Evaluation of pharmacovigilance systems in developing countries: the role of an international collaborative network

Patrick Zuber - WHO

Global Collaborative Network for Vaccine Safety Studies
Mérieux Foundation, 28-30 March 2011
SCOPE and MAGNITUDE: ALL WHO REGIONS, 332 country visits FOR ASSESSING/REASSESSMENT & FOLLOW UP: 1997-2010

101 NRA assessments conducted

- NRA assessment completed including follow up
- Not yet conducted
TOTAL POPULATION MONITORED THROUGH WHO* NRA ASSESSMENTS AND FOLLOW UP : 1997 - 2008

1997

- Not monitored: 5,580 M; 96%
- Monitored: 226 M; 4%

2008

- Not monitored: 4,270 M; 6%
- Monitored: 6,233 M; 94%

*World Health Organization

Source: World Health Organization/Immunization, Vaccines and Biologicals, as of 1st December 2008
NRA assessment process: 6-15 months

- Manufacturer request prequalification or country request
- WHO inform NRAs and propose previsit to plan for assessment
- Country Agree For the process
- WHO (HQ+ RO) Team visits country
- RO Team visits country
- WHO collaborative workspace open to upload information relevant to each indicator
- Self evaluation conducted
- Assessment confirmed or postponed
### WHO NRA assessment tools

**Function: PMS/AEFI surveillance, 1999-2007**

<table>
<thead>
<tr>
<th>NRA assessment tools (year of revision)</th>
<th>PMS/AEFI</th>
<th>Total indicators</th>
<th>Total sub-indicators</th>
<th>Total critical indicators</th>
<th>Total critical sub-indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>0</td>
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</tr>
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<td>2001</td>
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<td>2002</td>
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<td>0</td>
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<tr>
<td>2004</td>
<td>1</td>
<td>8</td>
<td>29</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>2007</td>
<td>1</td>
<td>8</td>
<td>25</td>
<td>6</td>
<td>16</td>
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</tbody>
</table>
8 components

1. Regulation/guidelines.
2. Quality management system.
3. Roles of key stakeholders.
4. Human resource management.
5. System to review vaccine safety events.
6. Capacity to detect vaccine safety.
7. Regulatory outcome.
8. Feedback and communication.
STRENGTHENING NATIONAL REGULATORY AUTHORITIES (NRA)

POST-MARKETING/AEFI SURVEILLANCE AND DEVELOPMENT STATUS:
TOTAL POPULATION AS OF 2009

- **Unknown**: 119 million; 2% (36 countries)
- **Not implemented**: 3,139 million; 46% (78 countries)
- **Developed & least developed**: 2,304 million; 34% (33 countries)
- **Developed & economy in transition**: 1,259 million; 18% (46 countries)
- **Implemented**: 3,564 million; 52% (79 countries)
STRENGTHENING NATIONAL REGULATORY AUTHORITIES (NRA)
POST-MARKETING/AEFI SURVEILLANCE AND DEVELOPMENT STATUS:
TOTAL POPULATION AS OF 2009

IMPLEMENTED
564m.; 52%
(79 countries)

NOT IMPLEMENTED
3,139m.; 46%
(78 countries)

UNKNOWN
119m.; 2%
(36 countries)

Developed &
economy in transition
48m.; 1%
(7 countries)

Developing &
least developed
3,092m.; 45%
(71 countries)
Indicator PM06: Capacity to detect and investigate significant vaccine safety issues - Critical

<table>
<thead>
<tr>
<th>Group of countries</th>
<th>Number of Countries</th>
<th>Number of Countries with data available</th>
<th>Number of Countries with Indicator Implemented</th>
<th>% Implemented (of those with data available)</th>
<th>% Implemented out of the total countries in the region</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Industrialized</td>
<td>48</td>
<td>48</td>
<td>45</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>B. Upper middle income</td>
<td>39</td>
<td>13</td>
<td>5</td>
<td>38</td>
<td>13</td>
</tr>
<tr>
<td>C1. Lower middle income</td>
<td>57</td>
<td>17</td>
<td>5</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>C2. Low income</td>
<td>49</td>
<td>17</td>
<td>2</td>
<td>12</td>
<td>4</td>
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</tbody>
</table>
**Indicator PM06: Capacity to detect and investigate significant vaccine safety issues - Critical**

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Number of Countries</th>
<th>Number of Countries with data available</th>
<th>Number of Countries with indicator implemented</th>
<th>% Implemented (of those with data available)</th>
<th>% Implemented out of the total countries in the region</th>
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</thead>
<tbody>
<tr>
<td>AFR</td>
<td>45</td>
<td>12</td>
<td>1</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>AMR</td>
<td>29</td>
<td>5</td>
<td>3</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>EMR</td>
<td>15</td>
<td>6</td>
<td>2</td>
<td>33</td>
<td>13</td>
</tr>
<tr>
<td>EUR</td>
<td>24</td>
<td>12</td>
<td>3</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>SEAR</td>
<td>11</td>
<td>9</td>
<td>2</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>WPR</td>
<td>21</td>
<td>3</td>
<td>1</td>
<td>33</td>
<td>5</td>
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</table>
## Indicator PM06: Capacity to detect and investigate significant vaccine safety issues - Critical

