Report of the third meeting of the Steering Committee on Immunization Safety

Geneva, 10–12 June 2002

Immunization Safety Priority Project
Vaccines and Biologicals
World Health Organization
Acknowledgements

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The Immunization Safety Priority Project would appreciate being informed of activities related to its mission and to learn of individual or institutional interest in collaborating with the Project.

Visit our web page: http://www.who.int/vaccines-surveillance/ISPP/Index.shtml
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<tr>
<td>AD</td>
<td>auto-disable (syringes)</td>
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<tr>
<td>ADC</td>
<td>accelerated disease control</td>
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<td>AEFI</td>
<td>adverse events following immunization</td>
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<td>AFR</td>
<td>African Region</td>
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<td>ATT</td>
<td>Access to Technologies (WHO/V&amp;B)</td>
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<td>BASICS</td>
<td>Basic Support for Institutionalizing Child Survival</td>
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<tr>
<td>BCT</td>
<td>Department of Blood Safety and Clinical Technology (WHO)</td>
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<td>BSE</td>
<td>bovine spongiform encephalopathy</td>
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<td>CEE</td>
<td>Central and Eastern Europe</td>
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<td>CD</td>
<td>communicable disease</td>
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<td>CDC</td>
<td>Centers for Disease Control and Prevention (USA)</td>
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<td>CVP</td>
<td>Children’s Vaccine Programme</td>
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<td>DTP</td>
<td>diphtheria–tetanus–pertussis vaccine</td>
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<td>EDM</td>
<td>Department of Essential Drugs and Medicines (WHO)</td>
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<td>EDL</td>
<td>Essential Drugs List</td>
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<td>ECBS</td>
<td>Expert Committee on Biological Standardization</td>
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<td>EIP</td>
<td>Evidence and Information for Policy cluster (WHO)</td>
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<td>EMR</td>
<td>Eastern Mediterranean Region</td>
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<td>EMRO</td>
<td>WHO Regional Office for the Eastern Mediterranean</td>
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<td>ESAR</td>
<td>Eastern and Southern Africa Region</td>
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<td>EUR</td>
<td>European Region</td>
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<td>FDA</td>
<td>US Food and Drug Administration</td>
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<td>GAVI</td>
<td>Global Alliance for Vaccines and Immunization</td>
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<td>GMP</td>
<td>good manufacturing practice</td>
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<td>GNP</td>
<td>gross national product</td>
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<td>GTN</td>
<td>Global Training Network</td>
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<td>HTP</td>
<td>Health Technology and Pharmaceuticals cluster (WHO)</td>
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<td>HPV</td>
<td>human papillomavirus</td>
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<td>ICC</td>
<td>interagency coordinating committee</td>
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<td>ICN</td>
<td>International Council of Nurses</td>
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<td>IEC</td>
<td>Information, Education and Communication</td>
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<td>ISO</td>
<td>International Organisation for Standardisation</td>
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<td>Abbreviation</td>
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<td>ISPP</td>
<td>Immunization Safety Priority Project</td>
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<td>ISSC</td>
<td>Steering committee on Immunization Safety</td>
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<td>IVR</td>
<td>Initiative for Vaccine Research</td>
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<td>JE</td>
<td>Japanese encephalitis</td>
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<td>JRF</td>
<td>Joint Reporting Form</td>
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<tr>
<td>KAP</td>
<td>knowledge, attitudes and practices (studies)</td>
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<td>MoH</td>
<td>Ministry of Health</td>
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<td>MMF</td>
<td>macrophagic myofasciitis</td>
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<td>MMR</td>
<td>measles–mumps–rubella</td>
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<td>MNT</td>
<td>maternal and neonatal tetanus</td>
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<td>MS</td>
<td>multiple sclerosis</td>
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<td>NAPIC</td>
<td>National Plan of Action for Injection Control</td>
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<td>NA-DFC</td>
<td>National Agency for Food and Drug Control</td>
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<tr>
<td>NDC</td>
<td>nondeveloped countries</td>
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<tr>
<td>NIS</td>
<td>newly Independent States</td>
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<td>NGO</td>
<td>nongovernmental organizations</td>
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<td>NRA</td>
<td>national regulatory authority</td>
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<td>PATH</td>
<td>Program for Appropriate Technologies in Health</td>
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<td>PEI</td>
<td>Polio Eradication Initiative</td>
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<tr>
<td>R&amp;D</td>
<td>research and development</td>
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<td>RWG</td>
<td>regional working group</td>
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<td>SAGE</td>
<td>Strategic Advisory Group of Experts</td>
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<tr>
<td>SEAR</td>
<td>South-East Asia Region</td>
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<td>SEARO</td>
<td>WHO Regional Office for South-East Asia</td>
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<td>SIA</td>
<td>supplementary immunization activities</td>
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<td>SIGN</td>
<td>Safe Injection Global Network</td>
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<td>TDR</td>
<td>Special Programme for Research and Training in Tropical Diseases</td>
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<td>TGA</td>
<td>Therapeutic Goods Administration</td>
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<tr>
<td>TSE</td>
<td>transmissible spongiform encephalopathies</td>
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<tr>
<td>TST</td>
<td>temperature, steam, time</td>
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<td>TT</td>
<td>tetanus toxoid</td>
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<tr>
<td>VAR</td>
<td>vaccine arrival report</td>
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<tr>
<td>V&amp;B</td>
<td>Department of Vaccines and Biologicals (WHO)</td>
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<tr>
<td>VVM</td>
<td>vaccine vial monitors</td>
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<tr>
<td>WHA</td>
<td>World Health Assembly</td>
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<td>WHPA</td>
<td>World Health Professions Alliance</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WMA</td>
<td>World Medical Association</td>
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<tr>
<td>WMC</td>
<td>WHO Mediterranean Centre for Vulnerability Reduction</td>
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<tr>
<td>WPR</td>
<td>Western Pacific Region</td>
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<tr>
<td>WPRO</td>
<td>WHO Regional Office for the Western Pacific</td>
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The deliberations

The third meeting of the Steering Committee on Immunization Safety (ISSC) was held at WHO Headquarters, Geneva, from 10–12 June 2002. Progress made since the last meeting, held in October 2000, was reviewed and challenges currently facing the global implementation of immunization safety issues were considered.

Committee members, associate members and WHO regional and headquarters’ staff participated in the meeting.

Committee members noted the contribution by all partners to the progress made in immunization safety in the past 18 months and the increasing availability of auto-disable (AD) syringes. The Committee expects that the majority of target countries will be using AD syringes by the end of 2002. Progress highlighted included:

- the institution of injection safety support by the Vaccine Fund for a period of three years for countries with approved applications for other support through the Vaccine Fund;
- the technical support provided by the Global Alliance for Vaccines and Immunization (GAVI) regional working groups for preparation of injection safety plans;
- the use of accelerated disease control campaigns (measles and tetanus toxoid) to improve immunization safety and safe waste disposal; and
- the adoption of immunization safety as a core focus area for the Communications Unit in the UNICEF medium-term strategic plan.

The Committee also noted the following:

- that all partners need to recognize the importance of both immunization safety and coverage;
- that the infrastructure for the Polio Eradication Initiative (PEI) presents an opportunity for training of polio staff for planning, implementation and monitoring of safety issues;
- that the current revision of materials and training (mid-level management, immunization practice, etc.) offers an opportunity to emphasize safety issues; and
- that the adoption of a resolution on “Quality of care: Patient Safety” at the Fifty-fifth World Health Assembly can be used as an advocacy tool to improve safety.
The Secretariat presented the new 2002–2005 Strategic Plan for the Immunization Safety Priority Project (ISPP) to the Committee for review. The Committee took note of the expected result of the Plan which is to provide adequate support to priority countries to enable them to build a comprehensive system to ensure immunization safety.

Members agreed that remarkable progress had been made by all WHO regional offices in the development of strategic plans, organization of national injection safety assessments and support of countries in vaccine safety, monitoring of adverse events following immunization (AEFIs) and safe waste disposal.

In relation to GAVI, it was strongly recommended that eligibility for immunization safety support be extended to those countries that are eligible in terms of gross national product (GNP) but do not have approved applications for other types of support. It was also recommended that the Vaccine Fund consider extending injection safety support from three to five years.

All participants agreed that countries should be provided with technical assistance for the preparation of injection safety plans to encourage requests for GAVI support on safety-related issues. With regard to safe and efficient vaccine administration and disposal, Committee members noted that most of the country injection safety assessments showed that patients, health workers and the community are generally at risk. Because of this risk and the future unavailability of sterilizable equipment, countries using sterilizable syringes should be encouraged to switch over to AD syringes. The practice in some countries of disinfection of used syringes before disposal is a dangerous one, particularly as it increases the risk of needle-stick injuries for the health worker, and it should be discouraged. Countries receiving GAVI support for immunization should be encouraged to use these funds to meet the price differential between disposable and sterilizable syringes and AD syringes to ensure the financial sustainability of injection safety support. This would not only prolong the GAVI support period but also ensure the retention of funds in national budgets required for long-term financial sustainability.

Two-handed recapping of syringes - a practice which leads to a high rate of needle-stick injury - was noted from all regional reports. The Committee agreed that re-training of staff, on-site supervision of peripheral staff and marketing of safety to both health workers and the community are some of the strategies which can be used to address safety.

An integrated approach involving other programmes in the Ministry of Health (HIV/AIDS, essential drugs, clinical care, etc.) with clear delineation of roles is needed for the management of safety. Professional assistance should be sought to develop a promotion strategy based on local sociocultural practices for an effective communication campaign.

There is a need to increase country capacity in identifying and responding to risks attributable to injections for immunization. More investment is needed to develop needle-free technologies to lower risks for patients and health workers alike.
The use of appropriate incinerators has increased in all regions. Some of the challenges faced by countries include inadequate financial resources for the construction of incinerators nationwide and transportation of used injection equipment to incinerator sites. WHO regional offices should encourage sharing of success stories between countries on management of health waste. Further research is needed on cost-effective, environmentally friendly disposal of injection waste in countries.

The Committee noted that vaccine safety should be assured not only through quality control procedures but also through safety evaluation in preclinical and clinical trials and post-marketing surveillance.

All countries should ensure that an independent and fully functional national regulatory authority (NRA) is in place for monitoring vaccine quality appropriate to the source of vaccine supplied. Members noted with satisfaction the progress made by the Secretariat on NRA assessments and other follow-up activities. The weakest NRA function identified was clinical evaluation of safety and efficacy. Considerable efforts to provide NRAs with appropriate documentation to guide them in this area - for example, WHO guidelines for the clinical evaluation of vaccines: regulatory expectations - have been made. All WHO regional offices should support NRA networks for the exchange of information and assist countries with improving their regulatory functions. At country level, procedures to ensure completion of the Vaccine Arrival Report (a tool for assuring the quality of vaccines at the point of delivery) need to be put in place.

The Committee also noted that political commitment is needed for immunization services to work together with NRAs for the establishment of AEFI monitoring systems. It was noted that, while WHO provides professional expertise and liaises with manufacturers, NRAs and UNICEF for the investigation of AEFIs, more training on AEFIs is needed for health workers, NRA staff and the media. Training on AEFI reporting and preliminary investigation should also be organized for service delivery staff. The private sector should be included in reporting of cases. Countries should adopt global guidelines on AEFI for their own use. Members agreed that a good AEFI surveillance system helps to counter arguments from the anti-immunization lobby. Capacity building is needed in countries for investigation of AEFIs.

In the area of research, new approaches for vaccine delivery are being explored. Activities leading to safer and simplified delivery are seen as the priority. Examples include heat stabilization of vaccines and needle-free delivery systems. Priority research areas include mucosal vaccination (aerosol measles). The GAVI research and development (R&D) Task Force is focusing on pneumococcus, rotavirus and meningococcus vaccine development, use of sugar-dried vaccines and devices to safely remove or store needles after use.

A report on activities of the Global Advisory Committee on Vaccine Safety was presented at the meeting. The Committee would, at its next meeting, examine the latest issues on the safety of thiomersal, as well as possible links between hepatitis B vaccine and leukaemia, hepatitis B vaccine and multiple sclerosis, measles–mumps–rubella (MMR) vaccine and autism, diphtheria–tetanus–pertussis (DTP) vaccine and child survival, and Bell palsy following intranasal influenza vaccine.
The Committee initiated discussion on the issue of more closely integrating priority project activities into the core functions of the teams within V&B (mainstreaming). Members agreed that early integration might lead to potential reduction in the gains made by the project in highlighting safety issues.

It was agreed that the Committee would define criteria for the mainstreaming of the project at its 2003 meeting.

The meeting was considered successful as it resulted in frank and useful discussion between participants on key issues needed to improve immunization safety. The priority project has raised the visibility of safety and put it in its rightful place, to be considered equally with immunization coverage issues.

Recommendations

GAVI and the Vaccine Fund

The Steering Committee noted the tremendous impact GAVI has had on injection safety through increasing content of injection safety issues on the GAVI application form and the institution of financial support for countries without approved applications for other types of support. It recommended the following:

- facilitation/acceleration of the uptake of available safety support by providing technical support to countries through the regional working groups;
- broadening of GAVI qualification criteria to allow injection safety support to all GAVI-eligible countries, including countries without approved applications for other types of support;
- that, in view of the increasing need for safe disposal of used injection equipment and the concern about release of dioxins and other harmful substances into the environment by current incineration technology, GAVI take the lead in R&D funding for safer sharps waste management technologies than currently exist; and
- that support for injection safety be increased from three to five years to provide countries with a longer transition period for securing resources for the procurement of AD syringes.

NRA strengthening

Much progress has been made since the establishment of the Committee in capacity development and assessment of NRAs.

It was recommended that:

- countries receiving support from the GAVI Fund consider using funds received through this mechanism to strengthen NRAs;
- WHO continue strengthening NRAs through training and consultancies such that the NRAs have the capacity to investigate AEFIs and take proper regulatory action; and
- collaboration between NRAs and immunization services be reinforced.
Programmatic issues

The integration of management of injection waste into accelerated disease control initiatives and the gains made so far were commended. The Committee recommended that WHO:

- explore ways to make use of the infrastructure built for the Polio Eradication Initiative (need to train polio staff on safety issues);
- further integrate immunization safety into other accelerated disease control initiatives such as those of measles and tetanus;
- ensure training on safety of staff at all levels;
- endorse the use of incinerators as currently the best available solution for waste disposal; and
- continue research into alternative cost-effective, environmentally-friendly methods of disposal of injection waste.

Communication and advocacy

The use of programme communication, advocacy and social mobilization in immunization is not new. Immunization services need to work with other programmes, e.g. HIV/AIDS and clinical or curative care, to use appropriate communication strategies for immunization safety. The Committee recommended the following:

- promoting immunization safety with health workers and the community, using public concern about HIV/AIDS transmission as a lever, emphasizing the personal benefit that health workers will gain from increased safety, and adapting the communication strategy to the sociocultural setting;
- strengthening communication and advocacy activities by recruiting expertise for communication campaigns;
- strengthening capacity of interagency coordinating committees (ICCs) to address immunization safety;
- emphasizing immunization safety in WHO regional, intercountry and country meetings; and
- capitalizing on the World Health Assembly (WHA) resolution on patient safety to raise awareness on immunization safety issues.
1. Opening remarks

Dr Daniel Tarantola, Director, Department of Vaccines and Biologicals (V&B)

Dr Tarantola in his opening address to the ISSC meeting emphasized that the occasion represented a great opportunity to reflect on many issues that are changing the face of immunization.

He said the meeting coincided with a number of other meetings in the sphere of immunization, including one on vaccine research, which had brought many very dedicated people to Geneva.

Dr Tarantola reminded delegates that this was his first Steering Committee meeting as Director and successor to Dr Bjorn Melgaard. He extended thanks to: the Chair; WHO colleagues; members who had accepted a second two-year term; and the new members, Dr Robert Hall from Australia and Dr Mercy Essel Ahun from Ghana. He thanked Dr Liz Miller who had served a term and had had to step down due to workload, and expressed regret that members Ms Mavis Nxumalo, Mr Greg Sam and Dr Stefania Salmaso were unable to attend. Dr Nxumalo was currently orchestrating a mass measles campaign in the United Republic of Tanzania and assured the meeting that the safety aspects of that campaign would be well looked after.

Since the last meeting of the Steering Committee (October 2000), the Strategic Advisory Committee of Experts (SAGE) of the department of Vaccines and Biologicals had endorsed a number of its recommendations. These would be discussed by Alenka Kraigher.

Dr Tarantola mentioned developments in a number of areas, most of which had been discussed in depth at the last meeting of the Steering Committee.

- *The potential for progress in immunization safety through GAVI*: With the rapid expansion of this Initiative, safety has required more attention. This has been achieved with the opening of a subaccount on injection safety. More than US$ 30 million has already been awarded to countries through this mechanism, an impressive response to the recommendations of the Steering Committee.

- *The need for effective implementation, advocacy and partnership-building*: While safety remained a very strong priority for both V&B and the Health Technology and Pharmaceuticals (HTP) cluster, it has also become a strong priority for WHO as a whole, with the adoption by the World Health Assembly of a resolution on patient safety. This gives the priority project and the Steering Committee more grounds for advocacy.
The opportunity to build on improvements in health system infrastructure made through the Polio Eradication Initiative: Attempts are being made to take advantage of this in terms of improved safety, outreach and so on.

Cross-team initiatives: Progress has been made in this area with the establishment of joint NRA assessments.

Establishment of the Focus project: This is a cross-departmental and cross-regional pilot project to ensure immunization safety in two selected countries: one in the African Region (AFR) and the other in the Eastern Mediterranean Region (EMR), using a variety of WHO resources.

Increased visibility of safety on the immunization agenda: This has led to renewed energy in investigating and sharing information on possible adverse events following immunization (e.g. allegations linking adverse events with MMR, and thiomersal and aluminium in vaccines). More allegations are likely as vaccine use broadens further. As diseases disappear, people are unwilling to see any risk at all attached to vaccine use. This makes it very important that WHO be used as an open forum to consider the validity of allegations of adverse events.

Integration of the Initiative for Vaccine Research (IVR) into V&B: This increases the capacity to impact on safety through research into safer technologies, among other issues.

Future of the Immunization Safety Priority Project: It would be useful if the Steering Committee could set out its own achievement targets or else give input on mainstreaming of the project and the use of the Committee expertise in support of other priority projects.

Finally, Dr Tarantola reminded that the V&B SAGE meeting would immediately follow this Steering Committee meeting. ISSC recommendations would feed into the SAGE advisory process. In the interests of transparency and objectivity, members were invited to give declarations regarding interests, and the closed sessions would be open only to entirely independent members.

Discussion

Asked what WHO’s position was on possible reintroduction of smallpox vaccine, Dr Tarantola explained that undertaking a risk–benefit analysis faces the problem of the unquantifiable risk of criminal use of smallpox virus. Fortunately, however, it is not necessary to immunize an entire population to control smallpox.

Dr Carolyn Hardegree, Steering Committee chair

Dr Hardegree welcomed participants, who introduced themselves. She explained that the agenda for this meeting reflected the format of some of the issues being addressed in the priority project, and was also intended to follow up on some matters put forward at the last year’s meeting. In an attempt to get many more people formally involved with the discussion, many members of the Steering Committee had been asked to make presentations, and members of the regional offices were being asked to make comments in specific areas.
The agenda was adopted on the understanding that a few changes might have to be made.

*Administrative issues*

Ms A. Delo addressed the meeting on administrative issues.
2. Progress since the second meeting

2.1 Review of Steering Committee functions and recommendations

*Presentation (Dr C Hardegree)*

The Steering Committee has the following terms of reference:

- to review ISPP priorities and targets and propose modifications as appropriate;
- to review and critically comment on strategies to best achieve the targets and strengthen the capacities of countries and WHO and regional offices to achieve immunization safety;
- to assess progress of the immunization safety workplan, milestones and indicators;
- to advise on relative balance of focus, resources and activities;
- to provide guidance in specific technical areas as necessary and support in concept some of these issues;
- to identify opportunities for enhancing global visibility of immunization safety;
- to explore ways of maximizing synergies with partners; and
- to advise on the possible contribution of ISPP to other parts of WHO.

Dr Hardegree added that the presence of members of various organizations at the Committee meeting was evidence that much had been achieved in global visibility.

*Recommendations from the last Steering Committee meeting*

Many of the recommendations from the last meeting were focused on GAVI issues, but the messages were two-fold: we need a healthy child and safe vaccination, and we must link safety and coverage. There was concern that some coverage issues were being driven ahead without concern for safety. Dr Hardegree mentioned that progress in this sphere would be reported at the meeting.

