DRUG REGULATORY AUTHORITIES OF THE
EASTERN MEDITERRANEAN REGION

Report on the Joint WHO/DSI: Regional Meeting
Tunis, Tunisia, 2-8 November 1993

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE EASTERN MEDITERRANEAN
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1. INTRODUCTION

The Joint WHO/DSE Regional Meeting of Drug Regulatory Authorities in the Eastern Mediterranean Region (EMR) was held from 2 to 8 November 1993 in Tunis, Tunisia. This meeting was organized by the WHO Regional Office for the Eastern Mediterranean (EMRO), with technical and financial assistance from the Deutsche Stiftung für Internationale Entwicklung (DSE, i.e. German Foundation for International Development). The objective of the meeting was to improve the availability and accessibility of effective, safe and good quality drugs for the population by strengthening the knowledge and skills of senior staff of drug regulatory authorities (DRAs) in countries of the EMR through:

- Reviewing the follow-up activities taken to implement the recommendations of previous meetings of DRAs in the Region.
- Updating the knowledge and skills about current topics relevant to a DRA.
- Exchanging experience and information about drug quality control activities in the Region.
- Discussing practical approaches for developing a national quality assurance system.

2. OPENING SESSION

Dr Amor Toumi, Director of Pharmaceutical Services, Ministry of Public Health, Tunisia welcomed the participants. Mr Merchert, DSE, Germany, then addressed them. He indicated that the DSE as one of the sponsors of this meeting was pleased that, following the first meeting in Berlin, Germany, a few years ago, a second meeting had been convened in Tunis.

Mr Merchert continued that there are a number of good reasons to have such a meeting organized in the EMR, rather than at the headquarters of the professional and sponsoring agencies. The first and foremost in this case of drug regulations and drug information is the indisputable fact that Tunisia has made serious efforts and succeeded in setting up a feasible and functional system of computerized drug information that needs to be studied for use and adaptation in other countries of the Region. Mr Merchert emphasized the fact that improving drug control and the availability of good quality and affordable drugs will contribute to the well-being of the people in the EMR. He also indicated that there is still a long way to go to reach these objectives and set-backs have to be faced, particularly at times of economic recession and competitive struggle. However, in spite of all diverging interests, there is a political and professional will to overcome obstacles, to adhere to ethical and professional standards and to collaborate in setting up reliable structures at national and international levels in control and surveillance of drug supply and thus ensuring access to one essential element of health care. Finally, Mr Merchert expressed his pleasure that the DSE has been able to secure the cooperation of both international organizations and professionals, as proven by a number of courses and conferences organized in recent years.

Dr A. Saleh, Regional Adviser, Pharmaceutical, Diagnostic and Therapeutic Substances, WHO/EMRO, read out a message from Dr Hussein A.
Gdezairy, Regional Director, WHO/EMRO. In his message, Dr Gezairy referred to the recommendations of the first Eastern Mediterranean Drug Regulatory Authorities Conference (EMDRAC) and suggested that the participants discuss the implementation of these recommendations at both national and regional levels. The Regional Director then emphasized that the successful implementation of a national drug policy depends, to a great extent, on the establishment of a well-functioning national quality assurance system. This requires a competent inspectorate system, supported by proper legislation and drug quality control laboratories. It is, therefore, important to discuss how national capabilities in the implementation of a national drug policy can be improved through good management of drug inspection and drug quality control activities, as well as the development of human and financial resources. Dr Gezairy then referred to the regional initiative on self-reliance for vaccine production and welcomed the discussion of quality control of vaccines in this meeting. This will support the initiative of EMRO and give confidence in the quality of vaccines produced in the Region.

The meeting was then inaugurated by H.E. the Minister of Public Health, Dr El-Hedi M'henni, who welcomed the participants and emphasized the significant role of WHO in the pharmaceutical field, especially in the development of a sound national drug policy and an efficient national drug quality assurance system. Dr El-Hedi M'henni then emphasized the complex nature of drug use and the fact that the person who prescribes medicine does not pay the cost. The ones who pay are not directly involved in the choice, and once the drug is prescribed to the patient it becomes obligatory and indispensable. It is important, therefore, to take into consideration the economic aspects of drug use as well as assurance of quality. He indicated that drug quality should be of great concern to national DRAs and international organizations like WHO. It is also important to establish a set of rules and ensure effective ways of drug registration and inspection, so as to ensure the quality of locally produced or imported drugs available for consumers. The experience of the Tunisian drug quality control laboratory has to be mentioned as an example of efficient drug registration, post-marketing surveillance, and drug inspection. The Ministry of Public Health in Tunisia is encouraging investment in local drug production. This has resulted in the increase of local drug production, from 8% in 1988 to 35% in 1993, and it is expected to reach 60% by the end of 1996.

3. FOLLOW UP ON EMDRAC-1

The first EMDRAC meeting was organized with the following main objectives:

- Enabling DRAs in the countries of the EMR to identify and discuss common practical problems.
- Presenting an update on recent developments and on WHO initiatives and activities in the field of national drug policies.
- Identifying the means by which the DRAs can assist in the development and implementation of a national drug policy.
3.1 Drug Legislation

The first topic discussed in EMDRAC-1 was drug legislation. It was recommended that legislation should be practical and enforced by realistic penalties. Four areas should be considered in any new legislation: pharmaceutical services and pharmacy, human medicine, animal medicine, and poisons abuse.

Concerning legislation, WHO has provided consultancy to few countries. It seems that revision of legislation is not an easy step and is a very lengthy procedure. The legislation can, however, be updated by ministerial decrees. On many occasions WHO has adopted several resolutions calling upon Member States to take certain actions with regard to drug registration e.g. use of international non-proprietary names (INN names), WHO Certification Scheme and Ethical Criteria for Drug Promotion. The participants were requested to discuss why responses to WHO resolutions and recommendations of meetings like this are not very positive.

