Current Global Landscape of Pharmacovigilance

National Regulatory Conference 2013

Kuala Lumpur

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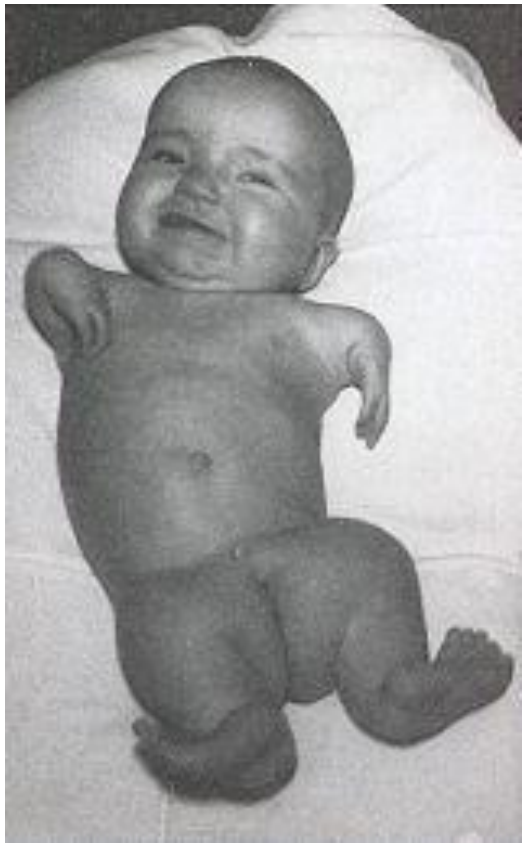
the UPPSALA MONITORING CENTRE

From spontaneous reporting to proactive surveillance

- History
- The development of the WHO Programme for Drug Safety
- DSURs/PBERs/PV Plans/REMs etc
- Monitoring effectiveness of PV
- Are we on the right track?

