A new era in Pharmacovigilance

Delivering the new approach to Pharmacovigilance in Europe

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Delivering the new approach

• What is state of play with negotiating EU Commission draft legislation?
• What is progress on key proposals?
• How are we moving forwards to delivery?

Personal reflections…
European Commission review in 2004 found……

- Unclear roles and responsibilities
- Complex reporting rules
- Differences at member state level
- Complex decision making procedures
- Lack of robust safety studies
The problem...

Drugs safety shake-up urged

EU watchdog calls for better monitoring • Slower release times sought for products • Comments set to spark transatlantic debate

How do we stop the Vioxx disaster happening again?

This question is exercising the minds of drug companies and scientists alike. A report in this week’s Lancet estimates there are 140,000 people with serious heart disease in the US caused by use of the painkiller Vioxx. The arthritis drug was withdrawn in September.

Dr. Graham agrees. "The US regulatory authority hasn’t acted on behalf of public health, but corporate interests. It was aware of the scale of the problem in June 2000 but was slow to act."

Are drug firms an unhealthy influence on your medicine?

Arthritis pill heart attack warning to 600,000 users

Drug firms warned to publish trial data after safety fears

Ministers set rules for medicines regulators

Pharmaceutical industry

Europe urged to keep eagle eye on drugs already in the market place

Sharper teeth for medicines watchdog

A bitter pill for pharmaceuticals to swallow

Andrew Jack hears the EUs top regulator call for more independent funding to do extra research on medicines already gained approval.
Historical perspective

- Wide consultation exercise involving stakeholders
- Draft EC legislative proposals published December 2008
- Council of Ministers Working Party
Progress in Working Party

ENVI-News
Newsletter from the European Parliament's Environment, Public Health and Food Safety Committee

Number 5/2010

Meeting in Brussels
Monday 26 April 2010: 15.00 – 18.00
Tuesday 17 April 2010: 09.00 – 12.30 and 13.00 – 14.30
Thursday 28 April 2010: 09.00 – 12.30

The Committee meeting will be web streamed and can be watched live on the EP web site at http://www.europarl.europa.eu

• Active negotiations in Council WP – 22 meetings
• European Parliament engaged - ENVI
• “Triologue” discussions
• Adoption at Health Council in Autumn?
• Possible coming into force in 2012?
Aim of EC proposals

Strengthening and rationalizing the community pharmacovigilance system with overall objectives of:

- Better **protection of public health**
- Ensuring proper functioning of the **internal market**
- **Simplification** of current rules and procedures
Specific objectives

• **Clear roles and responsibilities** for key parties and clear obligations against which they perform their roles

• **Rationalising decision-making** – full and equal implementation for all relevant products

• **Strengthened transparency & communication** – better penetration of warnings

• **Strengthened companies’ systems** while reducing administrative burdens

• **Proactive data collection** through risk management and rationalised single case and periodic reporting

• **Stakeholder involvement** via patient reporting, patients & healthcare professionals in decisionmaking

• **Simplification of pharmacovigilance procedures** with efficiency gains for both industry and regulators
Key Commission proposals

- Clear roles and responsibilities
- Streamlined and strengthened procedures
- Improved tools and good vigilance practices
- Simplification and reducing burdens
- Involving stakeholders
- Transparency
Roles and responsibilities

- Agency’s co-ordinating role at centre of system is reinforced – new tasks
- Member states remain core to operation of Pharmacovigilance – increased cooperation
- Scope clarified of MAH’s obligation to continuously monitor safety and inform authorities
The new Committee

- EUROPEAN COMMISSION
- EMA
- CMD(h)
- MEMBER STATES
- CHMP
- PHARMACOVIGILANCE WORKING PARTY
The new Committee

CMD(h)

EUROPEAN COMMISSION

MEMBER STATES

EMA

CHMP

PHARMACOVIGILANCE RISK ASSESSMENT COMMITTEE
PhVig Risk Assessment Committee

• **Mandate** – key role in Pharmacovigilance assessments, initial analysis of signals, PSURs and PASS, agreement of risk management systems

• **Status of advice**
  Recommendations to CHMP and CMDh must be respected if not explanation

• **Membership** Independent scientific experts or national authorities? Health professionals, lay members
Strengthened PhWP expertise

- Pharmacoepidemiology
- Biostatistics
- Risk management
- Risk communication
- Biotechnology
- Paediatrics
Streamlined procedure

• Clear and binding initiation criteria for Member States
• Ensure all relevant products concerned are considered including centralised
• Assessment by PRAC
• Ensures harmonised measures adopted
Current EU safety procedures

