

Implementing
Drug Safety
in 90 days



Rapid Pharmacovigilance Implementation in Developing Countries

“Some remedies are worse than the disease”

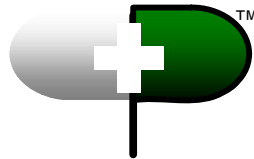
Publius Syrus, Roman writer, 1st century BC.

MORE AND MORE NEW PRODUCTS AND FORMULATIONS ARE BEING INTRODUCED DIRECTLY INTO DEVELOPING COUNTRIES; PUBLIC HEALTH PROGRAMS, USING THESE PRODUCTS, ARE BEING SCALED UP. UNFORTUNATELY THIS IS BEING DONE IN AN ENVIRONMENT WHERE THERE IS PRACTICALLY NO FOCUS ON PHARMACOVIGILANCE AND DRUG SAFETY, LEADING TO SIGNIFICANT RISK.

“RAPID” CAN CHANGE THAT, AND IT CAN DO IT 90 DAYS!

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"They poured drugs of which they knew little into bodies of which they knew less"
Voltaire (1700AD)



Our Mission

**TO CONDUCT PHARMACOVIGILANCE ON BEHALF OF
PUBLIC HEALTH PROGRAMS AND PRODUCT SPONSORS, AND
TO STRENGTHEN NATIONAL PHARMACOVIGILANCE CAPACITY
IN DEVELOPING COUNTRIES**

Our Approach

Complete safety data, especially for unexpected and serious adverse events, can only be captured through constant application of pharmacovigilance processes (preferably multi-country). It cannot be captured through clinical trials, which are typically conducted in an "artificial environment." For example, selected patients are usually not taking any other medications, do not have concomitant infections, are taking the drug short-term (during the duration of the trials only), are not children and not pregnant. Despite the obvious need for pharmacovigilance and existing regulations, very little is being done in this discipline in developing countries. Globally, only about 500,000 to 600,000 adverse event occurrences are captured—developing countries, which represent more than two-thirds of the world population account for less than 5% of all ADR data.

The RaPID program, a consortium of the leading organizations in pharmacovigilance, can help develop a short- and a long-term solution. The short-term solution could be implemented within 90 days, while the long-term solution, to build institutional capacity at the country level will take 3-5 years.

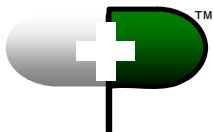
Our approach is to work with leading institutions from developed and developing world—this includes two WHO collaborating centers, the national regulatory authority of Switzerland, a pan-African health network and a leading academic and scientific research center in India. This consortium works directly with Ministries of Health, public health programs and public-private partnerships and product sponsors that develop and launch new drugs in developing countries.

Our work-flow includes the following steps:

- Assess and provide policy support for countries
- Design and establish country focused and disease focused pharmacovigilance systems
- Educate health professionals
- Gather adverse drug reaction data using health professionals and RaPID's 'P-Force'
- Enter data into a WHO approved and a globally recognized drug safety database
- Analyze data for causality
- Report findings to national regulatory agencies and international organizations
- Based on findings, provide recommendations for policy changes to WHO, Ministries of Health, PPP, and drug sponsors



Drug	Year	Examples of Serious and Unexpected Adverse Events Leading to Withdrawal of Drug
Thalidomide	1965	Phocomelia
Practolol	1975	Sclerosing peritonitis
Clioquinol	1970	Subacute neuropathy
Benoxaprofen	1982	Nephrotoxicity, oncholysis, cholestatic jaundice
Terfenadine	1997	Torsade de pointes
Rofecoxib	2004	Cardiovascular effects



Current Situation

Pharmacovigilance is defined by WHO as **“the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems”**

The objectives of pharmacovigilance are to:

- improve patient care and safety
- improve public health and safety
- encourage the rational and safe use of medicines
- promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

IN MOST DEVELOPING COUNTRIES, THERE IS NO CULTURE OF PHARMACOVIGILANCE AND DRUG SAFETY, AS A RESULT, THERE IS NO EVIDENCE ON THE SAFETY OF DRUGS IN PUBLIC HEALTH PROGRAMS.

Over 95% of Adverse Drug Reaction (ADR) data, a component of pharmacovigilance, is captured in developed countries. For example, some developing countries collect less than 100 ADRs per year, compared with several 100,000 ADRs in developed countries.

Further, the data from developed countries cannot be extrapolated to developing countries for several reasons:

- the type of drug use is different (developed countries do not use the co-formulated ARVs, and minimally use anti-TB, anti-malarial and anti-diarrheal drugs.
- Patient genotype and phenotype are markedly distinct than in developed countries, with a large number of malnourished patients and patients with concomitant diseases in developing countries relative to developed countries

The need to establish pharmacovigilance capability needs to be accelerated given that:

- New drugs are reaching developing countries in greater numbers and more quickly because of new funding from several donors, including the Bill and Melinda Gates Foundation
- Faster scale up of public health programs due to availability of new funding from major donors such as the Global Fund, World Bank, PEPFAR, PMI, and other major bilaterals.

