WHO Programme for International Drug Monitoring: strategies for Smart Safety Surveillance (3S) in low and middle income countries

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Group Lead: Medicines Safety
WHO
Safety & Vigilance in WHO

World Health Assembly Resolution 16.36 (1963)
INVITES Member States to arrange for a systematic collection of information on serious adverse drug reactions observed during the development of a drug and, in particular, after its release for general use.
WHO Programme for International Drug Monitoring

1968

2000

2016
Guidelines on Min PV Requirements and PV Public Health Programmes
PV Methods Spectrum

**Spontaneous Reporting**
- Denominator unknown
- Suspected ADRs
- All medicines

**Targeted Reporting**
- Denominator known
- Suspected ADRs
- Cohort specific medicines

  - Essential minimum reporting
  - Profile of ADRs for a specific medicine in a specific popn
  - AMPATH Kenya ARVs

- Denominator known
- Specific ADRs
- Cohort specific medicines

  - Incidence of a known ADR in a specific population
  - TSR of Tenofovir in Uganda

**Cohort Event Monitoring**
- Denominator known
- All Events
- Cohort specific medicines

  - Post-marketing surveillance of a new chemical entity
  - CEM of new antimalarials (ACTs)

**EHR Mining**
- Denominator known
- All Events
- All medicines

  - Using data available in patient records to enhance PV
  - Uganda
  - Ghana
Expand the network of WHO Collaborating Centres

- UMC 1978
- WHO CC Ghana
- WHO CC Oslo
- WHO CC Netherlands
- WHO CC Morocco
- WHO CC India
- WHO

Years:
- 2009
- 2010
- 2012
- 2017
<table>
<thead>
<tr>
<th>Full Members (20)</th>
<th>Associate Members (11)</th>
<th>Not yet members of WHO PIDM (7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia (2013)</td>
<td>British Virgin Islands (2008)*</td>
<td>Dominican Republic</td>
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<tr>
<td>Guatemala (2002)</td>
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<td>Jamaica (2012)</td>
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<td>Mexico (1999)</td>
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<td>Panama (2016)</td>
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<td>Peru (2002)</td>
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<td>Suriname (2007)</td>
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<td>Uruguay (2001)</td>
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<td>USA (1968)</td>
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<td>Venezuela (1995)</td>
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* British Overseas Territory
Total number of ICSRs submitted to VigiBase in the Americas

Total Number of ICSRs submitted to VigiBase

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Number of ICSRs submitted to VigiBase</th>
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<tbody>
<tr>
<td>Venezuela</td>
<td>13,35</td>
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<tr>
<td>Uruguay</td>
<td>1,801</td>
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<tr>
<td>United States (USA)</td>
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<td>Suriname</td>
<td>0,221</td>
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<tr>
<td>Peru</td>
<td>52,696</td>
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<td>Panama</td>
<td>0,263</td>
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<td>Mexico</td>
<td>77,585</td>
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<tr>
<td>Jamaica</td>
<td>0,234</td>
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<td>Guatemala</td>
<td>0,064</td>
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<td>El Salvador</td>
<td>0,43</td>
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<td>Ecuador</td>
<td>0,361</td>
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<td>Cuba</td>
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<td>Costa Rica</td>
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<td>Colombia</td>
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<td>Chile</td>
<td>11,462</td>
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<td>Canada</td>
<td>555,19</td>
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<td>Brazil</td>
<td>5,474</td>
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<tr>
<td>Bolivia (Plurinational...)</td>
<td>0,127</td>
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<td>Barbados</td>
<td>0,403</td>
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<td>Argentina</td>
<td>18,809</td>
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</tbody>
</table>

Millares
Reports for all Americas

Cumulative number of ICSRs submitted to VigiBase from countries in the Americas

Milliars

Number of ICSRs submitted to VigiBase

Year

US and Canada

Central and South America
Reports for Central and South America

Cumulative number of ICSRs submitted to VigiBase

- Colombia
- Mexico
- Peru
- Cuba
- Argentina
- Venezuela
- Chile
- Uruguay
- Costa Rica
- El Salvador
- Barbados
- Ecuador
- Panama
- Jamaica
- Suriname
- Bolivia
- Guatemala
WHO Global Database: VigiBase