Regulations of herbal remedies were also discussed in EMDRAC-1. It was recommended that DRAs regulate the marketing and use of herbal remedies in accordance with the guidelines developed by WHO. Few countries have, however, formulated rules for the registration of herbal remedies. These countries include Egypt, Iran, Saudi Arabia and Tunisia. The participants can update this information and indicate any action taken in this respect. In response to this recommendation, EMRO also organized an Inter-country Meeting on Traditional Medicine and Primary Health Care, held in Cairo, Egypt, in 1991. The participants of this meeting emphasized the need to develop a national policy on traditional medicine and called upon WHO to develop guidelines for the formulation of such a policy. EMRO is going to organize a meeting of experts in December 1993 to develop such guidelines.

It should also be noted that Gulf Cooperation Council countries have also shown interest in this topic and a consultation is going to be held in Riyadh, Saudi Arabia, in November 1993, to discuss quality control and the rational use of medicinal plants.

3.2 Drug Registration and Drug Regulatory Authorities' Functions

The participants of EMDRAC-1 identified the following problems as the more common obstacles facing DRAs: lack of skilled personnel; inadequate legislation; and lack of proper facilities for drug quality control. It was concluded that DRAs should take responsibility to initiate the development of a national drug policy, to involve all parties concerned, to prepare the necessary legislation and regulations, and to coordinate the implementation of all components of the policy. WHO is very well equipped and ready to support national authorities in this important task.

The recommendation on the collaboration between drug quality control laboratories in the Region was followed up. Collaboration in testing drug samples and providing training courses were made through WHO. Again WHO is ready to support the national authorities in this important task.
Specific recommendations were taken to strengthen DRAs:

Training: It was difficult to implement recommendations of the previous meeting. However, a few contacts have been established with some universities in and outside the Region, to provide training in specific technical areas.

Drug promotion: Some action has been taken by a few DRAs in the Region. However, this still represents a major problem.

Pricing: Recommendations of the previous meeting have only been considered by a few countries. Drug prices are constantly increasing.

WHO Certification Scheme: The practical use of the system has been reviewed in two EMR countries. The system will be further discussed in this meeting in order to agree on practical steps to make the best use of this scheme.

Licensing fees: A few countries are trying to implement the recommendation of the previous meeting. It seems, however, that many administrative problems prevent the full use of this proposal.

On discussing the follow-up on the recommendations of EMDRAC-1, it was suggested that Member States should identify priority areas for the implementation of these recommendations and develop national plans in collaboration with WHO on how to implement such recommendations. Such plans can include training, operational research, or other specific activities.

The problem of drug pricing was raised and it was indicated that Member States and WHO should give more attention to how Member States can develop an appropriate drug pricing policy. It was indicated that WHO can support Member States in presenting the plan of action developed by the pharmacy departments of ministries of health to policy-makers.

4. LOOKING FORWARD TO ICDRA-7

Ms A. Wehrli, WHO/HQ, stated that since the organization of the ICDRA conferences in the early 1980s in Annapolis, U.S.A., five such conferences have since been held. The organization of these conferences has been formalized and the programmes were carefully planned in preparatory meetings attended by representatives of the host countries, of the country which hosted the previous ICDRA, a representative from at least one country within each of the WHO Regions, and the WHO secretariat.

The preparatory meeting for ICDRA-7 was held in Amsterdam in November 1992 and a first draft programme was prepared, which has since been further developed. As usual there will be plenary sessions and parallel workshops. The main topics for the plenary sessions are:

- Counterfeited, spurious and substandard drugs
- Current topics (e.g. iodine tablets, INNs for blood coagulation factors)
- WHO ethical criteria for medicinal drug promotion
- Workshop recommendations
The main topics for the three parallel workshops are quality assurance, regulation, and harmonization.

The draft programme was sent to WHO Member States with an application for participation in this meeting. The other topics are workshop on regulation and workshops on harmonization.

Over the years the participation of regulators from developing countries, with exception of the ICDRA conference held in Japan in 1986 (23), has steadily increased, e.g. Sweden 1984 (39), Paris 1989 (39) and Ottawa 1991 (43). Ms Wehrli expressed her wish that this trend will continue for the forthcoming ICDRA 7, which is to take place in Amsterdam between 10-20 April 1994. Both the Government of the Netherlands and also the DSE have agreed to make special efforts to allow a maximum number of participants from developing countries to attend. Special efforts will also be made by WHO/HQ and Regional Offices to sponsor candidates from developing countries.

Ms Wehrli continued that ICDRA conferences have also acted as incentives for organizing meetings of drug regulators on a regional basis and this meeting can be seen as such a regional ICDRA meeting.

5. NATIONAL DRUG POLICY

Ms Helling-Borda, WHO/HQ, presented the work of the WHO Action Programme on Essential Drugs (UAF), including the importance of framing and implementing a national drug policy, and of establishing a strong drug regulatory and quality assurance system within such a policy and UAF's newly developed indicators, which are tools for systematic assessment of progress. The following summarizes her presentation.

The programme started in 1981. Its objectives are to assist developing countries in making essential drugs accessible to those who need them; to assist WHO Member States in developing and implementing national drug policies and essential drugs programmes; and to promote rational drug use.

The Programme which has a financial budget of US$ 20 million has adopted a so-called "4+4+4" formula for the purpose of depicting its programme strategy. The formula presents the four major areas of work, the four technical areas of intervention, and the four principles which underlie its activities. Taken together, they provide the conceptual framework for the programme's priorities and approaches which, in application, are tailored to each country's particular needs and circumstances.

The elements of the programme's 4+4+4 formula are:

Programme of work

- Country support (65% of the biannual budget)
- Development work (9%)
- Operational research (7%)
- Management activities (19%)
to monitor progress made in the national drug policy implementation, systematic assessment tools are needed which are simple, objective and reliable, i.e. indicators which can be used nationally by various programme managers and globally by international organizations, bilateral donors, and non-governmental organizations (NGOs). The indicators for monitoring national drug policies in developing countries, still in draft form, are of two kinds, qualitative indicators and quantitative ones.

Examples related to legislation and regulation of qualitative or structure indicators measure the capacity of the pharmaceutical supply system and are posed as questions which can provide a "yes" or "no" answer, such as, "Is there a Drug Act which has been updated in the past ten years?", "Is there a DRA whose mandate includes inspection and legislation?".