How we started



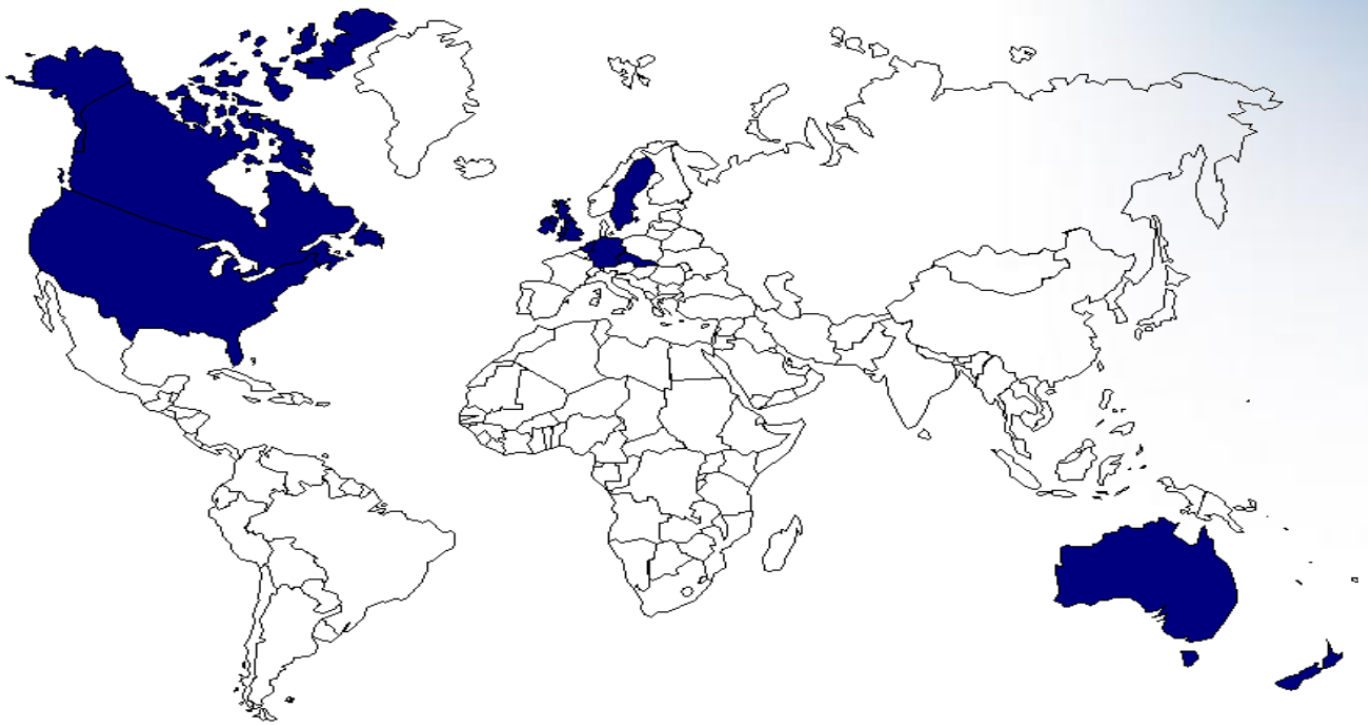
- Thalidomide 1961

- WHO Programme for International

Drug Monitoring 1968

WHO Drug Monitoring Programme

Founding Members 1968



WHO Programme members
June 2012

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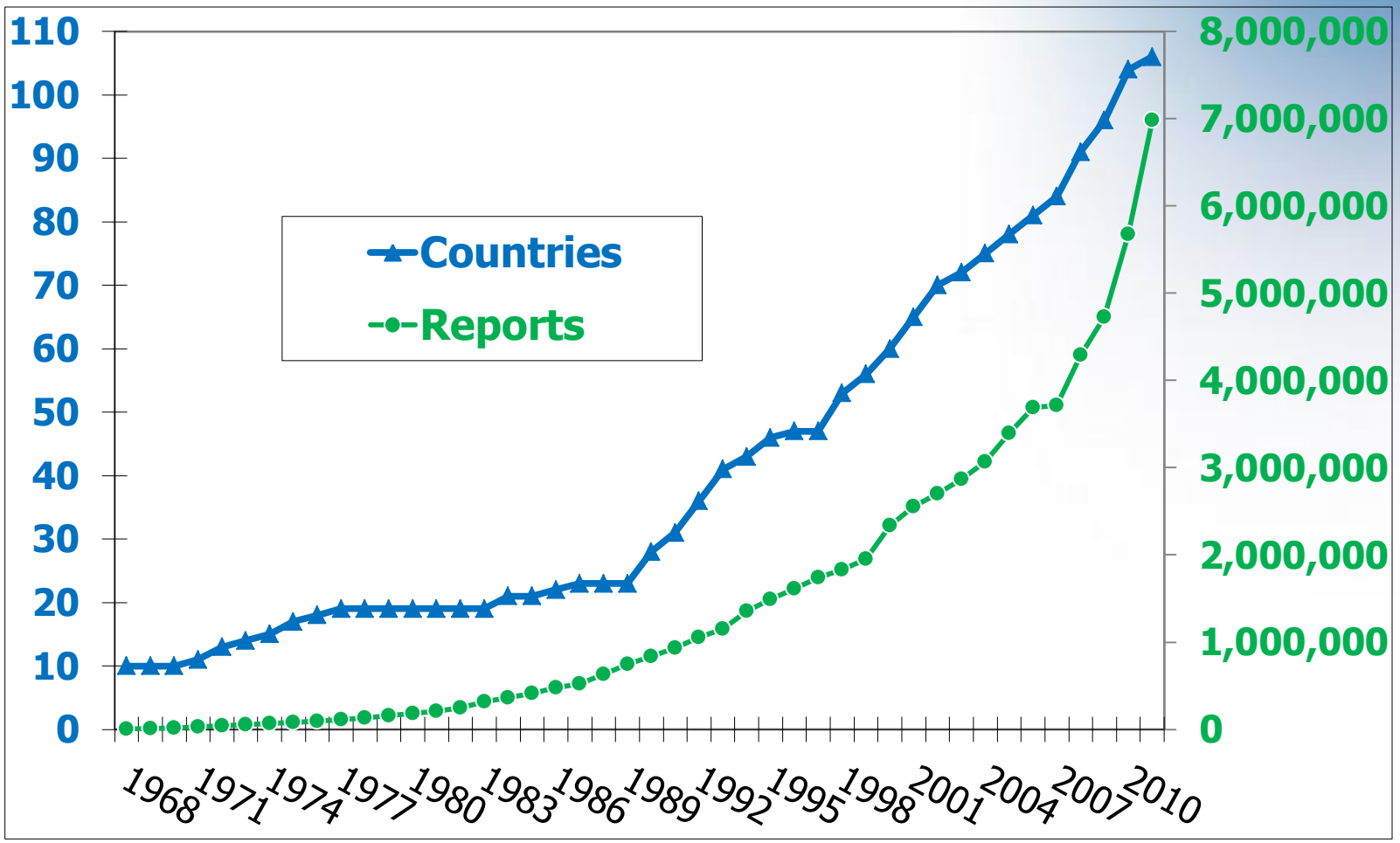
Countries and Reports