2014-12-31

10 302 935

1968
1970
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10 000 000
12 000 000

Americas
Africa
Asia
Europe
Oceania
Very limited reporting from LMIC
Barriers to end-to-end Pharmacovigilance
Snapshot: 3 Main problems

A. Limited reporting
B. Low local capacity / capability to analyze data collected
C. Low NRA capacity / capability to take action from alert signals received: Only a small fraction (3 in 55 according to 2010 survey by WHO) of the NRAs regularly take specific actions from signals received; most of these decisions are a replication of what was done by the SRAs
The Product Pipeline

A majority of the products will be launched exclusively or simultaneously in LMIC (23 within 5 years)

A majority of the products will be developed in resource rich settings that do not consider the characteristics (morbidity) of the LMIC where they will be launched.

Limited data package when the products are launched in LMIC:
- 'LMIC-only' launch: no experience from HIC for LMIC to rely upon
- 'Simultaneous' launch: trial designs, developer's landscape limit what we know

Launch plan and limited PV capacity multiply risks

Geographic distribution of product launches, assessed by relative risk (2016-2018)

Risk-based assessment

• Anticipated product pipeline
• Anticipated or potential post-market safety risk
• Pharmacovigilance capacity in launch countries
• Timing of launch

Source: BMGF SSWG Report
<table>
<thead>
<tr>
<th>Risks to</th>
<th>Potential Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients &amp; families</td>
<td>Adverse events: inadequate treatment, Illness, hospitalization, congenital anomalies, severe disability, even death</td>
</tr>
<tr>
<td>Governments</td>
<td>Legal liabilities, loss of confidence/credibility/productivity</td>
</tr>
<tr>
<td>Sponsor/MAH</td>
<td>Legal &amp; ethical issues; loss of credibility</td>
</tr>
<tr>
<td>Resources</td>
<td>Wasted money, loss of viable products</td>
</tr>
</tbody>
</table>
WHO-BMGF dialogue: Risk based prioritization of PV activities

- Assess Product launches over 10 years
  - Anticipated / potential risks with products
- Assess Time frame for product launch
  - Capacity for PV in launch countries

Tailor efforts to identified gaps in target countries
Protocols & operational guidelines
End-end vigilance (pre and post approval)
WHO-BMGF Strategy for PV in LMIC: Smart Safety Surveillance

**Vision**

Ensure timely and adequate reporting, review, and action on adverse events in low- and middle-income countries where priority Global Health products will be introduced.

**Proposed approach**

- **Adopt a stepwise approach:**
  - New medicine (NCE)
  - New vaccine
  - (Dx)

- **Develop holistic plans** that cover policy, infrastructure and resources

- **Leverage existing** infrastructure, networks

- **Enlist additional partners** for end-end safety management

- **Launch** Technical Working Groups and multi-country platforms

- **Develop integrated plan to include manufacturer**

- **Build the ‘infrastructure’** progressively to enable sustainability

"Smart Safety Surveillance"
## Concept

### National Needs
- Awareness and Advocacy
- Capacity and competence
- Enablers and infrastructure (guidelines, structures, processes, Resources)
- More engaged Stakeholders (public health programmes)
- Scope (Dx, Med Errors)
- Legal framework

### Regional Resources
- Morbidity patterns similar (lessons learned/information)
- Advanced PV systems: fellowships, peer visits
- Multi-ethnicity: sentinel sites for special investigations/Risk characterization
- WHO Collaborating Centres
- Platform

### Work-sharing Areas
- Pre approval Clinical Assessments (RMP), Mutual Recognition, Reliance
- Post approval: Joint PV assessment committees
- PV Inspections
- Harmonization initiatives (industry obligations, standard Assessment templates etc)
Reliance (on other NRA for pre-approval Clinical Assessment)
- Min PV (Spontaneous) systems

Plus
- Joint (RMP) Reviews
  - Targeted investigations
  - Vigilance System Strengthening: all core functions

Plus
- Joint assessment; Technical support to other NRAs
  - Sentinel sites/safety studies/signal validation
  - Host multi-country platforms (PV and risk assessment committee)