Examples of quantitative or process indicators to find out whether the policy is implemented are answers to questions such as, "What is the number of drug outlets inspected in one year, out of the total number of drug outlets in the country?", "What is the number of drug outlets in violation in one year, out of a total number of drug outlets inspected?".

The WHO Action Programme on Essential Drugs has field tested the indicators in five countries (Central African Republic, Guinea, Nepal, the Philippines and Tunisia) and is now in the process of revising the final draft of the DAP document entitled "Indicators for Monitoring National Drug Policies in Developing Countries". It is hoped that in their final form the indicators will provide a very useful common tool to monitor and assess progress within the elements of a national drug policy.

6. OVERVIEW OF DRUG CONTROL RELATED ACTIVITIES

6.1 Overview of Drug Control Related Activities by DAP/HQ

Ms Helling-Borda said that, in its operational support to countries, the WHO Action Programme on DAP undertakes situation analysis, problem identification, setting of objectives, and assists countries in developing master plans which include detailed activities, a time schedule and estimated costs for reaching the objectives. The organizational, technical, administrative and financial assistance related to drug control activities include reviewing and updating drug legislation, setting up registration systems, quality control and assurance mechanisms, strengthening inspection services, and upgrading good manufacturing practices. Human resources' development through workshops, seminars and study tours, and strengthening organization and management are vital elements in DAP's support to countries in drug control authorities. The development work has included the application of the DAP publication "Basic Elements of Drug Legislation and Regulatory Control" and WHO's Technical Report Series' recommendations.

A 15-country study to assess the operation of the WHO Certification Scheme and promote its use was further supported and coordinated by DAP in 1993. Study tours in drug regulatory control were arranged for nationals from a variety of countries as Benin, Bhutan, Burundi, Guinea, Indonesia, Malawi, Maldives, Myanmar, Thailand, and Republic of Yemen amongst others. In 1991 DAP
financed participation of nationals from 12 developing countries to the ICDRA meeting in Ottawa.

Intercountry DAP supported activities include meetings and workshops to develop joint guidelines for drug evaluation and registration, good manufacturing practice, herbal medicines, reference substance, etc. The Association of South East Asian Nations (ASEAN), the Andean Pact, and EMDRAC, where representatives of the drug regulatory control authorities of the Eastern Mediterranean Region meet, are examples of intercountry collaboration.

Finally, Ms Helling-Borda stated that in November 1993, DAP is also organizing a meeting in Niger with representatives from eight countries to review the functions and activities of the four regional quality control laboratories in the WHO/AFRO Region. Prior to the meeting, field visits to the laboratories were undertaken and questionnaires were sent out to assess the current operation and use of these laboratories.

6.2 Overview of Drug Control Related Activities by DMP/HQ

Ms A. Wehrli, DMP/HQ, presented the various activities of DMP/HQ, which supports the national drug regulatory authorities. These include guidelines for small national DRAs and computer software for handling drug registration data. DMP/HQ activities also include:

**Information on drug safety and efficacy**
- Essential drug model list and model prescribing information
- Monthly pharmaceutical newsletter and drug alerts
- Quarterly WHO drug information
- WHO collaborating centre on adverse drug reaction monitoring
- UN-consolidated list
- Internationally standardized drug nomenclature: INNs (WHA46.19: INNs Use and Protection)

**Pharmaceutical, quality assurance and control**
- Good manufacturing practices and WHO Certification Scheme
- International pharmacopoeia and basic tests
- Advice on setting up and running quality control laboratories
- Various advice c.g. stability
- Counterfeit drugs (joint WHO workshop, Geneva 1992)
- Guidelines for the assessment of herbal medicines, in addition to the following documents which are under preparation: guidelines for good clinical practice for trials on pharmaceutical products (consultative document published in WHO/D1); guidelines for good laboratory practice; guidelines on marketing authorization requirements for interchangeable multisource pharmaceutical products (meeting August 1993); guidelines for import procedures (meeting October 1993); model legislation (meeting November 1993); and guidelines on registration of pharmaceutical products (adaptation of DAP Tanzanian guidelines)
- Training of people from developing countries working in drug regulation and control, additional training support in collaboration with special
WHO country support programmes e.g. human reproduction/contraceptives and organization of biennial international conferences of DRAs

Of specific importance are the consultations organized by DMP on the role of the pharmacist:
- The role of the pharmacist in the health care system (report of New Delhi meeting, 1988)
- Quality pharmaceutical services benefits for governments and the public (report of Tokyo meeting, 1993)
- Good pharmacy practice (in preparation)

7. MANAGEMENT OF DRUG REGULATORY AUTHORITIES

Dr. B. Rowsell, Drug Regulatory Authorities, Canada, presented the management system of the Drug Regulatory Authorities in Canada. The Project Management System described in this document is the central management process whereby the Drugs Directorate of the Health Protection branch plans, monitors and evaluates its activities. The system provides a planning framework of up to five years and encompasses all activities (including professional, management, administrative, scientific and technical activities). It includes procedures related to operational planning, detailed planning, and implementation of results. The process is supplemented, as needed, by other processes such as periodic review meetings between managers and subordinates, periodic written progress reports, independent audit and evaluation of programmes and/or projects, and peer review of scientific and technical publications.

The objectives of the system are to:
- Ensure that the Directorate's programme is consonant with its mandate and broad objectives.
- Provide for long-term planning of the work of the Directorate and to provide a link with the departmental strategic planning process.
- Ensure that client needs are recognized and met.
- Provide a link between resource planning and operations, thereby ensuring effective and efficient use of financial and human resources in accomplishment of Directorate objectives.
- Ensure that adequate control of projects exists and monitor progress and results achieved, in a timely manner.

The activities of the Directorate are grouped into 27 project areas. The Review Committee evaluates each project area taking into account the following factors:
- Are the proposed projects consistent with Ministry of Health and Directorate goals?
- Are past achievements consistent with objectives?
- Have projects been well-managed?
- Have they been carried out effectively?
- Have they been carried out efficiently, i.e. cost/benefit?
Are the proposed goals consistent with goals for higher organizational levels?
- Will the proposed work provide a significant contribution to our knowledge?
- Will the proposed work provide a significant measure of health protection to the public?
- Is the proposed programme realistic in terms of resources available?
- What level of support is recommended for this project?