**GAVI**

The recommendations made to GAVI were that safety be accorded the same importance as coverage in the overall GAVI objectives, that coverage and safe service delivery be encouraged simultaneously, that disbursement of GAVI funds be dependent on immunization safety as well as coverage, and that an assessment tool for injection safety be used as a safety indicator for GAVI assessments. Furthermore, the Steering Committee recommended to GAVI that immunization safety be a priority activity.
for all GAVI task forces, particularly the one on advocacy, and that all GAVI partners endorse and adopt the WHO/UNICEF Joint Statement on the use of auto-disable syringes in immunization services. Finally, the Committee recommended that the development of safer injection and disposal technologies be a priority for GAVI partners.

Advocacy and partnership-building

In this area, the recommendations were: that the ISPP should communicate widely with all stakeholders; key messages should be a “healthy child and safe vaccination” and “strengthen NRAs”; donors supplying vaccines should be encouraged to fund waste disposal; and new partnerships should be developed.

In respect of the last two issues, Dr Hardegree stressed that waste disposal funding remained a problem, and that there was a real attempt to reach out and create new partnerships.

Technical and field-related issues

In these areas, it was recommended that standardization and strengthening of the curriculum on immunization safety should be key components in training of health workers; communication within and between regions related to available resources for immunization should be strengthened; system indicators to monitor progress at regional and country level should be developed; the capacity to monitor, analyse and manage adverse events should be developed further; and a systematic process for the quality control of all available AD syringes and other delivery systems should be developed in conjunction with NRAs.

Dr Hardegree added that the issue was not just a safe child. This Committee meeting would make the point that the health of the health worker was also an important issue to communicate. With regard to cross-regional activities, the meeting would hear about a pilot project involving two countries in two regions.

2.2 Review of recommendations from the June 2001 SAGE meeting

Presentation (Dr A Kraigher)

Important issues addressed at the SAGE 2001 meeting were:

- how to strive towards equity in immunization by achieving access and high coverage in every district of the world;
- how infusion of huge additional resources was driving the vaccine pipeline forward with new tools and technologies, creating the need for more partnerships in vaccine research;
- how GAVI would come to terms with a possible new mandate as an alliance for the whole global immunization agenda; and
- how to align the objectives of GAVI with polio eradication and other disease-control objectives.

Dr Kraigher listed the recommendations from that meeting which consisted of three parallel sessions devoted to innovation, immunization systems and disease control.
2.3 Progress report from the Secretariat

*Presentation (Dr P Duclos)*

Dr Duclos presented a brief overview of achievements of the whole Department in areas of immunization safety and set the stage for the ensuing presentations. In addition to outlining progress made since the last meeting, his presentation covered the new strategic plan and some key issues.

**Immunization Safety: 2002–2005 strategy and workplan**

The strategies and workplan have been adjusted to some extent to benefit from the experience and recommendations of the Steering Committee. It was important to build on progress that had been achieved and to have a much stronger country focus.

In the Strategic Plan\(^1\) of the Department of Vaccines and Biologicals Target 6 singles out the greatest chunk of the work in immunization safety: “Establish a comprehensive system to ensure the safety of all immunizations given by national immunization services”.

What is involved here is the provision of adequate support for building up capacity in priority countries for a comprehensive system that ensures immunization safety. There are, of course, limits to what WHO and partners can achieve.

The critical indicator is the proportion of non-developed countries (NDC) with sterile injection practices. This category includes least-developed countries, developing countries and economies in transition.

There are four products in Target 6:

- assurance of vaccine safety through quality control procedures and quality specifications;
- tools to ensure vaccine quality and safety up to vaccine administration;
- safe and efficient vaccine administration and disposal technologies; and,
- mechanisms to monitor and respond to AEFIs.

With regard to safe and efficient vaccine administration and disposal technologies, the major areas of work are injection safety assessment and monitoring; provision of technical assistance to regions and countries on injection devices, practices, sharps disposal and management; advocacy for injection safety; and waste management costing studies.

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\(^1\) *Vaccines, Immunization and Biologicals: 2002–2005 Strategy*  
(Who document WHO/V&B/02.02).
The milestones most relevant to countries for safe and efficient vaccine administration and disposal are:

- 40 countries will conduct an injection safety assessment and develop a plan to meet identified gaps by the end of 2002;
- 50 of the poorest countries will use the safest recommended devices and practices by the end of 2002;
- all NDC will be using only AD syringes for immunization by the end of 2003; and
- 80% of NDC will have sterile injection practices by the end of 2003.

With regard to AEFI management, emphasis has been put on strengthening countries’ systems for AEFI monitoring and management, providing assistance to countries in managing AEFIs, and making use of the Global Advisory Committee on Vaccine Safety. Countries planning a measles mass immunization campaign have been prioritized to ensure that they have an AEFI monitoring system in place.

The goal is that by 2003 all countries with NRAs will have an AEFI monitoring system (which includes collaboration between the NRA and the immunization system); and that 15 AEFI monitoring systems will have been established or strengthened.

There are other targets in the Strategic Plan that have safety aspects integrated, notably:

- Target 1: preclinical evaluation of new vaccines and delivery systems (novel delivery systems).
- Target 4: new technologies and methods for the standardization and control of biologicals.
- Target 5: assurance of adequate supply and quality of all vaccines up to administration (this takes into consideration the issue of distribution system, global supply, regulatory system).
- Target 7: strengthen key functions and managerial capacity at national and district level (involving a number of activities such as microplanning).

**Progress report**

After presenting the Plan, Dr Duclos took up the following questions: Have the Committee’s recommendations been addressed? Will the 2003 objectives be met, and the joint statement by WHO, UNICEF and the UN Population Fund (UNFPA) on use of AD syringes be complied with?

The use of indicators is important in such discussions. Simple indicators include the percentage of NDC with national safe injection plan detailed down to district level; the percentage of NDCs using AD syringes; and percentage of countries with a monitoring system for AEFIs. The percentage of NDCs with sterile immunization injection practices is a composite indicator, as is the percentage of NDCs having proper sharps disposal and sharps waste management. These use an algorithm, are based on a number of sources and avoid placing an extra burden on the countries in terms of data collection.
Sources of data include the Joint Reporting Form, GAVI, injection safety assessments and NRA assessments. There has been major progress in data collection, in streamlining the process and creating a cohesive approach. The presentation included a number of slides to illustrate available data and indicate progress, for example Figure 2.1 showing the estimated percentage of NDC with sterile immunization practices, and Table 2.1 showing baseline estimates.

**Figure 2.1: Estimated percentage of NDCs with sterile immunization injection practices, 2000**

![Bar chart showing the estimated percentage of NDCs with sterile immunization injection practices in 2000.](chart_image)

**Table 2.1: Baseline estimates (2000): percentage of NDCs meeting other indicators**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>N</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe injection plans</td>
<td>188</td>
<td>20</td>
<td>4</td>
<td>76</td>
</tr>
<tr>
<td>AD syringes for routine immunization</td>
<td>188</td>
<td>44</td>
<td>51</td>
<td>5</td>
</tr>
<tr>
<td>&quot;Proper&quot; sharps disposal</td>
<td>102</td>
<td>47</td>
<td>21</td>
<td>33</td>
</tr>
<tr>
<td>&quot;Proper&quot; sharps management</td>
<td>102</td>
<td>32</td>
<td>33</td>
<td>35</td>
</tr>
</tbody>
</table>

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2 The definition of “proper” was based on current WHO recommended practices and taking into account the existence of a policy, plan and/or budget; supply of required materials or equipment; and practices. Baseline estimates were measured by an algorithm developed by WHO using data reported through the WHO/UNICEF Joint Reporting Form 2000, and data from injection safety assessments (based on the standard Tool for the assessment of injection safety, WHO document ISSC Steering committee on Immunization Safety. WHO documents WHO/V&B/01.30).
A preliminary update from the 2001 joint reporting form shows rapid progress compared with 2000.

- Use of AD syringes: 60% (versus 38% in 2000) of countries in AFR; 35% in EMR (51% of population);
- Use of safety boxes: 63% (versus 46% in 2000) of countries in AFR; 71% in EMR (75% of population);
- Use of incinerators: 71% (versus 55% in 2000) of countries in AFR. See Table 2.2 for more data showing progress in incineration in AFR, implemented in connection with mass measles campaigns.
- An injection safety assessment was carried out in 17 countries in 2001. Assessments have been useful for advocacy, and for promoting the quality cycle of evaluation, assessment, planning, implementation and evaluation.

Projections for the future use of AD syringes forecast a steep rise, especially since China is to be supplied with hundreds of millions of AD syringes (and vaccine) by the Vaccine Fund. Much promise is also shown in recent developments in incineration of injection waste implemented for measles campaigns in Africa.

Table 2.2: Injection waste treatment with de Montfort incinerators in five African countries in relation with the 2001 measles mass vaccination campaigns

<table>
<thead>
<tr>
<th>De Montfort incinerators built (number by district)</th>
<th>Benin</th>
<th>Burkina Faso</th>
<th>Ghana</th>
<th>Mali</th>
<th>Togo</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 (1)</td>
<td>53 (1)</td>
<td>3 (1)</td>
<td>55 (1)</td>
<td>137 (4)</td>
<td></td>
</tr>
<tr>
<td>Weight of injection waste produced</td>
<td>37</td>
<td>68</td>
<td>30</td>
<td>133</td>
<td>31</td>
</tr>
<tr>
<td>Rate of injection waste burned in the incinerators (tonnes)</td>
<td>80%</td>
<td>56%</td>
<td>5%</td>
<td>70%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Boding well for the future, a study in Cambodia has shown steeply declining costs of waste management with increased levels of activity and higher coverage. The costs are lowest with local production and use of incineration for both campaigns and routine immunization.

Progress is also clear in the increased number of countries exercising AEFI regulatory functions. However, there is still a long way to go. See Figure 2.2 for the situation in 2002.
Key issues

Major progress has been made in a short time, in particular due to the impact of GAVI, which has gone beyond support from the Vaccine Fund to vastly increased visibility and advocacy. To try and achieve so much in a short time has been very challenging.

While AD syringe availability is no longer an issue, there is still a problem of resources when it comes to buying AD syringes and follow-up activities, and there are conflicting priorities at all levels.

Among other key issues are the following:

- Waste management is an issue in terms of cost and integration into a wider context as well as in terms of acceptability of some of the options.
- There is the problem of poor countries for which GDP per capita is low but not low enough for the country to be eligible for GAVI support.
- There is a long way to go in the training of health professionals.
- Despite progress in some regions, in terms of advocacy, there is still some prejudice against AEFI monitoring.

Finally, there is hope in terms of the Fifty-fifth World Health Assembly resolution on Quality of Care and Patient Safety, which can be a very useful advocacy tool.
2.4 New GAVI emphasis on immunization safety/GAVI update on injection safety

*Presentation (B. Stenson, M. Dabl-Regis)*

The emphasis on safety in GAVI material has increased. On the basis of guidelines and forms used in the application process for Vaccine Fund support, Mr Stenson calculated that content on safety of injections rose from less than 0.5% in the versions of May 2000 to over 6% in those of August 2001.

When it was launched in Davos in January 2000 it was announced that “GAVI promotes the use of new and safe technologies”, a humble beginning to what is now the increasing role of GAVI in injection safety.

The first version of the guidelines regarding country support (May 2000) stated, among others, that countries applying for support should plan to achieve safe injections as part of multi-year planning, and that all the new vaccines should be bundled with AD syringes and safety boxes.

The first revision of the guidelines (September 2000) required that efforts to improve the safety of immunization be documented and that there be plans of action to ensure safe injections and strategy (or statement of intent) regarding final disposal.

Another development followed when Nepal was provided with Hepatitis B vaccine from another donor without the safety equipment. A debate ensued whether GAVI should intervene and provide safety equipment without the vaccines, or put the burden on the donor. The latter path was chosen: the Fund would not provide AD syringes for vaccines funded from other sources.

In the next revision of the guidelines (November 2000), it was required that there should be a planned transition to AD syringes in accordance with the joint statement of 1999, and that a copy of the plan to achieve safe injections be attached to applications to the Fund.

In its London meeting of June 2001 the GAVI Board decided on a new approach. Improving safety of immunization was considered critical to GAVI’s mission, deserving special focus. The Task Force on Country Coordination was to work on new tools to monitor safety, and there would be special emphasis on safety in the guidelines for annual progress reports and mid-term reviews. It was also stated that further research on management of medical waste was required. Finally, there was a decision on a new policy to open a third window for safety: funds for AD syringes should be provided on the basis of a review of the injection safety plan.

This decision formed the basis for the current policy for injection safety support. Support is provided in the form of safe injection supplies according to the standard immunization schedule for three years, or the equivalent sum is provided if AD supplies are already secured.
The requirements for injection safety support are:

- approval for other type of support;
- a national policy for safety (or plan to develop one), a comprehensive injection safety strategy and an action plan for safe injections and waste disposal.

**Status of approvals by mid-2002**

Overall there are 74 eligible countries, 60 of which had been approved for support by mid-2002.

Injection safety: 42 countries had submitted applications, 25 of which had been approved; 12 applications were to be resubmitted and 5 approvals were conditional.

Total funds committed: US$ 47.5 million over three years, including the results of the latest review.

**Issues**

Dr Dahl-Regis then addressed the meeting on the issues still facing GAVI and the Vaccine Fund.

- Countries not qualifying for GAVI/Vaccine Fund support (e.g. Cuba and Honduras) should benefit from injection safety support.
- Injection safety support is for only three years, whereas vaccine support is for five years.
- The Vaccine Fund will not supply AD syringes for vaccines funded from other sources.
- Injection safety support is not covering all immunizations in some countries. There is the issue of parallel use of approved and non-approved vaccines.
- Is comparable quality control applied to AD syringes?
- Some countries maintain there is lack of clarity and information in the guidelines, and there is a question as to whether sufficient technical support is given to countries for drawing up safe injection plans.
- Advocacy and communications have been incorporated into the multi-year plan, but how much is enough when we move towards sustainability, particularly financial sustainability? What are the commitments of governments and various partners?
- A number of core indicators have been identified, but others are missing; how are we measuring advocacy, for example? At the same time, as much as we need indicators we have to make this simple for countries.
- When we look at assessing country capacity and the role of the ICC, the minutes of ICC meetings reflect that there is little discussion about injection safety. The ICC should be strengthened.

In conclusion, Dr Dahl Regis reminded the group that the Alliance has presented specific opportunities for exchange of information on best practices, introduction of new vaccines, raising immunization coverage and also injection safety.
Discussion

Points raised included the following.

On monitoring safety:

- Of 13 core indicators in the V&B strategic plan, only one specifically addresses the safety issue, namely: the proportion of districts in one country supplied with an adequate number of AD syringes during the year. The 2002 Data Quality Audit has also included presence or absence of monitoring of adverse events and safety supplies at district and health centre level.
- One out of 13 core indicators amounts to about 6% devoted to safety.

On injection safety plans:

- For Vaccine Fund support it is a requirement that countries have a safety strategy, but this does not have to be far-reaching. This contrasts with the precise request for an action plan for injection safety in the case of applications for support for injection safety.
- Some countries lack guidance, and guidelines to assist countries to produce a good injection safety plan may indeed be lacking.

On monitoring:

- There is a system of follow-up and monitoring based on annual reports from the countries, and it is stated that these should be satisfactory for the country to continue to receive support.

On integration of the safety aspect into GAVI activities at operational level:

- It was suggested that supplies are received but that there is no real idea of how training will be provided, and there is a severe lack of knowledge and safety consciousness in the field.

On the subject of an injection safety role for ICCs and possible technical support from regional offices:

- WHO and UNICEF have to play a leading role to strengthen the capability of ICCs as regards safety of injections. Since the regional offices do not have the resources to help everyone, ICCs should perhaps be expanded to include other groups to increase competence. WHO and UNICEF should do some advocacy to bring those who are funding health in general to the ICC.
- Although ICCs can be advocates for injection safety, the Ministry and the technical agencies (WHO and UNICEF) are the ones to provide the expertise to train the staff.

On the contribution by mass immunization campaigns:

- The measles group has taken a lead in including safety as a comprehensive part of a campaign. Monitoring of all safe injection events is part of the whole plan. The partners provide all the safety equipment needed as well as training for health care workers.
On quality control of AD syringes:

- The Device Manufacturers Association members abide by a code of ethical standards.
- UNICEF has two areas of quality assurance, one of which applies prior to UNICEF supply and the other after supply. This includes compliance with WHO specifications. In addition, UNICEF conducts inspections of the production plants and production run samples. In the last 18 months UNICEF has instituted requirements for successful field-user trials. After procurement UNICEF carries out random inspection of the facilities, inspects large orders, carries out random product inspection and has a feedback mechanism.

2.5 Opportunities within EPI to improve safety

*Presentation (J. Bilous, B. Aylward)*

The Immunization Safety Priority Project has done a tremendous job in raising awareness about safety in general. In particular, injection safety has a much higher profile in health ministries around the world.

As a prelude to discussing the opportunities for improving the safety of immunization services, the priorities of the Expanded Programme on Immunization (EPI) for 2002–2005 were outlined:

- Increasing coverage: GAVI has set a goal of reaching 80% of children in all districts of at least 80% of developing countries with routine immunization by 2005. Only 38 countries, or 20%, have achieved this coverage at national level.
- Polio eradication: The major goal is to interrupt transmission of wild poliovirus.
- Measles control: Priorities are to achieve 90% coverage and implement a second chance of measles vaccination in order to halve mortality from measles by 2005.

What are the opportunities to improve safety?

*Organizational structure*

At HQ attempts are being made to reorganize EPI to provide the kind of support needed and to be more proactive in immunization safety.

*Accelerated disease control initiatives (ADC)*

In addition, there are opportunities for improving immunization safety provided by accelerated disease control initiatives at a country and even global level. See Figure 2.3 for ADC-funded resources that could be used to strengthen safety. Most of this infrastructure is already playing a role in safety, but could be further exploited.
Apart from interrupting polio transmission and developing post-certification policies, major goals in the PEI are to ensure broader use of the polio infrastructure. The goals are to use this infrastructure to strengthen routine immunization as regards: cold chain and safety, microplanning and management, vitamin A administration and social mobilization. This infrastructure can further be used in surveillance for measles and other childhood diseases, epidemic-prone diseases, monitoring of coverage and adverse events.

For strengthening immunization systems, in particular immunization safety, the human resources infrastructure is most valuable. A survey showed that 41% of the international and 75% of the national polio-funded staff were already working on issues connected with immunization safety and that a substantial amount of their time is already taken up with areas that could involve immunization safety.

A number of strategies introduced by accelerated disease control have particular relevance to safety. These include supplemental immunization activities, strengthened monitoring and surveillance and use of ICCs for advocacy.

**Capacity building**

Another opportunity is presented by a complete overhaul of training materials: *Immunization in Practice* and the *Mid-Level Managers Guidelines*. In both of these guides more attention is being given to immunization safety; and this is an opportunity to systematically re-train government officials in the field with an emphasis on safety.

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### Table: ADC/EPI infrastructure

<table>
<thead>
<tr>
<th><strong>ADC-funded resources</strong></th>
<th><strong>Role in safety</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human resources</strong></td>
<td>Partial</td>
</tr>
<tr>
<td>• International and national staff</td>
<td></td>
</tr>
<tr>
<td>• Consultant support</td>
<td></td>
</tr>
<tr>
<td><strong>Infrastructure</strong></td>
<td>✔</td>
</tr>
<tr>
<td>• Vehicles, cold chain</td>
<td></td>
</tr>
<tr>
<td>• Communications equipment</td>
<td></td>
</tr>
<tr>
<td><strong>Institutional arrangements</strong></td>
<td>Partial</td>
</tr>
<tr>
<td>• Technical forums, LabNet</td>
<td></td>
</tr>
<tr>
<td>• Interagency coordinating committees (ICCs)</td>
<td></td>
</tr>
<tr>
<td><strong>Strategies</strong></td>
<td>Partial</td>
</tr>
<tr>
<td>• Active surveillance</td>
<td></td>
</tr>
<tr>
<td>• Pulse immunization</td>
<td></td>
</tr>
<tr>
<td><strong>Processes</strong></td>
<td>Partial</td>
</tr>
<tr>
<td>• Strategic plans, advocacy</td>
<td></td>
</tr>
<tr>
<td>• Microplanning/administration/management</td>
<td></td>
</tr>
</tbody>
</table>
**Introduction of new vaccines**

Introduction of new vaccines also presents an opportunity to improve safety. Apart from GAVI contributions, the many non-GAVI countries that are introducing vaccines are working in the area of adverse events and injection safety.

**Next steps**

The next steps are to systematically address safety training of polio-funded staff; to include safety in long-term human resources planning, making sure all technical consultative groups and ICCs recognize the issues of safety; to reflect safety in revised materials; and to exploit opportunities in new vaccine introduction and measles and other campaigns.

