Pharmacovigilance in Israel
The Way Forward
4th Jerusalem Conference on Quality and Pharma Sciences
21 May 2014

Dr. Grainne Quinn
Perrigo PLC
Pharmacovigilance

• Pharmacovigilance (PhV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

• The aims of PhV are to enhance patient care and patient safety in relation to the use of medicine and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines.

World Health Organisation
• “Those who don’t know history are doomed to repeat it”.
  
  – Edmund Burke
History of Pharmacovigilance

- 950 BC – Adverse effects of drugs documented by Homer
- 1540 – UK College of Physicians appointed Inspectors
  "To search for corrupted or defective medicines that might not be convenient to a man’s health"
- 1785 – First documented accounts of digoxin toxicity
- 1937- Elixir Sulfanilamide Incident
- 1950s – early 60s - Thalidomide
History of Thalidomide

• Anti-emetic first marketed in 1949

• “..can be given with complete safety to pregnant women and nursing mothers without adverse effect on mother or child..”

• Cases of Phocomelia
  – (0 cases 1949 – 1959, first case described 1960, 477 cases 1961)
  – Data from animal experiments incomplete and unreliable
  – Teratogenic effects subsequently reproduced in all species tested

• 1964-leprosy patient treated with unanticipated benefit-early benefit/risk management
Thalidomide Risk Management Today

• Authorised for use for treatment of multiple myeloma, ENL
• Subject to Risk Management Plan/activities, including pregnancy prevention programme (PPP)
• Registration of Physicians/pharmacies/patients
• Consent form for patient/partner
• Educational materials for HCPs/patients
• Special prescription requirements (i.e. issued within 3 days of a negative pregnancy test and limited to 4 week supply of product)
• Special dispensing requirements (i.e. dispensed within 7 days of the prescription date and within 10 days of a negative pregnancy test)

• The voice of the patient/consumer?
Establishing a pharmacovigilance system
The Purpose

• Patient/public health protection
• Effective early warning system
• Continuous surveillance over life-time of a medicine
• Facilitates risk identification and evaluation
• Communication of issues with safety implications
• Avoid drug “scares”
Establishing a System

- The people, processes and database systems required
- Time, dedication, expertise and continuity
- Education of pharmacovigilance staff
  - Data collection and verification
  - Interpreting and coding of events
  - Coding of medications
  - Case causality assessment
  - Signal detection
  - Risk management
- Collect data locally/nationally but consider data globally also
Assessment of Adverse Reaction Reports

- Review, evaluation, processing & follow-up of individual adverse reaction reports
  - Meaningful causality assessment vs quality of data
- Assessment of cases in context of cumulative data
- Exchange of relevant cases with partners and regulators
- Monitoring of new/emerging/established safety issues
- Initiation & implementation of safety-related regulatory action
- Internal/external review of cases/cumulative data
The PhV Quality Management System

- The characteristics of the system designed to produce outcomes relevant to the objectives
  - Compliance
  - Preventing harm
  - Promoting safe and effective use

- PhV QMS covers
  - Organisational structure
  - Responsibilities
  - Procedures
  - Processes
  - Resources/ resource management
  - Compliance
  - Records management
  - Business continuity planning
  - Predefined reviews, can be risk based
Good Pharmacovigilance Practice Metrics: Risk-based inspections

• MHRA: risk-based inspection process for GPvP commenced in 2009
• Marketing authorisation holders complete a compliance questionnaire every two years, voluntary
• Risk score assigned based on
  – # licenses
  – Mergers between systems
  – # activities/# FTEs
  – Expedited submission compliance
  – Change of Qualified Person in PhV (QPPV)
  – Outsourced activities
Global Regulatory Environment

• “FDA and European Medicines Agency strengthen collaboration in pharmacovigilance area”
  – FDA News Release 19 Feb 2014

• “In an increasingly globalised pharmaceutical market, collaboration between medicines regulators is essential. Medicines’ regulators are inter-dependent: any action taken in one territory has repercussions on the rest of the world”
  – Guido Rasi
Israel
משרדה: דירוג תופעות לוואי וידיעת בטיחות חולים