<table>
<thead>
<tr>
<th>DTP3 coverage</th>
<th>Number of Countries</th>
<th>Number of Countries with data available</th>
<th>Number of Countries with Indicator Implemented</th>
<th>% Implemented (of those with data available)</th>
<th>% Implemented out of the total countries in the region</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50%</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>51-70%</td>
<td>15</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>71-80%</td>
<td>17</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>81-85%</td>
<td>19</td>
<td>6</td>
<td>2</td>
<td>33</td>
<td>11</td>
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<tr>
<td>86-90%</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>33</td>
<td>10</td>
</tr>
<tr>
<td>&gt;90%</td>
<td>79</td>
<td>31</td>
<td>9</td>
<td>29</td>
<td>11</td>
</tr>
<tr>
<td>Health Expenditure (US$ per person per year)</td>
<td>Number of Countries</td>
<td>Number of Countries with data available</td>
<td>Number of Countries with Indicator Implemented</td>
<td>% Implemented (of those with data available)</td>
<td>% Implemented out of the total countries in the region</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>---------------------</td>
<td>----------------------------------------</td>
<td>-----------------------------------------------</td>
<td>---------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>&lt;25</td>
<td>38</td>
<td>16</td>
<td>2</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>25-75</td>
<td>81</td>
<td>22</td>
<td>4</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>&gt;75</td>
<td>26</td>
<td>9</td>
<td>6</td>
<td>67</td>
<td>23</td>
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### Indicator PM06: Capacity to detect and investigate significant vaccine safety issues - Critical

<table>
<thead>
<tr>
<th>HDI</th>
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<th>Number of Countries with Indicator Implemented</th>
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<th>% Implemented out of the total countries in the region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very High</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>High</td>
<td>38</td>
<td>16</td>
<td>4</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>Middle</td>
<td>41</td>
<td>14</td>
<td>5</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Low</td>
<td>42</td>
<td>13</td>
<td>1</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>NA</td>
<td>22</td>
<td>3</td>
<td>1</td>
<td>33</td>
<td>5</td>
</tr>
</tbody>
</table>
PMS network encompasses all activities to support national systems

**Global capacity building and harmonized tools**
- WHO and partners
- Brighton Collaboration
- CIOMS/WHO working group

**Global analysis and response**
- GACVS
- Other global or regional advisory bodies

**National AEFI surveillance, investigation, and response**
- Immunization programme
- Regulatory authority
- AEFI review committee
- Other support groups

**Global detection and evaluation**
- WHO PIDM
- Global vaccine safety data link
- Other partners

**Product monitoring**
- Vaccine manufacturers
- Licensing authorities in country of manufacture
- Procurement agencies
Vision for the Global Vaccine Safety Blueprint

All countries ensure effective vaccine safety monitoring so that unwanted vaccine reactions are minimized and public confidence in vaccination is maintained.
Three levels of engagement for the Global Vaccine Safety Blueprint

- Building capacity for effective vaccine safety monitoring so that all low- and middle-income countries have at least a minimal capacity.

- Enhancing the level of vaccine safety activity in countries that manufacture vaccines and in early introducers of newly available vaccine so that these countries have the ability to carry out active surveillance and database studies.

- Fostering international collaboration and encouraging global strategic planning so that national systems are adequately supported, all vaccines are under adequate post-marketing surveillance and vaccine safety information is shared internationally.
Minimal capacity at country level (as of 29 March 2011)

Vaccine safety monitoring structure:

- a national system of spontaneous reporting with a national database of AEFI reports;
- a national AEFI advisory committee;
- a clear communication strategy for routine communication and crisis communication;
- a national vaccine pharmacovigilance centre with designated staff collaborating with the WHO Programme for International Drug Monitoring;
- links to external technical support if required.

Managerial requirements:

- a proper regulatory framework (provisions for monitoring and management of AEFI),
- clear lines of accountability identified for the conduct of vaccine safety work;
- a management plan is developed, periodically evaluated and revised in order to ensure continuous quality improvement in the conduct of national vaccine safety activities;
- a commitment to sharing information on vaccine safety with other countries.
International resources considered for Blueprint

- **Capacity building:**
  - Decentralized pool of experts (institutional development, crises management, training).
  - International research groups (active surveillance projects and computerized databases).
  - Global rumour monitoring.
  - Global AEFI database.

- **Standards:**
  - Harmonized methodologies.
  - Case definitions.
  - Updated safety profiles for prequalified vaccines.

- **Electronic tools:**
  - Communication of vaccine safety issues.
  - Case verification and sharing of data.

- **Quality improvement:**
  - Best practices registry.
  - Performance indicators.

- **Expert advice:**
  - Independent advice on global vaccine safety issues.
  - Expert advice on implementing Blueprint strategies.
Anticipated challenges

- Ownership from national stakeholders.
- Making institutional planning attractive.
- Integrating project approaches with systems building.
- Adapting methods and definitions to local clinical practices.
- Enhancing collaboration between regulatory authorities and immunization programs.
- Endorsement from WHO governing bodies.
More anticipated challenges

- Communicating about vaccines-related risks.
- Defining milestones and priorities.
- Agree on common reporting formats (definitions, dictionary, language…).
- Attracting new players and making space.
- Clear rules of engagement with industry.
- Sufficient and predictable funding…