Global Collaborative Network for Vaccine Safety Studies Meeting
Annecy March 2011

Introduction to the Panel Discussion:

Lessons from the 2007 meeting
“Global Vaccine Safety DataNet”
held at the Merieux Foundation September 2007

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History

- A meeting was held at this center in September 2007 to discuss the desirability and feasibility of a global vaccine safety data network.

- Participants included representatives from 22 countries including potential investigators, regulators, manufacturers, governmental and WHO, IVI, PATH, Sabin Institute, GAVI WHO representatives.

- The consensus of those attending was that establishing a global network of collaborating sites dedicated to the assessment of vaccine safety using clinical databases was both feasible and desirable.

- It is the purpose of this presentation to review what has happened since and also to discuss what is required now to move this effort forward.
Countries that Participated at the 2007 Meeting

- Canada
- USA
- Costa Rica
- Chile
- Belgium
- Denmark
- Finland
- Germany
- Italy
- Switzerland
- UK
- Australia
- New Zealand
- Bangladesh
- China
- Singapore
- Thailand
- Vietnam
- Mexico
- Brazil
- South Africa
- Australia
- New Zealand
Background

- Vaccines are amongst the most effective public health interventions

- In many areas of the world, the very effectiveness of vaccines has eradicated public memory of the diseases they were designed to prevent.

- Safety scares have the potential to compromise or curtail vaccine safety programs both in the developing and developed world.

- Safety scares now are globalizing in impact.
Common Threads in Recent Vaccine Safety Issues

- Often there is a lack of scientific evidence confirming a causative association with vaccine
- Because of the internet and effective global communication, scares which began locally have had a global impact.
- For rotavirus and intussusception, findings from the US stopped the vaccine in the developing world even though the risk-benefit may have been positive in many countries.
Current Trends

- Vaccine development and manufacture of vaccines for export was once limited to Europe and the USA. This is no longer true with development of vaccines in Cuba, Brazil, India and China for actual or potential export.

- Globalization of information exchange and of safety scares requires a coordinated response.

- Evaluation of rare events require large exposed populations… larger than may exist in one country alone.
What Data is Needed for a Data Network?

vaccine Data

Exposure information at a minimum for cases

Computerized Hospital And/or Clinic Diagnoses

Outcome or Possible “Adverse Event”

Demographic Data on A Population

NOTE:
• Can do case series with Outcome alone or case control with Outcome and Demographics.
• With all three, can calculate rates and attributable risk
Importance of Broad Based Participation

- With globalization of vaccine manufacturing, globalization of evaluation is required.

- Increasing focus on development of vaccine targeting the developing world requires safety evaluation infrastructure in the same geographic area.

- Potential variability in susceptibility to adverse events requires a diverse population to evaluate vaccine safety.

- Increased use of existing vaccines and the targeting of new vaccines to lower and middle income countries makes them especially vulnerable
  - Lack of assessment, analysis and communication infrastructure
  - Susceptibility to vaccine scares with both local and regional impact
Global Vaccine Safety Data Network

Why now: Risk of the Status Quo

- An unsubstantiated vaccine safety scare can incapacitate a valuable vaccine program.
  - Hep B in France, MMR in the UK
  - Potentially dengue or malaria in developing countries

- Without a ready infrastructure, responding to such a scare or safety issue could take so long that the program could be dead by the time an analysis is done.
  - This undermines public confidence and makes future scares more likely

- Lack participation of local experts can undermine credibility of results
  - Not only results are necessary but also communication
Benefits of a Global Vaccine Safety Data Network

- Establish ready infrastructure for evaluation
- Allow evaluations of safety concerns across a large population
- Allow retesting of results from one country in another setting
- Provide a basis for mentoring and facilitating development of infrastructure and new techniques where they currently do not exist.
- Support development of local expertise for analyses as well as for credible communication.
Specific Proposal Presented in 2007

- Establish a Global Vaccine Safety Data Network with diverse participation focusing on available computerized data
  - At a minimum, hospitalization data needs to be available
  - Work with sites to encourage availability of vaccine, outpatient, and other data.
  - Does not need to be country-wide and not all countries in a region need to participate

- Define infrastructure required to standardize data management and data sharing and to facilitate scientific exchange.
Asia

- Bangladesh has regional registry but no computerized hospital diagnoses

- China
  - Immunization registry by region. Jiangsu province has all children with ~1 million
  - Hong Kong also has computerized hospital diagnoses but not immunizations
  - Hospital diagnoses regionally as well nationally in clinical databases