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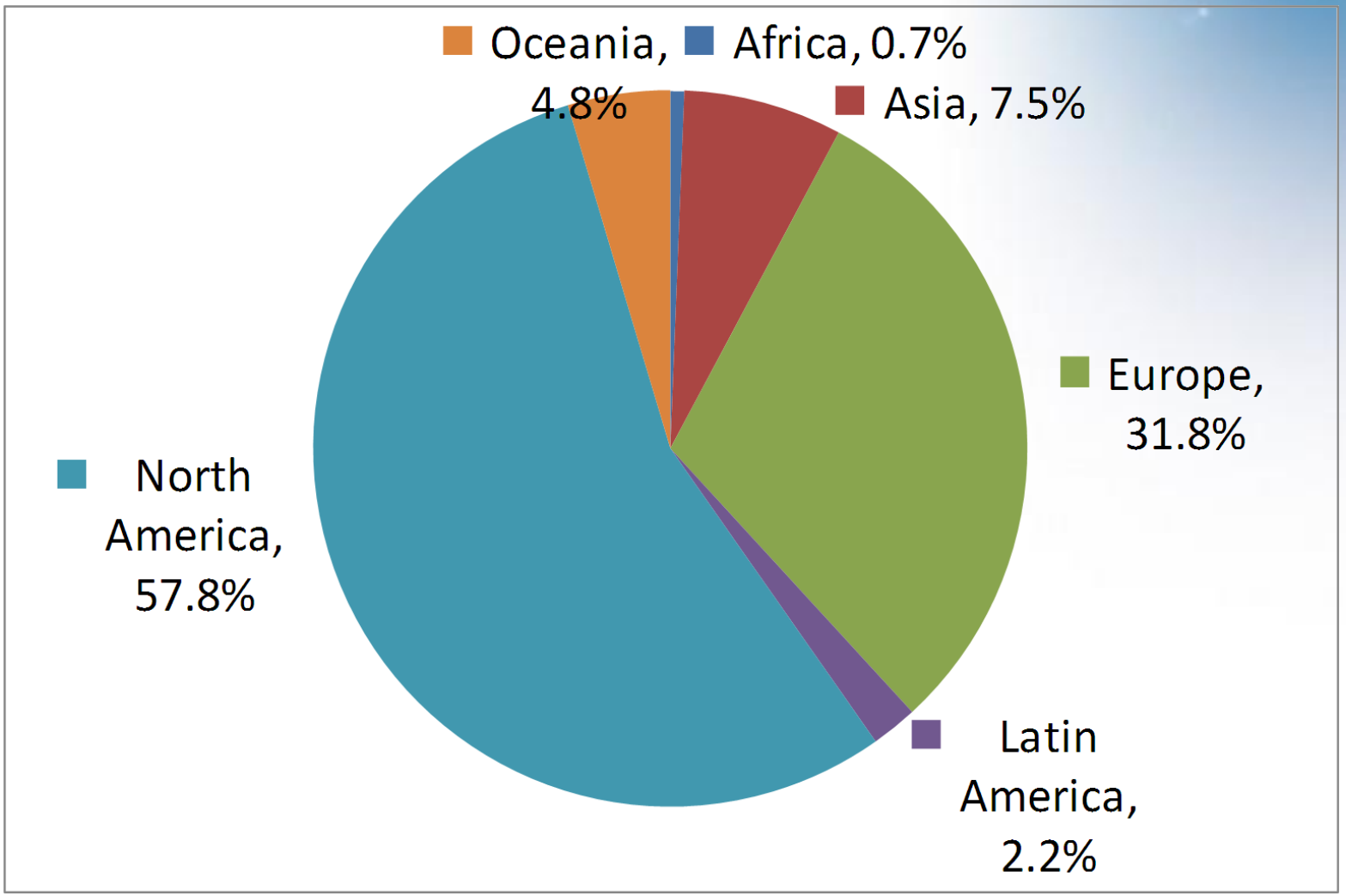
Contributions by Region



