Establishing a good Pharmacovigilance system: Essential elements

2 January 2014
Petach Tikva

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IFC Strategic Safety Consulting
Adverse Reactions are the 4th to 5th cause of death in US and EU

Who saves one life saves the world

Talmud
Agenda

- What is ISOP-ISRAEL?
- HOT TOPICS IN PV: program 2014
- Key Elements for Establishing a Good PV System: I. Fermont
- Where we are coming from and where we are going? Teva's Experience in PhV – Dr. Hedva Voliovitch, Vice President of Global Patient Safety & Pharmacovigilance, Teva
- Experience sharing
Our Vision

- Improve and harmonize Pharmacovigilance systems in Israel
- Increase awareness on patient’s safety
- Gather all stakeholders
- Be a think tank
- Support a mechanism for data sharing
- Use Epidemiology for risk detection

Join forces with Ministry of Health towards the implementation of a new regulation.
Our Actions

- Endorsement of ISOP ISRAEL by ISOP International President
- Tel Aviv University Public Health School involvement
- Abstract and communication: Biomed 2013, Israstem 2013
- ISOP Annual meeting: poster and endorsement by the Executive Committee

Set up of the educational program
- Hot topics in PV
- Basic course for Healthcare professionals
- Intensive summer course 2014

- Starting a joint collaboration with Paris University, and other ISOP chapters
- MOH support for Hot Topics in PV
- Website and LinkedIn group
Hot Topics in PV

Next meeting : PSUR/PBRER
9 March Tel Aviv
with Pharmacist association

- SDEA Safety data exchange Agreements SDSM
- Safety databases and electronic transmission to Eudravigilance
- Literature survey
- Quality in PV : Audit-Inspection-PV System Master File
- Risk Management Plan
# Advisory Board

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Irene Fermont, MD,</td>
<td>Coordinator</td>
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<td>Hedva Voliovitch, MD,</td>
<td>Secretary</td>
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<td>Yehoudit Wexler</td>
<td>Advisor Educational Program</td>
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<td>Mira Marcus-Kalish PhD,</td>
<td>Academy Advisor</td>
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<td>Dr. Luis Brezka, PharmD,</td>
<td>Industry Advisor</td>
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<td>Prof Daniel Cohen</td>
<td>Academy Advisor</td>
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**Irene Fermont, MD,**  
IFC Safety Strategic Consulting

**Hedva Voliovitch, MD,**  
Head of Global Pharmacovigilance, Teva

**Yehoudit Wexler**  
President, Bioforum

**Mira Marcus-Kalish PhD,**  
Director of International Research Affairs & Senior Researcher for ICTAF, Tel Aviv University

**Dr. Luis Brezka, PharmD,**  
Head Global Safety, Kamada

**Prof Daniel Cohen**  
Director of Public Health School, Tel Aviv University
Special Thanks

- Hedva for hosting us and launching this cycle
- Yehudit for her vision and unfailing support
- Shifra Hoch and Tamar Oren for the organisation
Next steps

- Registration to ISOP ISRAEL is free
- PLEASE REGISTER TO ISOP*
- Official creation: ISOP annual meeting Oct 2014
- Intensive Summer Course Tel Aviv University
- Bioforum seminars
- Involve Koupot Holim and Clinical Pharmacology
- Finalise the website
- Include HOT TOPICS presentations in the website and linkedIn group

* ISOP registration:
From dream to reality
the Israeli vocation!

It’s now in our hands!
Key Elements for Establishing a Good PV System

What EU regulation tells us?
Where to start?
EMA IMPLEMENTATION PLAN
Priorities

Activities
- Contributing to Public Health
- Improving transparency and communication
- Simplifying the processes
4 main domains of activities

- Collection of key information on the products
- Better analysis and understanding of the safety data
- Regulatory actions to safeguard Public Health
- Communication with all stakeholders
### Good Pharmacovigilance practices Module 1

#### Critical pharmacovigilance processes (1/2)

<table>
<thead>
<tr>
<th>Process</th>
<th>Details</th>
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<tbody>
<tr>
<td>Business continuity</td>
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<td>Continuous safety profile monitoring and benefit-risk evaluation</td>
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<td>Risk management systems; effectiveness of risk minimisation</td>
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<td>Handling of ICSR</td>
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<td>Signal management</td>
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<td>PSURs submission and assessment</td>
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<td>Responding to requests from NCA</td>
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### Critical pharmacovigilance processes (2/2)

<table>
<thead>
<tr>
<th>Interaction between PV et quality defect systems</th>
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<tbody>
<tr>
<td>Communication with NCA on safety concerns and changes to the risk-benefit balance</td>
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<tr>
<td>Communication to patients and HCP on changes to the risk-benefit balance</td>
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<tr>
<td>Keeping product information up-to-date; incl. assessment and recommendations from NCA</td>
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<td>Implementation of variations to MA for safety reasons</td>
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1rst step: establishing a workplan

- Regulatory references are moving: interim periods different for each process
- Inspectors will be looking at your processes evolution
- Start with a workplan
  - To be included in the PV System Master File
## Workplan

