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3.63 TRILLION

MEDICINES POPPED WORLDWIDE IN 2015

With 10% of 3.63 trillion medicines popped worldwide in 2015, India is the world's third-largest medicine market. It stands to scientific reason that these drugs will have side effects. Yet, in 2013, India reported no more than 2% of globally occurring adverse drug reactions (ADRs), jargon for side effects of medicines, logged in Vigibase, a database maintained by the Uppsala Monitoring Centre, a World Health Organisation collaborating centre for international drug monitoring.

It isn't as if drugs have fewer side effects in India. **Serious effects were seen in 6.7% of patients, a 2014 study reported.** Other studies have cited drug side effects as the reason for 3.4% of hospital admissions in India, 3.7% hospital readmissions, and 1.8% mortality. In the developed world, adverse reactions are believed to be the fourth-leading cause of death.

Within India, the ADR reporting rate (ADRs reported per million population) has almost doubled in the last three years to 40, but it is lower than 130, the average ADR reporting rate for high-income countries, and clearly disproportionate to the country's population and medicine consumption.

Adverse Drug Reaction (ADR) Reporting in India

	Reports	Population (in million)	ADR reporting rate
2006 to 2008*	11633	1175	1
2013**	27867	1252	22
2014**	40810	1260	32
2015**	50450	1277	40

Source:

* [An update on the Pharmacovigilance Programme of India](#)

** [Pharmacovigilance Programme of India](#)

IN OTHER WORDS, INDIA ADDRESSES THE PROBLEM OF ADVERSE DRUG REACTIONS BY IGNORING OR NOT REPORTING THE DATA. THAT COULD PROVE COSTLY, SAID EXPERTS, IF IT ISN'T ALREADY.



IGNORING INDIAN DATA MAKES DRUGS MORE UNSAFE

"ADR reporting is important because it gives Indian regulatory authorities realistic data to base drug usage decisions on," said Y. K. Gupta, professor and head, Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), and national scientific coordinator, Pharmacovigilance Programme of India. "Using only global evidence without Indian data isn't an ideal situation because people of different ancestry may respond differently to medication."

Reporting the side effects of a drug could help determine if the medicine should stay or be pulled off shelves. A medicine labelled safe for clinical use after trials could still be found to be dangerous—as it happened with Rofecoxib, a non-steroidal anti-inflammatory drug, a runaway success after its 1999 launch.

Between its launch and 2004, Rofecoxib reportedly caused between 88,000 and 140,000 cardiac events. This forced Merck, a pharma multinational and the drug's maker, to voluntarily withdraw it from the US market, in turn prompting a ban in India, although no significant cardiac event was reported as a side effect.

140,000

CARDIAC EVENTS

"ADR reporting is still too low vis-à-vis the country's 1.28 billion population," said Harihar Dikshit, head, Department of Pharmacology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, one of 150 Indian ADR Monitoring Centres.

Pharmacovigilance Programme of India (PvPI)



CARELESSNESS, INSENSITIVITY AMONG REASONS FOR INDIA'S POOR REPORTING OF SIDE EFFECTS

SOME KEY REASONS BEHIND INDIA'S POOR TRACK RECORD IN REPORTING ADRS:

- ✓ Nurses, who are most likely to see a patient suffer a side effect, are expected to inform the treating doctor but seldom do. "Reporting ADRs is not mandatory for doctors in India, nor is staying updated with ADRs," said Akram Ahmad, previously of the Department of Pharmacy Practice, Annamalai University, where he conducted some of the studies quoted in this story.

"Doctors in India are careless in prescribing medicines, because they know they will not be held accountable for their actions, and are equally careless about reporting ADRs," said Kunal Saha, a US-based doctor who has waged a decade-long legal battle after his wife Anuradha Saha died of side effects of a drug overdose when she was being treated for a skin allergy in 1998. Settling Saha's case, the Supreme Court ruled that medical negligence includes not informing patients about the possible side effects of a drug. "Physicians prescribe new drugs at the behest of medical representatives even without reading the drug pharmacology, driven by the promise of gifts, despite this being illegal," said Saha. "Patients are prescribed excessive doses, unwarranted drugs or unwarranted combinations."

- ✓ Some doctors don't know that drug side effects should be reported to any one of 150 ADR monitoring centres across India, nor are they adept at recognising a drug side effect.
- ✓ Half of India's population depends on drug stores not run by pharmacists, and on doctors holding alternative medicine qualifications who aren't permitted to prescribe allopathic medicines in many states, said Ahmad. "Neither of these two will report ADRs."
- ✓ "Doctors are focused on growing their practice. They spend very little time diagnosing patients' symptoms, let alone explaining the drug regimen and asking them to report back any adverse reaction," said Ahmad.
- ✓ Scarce data preclude regulatory action on questionable drugs
- ✓ Drug side effects in India are scarcely reported, even in scientific literature.
- ✓ A 65-year-old woman with cardiovascular disease developed chest pain after being put on Nimesulide, a popular pain-killer, for fracture-related pain, as this 2003 study reported. Swapping Nimesulide with an alternative, Ibuprofen, quickly alleviated the chest pain.

