EDITORIAL

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African Heat

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It is common for Northern Europeans and North Americans to seek warmer climates in the autumn, but for anyone interested in pharmacovigilance the 'hottest' location was certainly Accra, Ghana. Within the University of Ghana Medical School, the Uppsala Monitoring Centre (UMC)-Africa and the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance have not only been in operation for about 1 year but Accra was also the location for the WHO Programme for International Drug Monitoring Annual Centres Meeting (31 October–3 November), as well as the 10th International Society of Pharmacovigilance (IsoP) Annual Meeting (3–6 November). The two meetings were therefore back-to-back with a joint meeting day.

The agendas of the meetings give some insight into their current relevance and to the current state of pharmacovigilance in sub-Saharan Africa and resource-poor settings in general.

1. Forging Ahead in Africa

One of the most exciting general pharmacovigilance happenings to report from Accra is the rapid progress of UMC-Africa.

For the last 4 years a WHO project to train-the-trainers has brought together senior health professionals with a keen interest in pharmacovigilance from about 20 African countries. At the most recent workshop for this group in Togo, in September 2010, the group affirmed their support for the WHO-UMC Centre in Accra, and also proposed that a future structure should be an African free-standing, self-sustaining network coordinated from Accra. Such a proposal from a group of senior African pharmacovigilance experts should go a long way to provide assurance to donor organizations that pharmacovigilance in Africa is a serious public health consideration, which has serious support from high-level professionals and policy makers.

A consequence of this is that those involved in drug donations to Africa should include public health outcome measures for *both* effectiveness *and* safety, which must be considered by, and made relevant to, the work in each of the existing national pharmacovigilance programmes. The new African network has already contributed new ideas and approaches to global pharmacovigilance, being at the fore of patient safety development, widening the scope of pharmacovigilance in general and in taking active communication to the public seriously. I expect that the network will continue to thrive and develop as an independent group. It will certainly be supported in doing so by the UMC and WHO, and I hope others will also help UMC- and WHO-Africa to do their job, whilst respecting their national and regional autonomy. Africa cannot afford to add a load of iatrogenic harm to its other disease burdens.

1.1 Pharmacovigilance Toolkit

This is an early success of UMC-Africa and is a compilation of information, tools and resources for those working in pharmacovigilance that is planned to be available on the Internet by the year's end. It will ultimately have a hierarchical structure, to allow the user to dig down as more detail is added. It will also be available in other formats such as DVD. This is an exciting development and will provide pharmacovigilance practitioners across the world with easy tools, software, standard operating procedures, templates and

PDFs of useful publications to ensure that their practice is not unnecessarily hampered. It will also promote standardization in practice in line with the minimum requirement concepts of WHO, the Global Fund and other Global Health Initiatives who are funding the development and maintenance of the Pharmacovigilance Toolkit.

2. WHO Annual Meeting

It was the 33rd Annual Meeting of Representatives of the National Centres participating in the WHO Programme for International Drug Monitoring. As usual the agenda was largely built around requests from Programme members. On this occasion the meeting was effectively prefaced by a longer term Global Strategy proposal that has been initiated by WHO-HQ, endorsed by the Advisory Committee on Safety of Medicinal Products (ACSoMP) and will integrate with the UMC's 4-year planning cycle.

Once the suggestions of the meeting are incorporated, the Strategy will be available to a wider audience.

Several other topics of the meeting reflected emerging issues with strategic impact. Some of these were:

- ADR reporting directly from the public: a discussion of different approaches that are being used or considered. This is also linked to different views on the impact of such reports that represent different views of drug safety concerns, and also give new slants on patient safety matters, particularly how drugs are used and the qualitative impact on patients' lives.
- The new pharmacovigilance legislation for the EU, which will once again shift the direction of pharmacovigilance not only in the EU, but in all countries as they consider the new proposals.
- There were working groups on:
  (1) The role of pharmacovigilance centres in preventing medication errors. This relates to consumer reporting, but is also a necessary widening of the focus of pharmacovigilance. Some say that this is not the purpose of pharmacovigilance, but it seems absurd to introduce separate bodies for this in resource-poor countries when pharmacovigilance already has a major goal to improve the safety of therapy. Not all countries either want, or can afford, separate medication error monitoring and prevention groups, and some developed countries are even now beginning to re-examine the positioning of their patient safety agencies.
  (2) How to improve the quality of individual case harm reports (ICHR) [a more accurate term for the recently accepted individual case safety reports (ICSR), since the content is about harm, not safety]. We know we do not always receive good quality information on ICHRs, but it really is time to revisit the topic in the light of consumer reporting and patient safety. The promotion of pharmacovigilance to the public (see the 'How to improve awareness of drug safety issues' workshop mentioned below, as well as the session on communication held at the ISoP meeting) so that they know what we do and understand their opportunity, and indeed responsibility, to further drug safety seems to be linked to this topic.
  (3) Establishing new pharmacovigilance centres: the difficulties and solutions, a particularly important topic for the Programme now that there are 101 full members and over 30 associate members. Indeed a true problem of success!
  (4) Adverse effects following immunization (AEFIs) and the challenges of causality assessment and signal detection of such events. This is a frequently mentioned challenge, given the greater rarity of harm from vaccination, the more universal coverage and therefore difficulties in carrying out controlled investigations of harms, and the persistence of at least some of their effects.