**Discussion**

The following points were brought up.

On utilizing staff funded by the polio programmes:

- It would be a great missed opportunity not to use the expertise built up in the field to move on into improving injection safety. We should not repeat what happened to the smallpox programme when, at the end of 1977, the resources disappeared into the desert sands.
- Since most of the polio staff have training in the area of surveillance this facilitates adverse event investigations. Issues related to injection safety are a greater challenge. In most of the heavily populated countries or countries with a large number of polio programmes-funded staff there are processes in place making it easy to investigate and revise the skill base of people. In many other countries, however, WHO and partners will systematically need to address training needs. Injection safety will fit into a broader training programme for many of these staff.
3. Assurance of vaccine safety through quality control procedures

3.1 Global perspective: standardization for quality and safety

Presentation (I. Knezevic)

Ensuring consistent safety and quality of a vaccine is an essential element in any successful immunization service. Safety of immunization must be assured through every stage of vaccine development: production and control, preclinical and clinical testing, licensure and post-marketing surveillance and use of vaccines. The inherent variability of the starting materials poses particular problems, as does the complexity of the production process.

Safety of vaccines is not an absolute term but rather should be seen as a risk–benefit assessment. There is no vaccine that is 100% safe. Over time, the concept of vaccine safety has changed. Earlier, it was looked at passively, as part of the process of trying to achieve safety and immunogenicity. Today, safety receives much more attention. In this respect, there are a number of questions in the area of novel vaccines that need to be solved. Special attention needs to be paid to long-term safety (e.g. the issues of adventitious agents, which need to be looked at for evidence of safety rather than lack of evidence of harm, reverse transcriptase, and genetic stability).

In vaccine characterization and quality control, it is important to differentiate between full characterization during development, which is a pre-requisite for licensure, and lot release, when tests are performed routinely. Introduction of novel techniques is necessary to fully characterize vaccines (even classic vaccines like BCG, mumps). HIV and Haemophilus influenzae type b (Hib) vaccines also present this challenge.

Quality control is important but not sufficient to assure quality. Norms and standards comprise an important tool for vaccine evaluation and are set by the Expert Committee on Biological Standardization (ECBS). WHO guidelines, recommendations and requirements for production and control have been expanded, with more guidelines regarding vaccine evaluation on pre-clinical and non-clinical testing, clinical trials and post-marketing surveillance.
How can vaccine safety be assured?

- General issues in vaccine production and control should be examined (e.g. cell substrate, adventitious agents, bovine spongiform encephalopathy or BSE, thiomersal, vaccine stability) as well as specific questions regarding safety of individual products, as in rotavirus vaccine.
- It is also important to look at safety vs. efficacy.
- The design of pre-clinical and clinical studies is another critical safety issue: if one is not looking specifically at safety questions one will never find the right answers.
- Regulatory requirements should be science-based to ensure safety of vaccines.

3.2 Building on the work of the ECBS

*Presentation (J. Milstien)*

**Access to Technologies (ATT)**

The work of ATT builds on the work of the ECBS in four areas: prequalification of products for supply to UN agencies; strengthening of NRAs; the Global Training Network (GTN); and NRA networking.

**Pre-qualification process**

The guidelines put out by the ECBS for quality of vaccines, NRAs and so on are made concrete by using them as the defining rules in the process of prequalification of products. Based on the pre-qualification process, WHO provides advice to UN agencies on which vaccines are acceptable for purchase. Countries that want to buy vaccines also use this list, which is published on the internet. The procedure involves the following:

- It includes an initial assessment, which is published, a reassessment every two years and continuous monitoring and updating of the list.
- It relies on effective functioning of the NRA of the producing country, in line with ECBS guidelines and published documents.
- Part of the procedure is monitoring compliance with specifications of the UN agency tender based on the specific vaccine production guidelines of the ECBS.

**NRAs**

On the basis of the guidelines developed by the ECBS as to what the NRA should do, WHO has developed an assessment tool that looks at six essential functions. This has been used in a process that includes an assessment, development of a plan to meet the gaps, implementation including technical support, and a follow-up process (see Figure 3.1).
WHO has focused first on producing countries, and 30 out of 48 producing countries are now exercising all NRA functions (75% of the children in the world are living in countries that are being sourced by vaccines that are meeting all of the regulatory functions). So far NRAs in 10 out of 61 procuring countries, and 6 out of 82 countries that procure vaccines through UN agencies, meet all relevant requirements.

GTN
This network makes a major contribution to the strengthening of regulatory authorities (see Figure 3.2).
NRA network

This new initiative which is being developed aims to have a network of well-functioning NRAs to help with evaluation of new products and future regulatory challenges; to disseminate information and implications on new guidelines of the ECBS; to raise expertise of key NRAs and help them to share information; and to provide feedback to the ECBS on needs for country support in terms of safety and quality of biological products. The NRA network will build on networks established by the GTN.

Membership will be based on excellence of achievement in countries where vaccines are being produced. It will start with countries where the NRAs are already fully functioning, and build on that. Membership will not only be useful to the countries, it will also be a seal of approval and an indication that these NRAs will be able to deal with the challenges of novel technologies and so on. Countries are increasingly being called on to make regulatory decisions in areas where guidance by the ECBS is not yet available.
Discussion

The following comments were made with regard to NRAs:

- NRAs should be fully supported.
- The network is still in the planning stages. The proposal is that it would initially comprise fully functioning NRAs in the countries that have producers in the Developing Country Vaccine Manufacturers Network (producers that have pre-qualified products or will soon have them). WHO is specifically trying to develop information sharing. The way to ensure that children in developing countries get quality vaccines in the future is to enable development of quality vaccines in these countries.

In answer to questions on quality control and standardization, the following points were made:

- In clinical trials, you may need to look for specific adverse events and other problems of safety. There is a need for workshops to look in detail at many elements of safety, e.g. good clinical practices (GCP) in the field; in particular, workshops in countries where trials are going on might help regional staff to deal with problems more easily.
- In applying the criteria used to declare that a vaccine is of assured quality, WHO looks at the functioning of the regulatory authority, not specifically at the individual decisions that the authority might have made. WHO recognizes that authorities in different places will take different decisions, based on risk–benefit evaluations relevant to their individual situations. WHO would appreciate feedback on this concept, which is essential to perceptions of equity.
4. Tools to ensure vaccine quality and safety up to vaccine administration

4.1 Ensuring quality of UN-supplied vaccines at country level: review of situation

*Presentation (N. Dellepiane)*

The prequalification process (mentioned above) is the first step in assuring quality of vaccines purchased and supplied by UN agencies. The second step is to continuously monitor the quality of vaccines that are being supplied. This involves: random testing as well as follow-up of complaints from the field and assistance on receiving reports of AEFIs. The third step of this quality-assurance system is to make sure that the quality of the vaccine is maintained at country level.

The problem is that once the vaccine leaves the manufacturing country quality may be compromised during transport to the receiving country, or compromised in the receiving country at different levels.

Surveys have been done to try to identify the points where problems might occur. The main areas of concern are:

- **Shipments**: Problems include inadequate advanced notice, route deviations, and hold-ups out of the cold chain.
- **Receipt/rejection**: In many cases there are no standardized procedures and although quantity may be checked, quality aspects may not.
- **Storage**: Problems include cold chain failures, and an inadequate recording system.
- **Release for use**: NRA release certificates are not always checked in the receiving countries and sometimes the manufacturer’s release certificates are mistakenly checked instead (vaccine is meant to be released by the NRA of the producing country, an important insurance, especially when the receiving country does not have its own regulatory authority).
- **Distribution**: Bundling with diluents is not always done, or there are cold chain interruptions.
- **Point of use**: Problems here are associated with storage and cold chain, reconstitution, use of wrong diluents, administration and disposal.
Approaches to these problems include:

- implementation of vaccine vial monitors (VVMs) on all vaccines (improved detection of problems);
- global implementation of the vaccine arrival report (VAR) (see section 4.2 below); and
- development of quality guidelines for UNICEF and WHO country staff, immunization managers, national regulatory authorities and other relevant health staff dealing with the prequalification system, shipment and procedures at country level.

The guidelines should be published within the next few months. Implementation strategies have still to be worked out with the regional offices. The idea is to launch them at regional meetings, and to perhaps have focal points at regional and country level.

4.2 VARs

*Presentation (S. Hall)*

This project was first identified in the 1980s, and implementation began only a few months back. It involves a huge amount of work and many issues remain to be solved.

The purpose of the VAR is to:

- provide a tool to assure quality of vaccines at point of delivery;
- record vaccine ID (type, manufacturer, batch, expiry); and
- provide indicators for monitoring vaccine deliveries, including: maintenance of the cold chain during transport; compliance with shipping instructions; and adequate record-keeping.

There are several entities responsible for the reports:

- WHO and UNICEF developed the VAR and guidelines for implementation.
- The recipient government is the responsible party for completion of inspection and completion of the report, as it takes ownership of the vaccine.
- The UNICEF Country Office assists in implementation and reporting.
- The UNICEF Supply Division is responsible for record keeping, and is the focal point for follow-up (with the manufacturers/forwarder/WHO).

UNICEF makes approximately 1500 shipments a year to approximately 100 countries from 10 to 15 different manufacturing locations. Each shipment requires close collaboration of five parties: the manufacturer, shipping forwarder, UNICEF Supply Division, UNICEF Country Office, and government.

In 2001 UNICEF and WHO spent much time reviewing the VAR and developing instructions. Then in 2002 the organization began introducing it to the UNICEF Eastern and Southern Africa Region (ESAR) and for all GAVI-supported vaccine shipments.
The phased introduction has been used to identify problems and requirements in the follow-up on VAR incidents. Forms have not been filled in properly, release certificates have been incomplete, vaccine has arrived frozen, and so on. Much effort has gone into identifying problems and taking corrective action. During the introduction phase, approximately 20% of the countries required some kind of follow up.

Depending on the experiences during the introduction, the intent was for UNICEF to expand to two more regions during the second half of 2002 and to include VAR for all UNICEF shipments in 2003.

It was requested that the ISSC endorse the principle of a phased introduction of the VAR by UNICEF Supply Division, to allow for proper management and follow-up of the countries.

**Discussion**

The following points were made.

In answer to questions on the role of NRAs in the vaccine arrival process:

- WHO has divided the countries in three groups: the ones that need all the six functions (producing countries); the procuring countries, which need four functions; and the UNICEF group, which are being challenged to meet two functions. These countries tend to have embryonic regulatory systems. This is why it is necessary to have a prequalification system. If they have a regulatory authority able to check the certificates and release the vaccines, that is ideal. In other cases, the immunization service handles the whole thing.
5. Research and development

5.1 WHO Initiative for Vaccine Research (IVR)

Presentation (U. Fruth, on behalf of M.P. Kieny)

WHO’s Initiative for Vaccine Research (IVR) became functional in December 2001 when Dr Kieny was appointed as Director. IVR represents a synergy of WHO’s vaccine R&D capabilities and those within UNAIDS. This includes work on bacterial vaccines that was largely taken care of by V&B, HIV vaccines that were largely taken care of by UNAIDS, and parasitic vaccines that were dealt with in the Special Programme for Research and Training in Tropical Diseases (TDR).

The mission of IVR is to:

- guide, provide vision; and
- enable and support the development, clinical evaluation and worldwide access to safe, effective and affordable vaccines against infectious diseases of public health importance, especially in the disease-endemic developing countries.

Issues and challenges for IVR

Areas of work include: HIV, tuberculosis, malaria, rotavirus, dengue, Japanese encephalitis (JE), human papillomavirus (HPV), leishmaniasis, schistosomiasis, pneumococcus, meningococcus, *Shigella*, enterotoxigenic *Escherichia coli* (ETEC), measles, polio and new delivery systems. One of the first tasks as a result of the reorganization is to identify the specific roles of WHO/IVR.

IVR will identify gaps in knowledge and contribute to the global R&D agenda with other partners. The Initiative will make a contribution to: disease epidemiology that forms a baseline for clinical trials; forecasting of demand for new vaccines; product development with partners; clinical trials to evaluate appropriateness of any given product for developing countries; harmonization of regulatory procedures; and development of vaccination strategies.

WHO has given 12 years of active support to innovative vaccination technologies. This work has been based in an advisory group, with expertise in regulatory issues, vaccinology and product development, and has involved other agencies and industry as well as pioneers of a given technology. This group has concentrated on improved immunogenicity and simplified delivery.
The immunogenicity area has been devolved to the disease-specific committees. IVR is now concentrating on simpler and safer delivery systems, with the ambition of improving logistics, safety and access to full vaccination coverage. The main areas under focus are the heat-stability of vaccines, and, in particular, to render vaccination needle-free.

To meet the basic challenge of unsafe injection practices, such as reuse of unsterile equipment, incorrect disposal of sharps and mistakes in reconstitution, technologies under focus are: mucosal vaccination (oral, nasal, aerosol); transdermal vaccination, and new-generation jet injectors.

- When it comes to the problem of less efficient coverage by using injectable vaccines, the technology solutions being developed are safe, mass-immunization devices (jet injectors, nebulizers). A new generation of jet injectors is currently being evaluated, with a main focus on absence or presence of blood trace contamination.
- The current liquid measles vaccine may be able to be used on a global scale as an aerosol, as has been shown in Phase IV trials in a number of countries, including Mexico, where millions of children were vaccinated using existing vaccine formulations as an aerosol in nebulized form.
- Transcutaneous vaccination holds promise. The 2002 Global Vaccine Research Forum had a number of presentations in that area. Immunogenicity with those vaccines is reported to be good and side-effects may be controllable.
- To meet the challenge of losing immunogenicity through cold-chain failures, the technology solution under focus is thermostabilization of vaccines, with emphasis on sugar glassification. This technology, which stabilizes vaccine by incorporating it into sugar disaccharide formulations, holds great promise.

The new delivery systems operational framework within WHO is the bacterial team of IVR (IVR/BAC) led by Teresa Aguado. Worldwide, this group integrates with the GAVI R&D Task Force efforts. The modus operandi involves skilled staff at WHO, strong external advice (a steering committee), focus on proactive mechanisms, milestones for accountability, and an appropriate budget.

The New Delivery Systems Steering Committee has just been established. The Chair represents academia but has industry experience as well. Expertise on the committee includes specific technologies, regulatory aspects, clinical testing and industrial production (a non-active member).

GAVI support has an R&D component. It has recently selected three infectious agents for priority input: rotavirus, pneumococcus and meningococcus. The GAVI R&D task force has also been charged with the task of coming up with an agenda for technologies to streamline vaccination service delivery. Seven R&D agendas were short-listed, and the technologies that have recently been selected for priority input by GAVI are:
• in innovative management and reduction of cold chain dependency: sugar-glass dried vaccine;
• in tools to measure country progress and coverage: non-invasive oral field antibody tests; and
• in sharps waste management: device to safely remove/store needles after use.

Discussion

The following points were made:

• In answer to a question about animal models to understand safety issues, it was stated that the possibility to evaluate safety aspects in animal models is offered by IVR’s disease-specific committees.
• The current syringe and needle are over-engineered for their function. The ideal would be to engineer syringe and needle so as to be left with only a small amount of plastic that could be melted down at a couple of hundred degrees. However, industry has so far concluded that needles cannot be manufactured out of plastic.
• In answer to a comment about the high-tech focus of R&D and the need for low-tech delivery solutions to reduce waste disposal problems, it was pointed out that certain public health problems in developing countries require long-term input, which only WHO will take care of, because of market factors. IVR has only recently taken on devices with likely short-term gains. IVR is working together with partners on the Uniject™ approach, which would combine the tool with the appropriate thermostable vaccine. IVR is also working on solutions for waste disposal and waste avoidance. It has recently engaged on a more medium or long-term project, where a stainless steel needle might actually be replaced by a biodegradable needle that incorporates the vaccine.
• In the developing world the cross-over to the curative market is important so as to create a greater market incentive for safer injection technology (for 30 billion syringes globally as against the 220 million supplied by UNICEF in 2001). With the cross-over to curative we may see more companies putting money in it, and cross-over between the Safe Injection Global Network (SIGN) and V&B is important for that reason.
6. Safe and efficient vaccine administration and disposal technologies

6.1 Global WHO–UNICEF perspective

Presentation (E. Hoekstra/U. Kartoglu)

Safety goals
There has been major progress in achieving injection safety goals. Industry has increased its capacity to manufacture AD syringes to over a billion doses. UNICEF is expected to buy some 380 million AD syringes this year, an eight-fold increase since 1998. There has also been an eight-fold increase in use of safety boxes, which were introduced to reduce needle-stick risks.

The UNICEF–WHO–UNFPA joint statement of 1999 set the following targets:

1. From 2001 there would be no more contracts to purchase standard disposable syringes.
2. By the end of 2001, all countries should use only AD syringes or sterilizable equipment.
3. By the end of 2003 all countries should use only AD syringes.

In addition to setting these targets, it was requested that partners finance not only vaccines but also the safe administration of vaccines, AD syringes and safe management of waste.

In January 2001 UNICEF started procuring only AD syringes, except for BCG vaccine where such syringes would only be available in late 2002. In terms of the second goal, at the end of 2001, a number of countries were still using standard disposable syringes.

Meeting the third goal remains a challenge. In the case of campaigns, the effort to get donors to supply vaccine with syringes and safety boxes has been successful. The big challenge still is routine immunization.

UNICEF has been reluctant to insist that donors take over the responsibility for funding AD syringes as it believes that the countries should have the ownership. At this point many countries are paying for disposable syringes. The cost is approximately US$ 0.04 (4 cents) while AD syringes cost approximately 5.7 cents. UNICEF feels it would be counterproductive to ask donors to pay the full 5.7 cents, and that they may instead be asked to fund the price differential. Unfortunately, in the past donors have cut their vaccine support to compensate for AD syringe costs, and UNICEF does not want that to happen again.
Immunization is now one of the five core organizational priorities in the medium-term strategic plan, so emphasis on immunization will increase dramatically. There is a new indicator for safe immunization injection practices. The Programme Division has endorsed immunization safety as one of the basic principles and the Communication Unit has set itself a goal of becoming a world leader in communicating safety. The intention is to encourage providers to take care of injection safety and proper disposal with every immunization.

While the supply division ships bundled vaccines and AD syringes for all supplemental immunization activities, the challenge remains to make greater progress in routine immunization services.

With respect to safe disposal, Figure 6.1 shows a matrix of available technologies that was recently created at a workshop. The higher up in this matrix, the more efficient and more costly the technologies. On the right, the technologies are more environmentally friendly.

Examples of some of these technologies were discussed by the regions in later presentations (see below).

**Figure 6.1: Environmental and technological prioritization regarding waste disposal possibilities**
Introducing AD syringes and assuring injection safety in national immunization services

WHO is working on guidelines for AD syringes. These aim to assist policy-makers and programme managers in planning the introduction of AD syringes as part of a comprehensive national policy and plan of action to improve injection safety. These will be issued shortly as CD or hard copy.

An update of the document *Giving safe injections: using auto-disable syringes for immunization* is to be jointly published by WHO and the Program for Appropriate Technology in Health (PATH).

Guidelines for ensuring quality of UN-agency supplied vaccines at country level — a joint WHO/UNICEF publication due for publication — is for the use of all programme and regulatory authority personnel at country level, staff of partner and support agencies, and all who handle, store and use vaccines.

Recent advances in injection technology

Various studies have been done on pre-filled injection devices: 1995 TT (Bolivia), 1995–96 TT and HepB (Indonesia), 1999–2000 HepA (USA), 2000–2002 HepB (Indonesia – ongoing). There are studies planned for HepB in 2002–2003 (Viet Nam), and 2002 (China). During 2002 the TT device will be introduced in Afghanistan, Burkina Faso, Ghana, Mali and Uganda. It may be that the UniJect™ TT-filled device (already prequalified) does add an extra burden to the cold chain, but this is not thought to be the case with the Hep-B-filled device (on the way to being prequalified).

A favoured model of needle-free injector is currently going through US Food and Drug Administration (FDA) approval. A new feature is the protector cap to prevent the splash coming back into the device, i.e. it prevents contamination. The cap is disabled after one immunization.

Quality assurance for immunization injection devices

A recent project at WHO/ATT is quality assurance for injection devices, providing advice to UN procurement agencies. Norms and standards build a reference framework for design and development of injection devices; the safety of materials to be used; the manufacturing practices to be followed; and the consistency and quality of production.

There is regulatory oversight, with standard test procedures to check the functioning candidate devices. Finally, there is continuous post-marketing monitoring to assess the performance, quality and safety of the devices on a continuous basis, as well as their appropriateness for meeting the programmatic and operational needs. This is done in cooperation with the NRA and with full involvement of the appropriate national health authorities.
**Discussion**

Steering Committee members congratulated WHO and UNICEF on the progress in this area.