8. WHO MODEL SOFTWARE PACKAGE FOR DRUG REGULATORY AUTHORITIES

Ms Raffaella Balocco and Mr Williams Monterosso, DMP/HQ, presented to the meeting the WHO software on drug registration. They also demonstrated the various features of the system and the possibility of adapting it to national needs. A visit was also organized for the participants to see this system working at the DRA in Tunisia. The system has proved to be very efficient and several countries showed interest. DMP/HQ and EDP/EMRO will follow up the issue of installing this system and training nationals on its use.

9. DRA TRAINING NEEDS IN THE EMR

Dr Saleh presented this subject. EMRO is cooperating with various Member States to develop a well-functioning quality assurance system. The actual situation in the 22 Member States, however, varies considerably, so the type and need of technical support should be assessed accordingly. The various Member States can be divided into two main groups, those at an early stage of developing a quality assurance system and those with a developed national quality assurance system.

9.1 Member States at an Early Stage of Developing a Quality Assurance System

These Member States will first need training in planning and developing an appropriate quality assurance system. Such training should cover areas like conducting a situation analysis, identifying the objectives, and developing a plan of action for a certain period of time. At later stages, specific training courses will be needed on topics like training on physico-chemical drug quality control; drug inspection, especially within the drug distribution system; and good storage practices.

9.2 Member States with a Developed National Quality Assurance System

Several Member States have developed a national system including drug laws, a national drug quality control laboratory and an established drug inspectorate department. However, these Member States still need continuous support in the following areas:
- Updating of drug regulations, legislation and laws. This can be achieved by regional workshops on new approaches or strategies for updating drug laws.
- Advanced techniques in drug quality control. Training courses can be conducted in this field on bioavailability and bioequivalence studies; drug stability and expiry dates; and quality assurance of drugs and vaccines throughout the drug distribution system.
- Good manufacturing practices.
- Inspection of pharmaceutical institutions, including private pharmacies, hospital pharmacies and central medical stores.
- Management of the drug supply system. Training courses in this field can emphasize the strategies for guaranteeing the quality of drugs in the entire drug supply system.

The training needs in the EMR could, therefore, be divided into two main groups depending upon the country situation. The design of the training courses should be based on the needs identified by carefully prepared analyses of the participating countries. EMRO has various facilities for organizing training activities within its Region and would be very willing to cooperate with DSE in planning and implementation of the training proposals.

9.3 Outcome of Group Discussions on Training Needs

Development of human resources constitutes an improving component of drug policy. It is considered essential that each country should prepare a plan of action for training of personnel so that drug policies are successfully implemented. Each country, according to its economic and public health situation, has different needs and levels of training. Proposals for training needs and the possibility of providing training facilities for other countries were discussed and identified in various group discussions.

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<thead>
<tr>
<th>Country</th>
<th>Training needs</th>
<th>Capability</th>
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<tbody>
<tr>
<td>Iran, Islamic Republic of</td>
<td>Adverse drug reaction monitoring</td>
<td>Registration</td>
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<td></td>
<td></td>
<td>Drug evaluation</td>
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<td></td>
<td></td>
<td>Quality control analysis</td>
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<tr>
<td></td>
<td></td>
<td>(exchange with other countries)</td>
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<tr>
<td>Morocco</td>
<td>Good manufacturing practice inspection (recommends exchange of inspectors within EMRO)</td>
<td>Updating and revision of legislation and regulations; legal aspects</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Oman</td>
<td>Advanced physical/chemical microbiological analysis</td>
<td>Registration</td>
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<td>Country</td>
<td>Training needs</td>
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<td>Pakistan</td>
<td>Refresher course in registration/evaluation&lt;br&gt;Operational research, drug utilization studies&lt;br&gt;Drug distributions (control, storage, dispensing, transport)&lt;br&gt;Estimation of drug requirements, quantification&lt;br&gt;Bioavailability studies&lt;br&gt;Clinical pharmacy</td>
<td>Quality control analysis&lt;br&gt;Good manufacturing practices</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>GMP inspection&lt;br&gt;Testing of biologicals&lt;br&gt;Quality control analysis&lt;br&gt;Bioavailability/bioequivalence&lt;br&gt;Statistical analysis</td>
<td>Registration&lt;br&gt;Procurement</td>
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<tr>
<td>Syrian Arab Republic</td>
<td>Quality control analysis&lt;br&gt;Computers</td>
<td>-</td>
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<tr>
<td>Yemen, Republic of</td>
<td>Continuing education for health care professionals&lt;br&gt;Procurement; quantification&lt;br&gt;Medical supply control; storekeeping&lt;br&gt;Drug information; retrieval/dissemination&lt;br&gt;Microrbiological (on-the-job training)</td>
<td>-</td>
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<tr>
<td>All</td>
<td>Policy analysis, development of strategies, implementation, planning and evaluation</td>
<td>-</td>
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<tr>
<td>Collaboration needs</td>
<td>Meetings of inspectors to exchange reports, concerns and enhance capabilities&lt;br&gt;Exchange of reports of concerns (product failures)&lt;br&gt;Regional laboratory for vaccines, biologicals</td>
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10. EXAMPLES OF REGIONAL COLLABORATION IN THE PHARMACEUTICAL FIELD

Successful regional collaboration experiences in the field of pharmaceuticals in Europe and South East Asia, which are part of broader regional collaboration based on political commitment, will be briefly discussed.

Pharmaceutical Inspection Convention (PIC)

Recently, the PIC has looked into the expansion of its activities to interact also with official national drug quality control laboratories. A first meeting bringing together representatives of these laboratories from 20 countries took place in Wiesbaden, Germany in 1992. The result was very positive and the group concluded that work should continue to:

- Create a network of laboratories and exchange information.
- Organize common training activities.
- Develop guidelines.
- Share work in the case of special groups of pharmaceutical products.

European Community: Committee for Proprietary Medicines Products (CPMP)

The CPMP has issued a number of guidelines for the preparation of expert reports that have to be submitted for product registration.