Even in developed countries, which have, relatively speaking, stringent regulatory authorities, several drugs have been withdrawn from the market in the past few years, including: Alosetron (then returned to market with restrictions and a label warning), troglitazone, cisapride, cerivastatin, rofecoxib, valdecoxib. Several other products such as anti-depressants and NSAIDs have received additional warnings and restrictions based on data captured from drug safety activities. Similarly, drug safety data must also be captured in developing countries, where several million people are taking drugs for chronic diseases such as HIV/AIDS and tuberculosis. Many of these drugs are known to have a narrow therapeutic window and cause serious side effects.

It is also important to emphasize that clinical trials for new drugs are almost never conducted on patients with co-infections, or on children and pregnant women; whereas in the real world, all these groups of people will likely take the drugs at one time or another. For example, even in the United States, with almost a 100% literacy rate and well-informed health professionals and patients, it was noted that groups contraindicated to use specific medicines were using them frequently (as much as 20% in some instances), leading to serious adverse reactions. The situation in developing countries is likely to be much worse, but this data is not being captured.

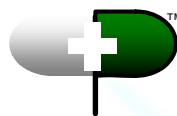
To gather this type of safety data, country-based systems for pharmacovigilance must be established. RaPID will help national program establish these and will also develop registries for children, pregnant women, people with co-infections, etc.



When implemented effectively, the information from pharmacovigilance allows for the intelligent, evidence-based use of medicines and has the potential for preventing many adverse reactions, thereby increasing effectiveness of national public health programs.

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About



Our team—Global Experience

The RaPID program team has significant Africa and Asia-based expertise in designing and implementing pharmacovigilance programs. In addition to developing country experience, our team has worked across the globe, including US, Europe, Japan, etc. The staff has provided consulting services in public sector and private sectors; in various life sciences industry including pharmaceutical, biotechnology, diagnostics, devices and vaccine industry; in clinical care settings from tertiary to primary care levels. Most of the team members are active on international advisory boards, and represent a wide range of academic and professional backgrounds that include:

- Public and private sectors
- Medicine, science, pharmacology, toxicology
- Management information systems and technology
- Out-sourcing and off-shoring capacity
- Operations systems capability

Consortium Lead Team Members

Paul Lalvani, Pharmacist, MBA (Kellogg), Executive Director, RaPID program

Sten Olsson, MSc., Pharmacist, WHO International Uppsala Monitoring Center, Head of External Affairs

Dr. Nilima Kshirsagar, MD, Ph.D, D cl. Ph, MNAMS, FNAMS, Previous Dean and Head of Department of Pharmacology, GS Medical College and KEM Hospital, Mumbai

Eva Ombaka, PhD, Pharmacist, Coordinator, Ecumenical Pharmaceutical Network

Jawahar Bapna, MD, PhD, Adjunct Professor Indian Institute of Health Management Research

In addition, technical support will also be provided by Swiss-medic, the Swiss National Drug Regulatory Authority



The WHO set up its International Drug Monitoring Programme after the thalidomide disaster. Since 1978 the Programme has been carried out by the Uppsala Monitoring

Centre (UMC) in Sweden.

An independent centre of scientific excellence, the Uppsala Monitoring Centre is responsible for the collection of data about adverse drug reactions from WHO member states from around the world, and the generation of signals of drugs which might possibly have problematic side-effects. Currently 82 countries are actively contributing to the database.



The Ecumenical Pharmaceutical Network (EPN) is an independent, apolitical non-profit Christian organization that works with its 80 pan-African members to provide health services in 31 countries. EPN's ultimate beneficiaries are in line with the 'Health for All' ideal; however there is a specific emphasis on the poor and the marginalized. The members include Christian Health Associations (CHAs) and Drug Supply Organizations (DSOs).



The RaPID™ program is hosted by O3i™, a New York-based, non-profit consulting organization. O3i's team has worked with the World Bank, WHO, UNICEF, various Ministries of Health and the Bill and Melinda Gates Foundation. Some of O3i's

board members are Directors of various UN agencies heading HIV/AIDS and malaria. The focus of O3i is its 'iii' approach:

INNOVATE—>IMPLEMENT—>IMPACT



Established in 1984 in Jaipur, IIHMR is the first of its kind of institution in India, with attention solely focused on health systems management. The Institute undertakes training, research and consultancy in health management and has collaboration with international organizations such as UNFPA, UNICEF, WHO, World Bank, ODA, DANIDA, KFW & GTZ, NORAD, CARE and USAID. International collaborations have been established with University of North Carolina, USA to offer masters programs to candidates from South-Asia.

“Primum non nocere” (First do no harm)

Hippocrates 500BC

Contacts

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