The following comments were made on the situation with AD syringes and means of promoting their use:

- The next challenge is procurement of syringes by countries themselves. Direct purchases by countries are increasing, but are still small in number.

- The projection is for a wider proportion of AD syringes to be supplied outside UNICEF, which has mainly supplied for campaigns in the past. Thanks to GAVI, the proportion of AD syringes for routine immunization is increasing. Up to May 2002, there were 10 countries doing all their routine immunization with AD syringes funded by GAVI.

- Countries should be made aware that funds are available to enable routine immunization to move over to AD syringes.

- Today it is hard to find suppliers of plastic sterilizable syringes. Countries should be made aware of the likelihood that sterilization will be more difficult and possibly more expensive than shifting to AD syringes in the future.

- The difference in price between disposable and AD syringes is narrowing. Instead of using funds to buy AD syringes for three years and then running out of funds, countries should rather use the money to fund the difference, so that the money lasts longer and sustainability is improved.

- Careful documentation is needed to show that AD syringes are a better choice. Data are available showing that (a) the health care system using sterilizable syringes does less well than the one using AD syringes or disposable syringes; (b) in India some 95% of health workers prefer AD syringes; although India is officially using sterilizable syringes, half the country is not, with mothers bringing their own syringes; (c) by switching to AD in Madagascar, coverage was increased.

- On future progress relating to safety of injections and AD syringes:
  - Every forthcoming measles campaign will go together with training on AD syringes, which will have a major impact on knowledge and training of the health care workers.
  - In Africa progress is being made: after training, countries want to apply this to routine immunization. The Vaccine Fund money for AD syringes will take a while to become available as most countries are still in the approval process, but eventually all countries with approved applications should be able to carry out all their routine immunization with AD syringes.
  - Coordination among partners must be improved. In some cases devices and vaccines are being donated by different parties without coordination with UNICEF or without any introduction plan.

- AD syringes are funded for a three-year period only. It is desirable to prolong this.
6.2 Regional perspectives

**African Region (M. Dicko)**

Assessments by WHO, BASICS and UNICEF using Tool C have shown that the risk for recipients is high in countries using sterilizable equipment. The introduction of AD syringes has ensured safety for the recipient. In one country using AD syringes the injections were found to be 100% sterile. In three countries using only disposables, 95–100% of injections were sterile.

The safety of the health care worker and the community is a problem in all observed countries. Case studies in three countries in the African Region (WHO and Centers for Disease Control and Prevention, CDC, 1999) showed there was a particular problem with recapping and safe disposal, and that bundling with safety boxes was no guarantee that immunization waste would be disposed of safely. The conclusions were that for all types of syringe there is an urgent need to stop recapping and improve disposal practices. There is also an urgent need for substantial improvement in supply, supervision and management of sterilization, or, if possible, to abandon this entirely in favour of AD syringes.

Fortunately, although there remain many issues to resolve in the African Region, with GAVI support, immunization safety is set to improve. In Africa, there are 34 Vaccine Fund-eligible countries. However, one does need to discuss countries that are not eligible, such as Gabon, where problems nevertheless exist. Also, campaigns will bring an increased number (and possibly rate) of adverse events concentrated over a short period of time, and a greater likelihood of programmatic error.

**Strategies**

It is evident that if immunization safety issues are not addressed immediately, they can affect negatively the entire immunization service and the health sector as a whole.

Dr Dicko shared some ideas on what the WHO Regional Office for Africa (AFRO) would like to achieve in creating a coherent regional strategy to ensure: safety of vaccines, injections and sharps disposal; the rapid detection and effective management of AEFIs; and effective communication with parents, community and the media.

Setting up and implementing an immunization safety policy and plan requires commitment, coordination, and resources. The strategy for that is to develop both internal and external partnership to address immunization safety issues, including involving national ICCs and GAVI; using disease control initiatives as an opportunity; and supporting countries to seize the opportunity offered by GAVI to get three years' supply of AD syringes and safety boxes for all immunization injections.

Progress has been made in used injection equipment disposal. But AEFIs are more problematic. EPI managers do not like to monitor AEFIs. There needs to be much reflection on how to achieve this monitoring.
Cascade training did not yield the expected results. In countries with strong district management it is possible to revitalize supervision and on-site support, but, with weak district management, additional training and supervisory support is required. AFR is considering using ICS teams (Increase Coverage and Safety Teams). In the case of training and workshops, the strategy includes using the Focus project in Burkina Faso (section 6.5) as a training ground for people from other countries; and organizing a workshop to discuss lessons learned and develop a regional strategy for immunization safety.

Rather than waiting until a country can be comprehensively covered with incinerators, it can start with small-scale activities. The strategy is:

- a de Montfort incinerator in each district conducting measles campaign in five West African countries and Kenya; plus Medecin 400 to be installed in three southern African countries;
- monitoring use and cost-effectiveness to better understand benefits and constraints of installing incinerators.

The problems of Africa are so immense that efforts need to be pooled. The ideas include: to use GTN and ATT for training on immunization safety (AEFIs, etc.), and for assessing and working with NRAs; to learn from the experiences of other WHO regions; to coordinate with the Bill and Melinda Gates Children’s Vaccine Program (CVP)/PATH and BASICS activities in their selected countries, to involve UNICEF; and to use SIGN to provide general framework, tools, guidelines and technical support.

**Region of the Americas (P. Carrasco)**

Injection safety in the Region of the Americas (AMR) was reviewed based on evaluation in nine countries and a special survey that was carried out as part of the Immunization Safety Priority Project.

The WHO Regional Office for the Americas (AMRO) looked at evaluations carried out between 1998 and 2001. Evaluation data were collected on survey questionnaires to document progress and impediments in the immunization systems, and prepare a plan of action over a period of two weeks using a multidisciplinary team. A mail survey was carried out on collection and disposal of used immunization injection equipment in 10 countries in 2002; and injection safety studies were carried out in two countries in 2001.

Looking at what type of technology was used to collect syringes, the questionnaires indicated that six countries were using plastic bags, and only three using safety boxes. As for methods of final disposal of syringes, a large proportion of countries were using landfill or burying, an indication of risk for the community. What countries called incineration was likely to be mere burning and did not reach the required temperature level.

The conclusions of the two-country study were that patients in the two countries are at risk of cross infection due to unsterile injection practices. Safe handling of vaccine is not 100%, therefore programmatic errors may cause untoward reactions in vaccine recipients. Furthermore, health workers often carry out recapping of used
needles and are therefore at *high risk* of contracting disease due to accidental needle-stick injuries. In one country 90% of health care workers recap used needles and 56% of health care workers reported accidental needle-stick injury, while in the other country 56% of health care workers recap used needles despite presence of safety boxes, and 18% reported needle-sticks.

Proper disposal of used injection equipment is perhaps one of most critical technological and logistic problems facing immunization services in the Region of the Americas. In many places the community may be at risk of infection from pathogens due to accidental needle-stick or reuse. It is thus important that countries assign adequate resources for sufficient syringes, safety boxes, regular supervisory visits, training and advocacy programmes.

AMRO should take advantage of every contact with countries to advocate for greater efforts on the part of the Ministry of Health (MoH) to make immunization services as safe as possible.

Investment in technology options, such as needle-less injection devices that will eliminate needles in order to reduce accidental needle-stick and the amount of dangerous immunization injection waste and thus protect the community, should be evaluated.

**Discussion**

The following comments were made in answer to a question on development of cartridges for safe injection devices:

- There should be a standard cartridge, or “bullet”, that could be put in any type of injection device.

- The concept is similar to that of the 35mm camera film cartridge that one can use in a variety of different cameras. One could thus arrive at an international standard for needle-less injection cartridges. Vaccine manufacturers could then compete to put the best vaccine in their cartridge. Device manufacturers could compete on the best device.

**European Region (D. Maire)**

The European Region (EUR) has developed a plan of action for 2002–2003. This plan focuses mainly on Eastern Europe, including Central and Eastern Europe (CEE), newly independent states (NIS) and Turkey.

The quality of immunization services is a priority in order to retain public confidence. High coverage has been sustained and countries show increasing concern about quality. The strategy is to strengthen countries' capacity to ensure the safety of immunization through support for the improvement of all programme components relevant to immunization safety.

The safety of immunization has four quality service components monitored by the AEFI surveillance system: procurement; cold chain and logistics; safety of injections; and waste disposal.
Achievements and challenges

There have been pleasing developments in the sphere of immunization safety. Following application by 11 countries for Vaccine Fund support, these countries now have, for the first time, clear plans for immunization safety. Introduction of AD syringes and safety boxes took place in the 11 countries, and a workshop on injection safety was held for eight of them. Assessments were carried out and a plan drawn up on waste disposal in Albania, Kyrgyzstan and Uzbekistan. Recently too, there have been important subregional meetings attended by 28 countries which focused on immunization safety and have had considerable impact. In the area of cold chain and logistics, 17 countries assessed their cold chain system and completed inventories for storage volume capacity, upgraded equipment and improved vaccine management. Cold chain studies were carried out in Albania, Kazakhstan, Turkey and the Ukraine.

In the area of vaccine management, procurement has been greatly improved, although there are still some challenges in terms of forecasting vaccine requirements. The challenges are to strengthen management and revise procedures to ensure quality performance regarding the following functions: temperature monitoring; national inventory; financing of equipment; stock management and wastage.

Among the main issues dogging immunization safety in Europe are: recapping of needles; preparation for recycling when discarding used equipment (needles soaked in chlorine as previously enforced in the former Union of Soviet Socialist Republics); reconstitution of lyophilized vaccines; and attention to safety during outreach activities.

A pilot assessment on injection safety, carried out in one country, found that sterile disposable and AD syringes were used for vaccination in 100% of health centres, and safety boxes in 94%; 26% of health workers recapped needles and 29% had suffered needle-sticks in the last year. Communities are at risk, as sharps were found around 31% of health centres, and only 4% of health centres had a written waste management policy.

Future directions

Future directions with respect to injection safety include: advocacy and communication activities for the introduction and sustained use of AD syringes; increasing health personnel awareness and knowledge; and assessments for evidence of risks to patient, provider and community, to be used for advocacy.

- Technology transfer will take place. Eight of the 28 countries are producing syringes and, since this is for both immunization and curative care, they will need to adapt production for both purposes. Plans of action will include discouraging disinfection of syringes after use.

With regard to waste disposal, support will be given to countries to: assess risks that waste disposal pose to the community; evaluate waste management systems in place; determine the best options for waste disposal and destruction; and develop policies and plans.
Discussion

On the issue of disinfecting needles before discarding (or recycling) them, the question was asked if one could forbid this without complete assurance that there would be safe disposal, and whether there were any data showing that it is risky to disinfect needles.

The following answers were provided:

- The risk is not only for the provider but also for the people who collect needles, as shown by the number of needle-sticks. After a few hours chlorine is not effective, but the provider may think that the equipment is still disinfected.
- There are data from Uzbekistan showing that when recycling the plastic after disinfection ceased, the rate of needle-stick decreased.

Eastern Mediterranean Region (J. Fitzner on behalf of E. Mohsni)

Before 2000, injection safety was not perceived as a priority in the region. In 2000, injection safety assessments were carried out in Oman and Egypt, and sensitization of the national immunization managers took place. In 2001, further injection safety assessments were carried out in Djibouti, Morocco, the Syrian Arab Republic, Sudan and Tunisia. A regional plan of action was then drawn up focusing on situation analysis. The WHO Regional Office for the Eastern Mediterranean (EMRO) also helped to draw up plans for Vaccine Fund-eligible countries, namely Djibouti and Sudan, and for countries that are not eligible for support from the Vaccine Fund (Cyprus, Morocco, Syrian Arab Republic and Tunisia).

Situation analysis

- Injection safety assessments show medium to high problems in all areas of injection safety, in some cases conflicting with information drawn from the WHO/UNICEF Joint Reporting Form (JRF) 2000. The assessments found that 47% of health workers in one country suffered from accidental needle-stick injuries. In a second country, the situation was also serious. Among other risks, two-handed recapping was performed by 83%, and close to 50% suffered needle-stick injuries in the previous 12 months. In a third country 82% of health workers performed two-handed recapping and 15% reported needle-stick injury in the previous 12 months, while sharps waste was found in the surroundings of 56% of the health facilities.

- According to the JRF 2000, AD syringes and safety boxes were used in seven countries and safety boxes had been introduced in eight others.

- Of six Member States eligible for Vaccine Fund support, three applied for injection safety, and two were approved while one was to resubmit; Afghanistan, Djibouti and Somalia were planning to apply.

- The National Plan of Action for Injection Control (NAPIC) project started in Egypt, as did the Focus project in the Syrian Arab Republic (section 6.5).
An integrated approach was agreed at the Communicable Diseases Control retreat (October 2001). The countries agreed to cooperate in capacity building in order to improve: programme development including managerial skills; basic epidemiology; partnership building; communicable diseases surveillance; and infection control including safe injection and anti-microbial resistance.

At the priority intercountry meeting on communicable disease (CD) control, Cairo, 17–19 February 2002, high-level national health professionals and national managers of CD programmes agreed to introduce an integrated approach and review/update national plans of action jointly.

In 2002, the regional working group (RWG) met to initiate the integrated approach. Data available at the regional office were analysed to review/update the regional action plan. An intercountry meeting was planned to follow up the implementation of recommendations. Various activities were held in collaboration with the HIV/AIDS programme. The 12th intercountry meeting of national AIDS programme managers (Beirut, 23–26 April 2002) focused on improving country plans for safe injection and infection control.

To support safe injection activities at country level, infection control programmes were planned for Egypt, Jordan and Sudan; assessment of infection control was carried out in Afghanistan and Jordan, and there was training of vaccinators, service providers and others, in nine countries.

**Discussion**

In response to a question on differing attitudes to the concept of training the trainers, it was explained that AFRO believes that from district level to peripheral level (where immunization takes place) there should be a revitalization of supervision and on-site support. The district people need to be trained, and then district staff should offer supervision to support people on-site.

In response to questions on cooperation between immunization safety and AIDS programmes, it was stated that the main issue for EMRO was lack of resources, and that the retreat in October (mentioned above) showed that the programmes shared a lot of concerns (including weaknesses in finance, management). The immunization area is driving the other areas.

EMRO was congratulated for having integrated communicable diseases and immunization, and for combining forces with regards to infection control and patient safety.
South-East Asia Region (S. Guichard)

In the South-East Asia Region 240 million routine infant immunization injections are carried out every year, which accounts for one-fourth of all the immunization injections provided worldwide. In 7 out of 10 countries the current national policy is for sterilizable syringes. Two countries are using AD syringes.

An injection safety assessment using Tool C has been completed in one country and will be undertaken in a second. An assessment was carried out in a third country as part of the field-testing of guidelines to assure vaccine quality at country level; a nationwide assessment (including curative care) was conducted in a fourth.

Available results are consistent with previous studies in other regions, showing large deficiencies in the safety of injections. There is a shortage of fuel for sterilization and no TST is used to monitor proper sterilization. Among health workers there is a low awareness of the risks associated with unsafe practices and a high incidence of needle-stick injuries. A big proportion of patients bring their own disposable syringes and needles.

The objective is that by 2005 the whole Region will be using AD syringes. GAVI is the trigger in this.

- In 2003, India will receive AD syringes from GAVI, UNICEF and PATH which, together with a donation of 1 million AD syringes, will cover approximately 10% of the infant immunization needs. For 2004 the estimate for coverage of the target population for AD syringes is 35% and, in 2005, 50%.
- In 2003, Bhutan will receive the DTP–HepB vaccine, and by 2004 all countries will have the tetravalent vaccine.
- Indonesia plans to introduce combo Hep–DTP in UniJect™ starting in 2004.
- Bangladesh has been approved for support. The country put together a new proposal for AD syringes for all immunizations a month ago.

Strategy and issues

The regional strategy covers: advocacy for AD introduction; technical support to develop national policy; and technology transfer for regional production of AD syringes. The WHO Regional Office for South-East Asia (SEARO) also intends to develop partnerships with environmentalists to identify solutions for safe disposal of immunization waste.

The advocacy strategy includes injection safety assessments, sharing of cost–benefit studies on AD syringe introduction in Madagascar, and information on the potential for AD syringes to boost immunization coverage (selling safety). SEARO will inform countries on the limited production of plastic sterilizable syringes for immunization, and update immunization managers on the regional production of AD syringes.
India has one manufacturer (its 0.5 ml syringe was to be prequalified in the third quarter 2002) with a current production capacity of 60 million, expandable to 300 million. In Indonesia, technology transfer has been initiated with one manufacturer that has a production capacity of 40 million 0.5 ml syringes. BCG syringes are expected to be available during the second half of 2002 from a single source (the requirement in SEAR for 2002 is 1 400 000 such syringes and, for 2003, it is 9 300 000).

A competitive market for AD syringes through global tender and regional procurement is being encouraged. An issue is what to do during the transition period, rehabilitating sterilization vs. accelerating AD introduction.

There are a number of issues regarding safe disposal of immunization waste. This has never been a priority agenda. There is an uneasy relationship with environmentalist activists due to lack of understanding, and there is growing concern in the region about an unhealthy environment (bans on plastic bags and so on), so that incineration is a sensitive issue. In addition, the existing infrastructure is very weak in most countries, despite the availability of studies and guidelines to comply with national legislation.

Among activities scheduled for late 2002 are: an injection safety assessment in Bangladesh; workshops on injection policy development in Bangladesh and Myanmar; an incinerator trial in Myanmar, and an activity plan for further expansion of the project. Potential for technology transfer in Bangladesh would be assessed, and the Indonesian transfer followed up. SEAR is also to review existing non-incineration technology in India with NGO/environmentalist group Shristi, to document success solutions with non-incinerator alternatives for urban areas. In addition, it is to finalize a protocol for a needle-puller field trial in cooperation with CVP/PATH, and the AD syringe inventory and regional vaccine policy.

**Western Pacific Region (W. Antkowiak)**

Immunization safety policies have been developed collaboratively between the ministries of health and the WHO Regional Office for the Western Pacific (WPRO), and adopted in Cambodia, Lao People’s Democratic Republic and Viet Nam. These define what constitutes a safe injection and acceptable equipment and outline introduction and waste disposal strategies.

**Challenges**

In several countries, injection safety and equipment disposal problems are very common.

- Open disposal, burial in pits or simple burning are almost routine.
- Widespread reuse/recycling of equipment is suspected and sometimes acknowledged.
- In the absence of locally available incineration, transport of used equipment is a major ongoing problem.
- Currently there is very limited monitoring and supervision of injection safety issues.
• There is limited government budget for injection safety training, even during campaigns.
• Proper monitoring of usage and anticipation of demand is needed.
• Public and private organizations are reluctant to adopt incineration.

Incineration may be seen as the best possible waste management solution until needle-less technologies take over. The Sicim incinerator is being installed (more about these under Progress below). Testing has shown that the Sicim incinerators produce dioxins and do not meet the standards set in the USA and various European countries, nor the revised standards set recently in Japan. A cost–benefit analysis is to be done looking at the disease burden produced by dioxins emitted by the incinerators as compared to the disease burden brought on by increased infection with hepatitis B and HIV in the absence of these incinerators. This is a touchy issue, and donors are very wary because of possible future environmental backlash.

Opportunities
There is growing public awareness of injection safety issues and acknowledgement of the injection safety problem by governments. Each country is developing plans of action. AD syringes are being locally manufactured, and there is increasing experience with using these syringes and safety boxes during campaigns. Experience with use of incinerators is also increasing. Another opportunity is that governments are beginning to address the larger issues of all medical waste.

Progress
In Cambodia there has been good progress. An application for Vaccine Fund support for injection safety has been approved, all provinces will use AD syringes by the end of 2002, and injection safety training is progressing. There is good collaboration between partner agencies. There are now 13 Sicim incinerators in Cambodia and another 7 or 8 will be added in the next year. They are easily assembled and burn well. Maintenance cost is very low. A recent study in one province showed that the cost of disposal of one syringe is US$ 0.08 (only routine) and US$ 0.02 if campaigns are included. The total cost for the province was about US$ 4500 per year (over 5 years). There were three main costs: safety boxes (29%); long-term training (16%); incinerator and housing (14% and 15%).

WHO support to Viet Nam has included: supervision and follow-up of the installation of 15 Sicim incinerators; training of local incinerator operators; and assistance with preparing for use of the incinerators for the measles campaigns in March 2002.

In the Lao People’s Democratic Republic WHO support has included installation of Sicim /Vulcain incinerators in three populous provinces. Incinerators in seven more provinces are planned for 2002. The country’s safety application to GAVI was approved in December 2001.