Nordic Council on Medicines

The Nordic Council is active in producing guidelines for drug regulation, and particularly drug registration, which rationalize the registration process in these countries.

Association of South East Asian Nations (ASEAN)

ASEAN was founded in 1967. Present members are Brunei Darussalam, Indonesia, Malaysia, the Philippines, Singapore and Thailand. Under the umbrella of ASEAN, a technical committee on pharmaceutical cooperation was created in 1979 with the objective to cooperate in the following areas under the first phase of a UNDP-sponsored project:

- Development of good manufacturing practice.
- Exchange of information on drugs.
- Development of adequate quality control laboratories.
- Collaboration in drug evaluation and control.
- Training and exchange of expertise.
- Production of regional reference standards.

The WHO Regional Office for the Americas has created a network of national quality control laboratories.
11. **ETHICAL CRITERIA**

Ms Wehrli presented WHO's revised drug strategy. WHO was requested to develop a set of ethical criteria for medicinal drug promotion and these ethical criteria were developed in an international meeting and adopted by the World Health Assembly in 1988 (WHA41.17). The resolution urged Member States (1) to take account of the ethical criteria in developing their own appropriate measures to ensure that medicinal drug promotion supports the aim of improving health care through the rational use of drugs; and (2) to monitor and enforce, where appropriate, the implementation of the measures they have developed.

In 1992, a further resolution was adopted by the Assembly (WHA45.30) stressing the lack of progress in this area and requesting that further action be taken to implement the ethical criteria. The same resolution also requested the Director-General to:

- Ask the Council for International Organization of Medical Sciences (CIOMS) to convene a meeting of interested parties in collaboration with WHO to discuss possible approaches to further advance the principles embodied in WHO ethical criteria of medicinal drug promotion.
- Consider other approaches and mechanisms in Member States to improve the implementation of WHO ethical criteria for medicinal drug promotion.
- Report the outcome of the meeting of interested parties and other actions of the CIOMS to the Forty-seventh World Health Assembly through the Executive Board.

In response to this resolution, a meeting was convened by CIOMS in Geneva, 5-7 April 1993. The report is to be submitted to the Executive Board. The following topics were in the draft report of this meeting and several recommendations were suggested for each of them:

- Education and communication
- Studies in relating to the ethical criteria and drug regulation and promotion
- National policies and actions
- International collaboration

Ms Wehrli presented some of the main reflections on the consultation:

- Concern about the fact that expectations about implementation of ethical criteria have not been met.
- While the consultation focused on developing countries, there are also problems in developed countries.
- Existing tensions between industry, government regulators, and consumers should be used to a positive effect.
- Common commitment should be capitalized upon and areas identified in which agreement and collaboration can proceed.
There has been success in bringing together participants into substantial agreement on a number of issues and actions to be taken. The report has been carefully constructed on the basis of contributions during the consultation and further commentary of participants during drafting and finalizing of the report.

It is clear, however, that a large amount of work still lies ahead. It is up to Executive Board of WHO and the WHA to take policy decisions to carry recommendations, modified as they see appropriate, towards implementation, including the important step of encouraging Member States to act in full support of the recommendations.

11.1 Group Discussion

The group reviewed drug promotion practices (commonalities and diversities) and the following is a summary of their findings:

Bahrain, Oman and Tunisia

- Media publicity not allowed; limited sampling is permitted.

Canada, Cyprus and Pakistan

- Promotion by medical representatives is not allowed; advertising of specific over-the-counter products through mass media is allowed; advertising of certain treatments for diseases is prohibited; promotional material is according to approved data sheets.

Holland and Switzerland

- Self-regulation; own codes.

Iran

- Face to face contact not allowed between medical representatives and physicians; sampling also is not allowed. Promotion only through scientific journals, public education about rational use of drugs.

Sweden

- Face to face contact not allowed between medical representatives and physicians; sampling also is not allowed. Representatives meet only drug committees, which make recommendations and formulate practices.

With this background of diverse nature, some common recommendations have been made by the group which are as follows:

- Ethical criteria of WHO for medicinal drug promotion should be the minimum requirement to be followed by the Member States. These should form a part of the National Drug Policy.

- The industry should be made to agree to this code which should be followed strictly by self regulation and monitoring through their national associations with punitive measure if possible.

- In order to promote the rational use of drugs, there is a need to organize consensus conferences to develop standard treatment
guidelines, which should be published at the national level and widely disseminated in the medical profession.

- There is a need to adopt a multidisciplinary approach to develop further standards and criteria for formulating policies in respect of promotional activities which support the aim of improving health care at large through rational use of drugs.
- Efforts need to be made to educate physicians and to provide them with unbiased information about the proper use of drugs, if possible by face to face contact with professionals which is considered to be the most effective means of carrying the message and influencing the attitude of the prescriber for promoting rational use of drugs.

12. WHO CERTIFICATION SCHEME

For many years WHO has expressed concern that drugs intended for export have not always been subjected to the same control procedures as those produced for the home market. In this case, developing countries lacking adequate drug regulatory systems and laboratory facilities for drug analysis are placed at a particular disadvantage. To redress this unsatisfactory situation, WHO has sought to extend and unify schemes already operated by the health authorities of some exporting countries which issue a certificate on request to foreign importers in respect of drugs that have been subjected to statutory control. Accordingly, definitive proposals relating to a certification scheme on the quality of pharmaceutical products moving in international commerce were issued by WHO in 1975.

The WHO Certification Scheme is accepted by health authorities. However, the following problems are frequently encountered:

- Responses are sometimes not timely.
- Requested data is not provided exactly.
- DRAs should recognize that the WHO Certificate has a prescribed format and content (DRAs can ask for additional information as part of registration requirements).
- DRA should prescribe an interval period for update/renewal of the WHO Certificate.
- Concern about the process for learning about changes/problems with products from manufacturer or by exporting DRA.
- Some WHO Certificates are issued by a regional/state centre rather than the national DRA centre.
- Supplying different packaging of the same drug.
- Some newly-generated drug industries do not use good manufacturing practice rules.

