

**Recommendations from the second meeting of the
Advisory Committee on Safety of Medicinal Products
27-29 October 2004, WHO, Geneva**

The WHO Advisory Committee on Safety of Medicinal Products (ACSoMP), constituted to provide advice on pharmacovigilance policy and issues related to the safety and effectiveness of medicinal products, held its second meeting in October 2004. The following is a summary of the minutes.

New Priority Areas:

Patient Safety

The Advisory Committee participated through a videoconference link in the launch of the World Alliance for Patient Safety held in Washington on 27th October, 2004. Given that half of drug-related adverse events are potentially avoidable, and given the scarce resources, it is important to avoid duplicative efforts. The existing expertise in the WHO Programme for International Drug Monitoring should be used to advantage in furthering patient safety solutions. The Advisory Committee welcomes the initiative to create a World Alliance for Patient Safety. This committee will explore how it might contribute to the scientific endeavours of the Alliance including by (a) the use of pharmacovigilance centres for reporting medication errors; (b) working together with the Alliance to conduct research on the impact of safety measures; and (c) devising training programmes on the safe use of medicines for health care professionals.

Safety of drugs in children

The Advisory Committee considered the importance of addressing the issues around safe drug use in paediatric population, monitoring of off-label use in children, developing treatment guidelines, use of anti-infective and anticancer drugs and to make sure that even under urgent conditions, as in the HIV pandemic with increasing number of infected children, the paediatric treatment protocols are not developed without adequate data that justify those decisions. The committee advised that a position paper should be developed and discussed in detail at the next meeting. WHO should also discuss the issue of pharmacovigilance in paediatric populations at the forthcoming meeting of the International Conference on Harmonisation (ICH) in Yokohoma in November 2004.

Essential Drugs and the WHO Model List of Essential Medicines

The Advisory Committee sees great opportunity to contribute to the work of the Expert Committee on the Selection and Use of Essential Medicines, the secretariat of which is hosted in the Department of Essential Drugs and Medicines Policy:

(i) The Advisory Committee offers to review safety issues for new applications for products on the Essential Medicines List (EML) as submitted by the secretary of the Expert Committee. (ii) The Advisory Committee will prepare a short description of pharmacovigilance and a model report form to be included in the formulary. (iii) The Essential Drugs and Medicines Policy Department will include pharmacovigilance in the training programmes. (iv) Applicants for the EML will include data from the WHO Collaborating Centre for International Drug Monitoring in their applications. (v) National

Pharmacovigilance Centres will be encouraged to promote reporting of adverse reactions to new drugs used in public health programmes and included or considered for inclusion in national EMLs.

Pharmacovigilance Planning (ICH E2E Document)

The ICH E2E document was commended as being valuable for all countries. It was recommended that WHO should develop a guidance document on how best to benefit from E2E guideline in developing countries. The committee also recommended that ICH E2E should be promoted in pharmacovigilance training programmes.

Issues continued from first meeting

Chlorproguanil-dapsone (Lapdap)

The Advisory Committee expressed concern regarding the discrepancies in labeling of safety of Lapdap in the UK and African markets. This should be drawn to the attention of the regulators in endemic countries. The Advisory Committee wishes to receive a copy of the WHO review of Lapdap safety, when it is available (even if that availability is for limited distribution only) and will decide on further action after receipt of the above report.

Pharmacovigilance for antiretrovirals

The Advisory Committee was updated on the progress of the '3 by 5' initiative and noted with satisfaction that pharmacovigilance is now recognized as important to the WHO HIV/AIDS Programme. It also noted the report on the training course for introducing pharmacovigilance into HIV/AIDS programmes. The following recommendations were made: (i) The need for training is reiterated to meet the pharmacovigilance requirements of the 3 by 5 initiative. A global vision for pharmacovigilance in training courses should be developed. (ii) Funding should be earmarked for pharmacovigilance activities, being a distinct part of the 3 by 5 related activities, and the Quality and Safety of Medicines (QSM) team needs to pursue that within WHO with the team in the HIV/AIDS Department of Treatment and Prevention Scale-up.

(iii) The national pharmacovigilance centres need to be adequately financed from the national treatment programme(s). (iv) There is a need for a dedicated budget in WHO/QSM for pharmacovigilance, that includes training and capacity building. (v) WHO should develop algorithms for treatment of adverse drug reactions associated with antiretroviral drug use.

Advocacy Document

The Advisory Committee noted the draft advocacy document and recommended that it should be finalized and circulated to the members of the committee. The committee recommends engagement of professional writers to assist with the advocacy document. However, recognizing the resource limitations for this purpose a request might be put to the World Alliance on Patient Safety; this would be in line with the objectives of the Alliance.

Pharmacovigilance in Public Health

The Advisory Committee noted that this manuscript was almost ready for publication. Final editorial changes will be made by the end of the year. A section will be added on “Where there is no pharmacovigilance centre”, with recommendations as to how countries might establish centres where they presently do not exist. The Advisory Committee does not identify further issues of commission or omission in the document

Reports from other WHO Programmes

Malaria

The Advisory Committee noted the report from the WHO consultant to the malaria programme on the progress made in introducing pharmacovigilance to malaria control programmes. They advised that there is a need to look at specific and at-risk populations, for example pregnancy, for all antimalarials. The malaria programme is also seeking assistance with the establishment, maintenance and analysis of the national pharmacovigilance data bases. The Committee will look into the matter.