- ✓ A 78-year-old man with heart disease was prescribed Nimesulide for a wrist injury. He developed breathlessness, blue pallor and restlessness, and quickly succumbed to further complications, another 2004 study reported.
- ✓ On the Naranjo scale—a scale developed by Canadian pharmacologist Claudio Naranjo and others to assess the causality for an adverse drug reaction—the complications the 78-year-old patient developed after taking Nimesulide scored two, indicating the drug could 'possibly' have been the cause of cardiac artery insufficiency, a shortage of blood in one or more coronary arteries.
- ✓ These events aren't recent: They occurred in Jawaharlal Nehru Medical College Hospital (JNMCH), Aligarh Muslim University, in 2003, well before the Indian government started to take pharmacovigilance seriously.
- ✓ "I observed those adverse drug reactions and have never prescribed Nimesulide since," said Syed Ziaur Rahman, associate professor, Department of Pharmacology, and deputy medical superintendent, JNMCH, Aligarh Muslim University.
- ✓ Nimesulide has been available in India since 1997. It currently sells as Nice (listed as a 'top brand' on Dr Reddy's Laboratories) and Nimulid MD (on Panacea Biotech). Nimesulide has never been licensed for use in the US, UK, Australia, New Zealand and Canada.
- ✓ "Hoping to drive further investigation on the drug, I presented these cases in academic conferences. But all that happened was Nimesulide became a 'hot' topic of discussion in academic meetings for some time," said Rahman.
- ✓ Over a decade later, a group of experts ruled that Nimesulide adversely affects the liver in children and should not be prescribed, said Gupta. So, Nimesulide was banned for children in 2011 (the Panacea website still lists Nimulid MD Kid as being available.)
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TO BAN OR NOT TO BAN: INDIA NEEDS DATA-DRIVEN ACTION

Reporting adverse drug reactions makes the experience of a few physicians available to the entire country.

For instance, in 2015, Indian authorities recommended the inclusion of advisory notes mentioning hepatotoxicity, haemorrhage and cardiovascular events as possible side effects of Sunatinib Malate, an anticancer drug, and cardiac dysfunction as a possible side effect of Pazopanib HCl, another anticancer drug.

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OVERVIEW

Pharmacovigilance, once called drug safety, has changed significantly over the past years. Expectations of the public (in particular concerned patients) and regulators have had profound effects on structures, processes, outputs, as well as objectives of concerned parties involved in Pharmacovigilance. Including – but not limited to – Regulatory Affairs, Quality Management, Compliance, Clinical Research, and, of course, Pharmacovigilance (PV).

PV may have once been considered a liability. However, an effective and sustainable PV is clearly an asset: Able to protect patient safety, hence allowing for appropriate life cycle management. Able to monitor and minimize drug risks, including off label use, hence significantly reducing liability risks. Able to provide expert input into labels and other publically available product information, hence training health care professionals and patients alike. Part of effective PV, and increasingly so since 2012, is a consistent PV Quality Management System, which is both sustainable and effective. This is a requirement, not an option. And it is tested thoroughly in PV inspections from regulators worldwide. An integral and essential part of that Quality Management System are PV audits, where all PV functions and many or most of the system components are checked. Thereby providing not only oversight (and insight) for the EU Qualified Person for Pharmacovigilance, but at the same time allowing for focus on the most essential changes that may be needed – as well as serving as an intense preparation for upcoming PV inspections.

COURSE LEADER



Dr Renald Hennig, MD, MBA, has more than 25 years of Pharmacovigilance experience – as well as even longer experience in conducting trainings, seminars, and workshops. He enjoys acting as a knowledge mediator.

He completed his medical degree in Hamburg, Germany, and originally worked in radiology and nuclear medicine, after which he started working for the pharmaceutical industry. His initial responsibility included training of sales reps (including preparation of the launch of a breakthrough drug), from which he went to Marketing and later to Pharmacovigilance. After holding global PV responsibility for a major company division for a number of years, he decided to change tracks. Since 2008 he is a Senior Consultant in his own company, co-owned with a colleague. SCRATCH has been serving as a PV service provider and provides consultancy and operational support in all areas of PV, including

QPPV services and PV audits. And yes, he has been PV inspected and audited several times.

He has written or co-authored Risk Management Plans and PV System Master Files, has been involved in recall and referral situations, tutored extensive 12 day PV training programs (Certified PV Manager, Frankfurt, Germany) – and has been trained in Training, Business Management and Coaching.

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