China is challenging because of its size. However, there has been progress in that AD syringes for HepB and all routine immunization were included for 12 western provinces and other poor counties in a successful GAVI application. There is some local production of AD syringes.
WHO will be working on issues in Papua New Guinea. Work is also to be done to find solutions other than incineration for the Philippines, as all incineration is banned there.

6.3 Country perspectives

Ghana (M.E. Abun)

The injection safety policy was revised in 2001 and a strategic plan drawn up. AD syringes have been in use in Ghana since 1996 in routine immunization (disposables for BCG), and for all mass campaigns.

Injection safety assessments and follow-up

The following are some of the findings of injection safety assessments in 1999.

There was a new syringe and needle used for every injection. Needle-stick injuries were reported by 80% of health workers in the previous 6 months; 60% of health workers were observed to be recapping needles; 68% of facilities used safety boxes; and there was supervised burning at 52% of facilities. Because of recapping the greatest danger was infection from patient to health worker (a risk of 48%), whereas the risk of patient to community infection was 28% and risk of infection from patient to patient only 2%.

Since then, a follow-up has shown that, despite bundling of vaccines and AD syringes for all routine immunization, there are interruptions in supply due to syringes and needles arriving after the UNICEF vaccines, or to some donors not including the syringes with vaccine, or to wastage and even pilfering. While safety boxes have been used for static services, there is irregular use for outreach. Lack of incinerators has also brought about disposal problems. Observation has shown that there is incomplete burning of used syringes and needles in pits.

Measles campaigns have provided an opportunity to improve injection practices and disposal. Before a measles subnational immunization day in 2001 there was retraining of all workers in safe administration and disposal. AD syringes and safety boxes were provided, and the boxes were delivered to sub-district level for burning. There was a specific health worker in charge of waste disposal. Pits, one per subdistrict, were dug for burning. No recapping was observed!

De Montfort incinerators have been built with WHO support in each of the 12 districts. These burn four safety boxes in 30 minutes. Health workers prefer the Gomoa (metal) design, which burns more boxes more quickly but raises environmental safety concerns about dioxins. The number of safety boxes burned was monitored.

Health workers were trained in AEFI monitoring in 2001. But there have been problems such as lack of cooperation in submission of forms. The opportunity to undertake retraining was taken with the measles campaign, with a column about AEFI included in the tally sheets. During that measles campaign about 800 000 children were vaccinated. There were 12 reported cases of rash, fever, abscess, vomiting and one serious anaphylaxis in one district, all of which were followed up.
After the campaign, the immunization services were approached by the NRA. Retraining of regional staff was done by the NRA in June 2002. An AEFI column was included on the monthly immunization returns form. Implementation was to start in August 2002.

Challenges

Some of the challenges include:

- introduction of BCG AD syringes and affordable safety boxes for all injections, not just for routine immunization;
- continuous education on safety for health workers, in particular to avoid recapping (in areas where the measles campaign did not educate workers on this aspect);
- ensuring proper disposal and destruction of used equipment in pits;
- resource mobilization for new incinerators, as one per subdistrict is not enough; and
- dissatisfaction with slow burning of de Montfort incinerators during mass campaigns.

Next steps

- The immunization services will collaborate with other directorates/institutions for help in monitoring and creating a unified injection safety policy. Efforts will be made to strengthen logistics at all levels; to explore local production of AD syringes and safety boxes; and to work with the NRA for AEFI monitoring. Continuous education will be given to both health workers and the general public on injection safety issues, using some GAVI funds for new vaccine introduction for this purpose. The planned measles campaign in 2002 would be used to improve vaccine administration and disposal practice.

United Republic of Tanzania (C. Akim)

Until 2001, the injection equipment used for immunization was sterilizable needles and syringes. An injection safety assessment was done in 2000 and 2001. This showed that 47% of all injection practices were unsafe. The assessment was then used for advocacy. In 2002, Tanzania had a BBC media campaign with introduction of posters and educational material. AD syringes and safety boxes were also adopted, as was the use of incinerators in district hospitals.

Injection safety assessments

The injection safety assessment showed that nearly half of all injections were unsafe, and that the majority of facilities did not follow safe disposal procedures. There was a general lack of awareness of the risks of unsafe practices, especially the risk of hepatitis B.

Among attention areas pin-pointed were: sterilizers in poor condition; needle-stick injuries to staff during sterilization and recapping of used needles; abscesses resulting from immunization injections; lack of safety boxes; unsafe disposal of loose needles/syringes and safety boxes and lack of awareness /action in the curative services.
**Action and progress**

Recommendations were made after the review, and the MoH and the ICC immediately took action. Findings were used as advocacy tools to get support for policy implementation and funding.

Steps taken included instructions to health workers on use of sterilizers, and UNICEF purchase of sterilizers and Kit Bs. Emphasis on monitoring and supervision was increased.

Use of AD syringes in routine immunization was implemented in 2002. For campaigns, their use started in 1999.

Through the BBC Media Campaign, efforts were made to raise awareness of risks of infection to motivate staff to take more care. Recapping of disposable needles and AD syringes was discouraged. Ideas for improvising safety boxes were promoted in the curative services, and staff responsibility for safe disposal was promoted through leaflets and the media campaign.

In the area of waste disposal national guidelines for safe disposal were drawn up by the MoH. Construction on low-cost incinerators began at district and health centre levels, and so far 13 such incinerators have been put up in 12 districts. These are dual chamber autocombustion models developed by de Montfort University, operating at 800°C to 1000°C. The MoH has put aside funds to support the construction of the incinerators in other districts. Labour is expected to be provided by individual districts.

Efforts were made to create partnerships for safe disposal with other MoH programmes and NGOs (to deal with the curative services).

In addition, there was wide dissemination of the *Healthworker* magazine (15 000 copies), with cartoons, interviews, competitions, as well as of eye-catching safe disposal leaflets. There were 10 000 colour posters promoting responsibility for safe disposal and 10 000 community posters to raise awareness of the risk of unsafe disposal. Finally, plans were developed to provide more materials using injection safety support from the Vaccine Fund.

**Strategies**

The injection safety plan for 2002 aims for achievement of: one sterile needle and one sterile syringe for each injection; AD syringes and safety boxes for all routine immunization injections; and incineration of safety boxes under supervision, as close to the point of use as possible.

Planned future activities are:

- behaviour change among health care providers and the community, through the design of messages targeting these audiences on the dangers of unsafe injections;
- advocacy to seek approval and support from high-level policy makers within the government and partners;
- training of health workers on one sterile needle and one sterile syringe for each injection, and the other policies set by the Ministry;
- efforts to accurately forecast equipment needs, effectively distribute supplies and equipment to the districts, and create a good monitoring system at all levels;
- training for health workers in injection waste management, with thorough supervision of safe injection practices;
- construction of 120 low-cost incinerators by 2003;
- development of IEC (Information, Education and Communication) materials for waste management and injection waste collection.

Should the application be approved, Vaccine Fund support will ensure provision of AD syringes and safety boxes (other sources of funding are from the Danish International Development Agency and the Government of the Republic of Tanzania), training, IEC materials, and monitoring and evaluation. The building materials for incinerators will be provided by the MoH while the labour is to be provided by the districts.

Discussion

The countries were congratulated on the considerable progress achieved. While there are impediments, they are trying to overcome them. Despite the heavy reliance on the Vaccine Fund to meet costs, establishment of incinerators was being incorporated in the health care system, which augured for future sustainability.

To questions about the major impediments, the following responses were offered.

- The major impediment in Ghana is the behaviour and attitude of the health worker, hence the need for a communication campaign targeting the health worker with the message: “We are concerned about you. We are concerned about your health.”
- The major impediment in the United Republic of Tanzania is the disposal problem. It is not cost-effective to put incinerators at dispensary level. There is therefore a problem of a system to transport safety boxes from the numerous dispensaries to the incinerators.

Asked how behaviour change would be monitored, Ghana suggested that the best way would be to do a survey. However, the country did not have the budget to do this annually. The 1999 survey would form a baseline.

Asked about cost benefit with regard to incineration, and environmental safety assessments and security issues, it was explained that Ghana had not done an environmental assessment as such but had used the information available from the de Montfort university. A problem with smoking was adjusted by engineers.
6.4 Linkages with the measles mortality reduction & MNT elimination

Presentation (A.M. Henao-Restrepo)

Maternal and neonatal tetanus (MNT) and measles represent around 60% of the deaths from vaccine-preventable diseases, which suggests that a certain level of priority should be given to reducing mortality linked to these two diseases.

In the Region of the Americas transmission has been stopped in most countries (an elimination goal was set for 2000). In the European Region there is a goal of elimination by 2007, and in the Eastern Mediterranean Region by 2010. There is also a goal for elimination in the Western Pacific Region (WPR), and strategies for elimination have been implemented in southern African countries. In sub-Saharan Africa and the South-East Asia Region (SEAR) efforts are being focused on halving measles mortality by 2005.

In the case of MNT, 57 high-risk countries were identified in 1999, mainly in sub-Saharan Africa, South-East Asia and some parts of the Western Pacific Region. The countries where accelerated disease control is needed are more or less the same for both diseases. These countries certainly also represent areas of low DTP coverage.

Strategies to reduce measles mortality include:

- improving coverage and quality of routine immunization services;
- ensuring a second opportunity for measles immunization (supplemental or routine);
- establishing effective surveillance for measles disease and monitoring of vaccine coverage;
- improving case management, including Vitamin A supplementation.

Eighty-one per cent of countries have already implemented a second opportunity. The number of measles doses has doubled in the last two years, and will continue to rise. In 2002, 47 countries will implement mass campaigns for measles, and 240 million children will be vaccinated. The magnitude of the challenge is not just the vast number of vaccinations. Many of the countries also face complex emergencies.

In the case of MNT, it is estimated that 21 countries will conduct supplementary immunization activities (SIAs) in 2002 to immunize 20 million women of childbearing age. Thus some 260 million injectable vaccines will be administered in 2002, many in countries where the infrastructure and services will be put under tremendous strain. Both the measles and MNT programmes of elimination are determined to meet the challenge of these weak infrastructures and to make a contribution to strengthening the systems and improving immunization safety.
Opportunities to improve safe and efficient vaccine administration and disposal technologies

Mass campaigns provide an opportunity to improve immunization safety, with respect to use of injection safety equipment, adequate injection techniques, disposal of sharps in safety boxes, and adequate waste management.

Lessons learned can be converted into action. In the area of planning, the importance of long-term plans of action for accelerated disease control, endorsed by the ICC, and of yearly workplans with a calendar of activities, has been recognized. So too has the importance of assessing immunization safety issues before mass campaigns, as has the need to draw up detailed campaign microplans, including local strategies for waste management and disposal.

In the area of implementation, more opportunities are presented by coordination among ADC initiatives. Thus common tools can be used for monitoring and supervision. Efforts can be made to coordinate training on immunization safety and share experiences of appropriate techniques for waste management and disposal. Social mobilization and advocacy efforts to promote behaviour change for safety can use the resources for measles, MNT and routine immunization through GAVI.

In the area of new technology, opportunities are presented by the development of UniJect™ for use with TT vaccine. In 2002 776,000 women of childbearing age will be vaccinated using UniJect™ in seven countries. In seven to eight years, aerosol administration of measles vaccine will be ready for introduction (see section 5).

Discussion

The following points were made in answer to questions.

- There is now political support to accelerate measles control.
- Problems with measles funding might be due to a lack of interest by some donors in giving a new focus to strengthening immunization services.
- WHO and UNICEF have been working for over a year to collect information from the WHO and UNICEF regional offices about vaccine demand, campaigns, vaccine to be used, resources available and production capacity. In 2002–2003 there will be about 350 million doses used in measles campaigns, almost equal to the global capacity, so there is unlikely to be a shortage of vaccine for the next four years. Of this about 20% will be in the form of measles–mumps–rubella (MMR) vaccine, well below the global capacity. However, heavily populated countries are to carry out campaigns, and WHO has stressed that these campaigns have to be carefully planned. On the negative side, of the 10 manufacturers of measles vaccine, only 7 are pre-qualified to provide vaccine to UN agencies. Only two have chosen to produce monovalent measles vaccine; the others produce combinations, which are more profitable.
- With respect to supply of AD syringes and safety boxes, it is important to know the exact month in which they are needed. WHO and UNICEF are doing their best to get information, including information on changes from measles vaccine to MMR.
- While PAHO has no problem with procuring vaccine, it has difficulty procuring syringes. There is a lack of elasticity. Greater coordination is needed.
6.5 Report on Focus Project

Presentation (S. Khamassi)

The WHO Mediterranean Centre (WMC), an international centre for action research, advocacy and training, focuses on access and coverage of services. Its mission is to identify constraints, facilitate sharing of experiences, field-test potential solutions to improve access, combat discrimination and promote social insertion.

Project “Focus” aims to ensure immunization safety through using the quality cycle and all the available tools and knowledge developed by WHO. It is targeting two countries in a concentrated and sustained way: the Syrian Arab Republic and Burkina Faso.

Focus’s objectives are to:

- ensure substantial and measurable progress in immunization safety;
- document the process that allows this progress;
- document key factors to ensure sustainability of this progress; and
- serve as a lesson to other countries.

Technical areas to be covered include:

- injection safety: availability of equipment; training on best injection practices; behavioural change;
- safe waste management: availability of equipment; training in safe waste collection and disposal; a strong communication component; and
- AEFI surveillance and management.

The project started with a national assessment and action plan to ensure immunization safety in the Syrian Arab Republic, 2002–2004. The first phase involved assessment of the situation: a survey on the safety of injections in the Syrian Arab Republic was done in July 2001 using a two-stage cluster sampling (WHO Tool C). Data from 80 health facilities were included in the analysis.

The results of the analysis highlighted a number of areas of risk: lack of sterility of injections, needle-stick injuries to health workers, two-handed recapping and sharps in the surroundings of health centres. In some health centres, this waste was dumped in an unsupervised area, or burnt on the ground.

According to these findings three major problems should be targeted in the national action plan: shortage of equipment and supplies; unsafe management of sharps waste; and the need for behaviour change.

Objectives of the national action plan are to establish an immunization safety unit at the MoH, and to work to promote behaviour change, ensure provision of equipment and supplies, and improve management of sharps waste. AEFI surveillance will be reinforced and progress monitored through regular supervision and evaluation.
Among important issues tackled were finding a focal point within the Ministry of Health. To bring about behaviour change, training sessions were planned with training of trainers and training of health care workers. How behaviour change will be assessed still needs consideration.

A further issue which required consideration has been whether to import AD syringes or transfer technology for local production. The Syrian Minister of Health decided on the latter solution to ensure sustainability. Until local production occurs, there will be a gap between the costs of disposable syringes and AD syringes: US$ 196 thousand for two years. Some donors have been contacted about funding the gap.

The shortfall in the budget needed to implement the immunization safety national action plan in the Syrian Arab Republic 2002–2004 is made up of: US$ 10 000 for production of communication materials for health workers and community (posters, TV spot, guidelines) in 2002; US$ 392 000 for importing sufficient AD syringes for two years; US$ 45 000 for building 90 de Montfort incinerators over two years (one in each health district). A costing for technology transfer for local production costing has yet to be determined.

6.6 Report on SIGN activities and annual meeting report

*Presentation (Y. Hutin)*

Injection safety is increasingly being implemented as a cross-cutting initiative. Policy management tools are rolling out, and curative-size AD syringes are arriving.

Ideally, SIGN should be seen as an intermediate coordinating mechanism and as a way to gain momentum. However, prevention issues should be carved out and integrated into other areas of work in WHO. HIV/AIDS prevention programmes should raise awareness regarding the risks of unsafe injections. Essential drug programmes should make sterile syringes and sharps boxes available, and address injection overuse. Donors and lenders should “bundle” supplies of injectables, vaccines and contraceptives with AD syringes. Health systems should manage sharps waste as part of their “duty of care”.

The HIV programme’s involvement in injection safety is reflected by the fact that the 10 key elements of national HIV prevention and care strategy now include: (a) infection control, including injection safety, and (b) health care worker protection. This is a huge breakthrough, although there is a lot of cultural work and adjustment to be done.

Since 95% of injections are given in the curative sector, national drug policies have a leading role in national policies for the safe and appropriate use of injections. As endorsed by the Essential Drugs List (EDL) expert committee (April 2002), with every supply of injectable drugs should be included the equipment necessary to give them in a sterile fashion, that is, disposable injection equipment (AD syringes when available), diluents and sharps boxes. This applies to national stakeholders procuring essential drugs, donors and lenders supporting specific programmes, and all in-kind drug donations.
The national drug policy should also aim at promoting the rational use of drugs, including restricting access to injectable medications, and promoting use of oral medications. Unnecessary injectable substances are to be “cleaned up” from the Essential Drugs List. Sharps waste management within health care waste management should include (a) a policy stating the responsibility of health care systems; (b) an integrated, comprehensive approach; (c) training at all levels; and (d) the choice of a waste treatment option of appropriate quality and safety. Managing waste is a management problem that goes beyond provision of incinerators.

In terms of policy management, tools are being rolled out. SIGN is working on an injection safety policy management planner, to be supplied on CD-ROM This tool will be discussed at the annual SIGN meeting in Cambodia in October 2002.

The lack of standards for curative AD syringes has been a setback in attempts to move this issue forward. However the Essential Drugs policy statement has given a mandate to work broadly on the curative sector. ISO standards are to be drafted for curative AD syringes. On the basis of the EDL expert committee statement, the department of Blood Safety and Clinical Technology collaborated with selected curative WHO programmes for them to endorse the bundling principle. SIGN has persuaded some curative WHO programmes to go for the bundling concept. This allows WHO to start with a procurement specification for curative syringes, after which the ISO committee will put together its standards. The curative sector is funded through a large variety of funding mechanisms and, within that sector, there is a very decentralized funding mechanism. The free market should be allowed to work within a system to ensure quality and safety, and to allow regional or national procurement for AD syringes at the best price.

How does all this affect work in immunization?

- Immunization managers can look for partners in their MoH (e.g. HIV managers, who are now encouraged to educate the public and health care workers about the risk that they can get HIV through a syringe).
- More technical assistance will be available for country level, including the communication component.
- The system to ensure safe injection equipment in the immunization sector can help build a broader system that includes the curative sector. The curative system can also help the immunization system to take into account issues of national production and regional procurement.

Discussion

A Committee Member commented on the subject of bringing together curative and immunization injection safety efforts, to which another pointed out that there are some essential differences that make this difficult, as the goal of rational use of drugs is to limit injections, whereas one wants to increase coverage with injectable vaccines (those with no alternative form of administration).

In response to this comment it was stated that the essence of reconciling rational use of drugs and increased access to safe injection equipment was that one should tell people not to receive an injection unless really necessary, but, if an injection is necessary, it should be sterile.
A further response to the above comment was that in Uganda there was worry that awareness of HIV was causing a fall in immunization coverage. A safety assessment showed, however, that the mothers who were aware of HIV were more likely to ensure their children were immunized.

6.7 Working in the field to improve safety

Presentation (J. Millogo)

Challenges
Among challenges and issues that have to be solved before one can begin to carry out assessments are:

- **Coordination among partners.** This can be difficult at field level, for personal or institutional reasons.
- **Coordination between government sectors.**
- **Conflicting priorities and agenda.** It is difficult to get meetings with immunization managers unless they have received a directive on the subject, as safety is not considered a priority.
- **Resistance to survey methodology.** This comes at the beginning, but enthusiasm is easily built up.
- **Operational issues.** Discussions on this can be endless. Even choosing a venue can be an issue.
- **Ownership.** It is important that the Ministry of Health have this.

Opportunities
Opportunities to improve safety include: increased public concern for safety; increased pressure for safety from HIV programmes; and availability of partners. Measles and TT campaigns also present an important opportunity.

Dr Millogo gave advice on various actions to help people in the field, including provision of guidelines, supporting assessments and advising on funding mechanisms beyond GAVI. He suggested further “small” steps, including information from HQ to field offices, and identification of someone inside the MoH as a go-between. It was important to keep in touch with key players, to make realistic recommendations and to follow up on their application.

Assessment results
Assessments undertaken in Guinea, February 2002 & Senegal, April 2002, highlighted the following.

- Patients are safety conscious and willing to pay for their own equipment.
- Injection practices are not necessarily safer in settings with higher qualified health staff.
- Routine immunization has collapsed in some areas.
- There is a high risk to patients and health workers from unsafe injection practices in both countries.
• There are risks to the community in both countries from sharps found in the areas surrounding health centres and, in Guinea, from waste dumped in unsupervised areas in health centres.

Discussion

Comments made included the following.

• It is important to be aware of difficulties such as unwillingness by some people to put emphasis on AEFI{s in case this lowers coverage of campaigns.

• In response to a question as to whether within the MoH the quality control department could be given responsibility of immunization safety, the reply was that this responsibility should remain within the immunization service.