- Rapid interim decision to address new emerging risk
  - Urgent Safety Restriction eg bupropion

- Prompt scientific opinion eg when new published data
  - Article 5(3) referral eg bisphosphonates

- Binding EU opinion on Phvig suspensions, revocations, and some variations
  - Article 107 referral eg aprotinin

- Risk benefit review when of Community interests involved
  - Article 31 referral eg ergot alkaloids, methylphenidate
Improved PhVigilance tools

- Risk management plans if new safety concern
- MAH reporting to include medicines used off-label
- Provision that can limit medicine to existing patients only
- Intensive monitoring of medicines for 5 years, with reference in PIL
“Black Triangle” scheme

Intensive monitoring scheme

Assigned to new active substances and established active substances if product is:

- a new combination of active substances
- administered by a novel route or drug delivery system
- significant new indication which may alter risk benefit

Report all reactions, including non-serious
Strengthened information

• Reference to intensive monitoring in PIL
• Essential information in box in Summary of Product Characteristics and PIL
Good Pharmacovigilance Practice Guide

- Published by MHRA in November 2008
- Practical guidance and examples
- Will complement EU legislative changes
Simplification

- Submission of all ADR reports to a single database managed by a single data processing network
- EMA to monitor published literature
- Adoption of a Pharmacovigilance Master File system
- Single assessment of PSURs for medicines authorised in more than one member state
• Approximately 550 agreed EU harmonised birth dates (HBDs) Published on HMA website

• 1275 additional active substances synchronised

• Harmonised birth dates (HBDs) also to be applied to generic products (existing and new marketing authorisations)

• MAHs holding MAs for generics are encouraged to submit PSURs based on the EU HBDs

• Since Jan 2008 approx 420 actives assessed
Member States acting as P-RMS

Allocated P-RMS for PSUR Work-Sharing

Member State

AT  25
BE  12
BG
CY
CZ  7
DE  17
DK  18
EE
EL
ES
FI  56
FR
GR
HU
IE
IS
IT  26
LI
LT
LU
LV
MT
NL  50
NO
PL
PT
RO
SE
SI
SK
UK  69
Involving stakeholders

- Introduction of public hearings as part of PRAC processes
- Patient and public to report suspected adverse reactions
Sources of ADR reports in 2009

- Healthcare professional: 47%
- Patient: 12%
- MAH: 41%
Patient reporting in UK

- Patients account for 12% of all ADRs
- Similar proportions of serious ADRs to healthcare professionals
PhVWP Lay observers

- New lay observers joined PhVWP May 2010
- Albert van der Zeijden, Chairman of IAPO
- Greetje Goossens, EMP counsellor
Transparency

- EMA to set up and maintain European medicines web portal
- Summary of committee meetings regarding pharmacovigilance activities
- Risk management plans
- List of medicines under intensive monitoring
- Initiation of procedures
Antidepressants and suicidal thoughts and behaviour

Antidepressants: PhVWP Recommendations for wording in SPC and PL (20.83 kb) January 2008

ACE inhibitors & Angiotensin II receptor antagonists (AIIRAs) in pregnancy

ACE inhibitors & Angiotensin II receptor antagonists (AIIRAs) in pregnancy - PhVWP recommended SPC wording (35.08 kb) January 2008

Antiepileptics and suicidal behaviour

Key statement on Antiepileptic Medicine & the risk of suicidal thoughts and behaviours (15.82 kb) July 2008
Agreed wording for SPC & Package Leaflet - Antiepileptics (12.02 kb) July 2008
Questions & Answers - Antiepileptic medicines, risks of suicidal thoughts and behaviour (16.3 kb) July 2008

Carbamazepine related Stevens Johnson Syndrome and association with HLA-B*1502

Agreed wording for SPC & Package Leaflet (9.33 kb) July 2008

Ibuprofen and low dose aspirin interaction

Bisphosphonates and Atrial fibrillation

PhVWP Assessment Report and recommended wording for SPC & PL (15.8 kb) October 2008

- 4: Credits & Disclaimer
- 5: Sitemap
- 4: Related Links
- 7: Newsletter

Conclusion

• Substantial progress made towards agreement of new pharmacovigilance legislation
• Now is time to consider how to deliver the changes, building on experience and current initiatives
• We need to get ready to measure the benefits
Keys to success

• All parties cooperating, sharing work
• Regulation proportionate to risk
• Harmonised implementation
• Stakeholder involvement
• Transparency
• Strengthening the evidence base