<table>
<thead>
<tr>
<th>עמוד 1 מזון</th>
<th>عدد המס' 1: אפריל 2012 נרשום:</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>2012</td>
</tr>
<tr>
<td></td>
<td>عدد המס' 2: פברואר 2013</td>
</tr>
<tr>
<td></td>
<td>מספר הגילוי: 6</td>
</tr>
<tr>
<td></td>
<td>תאריך הגילוי: יוני 1998</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

 tabletop

<table>
<thead>
<tr>
<th>המחלקה ל니חל סיכונים ומידעי תרופתי</th>
</tr>
</thead>
<tbody>
<tr>
<td>משמורת הביציאת</td>
</tr>
<tr>
<td>91010 ירושלים</td>
</tr>
<tr>
<td><a href="mailto:call.habriat@moh.health.gov.il">call.habriat@moh.health.gov.il</a></td>
</tr>
<tr>
<td>Tel: 02-5080234 Fax: 02-6474858</td>
</tr>
<tr>
<td>02-5080251 02-5080236</td>
</tr>
</tbody>
</table>

 קול הביציאת

2013 - תקנוץ הרתקחים (حتياجات) (תרכוש), התשע"ג – 2013

"QPPV" –Ａחהינא מעצב תרופי - "QPPV"

רודה ואדם בעלי רישוי ישראל וניסים של שנותיים בינקות
שפנייה על רישום למשת כઆerais מעצב תרופי
על פי גulado. על יניג הכתיש שלוחה ורמאה, יניג לומדת ג"ם
תפתץ. כהדרה ובחינת התוכן בטכנאי, התשע"ג-2012 יחל
השתעת, רדונה, רודה ואדם בעלי רישוי ישראל - הראה��ים זו
רופה בחטאת לודר שביל שאולת קלילות, החותם והוגה תפקידה.
Requirements in Israel “SOP 6”

- **Principle**
  - The Israeli Ministry of Health emphasises the importance of promoting public safety by only allowing safe, efficacious and high quality medicines on the market
  - The Ministry of Health views post marketing surveillance a critical responsibility

- **Requirements**
  - Pharmacovigilance system (also for Health Funds and hospitals)
  - Qualified Person in Pharmacovigilance (QPPV) responsible for all the pharmacovigilance activities; nominated to the Ministry of Health

- **Responsibilities of the QPPV**
  - Report any safety action by the manufacturer or any health authority
  - Report any new safety information
  - Changes in clinical information-foreign or domestic
  - Submission of foreign unexpected sADRs
  - PSUR submission
  - All company employees to be trained on the need for ADR reporting
Ministry of Health Website-AE Reporting

- Facilitates public and healthcare provider adverse drug event reporting
- Promotes a positive attitude to PhV
- Avoids under reporting
Current Challenges in Global Pharmacovigilance

- Worldwide Web-based sales and information

- Broadening scope of pharmacovigilance
  - overdose, misuse and abuse, off-label use
  - polypharmacy and interactions
  - increasing use of traditional and herbal medicines with other medicines
  - illegal sale of medicines and drugs of abuse over the Internet
  - increasing self medication practices
  - substandard medicines
  - medication errors
  - lack of efficacy

- Developing and emerging countries with overburdened healthcare systems

- Unsafe drug donation practices

- Counterfeit medicines

- Increased public awareness over safety of medicines with an increasing public scrutiny on the performance of the health professions, industry and regulators
In summary

- Responsibility for pharmacovigilance has to be shared to achieve the goal
  - scientists
  - clinicians
  - pharmaceutical manufacturers
  - drug developers
  - regulators
  - public policy makers
  - patients
  - the general public

- The risk of harm is less when
  - medicines are used by an informed health profession
  - by patients who themselves understand and share responsibility for their drugs

- When adverse effects appear - particularly when previously unknown in association with the medicine - it is essential that they should be analysed and communicated effectively (the role of pharmacovigilance) in partnership with regulators
References and acknowledgements

- IMB Website, accessed 12 May 2014
- “Reporting Adverse Events and New Safety Information”, IMOH SOP6, Updated October 2013
- Regulation 1, as amended, to the Pharmacists Regulations (Drugs), 5746-1986
- The Importance of Pharmacovigilance-Safety Monitoring of Medicinal Products. WHO, 2002

- Elena Kaplan, Medical information & Safety pharmacist, Perrigo Israel
- Maya Arieli, Medical information & Safety pharmacist, Perrigo Israel
Thank you

Questions?