Herbal Medicines

The Advisory Committee noted the recently issued guidelines for safety monitoring of herbal medicines, "WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems". They noted also the plans for inaugurating training programmes on how to set up a herbal medicines and traditional medicines safety programme.

Poisons

The Advisory Committee noted the recent developments in the International Programme for Chemical Safety in WHO which deals with poisons centre development and use of pesticides. The group has developed a manual for development of new poisons centres in the African region. A data management system INTOX has been developed. There is overlap in toxicovigilance and pharmacovigilance activities, something that particularly happens in the developing world. For the present, reports are not coordinated between respective centres. Collaboration between the centres for pharmacovigilance and the poisons centres is needed for this to happen.

Reproductive Health

The Advisory Committee was informed of the Continuous Identification of Research Evidence (CIRE) system which was developed in partnership between the WHO Collaborating Centre in Reproductive Health at the US Centers for Disease Control and Prevention (CDC) and the INFO Project at the Johns Hopkins Bloomberg School of Public Health's Center for Communication Programs (CCP) and WHO's Department of Reproductive Health and Research. The system identifies articles whose study objectives concern a topic addressed by WHO's Medical Eligibility Criteria for Contraceptive Use (MEC) or the Selected Practice Recommendations for Contraceptive Use (SPR). These articles are then reviewed to determine whether the evidence they provide is relevant to WHO guidance. Any updates to current guidance based on evidence from the CIRE system are noted on the electronic versions of the MEC or SPR.

Vaccines

The Advisory Committee noted the work and modus operandi of the WHO Global Advisory Committee on Vaccine Safety (GCVS), and considered the issues and operations of common interest. It was in particular noted that the GCVS meets twice a year, and has a budget of approximately 600 000 USD per biennium.

Specific Issues

Kava kava

The Advisory Committee resolved to commission an inquiry consisting of 3 persons, one of whom should be a member of the committee who should chair the inquiry; to consider all available information, published and unpublished, taking into account all relevant regulatory decisions and the basis for such decisions; the inquiry to report within 4 months. The membership of the committee would be decided by the chair of the Advisory Committee in consultation with the secretariat. The terms of reference would be finalized by the chair of the Advisory Committee together with the secretariat. The principal focus of the inquiry will be on the safety of kava.

Tenofovir

It was noted that the major toxicity of this medicine is renal. The drug also induces significant decrease in bone mineral density. The effect on the skeleton of children is not known and the data are awaited. The drug is also potentially hepatotoxic. A report will be prepared for the Expert Committee on the Selection and Use of Essential Medicines.

Emtricitabine

The consumption of this drug has been very low (and thus also the safety reports have been few in number). An emerging picture is available, that may be inadequate for the purpose of the Expert Committee on the Selection and Use of Essential Medicines. A report will be prepared and sent to the secretary of this Expert Committee.

Paracetamol/dextropropoxyphene (Co-proxamol)

It was noted that the UK relevant authorities are considering either curtailing the dose and use or discontinuing this drug. There is no good evidence of efficacy, but there are considerable safety issues including especially overdose, that includes cardiotoxicity. Many of the overdoses are unintentional. Sweden has controlled dextropropoxyphene and there does not appear to have been any obvious change in the safety profile of the drug. There is an indication of a long standing safety problem with the drug concerned and members of the Advisory Committee will inform the Medicines and Healthcare Products Agency (MHRA) of any further information that might add to the UK consideration of the safety of this combination analgesic drug. It was agreed that an article should be written on the topic for publication in the WHO Drug Information Journal.

Iron Dextran

The national pharmacovigilance centre in Sri Lanka requested the views of ACSoMP on iron dextran vs iron sucrose. The Advisory Committee noted the report prepared by one of the members of the Advisory Committee and agreed with the conclusion. In the absence of head-to-head comparative clinical trials it cannot be stated with confidence that iron sucrose (or any other formulation of iron for intravenous administration) is clearly safer than iron dextran. Comparisons of the safety of iron dextran for intravenous administration with other iron formulations do not allow of a clear recommendation in favour of iron sucrose versus iron dextran. The Sri Lankan national pharmacovigilance centre will be advised accordingly.

Polygeline and hetastarch

In 2003, the Ministry of Health, Sri Lanka received complaints from consultant anaesthetists in three teaching hospitals that they have noticed an increased number of anaphylaxis associated with the use of polygeline. Sri Lankan national pharmacovigilance Centre requested the ACSoMP to look into the matter. The Advisory Committee noted that the case descriptions and the investigation of the cases are insufficient for the committee to make a recommendation. An analysis of the literature does not enable the committee to advise the country further on its dilemma. The national pharmacovigilance centre of Sri Lanka will be advised accordingly.