In order to lessen these problems, it was suggested that WHO should be asked to enhance and facilitate the use of the WHO Certification Scheme in these countries. However, this subject is still a big challenge and needs elaboration from WHO.
13. INTERNATIONAL HARMONIZATION

Dr Ten Ham, WHO/HQ, reported on the second International Conference on Harmonization (ICH), held recently in Orlando, U.S.A. He explained that the Conference is an initiative of the Commission of the European Community, the US Food and Drug Administration and the Ministry of Health and Welfare in Japan. The objective is to provide a form for dialogue between DRAs and the pharmaceutical industry on technical requirements for registration of pharmaceuticals for human use. Some institutions outside the three parties, including WHO, participate in the discussions as observers. WHO tries to represent the interest of countries outside the three parties, in particular the developing countries.

The conference deals with three topics: quality, safety and efficacy, which are discussed in specific working groups. The project has raised great interest in the world of pharmaceutical products, in particular with the pharmaceutical industry. The first ICH, held in 1991 in Brussels, counted over 1000 participants, some 1600 participants attended the second ICH. Guidelines are being prepared on a variety of subjects in the three areas of interest. Draft texts on stability, on teratogenicity and on geriatric medicine are approaching final approval, while others are in various stages of development.

There exists a danger that the three powerful parties would be dictating to the rest of the world. However, through the observers', input from other interested countries is assured. Relevant documents emanating from the various working groups are circulated to the WHO Member States through WHO's information exchange system. Approved texts will be at the disposal of all drug regulation agencies in due course and they may consider incorporation in their national regulations if they so wish.

Various issues were discussed at the recent conference. Quality assurance of biotechnology products with the inherent need to resolve specific difficulties through development of new techniques and validation of quality testing methods were discussed in detail. The session on safety, mainly concerned with preclinical testing, discussed requirements for mutagenicity testing and formulated some rules. Carcinogenicity testing, particularly determination of the doses to be applied also received much interest. An important subject relating to clinical testing was the possible influence of interethnic differences on patient responding, an issue which is quite relevant to acceptability of foreign clinical data.

The main thrust of the ICH-project lies in the dialogue between interested parties which are being confronted with existing problems in drug registration and which have an opportunity to discuss them with colleagues and to receive advice from experts.

14. REGISTRATION AND CONTROL OF HERBAL REMEDIES

The criteria and the procedures for marketing authorization of medicinal products have been progressively harmonized in the EEC. In
future, EEC regulations will extend to all industrially manufactured medicinal products.

Criteria of quality, security and efficiency have been progressively harmonized, together with some aspects of the procedure for marketing authorization (delays, motivation of decisions, publication of decisions, etc.) and of the manufacturing process (quality control, inspections). Analytical, pharmaco-toxicological and clinical assays in accordance with EEC regulations do not need to be repeated within the EEC. The control certificates of the batches performed by the manufacturer in the country of production are accepted by other countries of the EEC.

In spite of the extent of the harmonization of regulation, divergences of evaluation remain in the decisions of national marketing authorities. In order to reduce these divergences, a pharmaceutical specialties committee formed by representatives of EEC countries and members of the EEC Commission has been created. This Committee can be asked by EEC countries or by the EEC Commission to deliver advice on a particular medicinal product. Several items were also discussed:

- Legal requirements for phytomedicines in France
- The legislation of phytomedicines in Germany
- Basic guidelines accepted by European Countries about the quality of herbal remedies
- Role of the European Pharmacopoeia

France and Germany have established strict rules for the content of marketing authorization applications concerning phytomedicines and are presently leaders in Europe. Harmonization of the regulations concerning this matter is needed and it is hoped that better phytomedicines will be employed globally in the near future.

The following resulted from the group discussions on traditional medicine:

**Problems**

- Traditional social belief that every national natural plant is safe.
- Lack of public information.
- Illegal promotion.
- Inaccuracy of the dose.
- Limited indication.
- Difficulty of drug control at the herbal level.
- Pesticide residues.
- Problem regarding limited stability on plant origin.

**Suggestions**

- There should be strong legislation to ensure safety, efficacy, stability, etc.
- It was recommended that governments conduct utilization studies about the use of herbal medicines.
Registered herbs should only be marketed at pharmaceutical level; others still at the herbal level should be under control of regulatory authorities.

There should be a protocol for conducting herbal drug utilization studies with the aim of improving the control of herbal remedies.

15. DRUG INFORMATION SOURCES

Dr Ten Ham referred to the discussions at the previous Regional Meeting for Drug Information Officers held in Alexandria, Egypt in 1992. The issue of information flow was extensively discussed at a meeting in Geneva in December 1992, with the participation of drug regulatory bodies, academics, professionals, the media, and drug bulletins, both from developing and developed countries. The responsibilities of all parties involved represent a complicated network. Sharing of information is vital, and countries should collaborate with WHO to assure rapid exchange. Regulatory decisions of relevance, in particular those with a safety aspect (new contraindications and other restrictions), should be transmitted to WHO for further dissemination to Member States. Through this system, countries may receive impartial, independent information. Participants were once again invited to inform WHO of any relevant regulatory actions.

16. ADVERSE DRUG REACTION MONITORING SYSTEM

16.1 WHO Activities

Adverse drug effects may be monitored using various methods, each with advantages and disadvantages. Dr Ten Ham briefly discussed some of the more widely applied study designs and their relevance for developing countries. Spontaneous monitoring systems do not allow detection of late drug effects, and suffer from lack of validation and information on comorbidity and comedication. However, spontaneous reporting systems are easy and cheap and may raise signals of adverse effects at an early stage. Such a system may be initiated in developing countries without great investment of time and personnel. Controlled clinical trials are considered as the gold standard for investigation of safety and efficacy of drugs. However, in view of the highly selective groups of patients involved, an extra range of results applicable to the general population may not always be valid. The protocol may be complex and strict in process and control, and good clinical trial practices will be necessary. Such studies may only be carried out in well-equipped regional hospitals with sufficient facilities and infrastructure.

