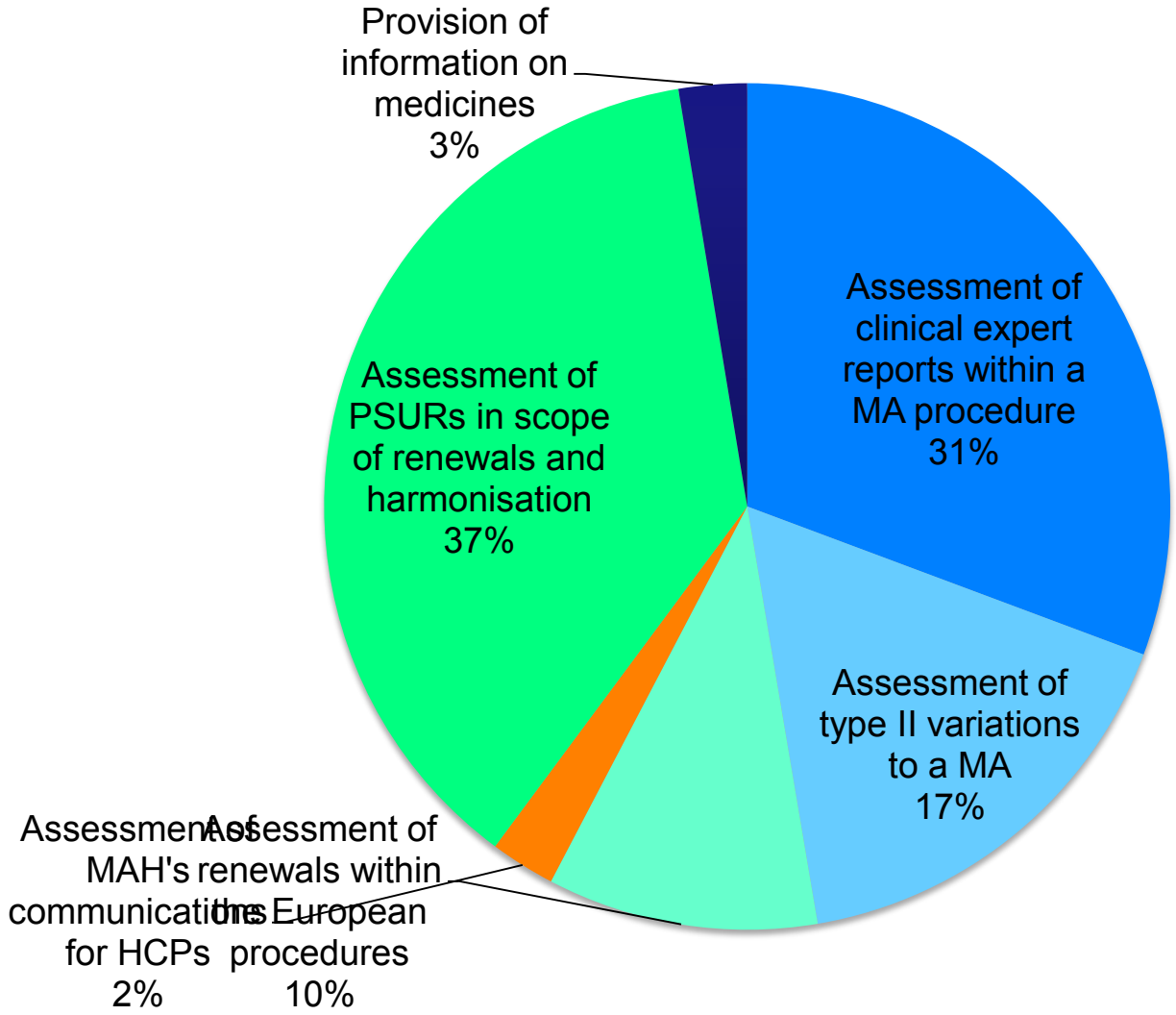
Pharmacovigilance Departement

Types of assessments carried out at the Pharmacovigilance Department in 2006-2012 other than assessment of ADR reports.



