



Safety monitoring

Moderators: Dr Gugu Nolwandle Mahlangu, Zimbabwe, and Mr Benjamin Kwame Botwe, Ghana

The following presentations give an overview of discussions and recommendations of a pre-ICDRA satellite workshop on safety monitoring.

The impact of regulation on the safe use of drugs: overview of the Workshop

Dr Jürgen Beckmann, Germany

The whole system of pharmacovigilance begins with risk identification and assessment. Any drug then has to be evaluated in terms of its benefits against its risks, and in comparison with alternatives. These considerations eventually give rise to regulatory measures. Ideally, a feedback system should be linked to the initial stage to monitor the outcome and evaluate the effectiveness and appropriateness of the measures.

In exercising self-regulation, the pharmacovigilance officer should detect drug-related hazards, assess the risk, eliminate or reduce the hazard, inform health care professionals and consumers on the regulatory measures, and assess the outcome of the measures. Different sentinels and indicators should be devised and put in place in various sectors of the health care system to obtain feedback on the effects of the regulatory decision. Cooperation among drug regulatory authorities should be encouraged and enhanced, with WHO serving as a facilitator.

Moreover, regulators should give attention to improving their sources of information, the interaction among regulators, and the

quality of information exchanged, and consider particular difficult situations with which the feedback system might have to cope.

A number of measures to improve the feedback loop were discussed at the pre ICDRA workshop on The Impact of Regulation on the Safe Use of Drugs. These are:

- Improvement of regulators' sources of information.
- Improvement in mutual interaction between regulators.
- Improvement in quality of information exchanged.

Some examples of particularly difficult, though relevant, situations with which any feedback based system will have to cope were presented.

Sources of information for regulators

Dr Benjamin Kwame Botwe, Ghana

Countries should broaden safety monitoring to include medical devices, traditional medicines, homoeopathic medicines, natural health products, lifestyle drugs, rationality of drug use (medication error, poor dispensing practices), and drug quality defects, such as counterfeit drugs.

A multisectoral approach to safety monitoring should be encouraged. Industry, academia, other regulatory bodies, health care professionals, technical agencies such as drug information centres and poisons control centres, consumer groups and patient groups should be involved locally, while international partners, such as WHO/UMC, CIOMS, ICH and other national regulatory agencies should also be involved.

Countries should develop and institutionalize outcome evaluation, feedback mechanisms, appropriate monitoring mechanisms, and success indicators for safety intervention.

WHO, together with its Collaborating Centre for International Drug Monitoring, should develop guidelines and assist countries to develop systems for outcome evaluation.

Crisis, pressure and controversy

Dr Stewart Jessamine, New Zealand

Unexpected events that require major regulatory action include product failure, manufacturing error, media interest and overseas regulatory action. Advance planning for such crises is essential, to ensure that sufficient resources are available. Crisis management is multifactorial, and a team of people, each with designated activities, is needed. Advice should be based on the best evidence available; uncertainties and the limitations of information should be acknowledged if they exist, and risk should be placed in the appropriate context. If possible, advice should be sensible, practicable and implementable by health care professionals and consumers alike. Identify target audiences and deliver key messages that are clear, complete and action-oriented. Regulators should also assess the impact of actions and of the communication strategy.

WHO should finalize and distribute its crisis management plans to its Member States. Moreover, countries should develop crisis management plans and test them periodically. WHO should also provide technical assistance and resources in crisis management, communications and research to member countries to develop crisis management plans. Most crises arise from existing adverse reactions, and the seeds of future crises can often be found in the data provided for the premarketing evaluation. Regulators should therefore be encouraged to develop postmarketing risk management strategies for products identified at the time of initial evaluation as posing a significant risk. WHO (via the Uppsala Monitoring Centre) should help Member States to identify criteria that indicate a product is likely to pose a significant risk.

Improving international drug monitoring

Dr Suresh Kumar Gupta, India

There should be greater transparency in the sharing of concerns related to pharmacovigilance between countries. To this end:

- A secure web-based intranet system should be established that will provide information on case reports, clinical data, evidence and proceedings from regulatory decisions.

- WHO should facilitate the sharing of information between countries.
- Systems should be developed to ensure the confidentiality and integrity of shared data.
- Legislation should be enacted to address concerns about privacy and confidentiality.
- Member States should be encouraged to post information, such as regulatory decisions, as soon as possible and preferably before the information is made public.

The database housed in the WHO Collaborating Centre for International Drug Monitoring could be strengthened by the following actions:

- Reviewing the standardization of definitions, harmonization of terminologies and reporting schemes.
- Assigning unique case identifiers to eliminate duplication of reports.
- Advocating for regular and timely reporting of cases by national centres.
- Opening the database primarily to people with legitimate interests in promoting public health and competence in drug safety monitoring.
- Advocating for a global policy statement on the sharing of information on adverse drug reactions and the need for ADR monitoring to override privacy concerns when the public health interest is paramount.

Pharmacovigilance is a truly global activity both in its conduct and impact; WHO-agreed definitions, tools and practices should be regarded as the sole world standards. The current WHO Programme for International Drug Monitoring should be strengthened in its role as the mandated global pharmacovigilance system. All ICH member states should be encouraged to participate actively in the WHO

Programme, and contribute to its development. WHO should continue to review regularly the Programme's definitions, tools, and procedures in the light of developments in safety in medicine, and the work of other groups.

Recommendations

There have been major advances in the area of pharmacovigilance and drug monitoring since WHO established its Programme for International Drug Monitoring in 1968 as the global standard for drug safety. These recommendations highlight important issues for action by regulatory authorities and WHO.

1. Regulatory authorities should expand the scope of their activities to include surveillance of medication errors, medical devices, homeopathic products, herbal medicines, natural health products and identify reports that may point to quality defects or to counterfeit products.
2. Regulatory authorities should improve efforts to evaluate the effectiveness of the various reporting mechanisms in operation in their countries.
3. Regulatory authorities should improve communication of emerging safety concerns. To assist in this and to ensure that confidentiality and security of shared data is maintained, WHO should develop a secure web-based communication system.
4. Regulatory authorities should be encouraged to develop post-marketing risk management strategies for products identified as posing a significant risk.
5. WHO should finalize and distribute its crisis management plan to Member States. This should be tested periodically. WHO should provide professional assistance and resources in crisis management, communications and research to Member States.

6. The WHO adverse reactions database utility should be strengthened by:

- Use of best methods to ensure timely reporting to WHO of case information, and by taking steps to increase national reporting rates.
- Assigning unique case identification codes to avoid duplication to all case-report recipients.
- Opening access to the WHO database to all stakeholders with a genuine public health interest and the ability to evaluate such case information.

7. The current WHO Programme for International Drug Monitoring should be supported by:

- Encouraging all WHO Member States including ICH member countries to participate actively in the WHO Programme, and contribute to its development.
- Periodically and regularly reviewing definitions, tools, and procedures in the light of developments in safety in medicine.
- Strengthening WHO's role as the mandated global pharmacovigilance system and recognizing WHO definitions, tools and practices for pharmacovigilance and drug monitoring as world standards.

8. WHO should convene an expert group to examine the special needs for assessing the safety and risk of medicines used in the treatment of HIV/AIDS, particularly in developing countries.

9. Progress should be reported back to the ICDRA.