Both strategic and technical issues were raised in an area of growing challenge in a session on methods supporting pharmacovigilance in public health programmes. In the areas of malaria, HIV/AIDS, tuberculosis, infestations and more to come, the monitoring of both effectiveness and risk when very large numbers of people are exposed to new drugs or therapeutic approaches – often in resource-poor settings – is an urgent and difficult challenge. Data must be collected over long periods in sustainable programmes that also consume resources. Cohort event monitoring (CEM) seems to be currently

the best compromise for such monitoring and the CemFlow software developed by WHO-UMC and piloted already in two sub-Saharan African countries will hopefully aid this work. This topic was continued in the Joint WHO-ISoP session described below.

The National Centres' meeting also considered new approaches to signal detection being developed by the UMC. The discussion covered the use of VigiBase (the WHO global database) for region- or therapy-specific drug safety issues. Another important new development reviewed was the use of electronic patient health records for medicine safety signal detection and follow-up.

Lessons learned from the influenza A (H1N1) pandemic were considered and shared in another plenary session.

Finally, a number of frequent safety concerns were considered in working groups. These were:

- optimizing pharmacovigilance activities to fight substandard and counterfeit medicines;
- building human resource capacity for pharmacovigilance;
- how to improve awareness of drug safety issues: 'social marketing' of pharmacovigilance;
- good practice for pharmacovigilance inspections/assessments.

3. Joint WHO-ISoP Meeting

Three key questions were posed in this meeting: Will Global Health Initiatives fund the establishment of pharmacovigilance systems in resource-limited countries? Integration of pharmacovigilance in Public Health Programmes – can this leverage the necessary financial resources for pharmacovigilance? Can the world afford not to have robust safety monitoring systems everywhere?

The challenges of pharmacovigilance in public health programmes are those of motivation. The main drive of public health programmes has been to deliver drugs to those who need them: a major set of logistic problems in resource-poor countries lacking infrastructure. For diseases such as malaria, the new drug combinations, artemisinin-combination therapies (ACT), have been untested in widespread human use. The pharmacovigilance challenge here is to assess short-term safety of such drugs, which will be mostly used as self-medications as most countries would invariably license them for over-the-counter sale.

Very different is the long-term monitored use of antiretroviral therapies for HIV/AIDS which require long-term monitoring of effectiveness and harms in a different socioeconomic and disease setting compared with their use in the US and European settings. Much experience is available from developed countries, but their use in resource-poor countries involves interactions with other endemic diseases such as malaria and tuberculosis and the drugs used to treat them, let alone the complications of widespread anaemia, malnutrition and the frequent challenges of mother-to-child transmission of HIV, necessitating the use of antiretroviral drugs in children either for prophylaxis against transmission or for management of HIV where it has been transmitted. For both HIV and tuberculosis, the follow-up of patients is challenging where trained health professionals are relatively few and under great time pressure, as well as lacking diagnostic support tools. My understanding is that dropout rates from HIV treatment are high and that follow-up of dropouts is almost impossible. In such settings the burden of recording and collating suspected harm from drugs or collecting new clinical events for analysis is thought by some as being a step too far, impractical and causing more damage than good. On the other hand, without a sufficient system of healthcare that records and monitors the good and bad outcomes of treatment, how can we argue that we do anything other than satisfy our consciences being self-congratulatory over mere delivery of drugs?

It is more than reasonable for donor organizations to express concerns at adding the cost of healthcare delivery and pharmacovigilance to their financial generosity, not to mention the need for 'exit strategies'. Those are weighty matters, but the economic priority dilemmas for the national recipients of donations are also clear. With all this in mind, it is especially pleasing that the debate over public health effectiveness and risk is now to the front of many donors' strategies and that many minds are considering the best ways forward.

The WHO and UMC have proposed, and are pilot testing, one possible method for monitoring effectiveness and harm, CEM, mentioned above. This is probably the simplest strategy to gain benefit-risk information other than spontaneous reporting which, alone, is not enough. Two issues have arisen from discussions around the pilot: one is the time necessary in the clinics to record the data and the other is to reach agreements over pooling data. These challenges must be resolved, and will be! Other partial answers seem to be the addition of more focused cohort studies and monitoring at sentinel sites or demography surveillance sites where more data collection is feasible.