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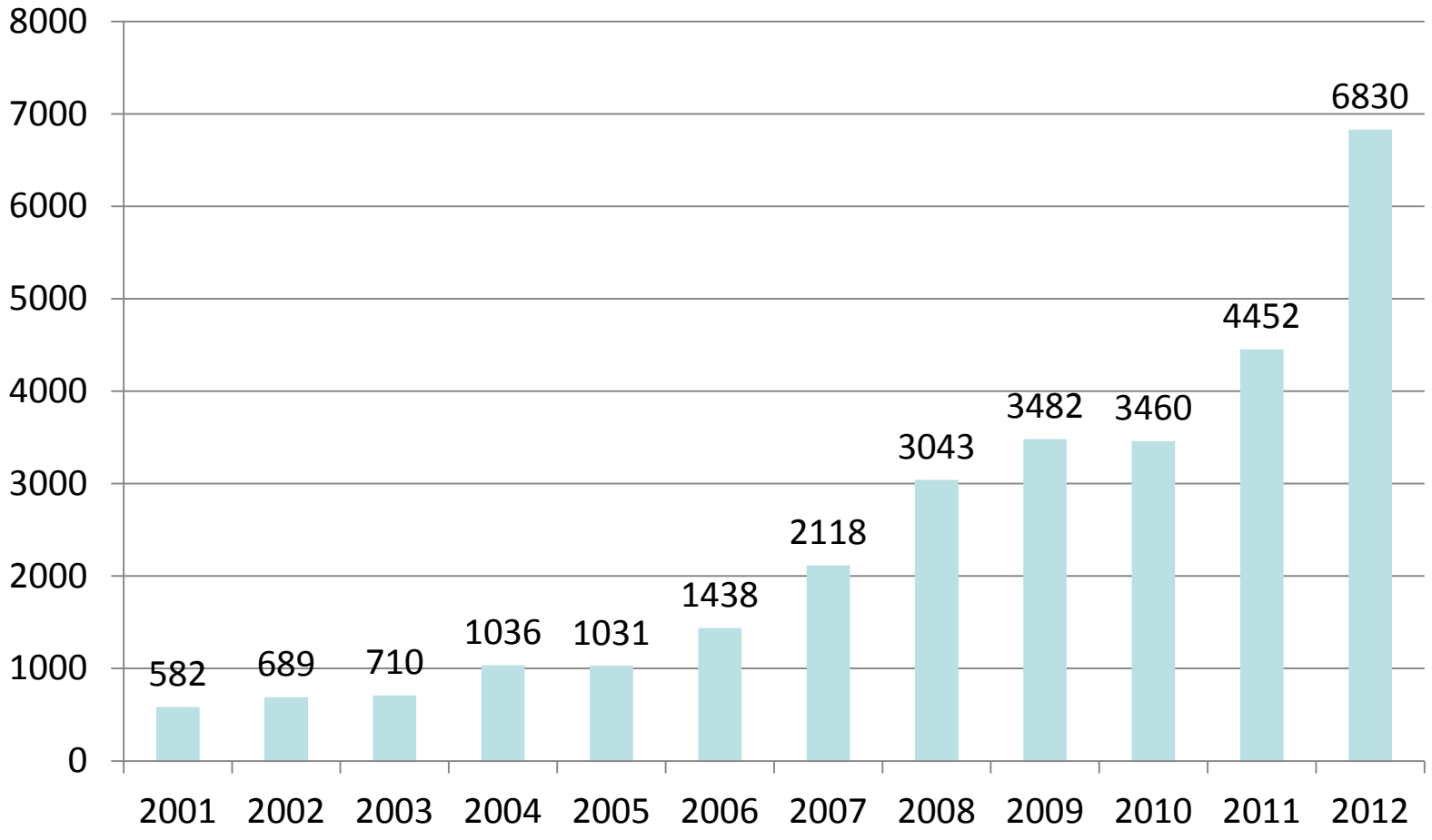
Source: *Annual Reports* on URPL from the years 2006-2012 kindly provided by the URPL