• Looking at the success of the polio eradication initiative one can conclude that advocacy at the highest level is one of the requirements for success.

6.8 Integration of waste management: success stories

Presentation (R. Carr)

The presentation looked at keys to success and a few success stories.

Policy for safe health care waste management should include designating a responsible authority and encompass a regulatory framework and guidelines. It is important to assess quantities of waste, whether for mass immunization or local curative services, and to integrate health care waste management into an overall waste management plan, if such exists.

In addition, a comprehensive system of health care waste management (both immunization and curative) should include the following:

• minimization and segregation of waste, as well as safe collection, handling, storage, treatment and disposal of waste;

• awareness and training on waste management, at regional or country level, including training of trainers, and education on risks and safe practices to inspire a demand among the public for better practices; and

• selection of options for the management of health care waste: incrementally improving solutions as resources become available; bearing in mind environmental friendliness; worker’s safety, sustainability; acceptability, and monitoring of safety and efficiency.

An examination of risks shows that the greatest health risk to patients, staff and community is due to the reuse of needles and syringes. However, risks to health workers and community can still be significant without reuse, if sharps disposal is not done properly.

In addition, burning health care waste at low temperatures produces dioxins, which are persistent toxins that can affect human health and the environment. It can also release mercury and other heavy metals that can affect human health and the environment. The risks from dioxin and mercury due to burning health care waste are unknown.
In seeking a technological solution for managing waste, it should be borne in mind that there is no one-size-fits-all solution. WHO is compiling a quick reference guide to available technologies. In choosing a technology, regulatory compliance must be looked at, as well as social acceptability. There should be awareness of environmental concerns, pressure groups and bans on burning in some countries.

The approach should be incremental. Immediate waste concerns should be tackled to reduce risks, and the situation should be improved incrementally as resources become available. Finally, one should think about the “polluter pays” principle — even syringes are a pollutant that we are adding to the environment.

Success stories

It is important to build on successes in other areas. There are now sufficient success stories from which to learn.

Cambodia has introduced a system of waste disposal and management into different provinces. This relies on strong planning, an appropriate treatment option, incinerators at provincial level, and trained people to monitor and handle the incinerators. (See WPRO: section 6.2.)

In India the Air Force Hospital has done a good job of managing health care waste, with budgeting, training and strict supervision. The nongovernmental organization (NGO) Shristi has been pushing for guidelines for medical waste management, doing public outreach work and training. SEARO is working closely with Shristi to evaluate treatment technologies.

Uzbekistan has had some success with pilot projects, thorough staff training in injection safety and waste management. Evaluation showed that provision of sharps containers and a waste treatment alternative were very successful. Finally, for the West African measles campaign, incinerators were installed at district level, to handle 200 out of 300 tonnes of waste. (See section 6.2.)

Discussion

The following points were made:

- On the role of WHO/HQ in promoting waste disposal: although WHO resources are fairly limited it is willing to provide technical advice. WHO has done country level assessments and workshops. The Organization has also produced guidelines for an action plan.

- In answer to a comment that there needs to be information on long-term risks of waste disposal technologies, and guidance to importers of incinerators:
  - WHO has created specific emission targets for incinerators. Waste segregation is necessary to avoid burning mercury, and a high incineration above 800°C. The issue of dioxins is tricky since one has to use optimal temperatures and to run the incinerator correctly. Dioxins get into the food chain, and how this process translates back to emission levels is complicated to work out. However, one can conclude that with good practices incinerators are an acceptable interim solution, until other solutions (e.g. steam sterilizers) are perfected.
WHO is also undertaking studies to estimate the risks of dioxin emissions into the environment from incinerators for immunization waste, against the risks associated with non-incineration. Dioxins are found globally, but over the last 15 years the concentrations in the environment and people’s blood have been decreasing. WHO cannot recommend technologies that create dioxin, but it can recommend the reduction of risks.
7. Strengthening of NRAs and mechanisms to monitor and respond to AEFI

7.1 Global perspective: progress in country support activities

Presentation (A. Bentsi-Enchill)

The aim of the V&B Strategic Plan is to establish efficient mechanisms, involving NRAs, immunization managers, and vaccine producers, to detect serious or potentially serious AEFIs and enable prompt and effective response, in order to minimize the negative impact on health and immunization services.

Data from the WHO/UNICEF Joint Reporting Form, in 2000, show that the percentage of countries that reported an AEFI system was 43%; 21% reported no AEFI system and 36% did not provide data. When these are compared with data reported by countries and data obtained through the NRA system, there are differences.

- Of 91 countries that report an AEFI system through the JRF, only 45% meet the NRA requirements for AEFI, 29% do not.
- Of 45 countries that report no AEFI system through the JRF, 16% meet the NRA requirements for AEFI, while 53% do not.
- Of the 78 countries that do not report data on the JRF, 33% meet the NRA requirements, 28% do not.

Overall 66 countries have had an NRA assessment conducted, 45 of which included surveillance of the AEFI function. 55 NRA assessments and follow-up visits are planned for 2002-3.

Within the Department, the activities are coordinated between ATT (which undertakes the NRA assessment) and other groups involved with the ISPP, EPI and Vaccine Assessment and Monitoring (VAM). Nine countries have so far been identified as targets for an AEFI assessment.

Common indicators have been developed for NRA assessments and NRA supporting activities. A revision of indicators to assess the AEFI function took place November and December 2001. A review/endorsement of indicators was made by advisory committees. In addition, WHO has developed an assessment tool/guide. The next steps are to test and finalize the tool, and include it in the GTN course on AEFI. WHO is also developing a shared/linked database to guide follow-up activities, based on assessment with common indicators.
The WHO GTN AEFI course provides skills and information to national level staff for AEFI monitoring and management. Currently there is one training centre at the University of Cape Town, South Africa. New training centres have been identified in Tunisia and Russia. Centres in WPR and SEAR are under discussion.

Different approaches have been considered for supporting countries with surveillance activities. First, one needs to know whether surveillance is being done because it is an NRA requirement or because the country recognizes it as a programmatic need. This has implications for ownership, commitment, resources (personnel, budget). There have been discussions around whether surveillance activities should be introduced in campaign settings. In special situations (e.g. the most populous countries), sentinel surveillance targeting selected regions might be more appropriate to initiate AEFI monitoring.

Challenges include questions relating to how to address fears that surveillance and increased awareness of safety issues result in negative impact. There are fears that surveillance creates a potential for assigning blame, identifying spurious associations and generating false hypotheses. Further, it is feared that surveillance may generate a huge amount of work.

WHO is engaged in developing resource materials that are easily accessible in multiple languages. Technical documents include: guidelines for monitoring AEFI; background information on AEFI; and an aide memoire for safety of mass immunization campaigns.

The immunization safety web site (http://www.who.int/vaccines-surveillance/ISPP/index.shtml) provides access to documents, fact sheets, press releases and so on.

7.2 Regional perspectives

*African Region (M. Dicko)*

The target is to establish a comprehensive system to ensure the safety of all immunization by national immunization services. Since 2000, an increasing number of countries have been supported from HQ and AFRO. Assessments of NRAs have been carried out with the goal of strengthening them. Following these, training has been conducted, including training of staff from NRAs and immunization services in specific functions. There has been a follow-up assessment conducted in South Africa, and in the next year more such assessments will be carried out.

Activities that support strengthening of NRAs include the assessment of overall vaccine management performance by countries (12 countries were assessed in 2001). In addition, WHO gives technical support to countries and collaborative support is provided by stronger NRAs (South Africa, Zimbabwe).

Of importance to immunization safety, AEFI monitoring systems are in place in Ghana, South Africa, Uganda, Zimbabwe. A system is also in place in Senegal which, as a producing country, still has many issues to address. Thanks to these systems, national staff have been better able to respond to AEFIs. Further, it is hoped that the vaccine assessments and support will increase the ability of countries to handle vaccines better.
Future plans include efforts to:

- ensure closer collaboration between the NRAs and national immunization services at national level;
- promote and support collaboration between weak and strong NRAs at regional level;
- continue capacity building at national level;
- continue technical and financial support to countries;
- ensure sustainability of programmes through financial support; and
- closely monitor action plans.

**Region of the Americas (P. Carrasco)**

To ensure vaccines of known quality, there is close collaboration with, and training of, the NRAs. They are invited to headquarters for four months, and taken to the field to work in other countries. Subregional workshops are held and information disseminated.

Progress in NRA strengthening can be summarized as follows:

- Harmonized registration requirements have been established for non-producing countries.
- AMRO is helping and training the countries to establish vaccine lot release mechanisms.
- AMRO has been supporting a network of National Control Laboratories, and a certification programme has been initiated to establish regional labs with capacity for specific vaccine testing.
- Training programmes are being designed and offered to NRAs to develop expertise in good manufacturing practices (GMP) inspections and clinical evaluation of vaccines.
- 11/20 (55%) of countries have a functioning NRA and four have been evaluated according to WHO/AMRO criteria for countries that import and/or have local production.
- There are now at least four locally produced vaccines — in the public sector — that meet GMP standards (four in Brazil, and one in Cuba). Columbia produces one vaccine that does not meet the standard. Although Venezuela has a good NRA, AMRO has not evaluated it to affirm how it meets this standard.

With regard to immunization safety concerns, the objectives are to augment each country’s managerial and technical capacity regarding immunization safety issues for quick response to all public concerns about vaccines, and for rapid, honest and efficient communication of results of the investigation.

Technical assistance is provided for investigation of serious events alleged to be vaccine-related. Three workshops have been held on partnership building with mass media (2001–2002) to improve the management of information regarding significant adverse events.
For advocacy purposes, articles are published, technical resolutions are adopted in the policy forums of the Region's ministerial conferences, and safety is on the agendas of meetings of national committees on immunization practices, professional societies and scientific congresses.

At workshops on partnership building with mass media, the focus is on improving immunization managers’ performance in managing information regarding significant adverse events causally related to immunization, sharing this information with the public and health workers. Three such workshops have been held involving 11 countries (2001–2002).

In the course of giving technical assistance during campaigns with MR vaccine, AMRO was able to estimate rates of adverse reactions in local population; to follow up pregnant women inadvertently vaccinated with MR vaccine (Bahamas, Brazil, Chile, Costa Rica); to improve knowledge on safety profile; and to set up or improve the monitoring system. The outcome was the suspension of the use of MMR with Leningrad Mumps Strain, and a recommendation for use of MR for mass campaigns, and confirmation that women inadvertently vaccinated with MMR/MR gave birth to normal healthy babies.

Rapid response was made to all alleged vaccine-related events in 2001–2002:

- Guatemala: there were two cases, with one infant’s death resulting from programmatic error, 2001 (mistaken use of neuromuscular blocking agent for diluent).
- Peru: six infants died following DTP vaccination, 2001 (viral infection, specimens under investigation).
- Cuba: three infants died after measles vaccination, 2002 (preliminary review indicates programmatic error).

Further training is required, supervisory activities need to be augmented both in terms of resources and quality, and much work remains to be done with the remaining countries to establish functional NRAs. In addition, appropriate investments are required to transform production facilities, equipment and procedures so that they comply with GMP and national/international requirements.

Important issues to face are:

- Do all countries, regardless of size, need to establish a viable NRA?
- Do all vaccines provided through UN Agencies need to be registered in a country?

**European Region (D. Maire)**

Most countries have an AEFI surveillance system already in place. Guidelines have been distributed and countries have established a list of AEFIs to be reported. Some countries are reporting from 0–10 cases of AEFI, others from 11–100 cases. 24% of countries reported more than 100 cases, and 24% reported at least one death associated with immunization.
Examples of handling adverse events

In one country, with the measles campaign in November 2001, a 16-year-old girl was hospitalized five days after MR vaccination, diagnosed with post-vaccination encephalomyelitis. The case was reported through the national AEFI surveillance system and reviewed by the national committee. The patient was re-hospitalized in March, with a diagnosis of retrobulbar neuritis, suggesting multiple sclerosis (MS).

It should be noted that the case was not mentioned in the report of the measles campaign and that the clinicians were not familiar with AEFI epidemiology.

In a second country a 12-year-old boy suffered from a sudden onset of serious headache two days after a first dose of hepatitis B vaccine. At the district hospital he was diagnosed with acute cerebral oedema, and later at the children's hospital in Tbilisi he was diagnosed with acute disseminated encephalomyelitis, presumably post-vaccinal. Another neurologist considered viral encephalitis as a diagnosis and recommended Zovirax. WHO was notified one month after the event.

Both cases were notified because of family pressure. In the first case, exchange of information in a network of experts could have led directly to the conclusion that it was a coincidental event. In the second case, the capacity for case investigation was limited, and thus it was difficult to prove non-association.

AEFI surveillance system example

The AEFI surveillance system in a third country was described. There are two parallel systems: one receives reports from pharmacists, dentists and hospitals, the other, through the MoH CD Department, from regional offices and hospitals. There is poor coordination and no systematic exchange of information between the two systems. The former has a poor capacity for follow-up. In addition there is a lack of clear definitions of AEFI to be reported. It is estimated that although only 10 AEFI were reported, 100 reports were generated.

Future

EURO will continue to assist countries in establishing AEFI systems, to assess existing systems and to revise a list of reportable cases. Involvement of health professionals, including those from the private sector, will be promoted. A system of performance indicators will be established. Finally EURO will facilitate establishment of a regional network for AEFI systems, identify regional experts and continue with GTN courses.

South-East Asia Region (S. Guichard)

In the South-East Asia Region, India, Indonesia and Thailand produce vaccine. India and Indonesia also export, while Thailand produces for the domestic market only. India has some 34 manufacturers. Bangladesh, the Democratic People’s Republic of Korea and Myanmar produce some vaccines but, there, the NRA is not functioning. Nepal and Sri Lanka procure vaccine from prequalified manufacturers. Others procure through UN agencies.

Three countries had NRA assessments in 2002. The rest of the countries had all been assessed previously.
In the second half of 2002, in India, there was to be GMP training in Pune, and OPV fillers were to be encouraged to apply for WHO prequalification; there were also to be GMP inspections of nine manufacturers with potential to export vaccine, and AEFI surveillance was to be carried out in selected Indian states. With regard to the OPV fillers, a new process was introduced in 2002 (UNICEF buys between 400 million and 500 million OPV doses from the local market).

In Nepal, Myanmar and Bangladesh, technical support was to be provided to develop guidelines and procedures for reporting. In Sri Lanka, a GTN training centre for AEFIs was to be established. Bhutan, Maldives and Democratic People’s Republic of Korea were to have NRA assessments.

NRA follow-up visits were to take place: in Sri Lanka (November 2002); Thailand (November 2002); Myanmar and the Democratic People’s Republic of Korea (September 2002); India (September and December 2002).

Western Pacific Region (W. Antkowiak)

NRA assessments were carried out in 1998–2002 in Australia, China, the Republic of Korea, Philippines and Viet Nam, which are all producing countries. These showed that all vaccines produced in Australia and the Republic of Korea were of assured quality. In China half of the vaccines met assurance quality standards, in Philippines all but DTP met the required standards and in Viet Nam only measles and DTP did so.

In 2001, of a total of 37 member states and territories, 26 countries were targeted for NRA activities. Of eight countries that procure their own vaccine, four exercised all necessary NRA functions (four did not), and of five producing countries, three exercised all necessary NRA functions (two did not). There were 13 countries that procured their vaccine through UNICEF.

For the percentage of vaccines of assured quality produced in WPR in 2002 see Figure 7.1.
There is one GTN centre in Japan for quality control, one in Australia with a focus on licensing, and one is being considered in the Philippines with a focus on AEFI surveillance.

**Priorities**

After NRA assessments, the priorities for China include GMP: training and technical experts to assist NRA audits in vaccine manufacturers; clinical evaluation of safety and efficacy of clinical trials; and AEFI surveillance (a team will visit to plan training and development of guidelines).

In Viet Nam, priority activities include: developing a legal basis for the regulatory system (in process); AEFI surveillance (organizing training and developing guidelines); and GMP (training and assistance of technical experts in NRA audits).

In the Philippines, priority activities following NRA assessments include considerable strengthening of AEFI surveillance. Lot release, laboratory access, GMP and clinical evaluation have not yet been implemented.

Priority activities in Australia include: developing a memorandum of understanding (MoU) to plan long-term use of Therapeutic Goods Administration (TGA) expertise for strengthening NRAs in WPR countries; and identifying funds to cover TGA participation/expertise in NRA activities. Priority activities in the Republic of Korea include: strengthening the laboratory quality system through GTN training; seeking potential for OPV and measles production; and assessing the potential for a GTN training centre on GMP.
There is increased commitment on the part of WPRO in support of regional/country activities. In the past few months internal changes have been made in WPRO to strengthen focus on these issues. In general, it is working on the following:

- system development (Viet Nam and the Philippines), AEFI surveillance and laboratory access (all) and GMP inspections (Viet Nam, China, Philippines);

- supplementing the budget to fund GTN trainees from HQ.

Discussion on NRAs

The following points were made:

- It was suggested that the GTN AEFI course could be complemented with rotation to further develop skills, as it dealt with rare epidemiology. It was pointed out that rotation can be costly. The training in GTN is designed to help managers from NRAs and immunization services to develop an AEFI surveillance system and to plan together at country level. An assessment is carried out in the countries and skills can then be strengthened by providing more GTN education, or a technical expert can be provided to implement the function.

- The way to proceed is in steps. Producing countries to fulfil the six functions are the first priority. The second priority are the procuring countries. Most of the procuring countries do so independently, so it is important that they know what they need to do. UN-supplied countries are the lowest priority, as they receive the support of the centralized system. In terms of producing countries there are new challenges posed by new vaccines. Not only must clinical trials be run and the data evaluated, but protocols must be checked. There are new regulatory pathways that have to be thought about, requiring creativity. The NRA network would look at the specific expertise that needs to be added to these countries, in clinical evaluation and specific GMP issues.

- The GTN centre in South Africa is working on developing a programme for follow-up activities for countries that have had staff trained through the GTN course.

- Some countries have moved fast and others have not. This may be due to lack of commitment at government level. China has reached five functions and is expected to reach six functions by the end of next year. A regulatory system has now been developed in Viet Nam and it has achieved five out of six functions.

- Some countries in AFR have started to do AEFI surveillance (e.g. Guinea, Mali), but not enough is done to follow up on the GTN courses to allow this to develop properly. Also, at immunization managers’ meetings the agenda should include the AEFI component.

- Industry is interested in having competent NRAs to protect vaccines from falsely attributed blame. Industry also has an interest in understanding the evolving safety profile of a marketed product. One might consider exploring ways for industry to help in the training.
7.3 Country perspectives

China (Y.U. Jingjin)

The presentation dealt with what has been done and what is to be done in China to further immunization safety.

Vaccine quality control

Before 1998, the Ministry of Health (MoH) was responsible for all aspects of vaccine quality control. The State Drug Administration Bureau (SDA) was established in 1998 (both ministries are under the State Council), and the SDA took over responsibility for legislation for vaccine quality control, new vaccine licensing, monitoring of vaccine quality, and AEPI surveillance.

Regulations related to vaccine quality control include a new Biologics Inspection Act, the National Requirements for Terminology of Biologics (6th edition), and the new National Drug Law, which was put into effect on 1 December 2001.

Good manufacturing practices are included in the new National Drug Law, which laid down stronger requirements for those enterprises responsible for the research, production and distribution of drugs. On 12 October 2001, the SDA issued a notice to accelerate the process of GMP accreditation of drugs, and allowed all the enterprises without GMP accreditation to produce only until 1 July 2004. Based on GMP requirements, 30 vaccine production lines from 15 manufacturers were accredited by the National Regulatory Authority by February 2002.

Injection equipment quality control

The Inspection and Management Regulation of Medical Devices was put into effect on 1 April 2000, requiring licensing of production and distribution enterprises and products. Reuse of disposable medical devices was prohibited and it provided for destruction of medical devices.

In addition, there are a number of regulations distributed by the SDA relating to registration and inspection of medical devices. The main requirements introduced were as follows:

- The provincial health bureaus were required to strengthen the inspection of clinical use of disposable transfusion devices (including syringes), in particular focusing on the medical agencies at county and lower levels, including private clinics.
- The medical agencies were required to strengthen the management of clinical use of disposable transfusion devices by developing and strictly enforcing related regulations, and to pay greater attention to procurement of quality equipment and disposal after use.
- The disposable medical devices could only be procured if the manufacturer could show the licence for production, the quality certification and the health authority permission.
After utilization, the disposable medical device had to be sterilized, destroyed and properly disposed of following the requirements of the local health bureau, to avoid reuse and entering the community.

The local health bureau was asked to specify the facility or manufacturer within its administrative territory to be responsible for collection and disposal of single-use transfusion devices and syringes.