<table>
<thead>
<tr>
<th>Topic</th>
<th>Task</th>
<th>Deadline</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Training PV staff</td>
<td>GVP module 1,2,3,…</td>
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<tr>
<td>PV System Master File</td>
<td>Implement Update</td>
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<td>SOPs update</td>
<td>SOP ICSR, SOP PSUR,…</td>
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<td>New tools development</td>
<td>Benefit risk algorithm</td>
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<td>Signal detection</td>
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<td>Crisis management</td>
<td>SOP simulation</td>
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<td>Regulatory survey</td>
<td>Organisation Implementation of changes</td>
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<td></td>
<td>Interim period</td>
<td></td>
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<td>Quality plan</td>
<td>Audits, auto-inspection</td>
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<td>Contractors, affiliates, …</td>
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<td>End of the process</td>
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The Pharmacovigilance
& Risk management systems
A holistic approach
PHARMACOVIGILANCE & RISK MANAGEMENT SYSTEM

- Pharmacovigilance system

Safety Profile Surveillance B/R Assessment

- Spontaneous reports (post-marketing) Compassionate Use & Literature cases
- Clinical Trials SAEs & SUSARs
- Links with Products complaints and Medical Information/contractors
- Assessment of expedited reporting criteria Interim

ICSR : Case management

- Include off-label, misuse, medication errors
- Strengthen medical analysis and Company comment
- Flag your events of interest & critical events
- Literature search: 2-3 databases + internet
- Check National Competent Authorities reporting criteria
- Check Eudravigilance changes
- Periodic reconciliation with medInfo-complaints and contractors
- One system, one database for pre and post marketing
- Strengthen medical analysis
- One approach for all periodic reports
  - Link all your reports: DSUR-PSUR-RMP, etc..
  - Compare to cumulative
  - Update your Reference Safety Information
    - SmPC
    - CCSI Company Core Safety Information
    - Development CSI
    - Investigator Brochure
PHARMACOVIGILANCE & RISK MANAGEMENT SYSTEM

**Pharmacovigilance system**

**Technology**
- PV databases
  - Web access
  - E2B compliant; XML format
  - Editing CIOMS – Medwatch
  - Line listing ans Summary Tabulations
  - Electronic reporting
  - Data reconciliation
  - Queries and signal detection
  - Data migration

**Safety Data base**

**Electronic-reporting Eudravigilance & National Competent Authorities**

**Eudravigilance Certification**
- Electronic transmission
- Registration & Validation in EV + NCA
- Affiliates, contractors, 3rd party provider
- Certification and registration of products in XEVMPD
- Check your back log!
PHARMACOVIGILANCE & RISK MANAGEMENT SYSTEM

Risk Management system

Pharmacovigilance system

Technology

- Safety Data base
- Call Tree
- Internal Communication
- Electronic-reporting

Workflows /contractors
- Safety Plans
- SUSARs distribution to Investigators & IRB/EC

- Stand by duty 24/7: organise, test and control
- Call tree: your contractors
- Dedicated lines for fax & tel
Review roles of EUQPPV & local QPPV
Registration of EUQPPV : EMA & NCA
Back up : transmission reports
Test availability 24/7/365

PV Training Plan
Training records

PV System Master File
Quality Plan : audits, metrics, readiness to inspection, providers, contractors
SOPs, Instructions to be updated
Detailed Description of PV System
Regulatory survey

For 3rd countries exchanges
Safe Harbour
Agreements for data protection CNIL

Safety data exchange agreements
1rst to be inspected
Set up of a proactive Risk Management approach!
- RMP : links to PSUR-DSUR, REMS

- Developmental Risk Management Plan (CIOMS VI)
- Start writing Safety Specifications

- Organize solicited or non solicited case handling

Think: ACTION!
- Educationnal material
- Measure Efficiency of actions : PSURs

- Anticipate: SOP, training, simulation
- Safety Committee will be the crisis committee

Risk Management System

Risk Management Plan

Safety in Clinical Development plan

Post-Authorisation Safety-Efficacy Studies PASS+PAES

Risk Minimization Actions & Risk Communication

Safety Crisis management
PHARMACOVIGILANCE & RISK MANAGEMENT SYSTEM

Pharmacovigilance system

- Safety Profile Surveillance B/R Assessment
  - Spontaneous reports
  - Compassionate Use and Literature cases
  - Clinical trials SUSARs-SAEs
  - Links with Products complaints & Medical Information
  - Assessment/expedited reporting criteria
  - Study Safety reports
  - DSUR
  - PSURs

- Technology
  - Data base organization
  - Communication Call tree
  - Electronic reporting Eudravigilance

- Resources And Structures
  - Role of the EU QPPV and the local QPs
  - Pharmacovigilance Training
  - Quality Assurance / Quality controls
  - Filing/Archiving Organization
  - Data protection
  - Safety agreements

Risk Management system

- Risk Management Plan
- Safety in Clinical Development plan
- Post-authorisation Safety Studies
- Risk Minimization Actions and Communication
- Safety Crisis management

Signal detection

Answers to queries from Competent Authorities
Handling of urgent safety matters

Links with Products complaints & Medical Information

DSUR
PSURs

Periodic reports

- Study Safety reports
- DSUR
- PSURs

Individual reports

- Spontaneous reports
- Compassionate Use and Literature cases

Risk Management Plan
Safety in Clinical Development plan
Post-authorisation Safety Studies
Risk Minimization Actions and Communication
Safety Crisis management

Filing/Archiving Organization
Data protection
Safety agreements
STRENGTH & ENERGY with LAVOCAT products

IRRADIATED FOOD

1930
Thank you for your presence

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