Case-control designs, although not useful to discover rate events, seem to be quite apt for use in developing countries and are not too expensive. They allow for retrospective hypothesis testing. Cohort studies require a very complex organization, in particular in countries where follow-up of patients during a considerable period of time is difficult. Also huge amounts of efforts, money, and personnel are required and so such studies may not be possible. However, an example of such a study carried out by WHO's programme on human reproduction to investigate long-term...
effects of an implantable contraceptive device (Norplant) demonstrates that such studies are possible. Another study intended to monitor the safe introduction of an antimalarial drug carried out in Thailand failed.

WHO tries to help countries (and pharmaceutical companies) when introducing new drug treatments. This has already been proven useful in the introduction of eflorenithine, indicated for sleeping sickness, but should be extended to other drugs used in tropical countries. New drugs should be followed up, as often little is known about the side-effects of drugs that have been in practice for many years.

16.2 Activities of WHO ADR Collaborating Centre

Dr Sten Olsson described the international system of Adverse Drug Reaction (ADR) monitoring and the global perspective on spontaneous ADR reporting. ADR monitoring is the science of systematically collecting information about adverse drug experiences with the aim of, through feedback to the parties involved, continuously improving drug therapy.

16.2.1 Spontaneous ADR Reporting

Spontaneous ADR reporting requires health professionals to be aware of the fact that medicines may occasionally cause unwanted effects and to be alert to the possibility that such events may occur among their patients. If they observe a suspected case of an ADR, they must also be prepared to report their suspicion for the information of their colleagues.

16.2.2 National or regional ADR reporting programmes

The major function of spontaneous ADR reporting systems is to provide early suspicions about unknown drug effects. Data from such systems are less well-suited for verification of generated hypothesis because of some inherent weakness. Compared to other methods, spontaneous reporting has several advantages.

16.2.3 National ADR monitoring programmes

National programmes for reporting of ADRs are operated in many different ways and adapted to local circumstances. Since no particular approach has been proven to be superior to any other from a scientific point of view, it is advantageous for the global community that many approaches exist. By pooling information acquired under different circumstances, as is being done in the WHO Drug Monitoring Programme, a more complete picture of risks involved in drug therapy may be obtained. It is, of course, important to realize that differences between countries exist and to try to understand how these differences influence results.

Legal status, organization and affiliation of national centres, sources of reports, what to report, reporting rate, handling of reports at the national centre, and feedback to reporters were discussed.
16.2.4 The WHO International Drug Monitoring Programme

The prime objective of the International Drug Monitoring Programme is the early warning function. The scheme was established in 1968 to assist in the detection of ADRs not revealed during clinical trials. By pooling drug experience reports from many countries, it is also possible to detect the very rare adverse reactions. Other functions and developments within the programme were also discussed.

Generally, the programme aims not only to develop the existing signal generation potential, but also to ensure that analysis and investigation of all important safety signals proceed consistently. This can only be done through cooperation with many people throughout the world with an interest in pharmacoepidemiology and drug safety.

The programme reaffirms its commitment to making a contribution towards improved drug information, drug utilization and drug therapy globally. In this endeavour the programme will continue working in the best interests of prescribers, dispensers, and patients in their demand for complete, accurate and up-to-date information about drugs and their effects.

17. QUALITY ASSURANCE OF VACCINES

Vaccines are used primarily for the prevention of disease in healthy subjects and must have high acceptability in relation to efficacy and freedom from adverse affects. Quality assurance plays a vital role in achieving this.

Bacterial vaccines may consist of killed cells, live attenuated strains, detoxified toxins (toxoids), purified antigens (polysaccharide or proteins), glycoconjugates prepared by chemical linkage of polysaccharide to protein, and genetically-engineered products.

The control of whole cell vaccines is based on assurance of excessive toxicity, confirmation of identity, and determination of potency against appropriate reference preparations. The control of live vaccines is dependant on confirmation of the identity and lack of virulence of the strain. Potency is established by viable count.

Toxoids are controlled for freedom from specific toxicity including capacity to revert to toxicity under in vivo conditions. Potency is assay by in vivo challenge in comparison with international standards on equivalents.

The polysaccharide vaccines are evaluated by physical and chemical methods for composition and molecular size. Safety is assured by freedom from abnormal toxicity and pyrogenicity.

Conjugate vaccines require physical-chemical evaluation of components and biological tests when toxic products are used. Potency of the final product is confirmed by immunogenicity assay in vivo.

Viral vaccines can consist of inactivated virus, live attenuated virus strains, viral sub-units, or ribonucleic acid (RNA) products. Evaluation tends
to be less extensive than from bacterial vaccines. The safety test includes examination for freedom from live virus in the case of inactivated products and for identity and lack of virulence of attended strains. Potency of inactivated vaccines is usually based on immunogenicity assay in appropriate animals. The potency of live vaccines is based on cell culture assays. The potency of split or sub-unit influenza vaccines is based on radical immunodiffusion assay of haemaglutinin content.

The development of quality control systems for vaccines can be a phased process with emphasis on safety assurance in the first instance. The more elaborate potency assays can be added at a later stage. A few procedures, such as the neurovirulence assay for poliomyelitis vaccines, are best left to specialized centres.

18. CONTROL OF BIOLOGICAL MEDICINES

Biological medicines comprise those products of biological origin used in the prevention or treatment of disease, with the exclusion of herbal and traditional medicines.

The control of biologicals involves essentially similar processes to those used for synthetic drugs with the exception that greater emphasis needs to be placed on batch monitoring because of the greater variability of biological materials.

The categories of biologicals include:

- Blood products
- Immunologicals (antisera, immunoglobulins, immunostimulants, cytokines, in vivo diagnostics)
- Vaccines (bacterial, viral, protozoal)
- Toxins
- Hormones and growth factors
- Biotechnology products (genetically engineered [r-DNA] materials, monoclonal antibodies, gene therapy products)

Some categories of organ/tissue transplants may also be considered as biological products.

The control of biologicals places emphasis on safety, potency, stability, and consistency. The major concern is the case of blood products in donor-derived viral conglutination especially with HIV-1 and 2, hepatitis A, B and C. The materials must be produced from screened donor blood and control requires examination of plasma pool samples, combined with vigorous inspection and licensing requirements. Final product testing may be performed but cannot alone assure safety. However, it is necessary for assurance of potency, quality and stability. Similar issues apply to immunologicals of human origin. This includes monoclonal antibodies which, in addition, may require screening for immune microbial pathogens and cytokine contamination.