Pharmacovigilance Departement



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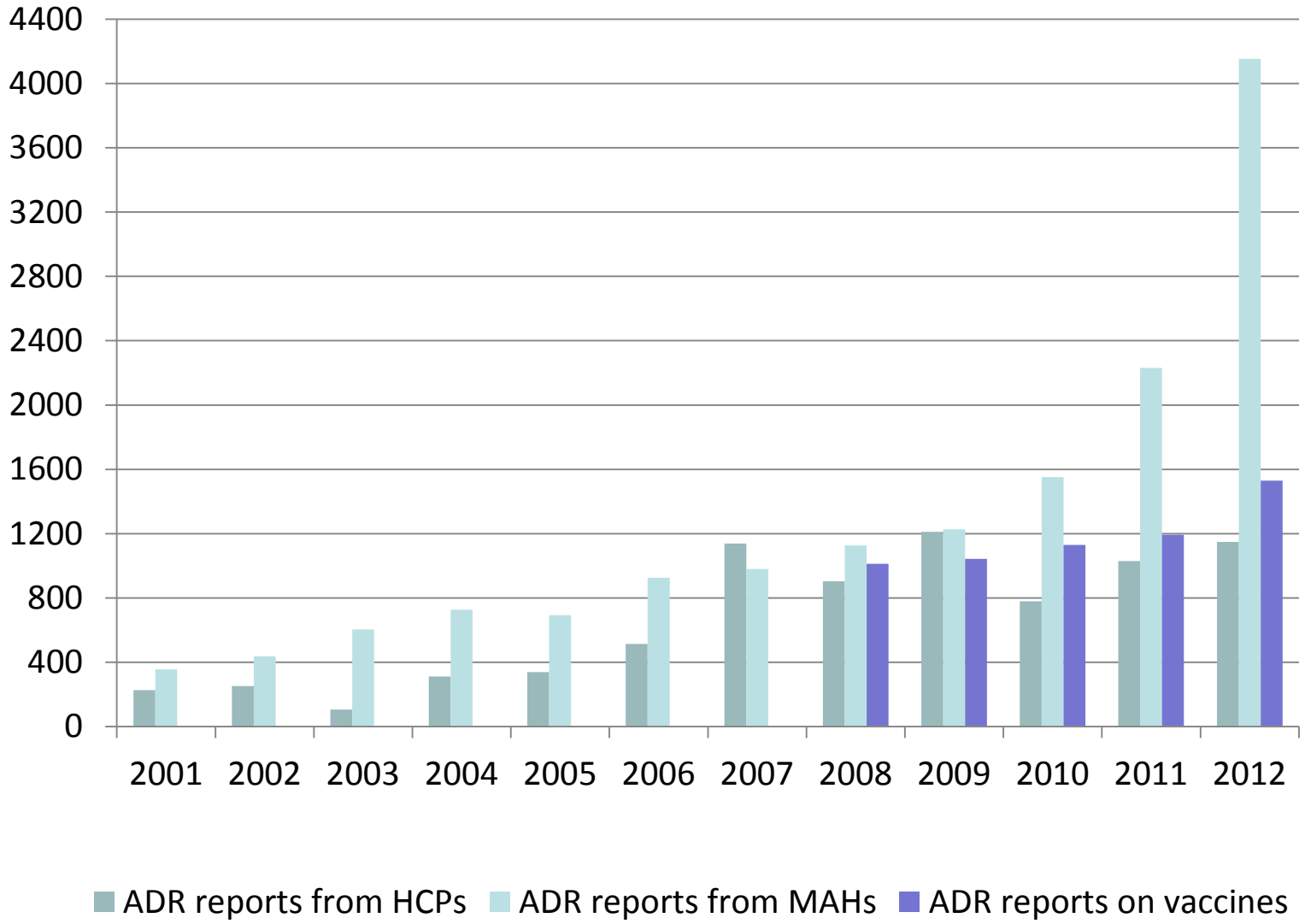
Source: Information kindly provided by the URPL

