New EU Pharmacovigilance Legislation
A Company perspective

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Agenda

- Legislation
- Objective of legislation
- Top Level Changes
- New Modules & Impact on MAHs
- Implementation Requirements

Legislation

Published: 31st December 2010
Regulation will apply from: 2nd July 2012
Directive will apply from: 21st July 2012

-"The legislation aims to save lives by strengthening the European-wide system for monitoring the safety of medicines"

-It is the biggest change for human medicines since the establishment of the EMA in 1995

-16 Modules will replace Volume 9A

Legislation

Reality check……

- Good Vigilance Practices (Wave 1)
  - Released for public consultation on February 21st, 2012
  - Companies'/EFPIA comments released
  - Final documents in June 2012
- EU Commission Questions & Answers (February 2012)

http://www.youtube.com/watch?v=IWwCj-GPeI0

Objective of new legislation

For all parties, the legislation aims to:

- Provide clarity on roles and responsibilities
- Minimise duplication of effort and increase efficiency
- Provide a clear legal framework for post-authorisation monitoring
- Risk-based approach and pro-active pharmacovigilance
- Increase transparency
- Engaging patients and healthcare professionals

Top level changes

- Legal requirement to have a quality system to support PV activities
- Introduction of the Pharmacovigilance System Master File (all products)
- RMP including risk minimisation strategy is required for all new MA applications from July 2012
- Reporting of non-serious cases within 90 days
- Additional monitoring will be brought in
  - Will replace UK Black Triangle
- Product authorisations may be granted with conditions

Module I: Pharmacovigilance systems and their quality systems

- Documentation to demonstrate
  - Resource
  - Business Continuity Plan
  - Job Descriptions and training records
  - Show hierarchical relationships
- Compliance Management
  - Effective communication with HCPs, patients, EMA and NCAs
  - Evidence of how scientific evaluation of risk is performed
  - Evidence of timeliness of ADR reporting
- Audits
  - Independent audits
  - Document corrective action plans and follow-up measures

Module II: Pharmacovigilance system master file (PSMF)

- PSMF is a legal requirement
  - applies to applicants of traditional herbal or homeopathic products
- Must be in place upon renewal or July 2015 at the latest
- Must be available 7 days following a request
- Master File must include all significant corrective action and preventative actions (CAPAs) impacting the PV system

PSMF Modular Content

- Qualified Person for PV details
- Organisational structure (Mergers/Acquisitions)
- Products
- Sources of safety data (all studies)
- Computerised systems and databases
- PV process & written procedures
- PV System performance
- Quality System
- Document and Record Control
- Logbook

Module V: Risk Management Systems

- Focus on risks in the context of benefit (not just managing risks)

- Additional Risk Minimisation Measures
  - Country specific or global (medical context)
  - Training of staff - communication
  - Measure effectiveness - how
  - EU vs ex-EU
  - Define roles and responsibilities company staff

Module VI: Management and reporting of adverse reactions to medicinal products

- New definition of ADR
- Non Interventional Research – AE Reporting (non-serious)
  - CU/Named Patient Use
  - Patient Support Programs
- Solicited vs Spontaneous
- Events not associated with AEs (Off label, misuse, overdose, etc)
- Consumer Reports (Non HCP)
- Literature Review
- Emerging Safety Issues

Expedited reporting requirements

	Serious HCP	Serious Consumer	Non-Serious HCP	Non-Serious Consumer
	EU / Non-EU	**EU / Non-EU**	**EU only**	**EU only**
Pre-July 2012	Y	N	N	N
Post-July 2012	Y	Y	Y	Y

Timelines for expedited reporting (calendar days)

	Serious HCP	Serious Consumer	Non-Serious HCP	Non-Serious Consumer
	EU / Non-EU	**EU / Non-EU**	**EU only**	**EU only**
Pre-July 2012	15 days	N/A	N/A	N/A
Post-July 2012	15 days	15 days	90 days	90 days

	Serious HCP	Serious Consumer	Non-Serious HCP	Non-Serious Consumer
Pre-July 2012	Serious expected or unexpected	N/A	N/A	N/A
Post-July 2012	Serious expected AND unexpected if occurred anywhere in the world	Serious expected AND unexpected if occurred anywhere in the world	Non-serious expected AND unexpected if occurred in the EU	Non-serious expected AND unexpected if occurred in the EU

What does this mean for the MAH?

The number of reports that need to be submitted to the Regulatory Authorities in the EU after 2nd July 2012 will increase dramatically, along with the quantity of reporting from pharmaceutical companies

Module VIII: Post-authorisation safety studies

- Can be voluntary or imposed by CA
- Studies may be imposed as a condition of licensing
- PASS should not be promotional
- MA should register PASS on EU PASS Register
- Progress reports may be requested at any time by HAs
- AE data should be collected as per Module VI
- Reports & results can be published
- Final report should be submitted within 12 months of completion

Module IX: Signal Management

- Monitor monthly
- Monitor all available data and perform signal detection activities including the validation of signals and communication to the EMA & CAs
- Apply the appropriate method of detection e.g. stat analysis, review of ICSRs or both
- Audit trials for signal detection activities

Module X: Additional Monitoring

- EMA to provide list of substances for additional monitoring
  - NA can request for another substance to be added
- Stay on the list for 5 years and a removal is tied to a renewal
  - Reviews are linked to fulfilment of obligations e.g. PASS
- Extensions to monitoring
- Products can be added to the list a second time
- Black symbol
- SmPCs shall be updated by way of variation to include/remove the symbol and associated statement

Implementation Requirements

- Review, update or write new processes, training, documentation
- Assess resourcing
  - more emphasis on evaluation, detection and response
- Engage with multidisciplinary stakeholders
  - Regulatory, Clinical development, Medical affairs, IT, QM & internal audit groups
- Document everything
  - Impact assessment
  - Implementation plan

Reality

- Challenging time for MAHs to understand what is changing
  - Important to continually assess the landscape to amend processes and maintain compliance
- Key is:
  - Complete and continually revise impact analysis
  - Have a well documented but fluid action plan for implementation

QUESTIONS?