Safe injection practices
The Plan of Action for Safe Injection Practice in Immunization in China, 1997–2000, had the objective of eliminating incorrect sterilization and injection practices in the immunization services by the year 2000, and of replacing disinfection through boiling of needles and syringes used for immunization by steam sterilization nationwide.

Strategies recommended in the Plan of Action covered the selection of appropriate sterilization and injection equipment, upgrading of the supply system, and monitoring and supervision etc. It also aimed to strengthen training of health workers and supervisors on correct immunization sterilization and injection practices, including development of systems for rapid information dissemination. Finally, funding was to be secured to ensure that the policies for safe immunization could be implemented.

With regard to AD syringes:

- the central government and GAVI were to introduce auto-disable syringes and safety boxes for immunization activities and cover the cost among 12 poor western provinces of China in the second half of 2002; and
- one million AD syringes were delivered to 18 provinces for training purpose in June 2002.

Work is also being done to strengthen management and supervision.

Surveillance of AEFIs
In October 1999, the MoH and SDA jointly issued the Act for Drug Adverse Events Surveillance. Surveillance centres for drug adverse events were set up at national level and in provinces, as was a reporting mechanism for AEFIs within the health system, and an expert panel at county level and above to investigate and deal with any reported adverse events.

Conclusions
While great progress has been made in immunization safety, there is still much to be done, particularly in the western part of China. Regulations to improve the production and quality of injection equipment and vaccines have been issued, but implementation of the regulations still needs to be applied throughout the country. High priority has been assigned to the problem and it is expected that increasingly rapid progress will be made in ensuring that all immunization is given safely.
Discussion on China

The presenter answered questions as follows.

To the question why the government is allowing some of the products to be produced without GMP until 2004, the response was that GMP application began in 1999, but, since China has more than 1000 manufacturers, it was difficult to achieve GMP implementation in a short time.

About the difficulties in setting up the AEFI system, the reply was that the SDA and the MoH are different departments. The resources come from the MoH but the management of the system and the reporting is the responsibility of the SDA. Many adverse events are now reported to the MoH because the local levels get some technical support from the MoH.

As to whether burning or burying waste is allowed in China and what technologies can be used in urban and rural areas, it was stated that both burning and burying are recommended.

Indonesia (L. Slamet)

Safety of vaccines depends on a system that ensures cooperation among key players, immunization manager, NRA, health workers and professionals. As Indonesia has a vaccine producer it needs to comply with all six functions of a national regulatory authority.

The findings of the WHO NRA assessment in October 2001 showed that:

- Through the National Agency for Food and Drug Control (NA-DFC), Indonesia has an independent and competent system to see that all vaccines are of assured quality (6.5 out of 7 indicators implemented).
- Indonesia has a fully documented system to register and licence vaccines (9 out of 10 indicators implemented).
- Surveillance for AEFIs has been organized but needs strengthening (4 out of 5 indicators implemented).
- A lot release system has been implemented but needs strengthening (3 out of 5 indicators implemented).
- A laboratory access function has been implemented but needs strengthening (9 out of 12 indicators implemented).
- The GMP inspection function has been fully implemented (9 out of 10 indicators implemented).
- Clinical evaluation of safety and efficacy has been implemented (4.5 out of 5 indicators implemented).
While the NA-DFC is responsible for vaccine quality, the immunization service, under the MoH, is responsible for national procurement and delivery of immunization. The two institutions collaborate on product availability, monitoring of cold chain and AEFI surveillance through the AEFI working group (see Figure 7.3).

The AEFI working group was established in 1998 with representatives from the MoH, NA-DFC, professional organizations and experts in medical law. It evaluates reported AEFI data and dose-safety aspects, and makes recommendations to the central level. It establishes AEFI guidelines, adopted from WHO guidelines, informing on the type of reaction to be reported. It also distributes the reporting form, which includes patient data, AEFI manifestation, vaccine use, treatment and follow-up action taken by the health worker.
The scheme of reporting and investigation is shown in Figure 7.3. The report is received by the district health centre from the community or the community can send it directly to the hospital. This would be sent to the provincial health office for investigation, assisted by the AEFI working group at the provincial level. The results are sent to the central level for any necessary decision to be taken.

If there is evidence that the problem is vaccine-related, the NA-DFC will review the batch file as well as other information for confirmation. The finding will be reported in the working group which will ensure any regulatory follow-up.

There are 13 provinces in Indonesia that reported a total of 43 AEFIs in 2000, involving BCG, DTP, polio, measles vaccines. Of these, 10 AEFI cases were severe but evidence was inconclusive as to causal relationships. No AEFI reports from private use were processed.

If the investigation showed there was a product-related AEFI, immediate action could be taken, namely: recall of a batch, reassessment of quality and safety, and review of product information. The AEFI working group needs to be strengthened for causality assessment, supported by substantial data on epidemiological aspects.
Discussion on Indonesia

Indonesia was congratulated for its progress in this area.

Dr Slamet answered various questions:

- On whether the CDC was responsible for the investigations in Indonesia, the reply was that the first field investigation is done by the CDC and, when there is an indication that the adverse event could be vaccine-related, the inspector from the NA-DFC joins the investigation.

- On the barriers to setting up the working group, he stated that the AEFI programme was started in 1993. In 1998 the MoH set up a working group. The key to the establishment of the working group was political will from the CDC and from the NRA.

- On whether a clearly programmatic case would ever involve the NRA, he replied that the local health authority will find out first if it is a programmatic error or not. The NA-DFC is informed but not involved. If the district working group suspects it is vaccine-related it informs the NA-DFC to get guidance.

- On how far this awareness of AEFIs has trickled down to the health worker in the clinic, the health worker in the clinic sometimes does not have enough data to identify reasons for the AEFI. The working group has proposed more training for the health workers so that they can conduct a preliminary investigation. The provincial AEFI working group needs strengthening.

- On why so few AEFIs were reported out of the huge population of Indonesia, he concurred that the AEFI working group needs to look at this underreporting. This may be partly because there is already a filtering at the local level and only those they are sure about are reported to the central organization.

- On compensation, he pointed out that the guidelines do mention compensation but do not say how or how much.

- On AEFI reporting in the private sector, the data shown do not yet include the private sector. The private sector is still reserved about reporting. Most immunization is done by the national immunization services. At meetings with the AEFI working group private doctors are invited.

Other general comments made have been included in the discussion in section 7.4.
7.4 Investigation of vaccine safety

Presentation (P. Duclos)

Global Advisory Committee on Vaccine Safety

The Global Advisory Committee on Vaccine Safety was founded at the end of 1999. It has been fully operational and has met regularly. The role of the Committee is to be proactive and fully independent, and to review the best scientific evidence. It decides what issues of global importance to bring to the table. The Committee is multidisciplinary, and advisory to the Director of V&B and SAGE.

The issues it was involved with in 2001 include: macrophagic myofasciitis (MMF); immunization and autoimmune diseases; safety of thiomersal; potential vaccine contamination by transmissible spongiform encephalopathies (TSE); yellow fever vaccine-related deaths; AEFIs following mumps vaccine; and child survival following immunization.

The last point related to findings in Guinea-Bissau published in the British Medical Journal in December 2000, indicating lower survival with DTP vaccination and increased non-specific survival with other vaccines. There are now 10 data sets outside Guinea-Bissau relevant to that discussion. Further studies included WHO-sponsored studies carried out in: Burkina Faso; Bangladesh (Matlab); Indonesia; and Papua New Guinea. These studies have not confirmed the Guinea-Bissau results. Part of the difficulty is control groups, as it is unethical not to vaccinate children, particularly where there is high endemicity.

The next meeting of the Global Advisory Committee on Vaccine Safety, scheduled for later in June 2002, was to look at the latest evidence on the safety of thiomersal; the purported links between hepatitis B vaccine and multiple sclerosis; hepatitis B vaccine and leukaemia; and the onset of Bell’s palsy following use of an intranasal flu vaccine.

Investigation of AEFI and response to crises

A fraction of reports of adverse events needs full attention. On the basis of the recommendations from the last meeting, V&B has significantly increased resources to assist with investigations of adverse events.

Often with individual cases, it is neither possible to show a link with the vaccine nor rule it out. However, in many instances it can be shown that the vaccine did not cause the situation, which is extremely useful in protecting the vaccine from undue blame. When it comes to serious programmatic errors, there are legal implications, but at least the situation can be corrected.

An important issue is that of liaison with the manufacturer, UNICEF, the NRA and with other countries. Sharing of information proactively is desirable so that other regional offices are not taken by surprise. However, when programmatic mistakes have legal implications it is not always possible to share as much as one would wish.
There is a lack of resources for WHO or UNICEF intervention, yet sometimes the potential consequences from a case might be such that intervention is needed. For example, the case may be incorrectly handled by the clinicians in the country, so that instead of giving urgent treatment they wrongly blame the vaccine.

Global activities with an impact on the ability to handle AEFIs include: development of standard definitions (through the Brighton collaboration), the Cochrane AEFI review, starting with Hepatitis B, and collaboration with the Uppsala monitoring centre to improve signal generation. Support is given to develop investigative capability. In addition, there are studies in progress on rates of anaphylaxis.

**Discussion on AEFI reporting and investigation**

The following comments were made:

- **On assessing functionality:**
  - There is a fear that if too much gets reported it will be damaging. The challenge of AEFIs is assessing the full functionality of the system. If a country has a large population and a small number of reported adverse events, it is evident that something is amiss. However, it is not necessarily a problem if there are few reports at national level.
  - We know the sudden infant death syndrome (SIDS) occurs in all countries, with a peak in the third month of life when a lot of vaccines are given. Indirect methods have estimated 30% or 40% of SIDS cases are reported, which might be a marker.

- **On country experiences with AEFI management:**
  - In Australia management of AEFIs is strongly linked to the surveillance system. This has encouraged the private sector to collaborate.
  - In the USA something similar to the system in Australia has been established. The Clinical Immunization Safety Assessment Center (CISA) concept is that one cannot expect the average primary care doctor to manage a rare case, so there is a referral system, and with time the primary care doctor learns the proper treatment. This new centre will further understanding of AEFI, and protocols for treatment will be posted on the web.

- **On the subject of encouraging report-back:**
  - To get the baseline worker to report something that he/she or a colleague might have caused, it might be better for an adverse event reporting system to be called a vaccine safety reporting system.
  - The second part of a series published by V&B, *Supplementary information on vaccine safety. Part 2: Background rates of adverse events following immunization* (unpublished document WHO/V&B/00.36), is currently undergoing revision.
  - Information on a clearly established referral system needs to be shown to the health worker.
• On the subject of compensation there was lively debate:
  – Giving compensation adds to the confidence of the public that the
    immunization services will take responsibility for programme errors.
    However, concern over the costs of compensation could be a constraint in
    getting the immunization services to report adverse events.
  – Medical care for the person suffering from the adverse event is an ethical
    issue, and the national immunization services have an obligation to provide
    services for children who have vaccine-related damage. The problem with
    paying compensation is that it can lead to blame and retribution in the
    courts. V&B is working together with the human rights section of WHO
    to work out a perspective on this, and feedback from the ISSC is welcome.
  – The US Compensation Act, which required that the health care provider
    report any adverse event specifically mentioned in the law, has been difficult
    to enforce.

• On routine reporting of AEFIs:
  – Immunization services might consider publishing tables on surveillance of
    disease, immunization coverage, and surveillance of safety, stating the
    number of cases that required investigation.
  – With respect to manufacturers’ reporting, it is the prerogative of the NRA
    in the country to decide what has to be reported. In Canada, for example,
    industry was expected to report a serious situation immediately, but regular
    mandatory reports were not seen to be very useful.

• On the subject of giving a WHO seal of approval for GMP:
  – The pre-qualified manufacturers listed on the WHO web site come under
    functional NRAs that enforce GMP. WHO also has a list of countries that
    have fully functioning NRAs that enforce GMP.

• Regarding weaknesses in the system:
  – It must be possible to deal with emergencies, especially during measles
    campaigns
  – In order to be able to make regulatory decisions information must reach
    the NRAs. If vital information is not given to the NRA, the immunization
    services are not properly fulfilling their responsibilities.
  – Yellow fever (YF) has become a very big issue, so there is now a high level
    of sensitization for reporting YF vaccine reactions.
  – There is an advocacy problem that the NRAs and immunization services
    could tackle together: on the one hand the immunization services do not
    realize that they have a broader impact on the safety of vaccine, aside
    from rectifying programmatic errors, on the other, the NRA may be
    ignorant of the needs of the immunization services.
  – The most common weakness factor is a blockage in the system at political
    level because both parties want to do a particular task. Responsibilities
    need to be agreed on, and activities then reported back to the other party.
8. Communication and advocacy strategy

8.1 Progress and gaps

Presentation (S. MacKay, M. Agha)

When someone brings a child for immunization, they are putting their trust in the immunization services. For that reason immunization safety is not an option but an obligation.

Progress

There has been much progress since the last meeting.

A window of opportunity has been opened by the GAVI partnership, with its promise to every child. The task force for advocacy and communication, currently being strengthened, is to give a stronger focus to immunization safety. The requirements to include information on injection safety assessments and plans in the GAVI applications process have presented an opportunity to find more about the needs of the programmes in terms of communication support.

There has also been progress in terms of publications giving a voice to immunization safety. Recently the WHO–UNICEF joint technical update for programme managers devoted a whole issue to safety. Another step forward has been the 24-hour service offered on the web sites of the partners.

The SIGN toolbox has a number of tools that are complementary to the immunization-specific tools. Last year, a behaviour change strategy was put together to promote the safe and appropriate use of injections. It is an easy step to adapt this as a strategy for safer immunization. This strategy was very action-oriented: sterile needles, use of safety boxes, waste management.

In 2000–2001 there were a number of communication and advocacy activities in the African, Eastern Mediterranean and Western Pacific regions, through partnering with Egypt, Mongolia and the United Republic of Tanzania. Exciting quality materials were put together in partnership with the countries.

Gaps

A fairly obvious gap is that immunization services are not reaching all children, one reason being that fear of safety issues is holding them away. Thus there is a real reason to increase community demand for safe immunization services. Ownership is key. Every parent should want to immunize their child.
There is a need for strong media partnerships, especially at country level. Having journalists interested in the issue can pay dividends before adverse events erupt.

Adverse events result from unsafe practices, so training is another key element, as well as supervision and monitoring. These might be called communication issues as it is often the quality of the supervision and the way the supervisor interacts with the person supervised that makes a difference to attitudes towards patients.

The health workers at the periphery sometimes have a huge burden of work and are not rewarded financially, so it is not surprising that the services they provide are affected. Our studies have shown that many of the health workers feel “if the system does not care about me, why should I care about anyone else?”.

Thus there is much work to do to train and motivate workers. Unless the status of the health worker is raised, good service cannot be expected.

Finally, particularly in communication, there is a need to document progress.

**Opportunities**

There are many opportunities. At the World Health Assembly in 2002, patient safety featured strongly in the agenda. Immunization safety has much to share with the rest of WHO, so this is a strong lead element.

Creating consumer demand for safe immunization will ensure a sustainable momentum where health workers cannot simply fall back into giving poor service, because the community is expecting better service.

In creating consumer demand, we are really targeting the idea of parents’ ownership. Selling safety and quality of service leverages demand. Introducing new syringes and new vaccines can be seen as added-value service, all for free.

In improving service delivery, emphasis must be placed on improving customer care. It is much more than training. It is training plus. It explains why particular work should be undertaken. We should also remember that, in terms of incentives, it is important to thank the people in the field.

Some important issues need highlighting:

- There is a need to invest in more country-level activity, strengthening immunization services through intensified communication and advocacy activities, selling safety to create demand.
- Health worker training should be imaginatively strengthened and perhaps called something like training plus.
- Waste management should build on partnerships and bring in more environmental agencies.
- There is a need to strengthen country communication skills and create a bridge between immunization services and the creative people in the country.
In terms of monitoring, some suggested indicators (from the polio experience) are: looking at whether the multiyear plan has detailed information on advocacy, communication and training interventions; whether immunization safety issues are integrated into the immunization targets; what immunization safety communication interventions have been accomplished; what has been done to improve staff knowledge and skills of new vaccines and AD syringes; the percentage of districts that have integrated an interpersonal communication module within on-job refresher training.

In terms of SIGN work the strategy was tied to assessment tools so that countries would have to develop a new monitoring and evaluation system. The four simplest indicators looked at sterility for patients, used needles in sharps containers, environmental waste, partnership with HIV programmes doing population-based KAP (knowledge, attitude and practices) studies, looking for increased awareness of injection-related risks of HIV infection.

Discussion

The vision on selling safety had full support. The following comments were made:

- Consumer demand for safety is already there. In Sri Lanka, for example, one sees at least 50% of mothers with their own syringes. What we need now is to address these demands.
- In answer to a question on whether some countries should wait before investing in promoting safety and how countries perceive such an approach:
  - In Ghana there is a realization that demand must be created and that clients should ask for the service. But promotion to the health worker is needed most of all. To the health workers, “safety” means, first of all, safety for themselves, then safety for the clients, then for the community. Since receipt of GAVI funds, use of coloured posters in Ghana has had a big impact and proved a good way of promoting the programme.
  - In retrospect, some of the difficulties now being faced in the USA and other countries are due to the fact that consumer demand for safety was not accepted early enough. The consumer groups thus developed an “ideology” that the government did not care. So, although the immunization services are trying to reach out, there is constant confrontation. This is a lesson that a programme should start as early as possible.
  - In the United Republic of Tanzania the universal child immunization service had a lot of communication input and coverage went up. But because it was not a continuous process coverage started going down. Communication should be a continuous strategy since there are constantly new mothers with children to be immunized.
- There is a lack of expertise in communication in the countries.
- Governments, engaged in structural adjustment programmes, cannot increase the share for health worker salaries in the budget. If the programmes are to improve, the issue of motivation must be addressed. One of the ideas being discussed is supervision and on-site support. An idea to be tested in Togo is that the supervisor comes with half a day of remuneration for the health worker, which is paid if a task has been done. Other ideas are to allow the health worker to take home discarded equipment, or perhaps to lay on electricity to the health workers’ homes when it is laid on to the health centre.
8.2 Partnerships supporting the drive for safety

The International Council of Nurses (ICN)

The ICN is a federation of national nurses associations in 124 countries. One of the missions is to develop and promote the special contribution of nursing to society with respect to health and quality of life. When it comes to immunization safety, nurses are key players, in terms of training, supervision, or actually providing immunization. ICN would like to develop this function in partnership with the Steering Committee.

The ICN goals are to influence nursing, health and social policy; to assist nurses to improve standards of care; and to promote strong nurses’ associations around the world that network with colleagues at country level. The ICN has established partnerships for immunization safety with WHO and Merck Publishing (providing training materials, organizing symposia etc.). ICN also has a strong alliance with colleagues in the World Medical Association (WMA) and International Pharmaceutical Federation through the World Health Professionals Association (WHPA). Millions of doctors, nurses and pharmacists are represented.

Some of the activities over the last few years include disseminating ICN and WHO publications on immunization safety. One recent innovation is the ICN mobile library to reach out to associations with basic material in health care, including immunization safety. Kits have initially been sent to Zimbabwe and Kenya. Fact sheets on immunization safety have been distributed. A symposium was organized last year in Copenhagen, where the inclusion of nurses challenged many assumptions about safety. The WHO–SIGN Best practices was endorsed and disseminated. ICN is drafting a wall chart on immunization safety.

ICN has linkages with WHO immunization training partnerships, and is in the process of endorsing the bundling policy on AD syringes, since ICN feels nurses should come on board with this technology which is at the cutting edge of safety.

ICN is in a position to develop immunization safety guidelines and training materials, and this is where partnerships with WHO will be crucial.

A way to ensure a continuous interest in safety is to ensure continuous fitness. ICN is experimenting with providing credits to nurses who attend further education courses, allowing them to renew their licences to practice. This is a non-monetary incentive to keep safety on board.

An important question is how to ensure that all nurses receive information on new developments in terms of technology, adverse events and guidelines.

GAVI: the need for feedback

Two years into GAVI, the partners need feedback. The Alliance needs to set up a structure to receive this information without burdening the immunization services. One way of getting evidence is to have regional workshops with the media to get the stories, and to pay journalists to report.
• GAVI is a new alliance and looked at as a model. What is working and what is not needs to be reported.

• From anecdotes one knows there is such a fear of AIDS in Africa that Africans are very sensitized to injection safety. But evidence of this is needed.

• One of the things that has been seen with GAVI is that donors may change views if given adequate evidence. There may be some new mechanisms to explore to obtain funding (e.g. if the above-mentioned experiment in Togo is seen to work).

• Another reason for getting information is to recognize good work. Recognition of good work may even lead to new funding.