Pharmacovigilance Departement



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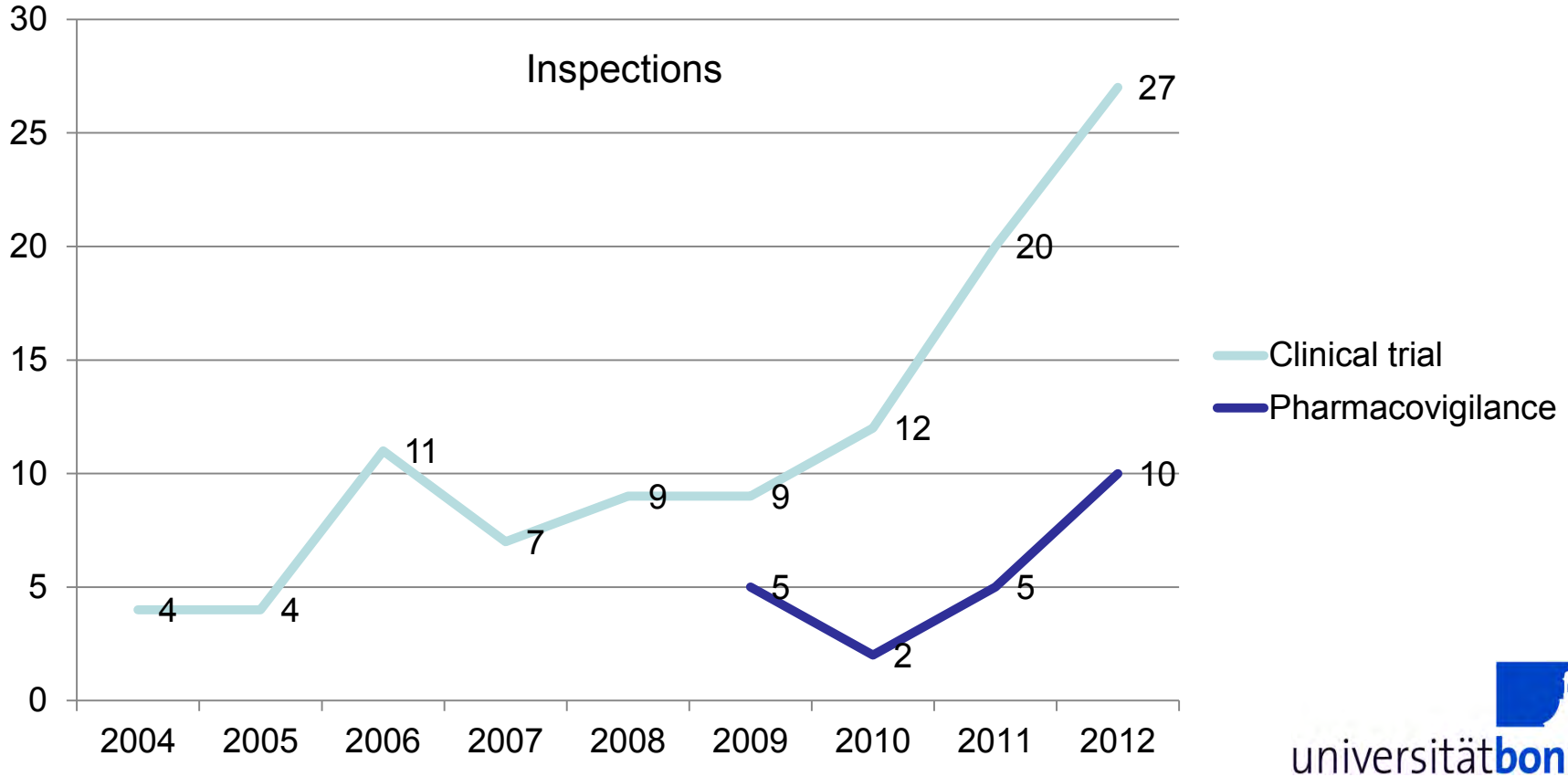
Source: Information kindly provided by the URPL

Inspections Departement

- Legal basis for pharmacovigilance inspections has been established in 2008 and in 2009 first pharmacovigilance inspections were carried out
- Initially 4 inspectors, currently 8 inspectors responsible for both clinical trials- and pharmacovigilance inspections



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ADR reporting – key facts

- Mandatory for prescribers since 2001
- Centralised system for collecting ADR reports at URPL
- No patient reporting
- No pre-paid ADR reporting form
- Source of reports: 40% → HCPs (mostly medical doctors) (in 2001- 2011) 60% → MAHs
- Half of the reports → serious ADRs (WHO criteria)
- Low reporting rate* → 7 (UK 233, France 194, Germany 116) * (Reports / million inhabitants / year), data from 2012
- Vast majority of ADR reports (96,6% in 2011) → known ADR (inlcuded in SmPC)
- 5 regional PV centres operating on a voluntary basis at pharmacology departments at university hospitals
- In 2010 the PV centre in Krakow submitted ≈ ¼ of all 779 reports submitted directly by HCPs

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Reasons for underreporting

The reasons for underreporting in Poland and in the EU are similar and include potentially modifiable factors.