3.1 Special Pharmacovigilance Stakeholders' Meeting

A special pharmacovigilance stakeholders' meeting, organized mainly by WHO and the Global Fund, involving several pharmacovigilance experts, public health programme specialists, regulators, donors, the pharmaceutical industry and global programmes members, effectively continued the discussion. This discussion was more specifically around a pharmacovigilance strategy document produced by the Global Fund and WHO as part of the Global Health Initiative. This 1-day pragmatic meeting allowed all the major stakeholders present to examine and identify with a robust strategy for pharmacovigilance in public health, and this is a good start for truly coherent progress.

4. ISoP Meeting

The theme of the meeting, 'Pharmacovigilance in a Global Village', was introduced by the ISoP President, Dr Alex Dodoo, and closely followed by the first related keynote speech which posed a question, 'how does one ensure safety during mass, rapid deployment of medicines?'

This beginning related to several global safety challenges as subjects of presentations and debate. Vaccine safety has been highlighted in the last year because of the challenges of monitoring the influenza A (H1N1) pandemic, which thankfully never became a major public health issue. Nevertheless, many countries contributed important study information on what monitoring was done in their countries, with presentations from four different country settings as well as a global overview from WHO-UMC. Thankfully, few serious suspected adverse reactions have been reported, but final analysis is still being undertaken; it is a reminder that predicting potential harm from a pandemic is very difficult and must be considered against potential benefit and harm from prophylaxis either by vaccines or by antiviral drugs.

The topic of ecopharmacology has been on the table for many years and there are now regulations in some countries relating to the potential for drug residues and metabolites to damage ecosystems. But what happens if the drugs or metabolites recycle to animals and humans? Eco-pharmacovigilance was a session in the meeting, and should be part of our concerns, even though the effects are more distant from the causes than usual. I think the challenge is going to be a further extension of the current problem of pharmacovigilance; how much will society pay for apparently rare or remote harm?

As mentioned above, safety of medicines for HIV, tuberculosis and malaria is a challenge related to massive roll-out campaigns, and which is in part due to their success. International aid organizations, in particular the Global Fund against HIV/AIDS, Tuberculosis and Malaria, have funded older and novel interventions for these diseases, but even the more tried medicines may not have been previously used in recipient countries, some of whom may have different disease burdens, nutritional status, drug phenotypes and healthcare systems. Though these organizations have encouraged countries to apply for financial support to undertake pharmacovigilance, it seems only a few countries are applying. This is worrying: one needs only to think that many people receiving treatment with antiretrovirals may need management for malaria and tuberculosis also and the high number of possible adverse events becomes apparent. This use of medicines mandates careful benefit-risk monitoring: success is not just getting the drugs out there, it is to know how many truly benefit from them and how many are harmed.

There was a session each on pharmacovigilance experience in North America, Latin and South America, and in the Western Pacific regions.

What might be preventable was a focus in both sessions, with discussions on risk management as well as common preventable problems such as hyponatraemia, interactions and allergies (at least preventable re-exposures!). Linked to the issue of preventable adverse reactions was a session on patient safety, which again focused on preventability, again a global challenge.

Risk management and developments in epidemiology were keynote topics. These were linked to a session on meeting EU regulatory expectations in pharmacovigilance. As mentioned above, the rapid development of EU regulations will affect all in the global village.

Language can often be a barrier in large meetings, often held in English, but this meeting bore in mind the wide use of French in Africa with a specific session, '*Pharmacovigilance à la carte*', delivered completely in French by speakers from around the world. There was also an interactive debating session on communication in drug safety, also underlining the general need for those in pharmacovigilance to take this topic very seriously. This links to the ongoing difficulty of obtaining enough sustainable funding for pharmacovigilance, a topic that was also on the meeting agenda.

Two separate sessions dealt with an old but continuing challenge – signal detection – and one on future thinking and perspectives in pharmacovigilance.

A final keynote speech explored some possibilities for further international cooperation in global pharmacovigilance, but the last seminar of the meeting was on the topic of 'Forensic Pharmacovigilance' – an exciting and provocative angle on pharmacovigilance and the law.

Three-day ISoP training sessions on 'Basic Concepts', in separate English and French sessions, and also on the 'Principles of Risk Management' followed the meeting.

The feverish activity within meetings lasted a few short days, and we left with good memories of warm, wonderful Ghanaian hospitality and balmy, tropical evenings.

5. Further Information

Further details of the meetings will be available on the following websites in the coming months:

- www.isoponline.org
- http://www.who.int/medicines/publications/newsletter/PharmNewsletter
- http://www.who-umc.org/DynPage.aspx?id=13136&mn=1512#11
- http://adisonline.com/drugsafety/Citation/2010/33100/ABSTRACTS__10th_ISoP_Annual_Meeting.9.aspx

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