- Singapore
  - Immunization registry all children, hospital diagnoses, no outpatient

- Thailand
  - Regional immunization registries as well as hospital and outpatient data

- Vietnam
  - Did pilot datalink study with 350,000 people in study area
  - No national immunization registry

- India
  - No national registry or hospital data
  - Immunization registry and hospital outcomes available at select sites.
Latin America

- **Brazil**
  - Comprehensive registry on all children and adults
  - National hospital data with 11 million people participating
  - OPD system regionally

- **Chile**
  - No national immunization registry
  - Hospital outcomes nationally at all hospitals

- **Costa Rica**
  - National immunization registry all children ~ 350,000 children < 7 years of age.
  - National hospital database

- **Mexico**
  - National immunization registry
  - Hospital diagnoses nationally
  - Ability to link using unique identifier
Canada and USA

- **Canada**
  - Manitoba province has 1.1 million people with immunization registry, outpatient and hospital data
  - Projected nationally in 2-5 years.

- **USA**
  - VSD in place for 14 years with 2% of US population
    - Immunization, outpatient and hospital data
    - Limited to selected HMO sites only
  - PRISM

Africa

- **South Africa**
  - No national registry although is being discussed
  - Hospital diagnoses at select hospitals
  - Experience with using databases for safety and efficacy studies
Europe

- Finland
  - Immunization registry in place in one region, nationally within 5 years
  - Hospital diagnoses selected hospitals

- Germany
  - No national immunization registry
  - Hospital and outpatient diagnoses nationally

- Denmark
  - National immunization registry ~ 1 million people
  - Hospital diagnoses nationally
  - Experience in analysis of computerized safety data

- Italy
  - Regional immunization registry ~600,000 children
  - Hospital diagnoses regionally

- UK
  - Immunization registry with 30 million participants
  - National hospital data and outpatient data.

- Switzerland
  - No national registry
  - National hospital diagnostic data.

- Belgium
  - Immunization data on about 60 percent of population
  - National hospital data
Survey summary 2007

- Capacity and experience varied widely, but by country rather than by region.

- Countries with regional or national data on immunization, demographic and hospital outcomes:
  - Australia, New Zealand, China, Singapore, Brazil, Costa Rica, Canada, USA, Denmark, Italy, UK, Mexico, Vietnam, Thailand, Belgium
  - Potential population > 75 million people

- Countries with hospital outcomes data without immunization registries:
  - Switzerland, South Africa, Chile, Germany, Finland

- Data systems and localization (national, regional) are variable.

- Several countries had experience using computerized data for vaccine safety analyses:
  - New Zealand, USA, Denmark, UK.
What has happened since?

- Several examples of studies of vaccine safety using clinical databases since 2007
  - VAESCO
    - Has demonstrated that multi country collaboration and data sharing is possible
    - Political and privacy issues have been addressed.
  - Global Collaboration to Assess the Risk of GBS following H1N1 pandemic influenza vaccine using clinical databases
    - Common protocol being used with representation from all continents
    - Case series approach
    - Proof of concept has been achieved
  - Additionally, several countries have performed safety assessments using clinical databases since 2007
    - Australia for intussusception following rotavirus vaccine and H1N1 influenza
Global Collaborative Network for Vaccine Safety
So where are we now?

- Need has been demonstrated and is generally accepted
- Feasibility of within country and intracountry collaborative studies has been demonstrated
  - VAESCO
  - Global Vaccine Safety Collaborative Network:
    - Pilot project to assess risk of GBS following H1N1 pandemic influenza vaccine
- However, the global network is only a demonstration project and would require resources to become sustainable.
- Apart from the IVI project in Vietnam, models for LMI countries need to be developed.
SO WHAT IS NEEDED?
What is needed to go forward?

- **RESOURCES**
  - To fund training and coordinate activities on an ongoing basis.
  - To prioritize work and provide analytical capacity
  - To assess data quality across sites
  - For demonstration project(s) in lower income countries to refine a sustainable model.

- A means of coordinating with potential audiences
  - National MOH and regulators
  - WHO
  - Manufacturers
Potential sources of funding support

- Two models which are not mutually exclusive
  - A central foundation which receives funds from donors, from a vaccine excise tax or similar source.
  - A central foundation which receives support from manufacturers with specific need to perform phase four studies.

- We have moved forward in the past four years, but progress has been slow. Unless a reliable source of support is identified and sustainable infrastructure established, international collaborations run a high risk of being unsustainable.

- Demonstration projects may be necessary to develop training and data sharing protocols as well as to develop models for LMI countries.