Questionnaire distributed among Polish medical doctors (from 1999)

1. Physician is too busy (69,7%)
2. Physician is unsure about the casual association between a drug and a reaction (67,8%)
3. The reaction is already known (58,1%)
4. Difficulties in pointing out the suspected drug (41,9%)
5. The belief that reporting does not influence a treatment scheme (21,3%)
6. Lack of financial gratification (13,9%)
7. The belief that only safe drugs are on the market (6,9%)
8. Ambition to publish a personal series of cases (4,7%)

Study on underreporting in Europe (from 1997)

1. Lack of confidence of making diagnosis
2. No available means for reporting ADRs (report forms, telephone numbers)
3. Lack of time and unclear reporting criteria

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Source: Maciejczyk A., Arcab A. and Czarnecki A. *Questionnaire on adverse drug reactions reporting.* Acta Poloniae Pharmaceutica – Drug Research 1999;56(5):403-406. Belton KJ and the European Pharmacovigilance Research Group. Attitude survey of adverse drug reaction reporting by health care professionals across the European Union. European Journal of Clinical Pharmacology 1997;52(6):423-7

The „new“ pharmacovigilance legislation

Regulation (EU) No 1235/2010 and Directive 2010/84/EU

- Revised definition of ADR (incl. medication errors and drug abuse)
- Patient ADR reporting
- Changes in timelines for transmission of ADR reports (serious 15 days, non-serious 90 days)
- Risk management plans with every new marketing authorisation
- Strengthening regulatory basis for PASS and PAES
- Web based ADR reporting
- National PV web portal with the “minimum information”:
  - → Public Assessment Reports (PAR)
  - → Summary of Product Characteristics (SmPC)
  - → Package Information Leaflets (PL)
  - → Summaries of Risk Management Plans (RMP)
  - → List of medicines subject to additional monitoring
  - → Information on possible ways of reporting ADRs
- Structured approach to signal detection → lead MS will be appointed for every substance authorized in the EU (13 substances currently for Poland)

Substantial increase in workload

Increase in nr of ADR reports to 20,000/year by 2022 is expected in Poland

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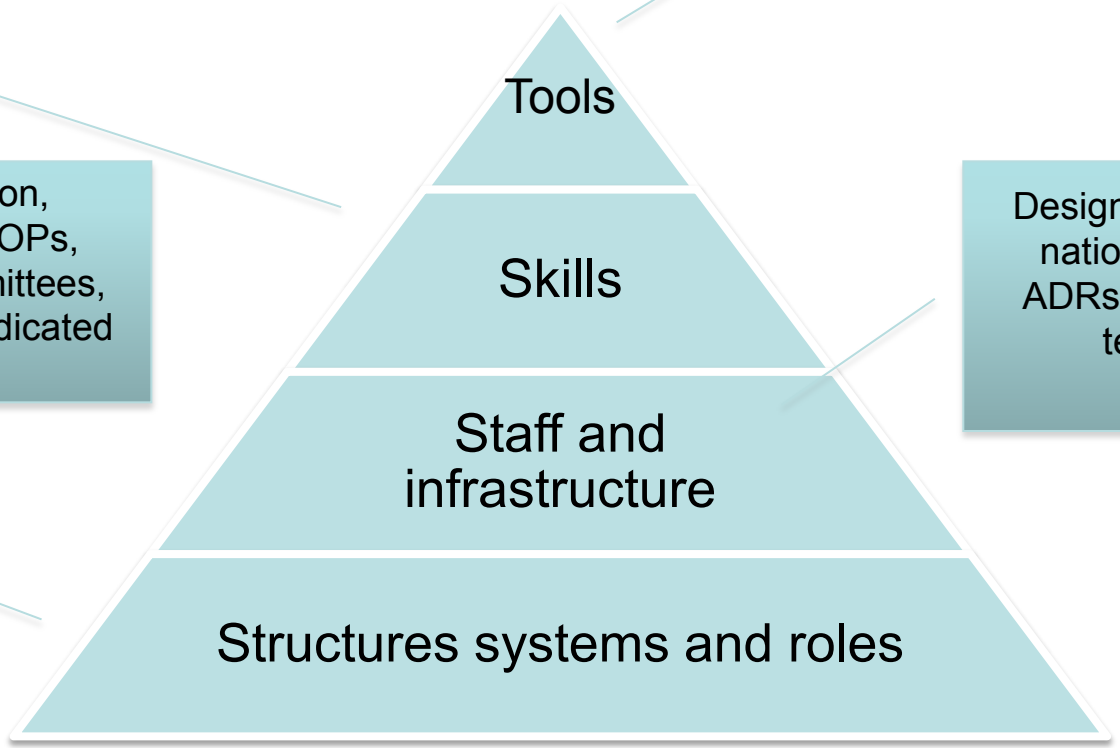
Implementation of changes and maintenance of pharmacovigilance systems requires a comprehensive approach

Training on PV, public education on PV

PV reporting form for HCPs and patients, PV database, national PV website



PV legislation, guidelines, SOPs, advisory committees, PV centres, dedicated budget

Designated staff for PV, national database of ADRs, communication technologies

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Adapted from: Strengthening Pharmaceutical Systems (SPS) Program. 2009. *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*.