• Looking forward, GAVI needs information for both implementation and advocacy. Advocacy includes deciding on common missions, influencing the right people, developing the right communication and communicating about success.

• The GAVI web site is to have a section on safety; and input is welcomed.

The World Medical Association

The WMA, an independent confederation of national medical associations, has a close relationship with WHO and supports the Steering Committee's commitment to immunization safety. WMA also works together with other associations representing health professionals, bound by their respective codes of professional ethics to care for all. WMA's input on issues is through policy-making.

It acts as a global representative to physicians in 75 countries to ensure highest standards of medical ethics, medical education, human rights, and professional care for patients.

At the last WMA, focus was placed on injection safety. The declaration that the health of a patient is a physician's first consideration was reconfirmed. Implied in this concept is “First, do no harm”. It was proposed that the national medical associations cooperate with their national governments or other appropriate authorities to develop policies on the safe and appropriate use of injections.

The physicians worldwide were urged to prescribe non-injectable medication whenever possible, to promote use of non-injectable medication, and if administering essential appropriate medication, to ensure safety and not harm the recipient, provider or community. They were also urged to use only safe disposal containers and not to utilize the covers of sharp instruments. In addition, they were urged to raise awareness of the risks raised by unsafe injections and to help in promoting behaviour change among patients and health professionals. It is hoped that these recommendations will be adopted by the various national associations, and that they will explore policies that ensure patient safety.
Discussion

Dr Music made a number of general comments on immunization safety:

- Immunization does much more good than harm. However, harm done by doctors, nurses and pharmacists is unacceptable. The Immunization Safety Priority Project needs to be put in the right framework, that of infection control and reduction of medical errors, and to be integrated thoroughly into every meeting on related issues that WHO supports or facilitates.

- The attributable risk from vaccines is very small, but we must bear in mind vaccines do not work in everyone, that vaccines do cause side-effects and that they are contra-indicated for some people.

- The attributable risk from an unprofessional health care system is very high. This reality must be accepted if it is to be effectively addressed.

- AEFI surveillance is a difficult issue. Cautious interpretation is the key. Most events reported are not causally related.

- Regarding medical waste, a filter that absorbs dioxin could be a temporary measure. The suggestion was made that WHO offer a modest reward for a technical solution.

8.3 Improving the immunization dialogue: The National Network for Immunization Information

Presentation (B. Gellin)

The Network began as a pilot project at the Infectious Diseases Society of America. In the USA, there is a lurking fear that immunization is perhaps not safe, and the increasing amounts written about immunization safety are one of the indications of rising concern. As expressed in one publication: It’s no longer enough to say, “Trust us, we’re the experts.” Dialogue is essential.

In considering which audiences to involve in this dialogue, it was decided that public information campaigns would be too costly. Instead the focus would be firstly on health care professionals, and then on policy-makers and the media. Still new, the Network involves seven associations: Infectious Diseases Society of America, Pediatric Infectious Diseases Society, American Academy of Pediatrics, American Nurses Association, American Academy of Family Physicians, National Association of Pediatric Nurse Practitioners and American College of Obstetricians and Gynecologists.

Research findings of interest in communication of immunization safety and risk

When talking about safety, one is often talking about risk. Of all the elements that the public uses to interpret risk information, the most important is trust. The health care professional is still the trusted source of information. According to unpublished CDC 2001 data, the first choice in seeking information about a concern is a physician.
Rather worrying was a small study from Canada, which showed that health care providers themselves do not have full confidence in the safety of immunization (see Table 8.1). Only 57% of nurses thought vaccination was safe. This needs to be rectified.

Table 8.1: Attitudes of vaccinators in Canada (Quebec, 1998)
In general, the vaccines that are recommended for use in infants and children are:

<table>
<thead>
<tr>
<th></th>
<th>GPs</th>
<th>Paediatricians</th>
<th>Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe</td>
<td>87%</td>
<td>88%</td>
<td>57%</td>
</tr>
<tr>
<td>Effective</td>
<td>77%</td>
<td>85%</td>
<td>52%</td>
</tr>
<tr>
<td>Necessary</td>
<td>92%</td>
<td>94%</td>
<td>68%</td>
</tr>
</tbody>
</table>

To be able to design educational and communication programmes, the issues must be examined. Research has shown that in the case of risk perceptions science is secondary to value judgements that people make concerning risks. None of the leading factors of how people make decisions are technical or scientific; and source credibility is key. Because of source credibility the Network has taken no funds from pharmaceutical companies, and is also very careful about taking government money. The Network has so far been able to rely on philanthropy.

In addition, to successfully communicate, one has to understand the audience. Parents have important misconceptions about vaccines and immunization practices. A telephone survey among parents of children under six found that 25% believe immune systems are weakened by too many vaccines, 23% think children get more vaccines than are good for them, and 19% of parents do not think vaccines are proven safe prior to use in the USA. Communication research findings show that parents are actually very interested in disease information, vaccine side-effects and so on. The vast majority of parents want an immunization recommendation (vs. simple provision of information). However, there is considerable variation in how people respond to, or prefer to receive risk–benefit information, showing the importance of pinpointing your various audiences.

Finally, all health care workers, from general practitioners to midwives, need to be kept up-to-date with developments in the debate and learn how to discuss, rather than dismiss, parents’ fears.
8.4 Role of polio adverse events in policy development in post-certification era

*Presentation (B. Aylward)*

Development of post-certification policy will be based on a scientific evaluation of risks, but final decisions will be based on political and economic decisions on perceived risk.

The disease is truly on the verge of eradication and we will soon be in the situation where the only paralytic polio is due to the vaccine. Outbreaks of circulating vaccine-derived polio (cVDPV) confirmed in the last couple of years in Hispaniola and the Philippines have brought this fact to the forefront of discussion. The risks of vaccine-caused paralysis in a polio-free world include vaccine-associated polio (VAPP) and immunodeficient long-term excretors of vaccine-derived poliovirus (iVDPV).

In addition, there is the risk from accidental or intentional release of wild poliovirus (from IPV manufacturing sites, laboratories and so on). In summary, the debate is being driven mainly by concern about cVDPV and fear of bioterrorism, sharpened by the events of 11 September 2001.

**Table 8.2: Possible cases of paralysis from vaccine-derived viruses in the decade after certification and possible strategies of prevention in the post-certification era**

<table>
<thead>
<tr>
<th>Paralysis category</th>
<th>Estimated No. of cases</th>
<th>Prevention strategy</th>
<th>Potential mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAPP</td>
<td>3000</td>
<td>stop OPV</td>
<td>n.a.</td>
</tr>
<tr>
<td>cVDPV outbreaks</td>
<td>300</td>
<td>stop OPV</td>
<td>pulse OPV</td>
</tr>
<tr>
<td>iVDPV</td>
<td>10</td>
<td>stop OPV</td>
<td>screen immunodeficients</td>
</tr>
</tbody>
</table>

Table 8.2 gives estimated risks based on the assumption that all countries continue current immunization policies with pulse immunization activities every three years. The prevention strategy could be to stop immunization with oral polio vaccine (OPV), using an acceptable mechanism.

Alternatives discussed are:

- Stop OPV followed by a surveillance and response strategy.
- Replace OPV with inactivated polio vaccine (IPV) in all countries.
- Develop a “new” polio vaccine.

The problem with the second possibility is that the costs would be huge (less than 7% of the world’s population uses IPV at present), and population immunity insufficient. The third possibility is very unlikely.
When it comes to the risk of polio from release of wild poliovirus, we have no evidence of such events in the past. A containment strategy is being implemented, and there are mechanisms to further reduce the risk if containment fails.

On looking at the determinants of post-certification policy, a number of issues are polio specific. We need scientific information and observational data to answer questions on the risks over time of circulating vaccine-derived poliovirus. Also to be taken into consideration are the risks of reintroduction of polio, bioterrorism, and so on, as well as Member State expectations.

Other general immunization policy considerations on burden of disease, cost, financing etc., also come into play. For example, a shift to IPV would draw resources from other new vaccines.

An important question is how big a role OPV safety considerations should play in developing post-certification immunization policy. There are a number of very vocal supporters supporting continued immunization with OPV. Others point out that the only children being paralysed in the post-certification era would be in lower and middle-income countries. Thus it is important to enlist expert committees from outside the polio eradication community to look at this issue from the context of the broader health programme.

Discussion

A number of points were made.

- On the subject of the Committee’s involvement with post-certification policy, it is important for the Committee to realize WHO’s role is not to advocate use or non-use of OPV or IPV, but to give countries enough information to make the decision themselves.

- The tragic consequence of 11 September is that it puts all the programmes back in the unfortunate stage of high immunization coverage, low disease and prominent adverse events. In the setting of polio we have zero disease and cases of vaccine-associated paralytic poliomyelitis. In disease eradication programmes, historically the cost–benefit equation is based on the ability to stop vaccination once certification is achieved. If it is no longer possible to stop vaccinations, it is also no longer possible to use the cost–benefit equation.
9. Summing up

Report of the Steering Committee of the priority project on Immunization Safety

*Presentation (C. Hardegree)*

The Committee’s deliberations and major conclusions and recommendations were presented by Chair C. Hardegree at the SAGE meeting on 13 and 14 June, which followed the Steering Committee meeting.

Dr Hardegree said that the Committee was pleased to note that many of the recommendations at the second Steering Committee meeting 18 months previously had been achieved.

**Programmatic Issues**

The committee noted the significant progress made by the ISPP in raising the awareness of immunization safety in the last three years. A number of programmatic issues had been discussed.

- Linkages to other programmes including polio, measles, MNT and SIGN were reported on and discussed, in particular the need to explore ways to make use of infrastructure built for the polio eradication initiative and to utilize skilled PEI staff, for safety issues in general. This would require significant training. There is a need to integrate immunization safety into other accelerated disease control initiatives such as measles and MNT and to train staff at all levels on safety issues.

- The question was raised as to whether mainstreaming the ISPP at this time may lead to a loss in the gains made for immunization safety. Safety is a major consideration in the polio endgame. The possibility of mainstreaming the ISPP should be reviewed in 2003.

- The Steering Committee noted the importance of system indicators for assessing improvements in safety, but noted also the importance of not overloading the system with too many of them. The Committee agreed in principle about the revised strategic plan but felt that it needed additional time to be sure it agreed with all the issues.
GAVI and the Vaccine Fund

The impact of the Vaccine Fund on emphasizing immunization safety was reported, illustrated by the fact that the injection safety content of country applications to GAVI had increased from 0.5% in May 2000 to over 6% in August 2001. The Steering Committee noted that when the GAVI Board met in June 2001 its recommendations were in many ways consistent with what the Committee had earlier recommended, including the recommendation for new tools to monitor safety, and a decision to fund AD syringes. The Committee was pleased to note the change in emphasis. Recommendations with respect to GAVI included the following.

- A number of countries still need support for immunization safety, including countries not eligible for GAVI support. Further thought needs to be given to how to facilitate this safety support.
- The Steering Committee recommended that injection safety funding from GAVI should be increased from three to five years in line with the support for vaccines and that eligibility for injection safety support be broadened such that all GAVI-eligible countries, including those without approved applications for other types of support, could apply.
- R&D funding should be considered for appropriate sharps waste management technologies.

AD syringes and injection safety

In the area of injection safety, the following issues were among those discussed.

- Immunization services have had a positive impact on the curative care sector such that the latter group’s interest in using AD syringes has increased tremendously. A baseline assessment made in 2000 showed the percentage of non-developed countries meeting various indicators. Only 44% of non-developed countries were using AD syringes and 47% had proper sharps disposal. By 2001, improvement was apparent. In 2001, according to the WHO/UNICEF Joint Reporting Form, AD syringes were used by 60% (versus 38% in 2000) of countries in the African Region. Safety boxes were being used by 63% (versus 46% in 2000) of countries in the African Region.
- During the last years, the use of AD syringes had risen further, and is projected to rise sharply during 2003. (see Figure 9.1)
- The high number of needle-stick injuries and other injection safety issues were highlighted in a presentation of findings from 1999.
- In 2001 an injection safety assessment had been carried out in 17 countries.
- The expected increase in number of manufacturers globally raises a number of quality control issues and the device regulations that are required. The Device Manufacturers Association is aware of the need to try to develop new needle-less technologies for injections.
- One region (the South-East Asia Region) has found that plastic sterilizable syringes are becoming harder to obtain, as fewer manufacturers are willing to make these, which suggests that it will be possible to show a cost benefit with AD use as sterilizable prices increase.
Waste disposal
An indication of progress in the area of waste disposal is that in 2001 incinerators were being used by 71% (versus 55% in 2000) of countries in the African region.

Given existing evidence, incinerators offer the best solution for waste disposal. However, medical waste needs to be considered in a comprehensive manner – a multidimensional, multisectoral approach, not just immunization waste disposal.

The Steering Committee emphasized the need for monitoring tools and support to countries for efficient and environmentally appropriate waste disposal mechanisms. It was felt that issues related to countries’ capacities are linked to (lack of) support of the MoH. Regional offices should be strengthened to support countries.

The suggestion was made that it may be time for EPI managers to begin a partnership with environmentalists to find environmentally-friendly solutions to disposal of used syringes.

Quality control, NRAs and mechanisms to monitor and respond to AEFI
The Steering Committee noted the importance of assuring safety through quality control and emphasized the importance of clinical studies in evaluating safety as well as the essential role of regulatory authorities, including those in importing countries.

The accelerated efforts to strengthen NRAs were noted with approval. The Steering Committee urged that resources be found to enhance the ability of WHO to carry out this activity.
In addition, the Steering Committee felt countries should be encouraged to strengthen their own NRAs, which involves national recognition that this is essential for their work and economy (e.g. they will not be able to sell a product outside their country if an appropriate regulatory authority is lacking).

The Steering Committee considered monitoring and response to adverse events. The issue of reporting came under particular focus.

- Some countries have been able to put in place the nucleus of a reporting system, others have been able to formalize a reporting system including development and use of outside expert committees to deal with some of their issues. The number of groups considering regulatory functions has increased; in particular producing countries are looking at their capabilities to monitor adverse events.
- The Committee noted the WHO activities in this area and that significant resources are needed to support countries. Training needs are significant.
- There continues to be a need for legislation with respect to reporting of adverse events in many countries; however, some country examples of new legislation and reporting systems were noted as encouraging. The Steering Committee believes lack of reporting can harm immunization services.
- The Committee was pleased to note the V&B effort to establish an NRA network which would allow support, and provide feedback to WHO. It looks forward to further details and updates.
- NRAs must have the capacity to investigate adverse events and to take regulatory action. Just to have a reporting system is not enough. It has to have the tools to be able to make a decision whether to withdraw a product, and understand how that impacts on the world.
- Close collaboration between regulatory groups and immunization services is essential. In some countries the NRAs have not known about problems with vaccine and been unable to take appropriate action.
- The GTN has now expanded into 13 training centres, including those dealing with reporting of adverse events, and many persons have been trained. Part of the training is geared (and probably needs enhancement) to interaction between NRAs and immunization services, and also to media interaction.

**Communication and advocacy**

Communication and advocacy were a major focus of discussion throughout the whole meeting of the Steering Committee.

- A healthy child and safe vaccination should be promoted. Emphasis was placed on “selling” safety. It was stressed that culturally sensitive information should be provided. A demand for safety should be created: the health worker must be made aware of the importance of safety and be motivated to provide it. The Committee heard about examples of nurses and medical associations trying to improve communication with parents and the media, to try to address safety issues.
- The Steering Committee agreed that the capacity of ICCs to address immunization safety needs to be strengthened and safety brought to the agenda on a regular basis at regional and intercountry meetings.
- It was stressed that WHO should capitalize on the WHA resolution on patient safety.

**UNICEF**

The Steering Committee heard from UNICEF that their mid-term strategic plan includes immunization as one of their core organizational priorities, but also heard that safety had been taken up by the communication unit as a focus area and that safety was to be a core issue in the new measles reduction plan.
# Annex 1: Agenda

**Monday, 10 June**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Speaker(s)</th>
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<tr>
<td>13.00–13.30</td>
<td>Registration</td>
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<tr>
<td>13.30–14.00</td>
<td>Opening session</td>
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<td></td>
<td>Opening remarks (including V&amp;B organizational changes)</td>
<td>Daniel Tarantola</td>
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<td>Introduction of participants</td>
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<td>Adoption of agenda, election of rapporteur Chair</td>
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<tr>
<td>14.00–15.30</td>
<td>Progress since second meeting</td>
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<td>Review of steering committee functions and recommendations</td>
<td>Chair</td>
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<td>Review of recommendations from the June 2001 SAGE meeting and interaction</td>
<td>Alenka Kraigher</td>
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<td>Progress report from the Secretariat</td>
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<td>Review of new strategic plan</td>
<td>Philippe Duclos</td>
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<td>New GAVI emphasis on immunization safety: current status of applications for safety support.</td>
<td>Merceline Dahl-Regis/Bo Stenson</td>
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<td>Are we meeting the challenge?</td>
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<td></td>
<td>Overview of activities and progress</td>
<td>Philippe Duclos</td>
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<td></td>
<td>What opportunities within EPI to improve safety?</td>
<td>Bruce Aylward/Julian Bilous</td>
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<tr>
<td>15.30–15.45</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>15.45–16.15</td>
<td>Progress since second meeting (continued)</td>
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<td></td>
<td><strong>Discussion</strong></td>
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<tr>
<td>16.15–16.45</td>
<td>Assurance of vaccine safety through quality control procedures and quality specifications. Global perspective</td>
<td>Ivana Knezevic/Julie Milstien</td>
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<tr>
<td>16.45–17.30</td>
<td>Tools to ensure vaccine quality and safety up to vaccine administration. Review of situation</td>
<td>Nora Dellepiane and UNICEF</td>
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<tr>
<td></td>
<td><strong>Discussion</strong></td>
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<tr>
<td>17.30–19.00</td>
<td><strong>Reception</strong></td>
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Tuesday, 11 June

08.30–09.00 Research update  Marie-Paule Kieny
09.00–10.30 Safe and efficient vaccine administration and disposal technologies
   Global WHO–UNICEF perspective  Umit Kartoglu/
                                    Edward Hoekstra
   Regional perspective
   AFRO  Modibo Dicko
   AMRO  Peter Carrasco
   EMRO  Julia Fitzner
   EURO  Denis Maire
   SEARO  Stephane Guichard

10.30–10.45 Coffee break

10.45–12.30 Safe and efficient vaccine administration and disposal technologies (continued)
   WPRO  Wayne Antkowiak
   Safe and efficient vaccine administration and disposal technologies, progress accomplished in Ghana  Mercy Essel Ahun
   Safe and efficient vaccine administration and disposal technologies, progress accomplished in Tanzania  Caroline Akim
   Linkages with the measles strategic plan and MNT elimination  Ana-Maria Henao-Restrepo
   Report on Focus Project  Selma Khamassi
   Report on SIGN activities and annual meeting report  Yvan Hutin
   Working in the field to improve safety  Jules Millogo

12.30–13.30 Lunch break
   Integration of waste management: success stories  Richard Carr

Discussion

15.45–16.00 Coffee break

16.00–17.30 Strengthening of NRAs and mechanisms to monitor and respond to AEFI.
   Global perspective  Adwoa Bentsi-Enchill
                    Lahouari Belgharbi
                    Emma Uramis
                    John Clements
   Regional perspective
   AFRO  Modibo Dicko
   AMRO  Peter Carrasco
   EURO  Denis Maire
   SEARO  Stephane Guichard
   WPRO  Wayne Antkowiak
Wednesday, 12 June

8.30–10.30 Have revised Jacqui. These times are now OK. ADSTrengthening of NRAs and mechanisms to monitor and respond to AEFI (continued)

- China review of progress toward strengthening NRA and impediments
  - Yu Jingjin
- Indonesia review of progress toward strengthening NRA
  - Lucky Slamet
- Dealing with investigation of vaccine safety
  - Philippe Duclos

Discussion

10.30–10.45 Coffee break

10.45–13.00 Communication and advocacy strategy (positive vs. negative)
  - Mahenau Agha
  - Progress and gaps
  - Susan Mackay
  - Status of partnerships in supporting drive for safety
  - ICN
  - National Network for Immunization Information
  - WMA
  - In the absence of wild type polio virus, what should the role of adverse events be in policy development?

Discussion
  (including on indicators that could be used for advocacy)

13.00–14.00 Lunch break

14.00–15.30 Summary of recommendations of the meeting
  - Rapporteur

Discussion
  - Mainstreaming of Priority Project

15.30–15.45 Closing remarks

15.45–16.00 Coffee break

16.00–17.45 Closed session (committee members only):
  - Finalization of recommendations
  - Discussion and adoption
  - Review of committee functions with regards to final recommendations
Annex 2:
List of participants

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