VigiBase™

- Database of the WHO Programme
- Run by Uppsala Monitoring Centre
- Reports from National Centres members of the Programme
  - Health Care professionals
  - Industry
  - Patients/Consumers
  - Literature etc

→ Spontaneous reports

Expanded Scope of PV

- Medication errors
- Counterfeits
- Lack of efficacy/Drug resistance
- Abuse
- Ecopharmacovigilance

Additional Methods

- Enhanced/targeted PV
- Cohort Event Monitoring
- Analysis of longitudinal medical records

Where does Pharmacovigilance happen?

- At home
- In healthcare facilities
- In academic institutions
- In regulatory/healthcare authorities
- In industry
- In public health programmes
- In politics

Towards proactive PV

- From IND/EU Annual Safety Report to DSUR (ICH E2F)
- Pharmacovigilance Planning (ICH E2E)
- From PSUR to PBRER (ICH E2C R2)

Development Safety Update Report (DSUR)

- Harmonization of requirements within the ICH region
- Shift of focus from regulatory compliance to benefit-risk analysis
- Consistency in safety data and periodicity
- Consistency among sponsors
- Decrease in number of reports generated (annual)

DSUR - Scope

- Information on current period and cumulative analysis overall
- New issues with impact on ongoing trials/overall programme
- Current understanding of known and potential safety issues
- Changes to current safety profile
- Update on clinical development programme

PV Planning (ICH E2E – 2004)

- New chemical entities, biotech products, vaccines
- Significant changes in established products
- New indications/populations
- New major safety concern

Structure

- Safety Specification
  - Identified risks
  - Potential risks
  - Important missing information
- Pharmacovigilance Plan
  - Based on Safety Specification
  - Ongoing safety issues
  - Routine PV
  - Action plan for safety issues incl. milestones

Implications for Drug Regulatory Authorities

- E2E documents need to be evaluated at the time of approval
- Milestones need to be monitored
- Results of additional PV activities need to be evaluated

PSUR (ICH E2C – 1996)

- Periodic Safety Update Report
- Periodic evaluation of relevant safety information in the context of patient exposure
- Common format and compatible timeframes
- High workload for marketing authorization holders as well as for Regulatory Authorities

PBRER (ICH E2C R2 – 2012)

- Periodic Benefit Risk Evaluation Report
- Formal evaluation of benefit
- Frequency of submission according to national regulatory requirements
- Overlap with other documents: modular approach -> sections with identical content

PBRER - Scope

- Evaluation of new, relevant safety information in the context of the benefit (efficacy) of the product
- Focus on new information but cumulative analysis required
- Information on ongoing clinical research
- One PBRER per active substance

ICH Guidelines

Relevant ICH Guidelines for PV activities can be found at:

http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html

What has been achieved?

- Clearer focus?
- Less workload for marketing authorization holders?
- Less workload for Regulatory Authorities?

How effective is PV?

- Do we get the right information to identify risks?
- Do we identify the relevant risks?
- Do Regulatory Authorities take effective risk minimizing action?
- How can we measure our impact on patient safety?

The right information?

Legal requirements, PV-inspections and guidelines focus on time frames and formats not on the clinical relevance of the information provided

-> Marketing authorization holders act accordingly

Example

- *A physician reported that a 27 yr old woman developed liver disorder and was hospitalized while under treatment with drug XY® for an unknown indication. Outcome unknown*

- Report forwarded to Authority within 15 days, no follow up

Relevant risks?

- What is more relevant to public health: the new (maybe non-serious) adverse drug reaction or known problems related to medicines' use that turn up again and again?

Effective risk minimizing action?

- Communication: are DHCP letters read and acted upon?
- Are prescribers aware of changes to the Product Information?
- What happens if a drug is withdrawn from the market?

Impact on patient safety

Wished for outcomes:

- More rationale prescribing
- Better health consciousness among consumers
- Less hospitalizations due to adverse drug reactions

Conclusions

- PV has expanded its scope
- We use new methodologies
- We have moved from spontaneous reporting to a more proactive PV
- The workload for DRAs and MAHs has increased
- The impact on patient safety has yet to be quantified

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