Implementation in practice

→ Deadline for the Directive to be transposed: **21 July 2012**
→ Transposed into national law on **27 September 2013**
→ Practical implementation on-going

The new PV legislation expedited the introduction of changes which once fully implemented will ultimately strengthen the PV system in Poland.

- 38 additional employees planed for PV department
- Patients involved in PV process → ADR reporting by patients
- Dedicated website to PV with more information for HCPs and patients
- Increased transparency
- Project of developing new national ADR database (on-going)
- Development of methodology for signal detection by a national expert (on-going)

+ ADR reporting has become mandatory for **all** HCPs

However:

- No e-reporting form yet
- Not all the minimum PV information requested by law is provided yet

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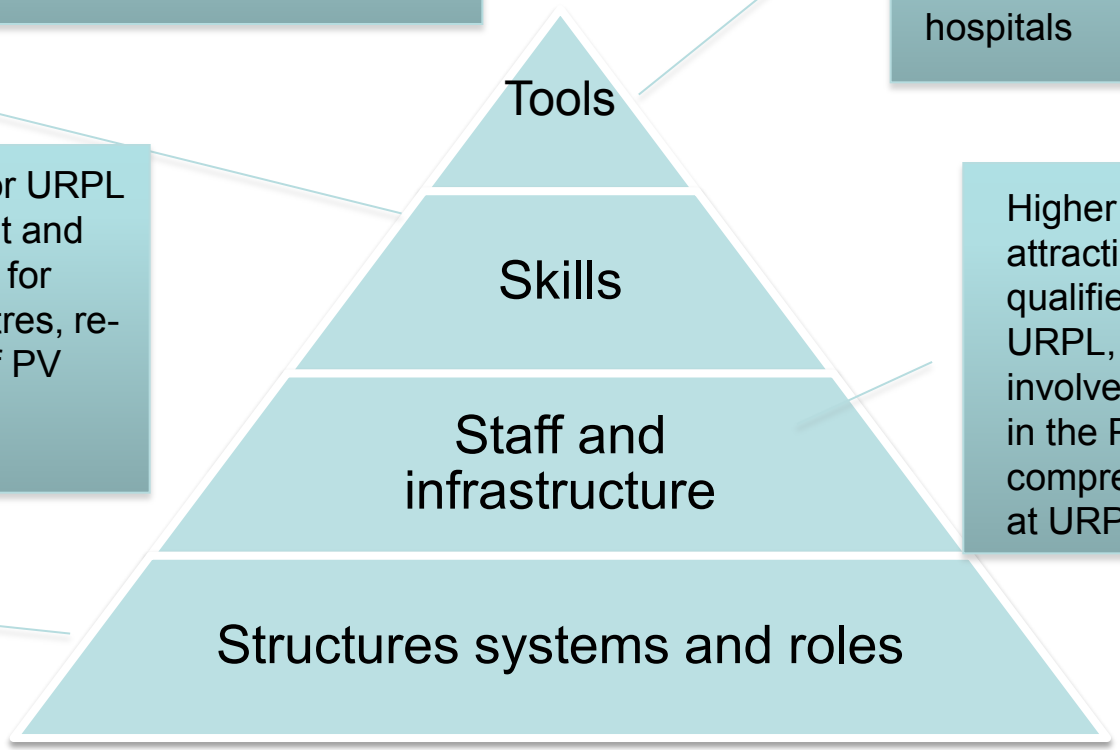
Proposals for further strengthening of PV in Poland

Stronger focus on training and career development at URPL, targeting HCPs in the course of their university education, PV trainings within obligatory continuing development of qualifications of HCPs

e - ADR reporting form incorporated into GPs computer systems, Drug Bulletin issued also in printed form and distributed to pharmacies and hospitals



Mixed funding for URPL from government and fees, legal basis for national PV centres, re-establishment of PV advisory group

Higher remuneration for attracting and retaining well qualified personnel at URPL, increasing involvement of pharmacists in the PV process, comprehensive IT systems at URPL

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Conclusions

1. The new PV legislation has triggered developments to the national PV system which will strengthen the PV system in future.

1. National PV systems and environment for introducing changes differ between member states and major reorganisation is needed in case of Poland – time and resources consuming process.

1. Incorporation of the PV in the national health policy and recognition of the importance of an effective PV system by the legislators is crucial.

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Thank You

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