Vaccines require examination to ensure freedom from living organisms in the case of killed vaccines, use of the appropriate attenuated strains for
live vaccines and adequate detoxification for toxoids. Potency is determined by biological assays against the appropriate international standards or reference preparations.

Many hormones are produced to a high level of purity and do not require biological evaluation. However, some, including growth factors, should be subject to potency assay.

r-DNA products present special problems. Although, in general, these products have proved to be of high quality with a good safety record, they may differ significantly from the rational product. Modifications of amino acid sequence, conformation, acylation, cross-links and deacetylation can drastically affect activity. Initial evaluation will require detailed molecular studies. However, routine batch testing can use simpler procedures and potency assays may be similar to those used for natural products.

The control of biologicals should be a comprehensive process involving the licensing authority, inspectorate, control laboratory, and epidemiological monitoring units with constant interaction between these. The development of a control system may be a phased process with initial emphasis on safety assurance and low technology processes. More advanced procedures can be developed later. The control of biologicals is not a static process and must keep pace with continued development and change of emphasis as new products emerge.

19. FORMULATION OF A NATIONAL DRUG POLICY (NDP)

Dr Saleh delivered a short presentation on the main components of an NDP. In his presentation, Dr Saleh referred to the following main components:

19.1 Situation analysis

It was emphasized that the formulation of an NDP requires a comprehensive qualitative and quantitative situation analysis to identify major problems and available facilities.

19.2 Objectives

It is important to define clearly the objectives of the NDP. It was generally agreed that the following objective should be adopted: "ensure the regular supply of a selected number of drugs of proven safety and efficacy and of good quality at all levels of the health care system at prices affordable by individuals and the community and that these drugs are rationally used".

19.3 Policy Components

Drug needs

Drug selection: The policy should develop the mechanism by which drugs to be selected at national levels, as well as each level of the public health care system, can be decided. The concept of a national essential drugs list
and the importance of a dynamic mechanism for the revision of this list was emphasized.

Drug quantification: Based on the morbidity pattern and the agreed upon standard treatment schedules, drug needs, at various levels, can be determined.

Drug supply

The policy should define the national framework of the drug supply system at all levels.

National drug production: Production of essential and generic drugs should be emphasized.

Drug importing: Drug importing should be limited to those of proven safety, efficacy, good quality, and of reasonable cost.

Drug distribution: The NDP should define the mechanism for management of the drug supply system, including development of management skills, procurement skills, good storage practices, the distribution network, and the information system within the distribution cycle.

Drug use

The policy should promote the national use of drugs, including rational prescribing, rational dispensing, and rational use by patients.

Drug information: The establishment of a national drug information centre providing up-to-date and scientifically valid information is emphasized. The publication of various drug information bulletins, formularies, and newsletters was mentioned.

Medical and pharmacy education: Rational use of drugs (RUD) should be part of undergraduate education in both medical and pharmacy schools. It should also be part of continued medical and pharmacy education. Professional associations and scientific societies should be involved in the promotion of RUD.

Public education: At country level, RUD needs to be addressed through a proper public education programme. This programme should also address the issue of self-medication and the use of traditional medicine.

Legal framework of the NDP

The enforcement of the policy needs both public education and the formulation of approved laws and regulations, as well as the establishment of an efficient enforcement body. The legal framework can cover the following:

Drug registration: The criteria of safety, efficacy, quality, and cost should be taken into consideration during registration.
Professional regulation: This covers registration of professional personnel and pharmaceutical institutions, including pharmacies and manufacturing units.

National drug quality assurance system: This system should ensure the quality of drugs available at national levels throughout their shelf-life. The system includes:

- Appropriate legislation, and good manufacturing practices, storage practices, laboratory practices and pharmacy practices.
- An efficient national drug quality control laboratory.
- An efficient inspection department.

Operational research

The policy should emphasize the importance of operational research to provide a practical solution for existing problems and suitable means of improving the services in the field.

Finance

The implementation of the policy requires clear identification of sources of funds. This emphasizes the importance of drug economics, clinical economics, as well as various systems of cost-sharing.

Cooperation at national, regional and international level

The fact that successful implementation of the policy requires close cooperation between the government, academic institutions, professional associations, and NGOs was emphasized. Cooperation at regional and international levels has proven to be very useful and the example of bulk procurement is a good one.

Following this presentation the participants of the meeting started to draft a national drug policy using the data and information they brought with them. It was finally agreed that this exercise will be conducted in a more comprehensive way at the national level and all parties concerned will be invited.

20. Recommendations

1. Member States should develop national drug policies as a basis for DRAs activities, with clear objectives and approaches, and should also establish monitoring and evaluation mechanisms. DRAs can formulate specific projects in areas of special importance (Canadian guidelines on management of DRA).

2. DRAs in the EMR should make use of systems available for exchange of product evaluation reports. Copies of evaluation reports should be requested from countries where the regulations allow free distribution of such reports.
3. The use of WHO software for drug registration by DRAs in the Region should be promoted and supported. DRAs with well-functioning systems should be used as training centres for other countries.

4. DRAs should formulate, with concerned authorities, the national plan for training within the national drug policy programme. The plan should indicate priority areas of training, with a timetable. The plan could be revised every two years.

5. DRAs in the Region should be encouraged to provide training facilities for candidates from other countries.

6. WHO should encourage bilateral collaboration in the area of training at regional and international levels.

7. Ethical criteria should be included in medical and pharmacy curricula.

8. Ethical criteria of WHO for medicinal drug promotion should be the minimum requirements to be followed by Member States. These should form a part of the NDP.

9. The industry should agree to this code and it should be followed strictly by self regulation and monitoring through national associations with punitive measures if possible.

10. Efforts need to be made to educate physicians and to provide them with unbiased information about the proper use of drugs, if possible by face to face contact with professionals, which is considered to be the most effective means of carrying the message and influencing the attitudes of the prescriber for promoting rational use of drugs.

11. WHO should be requested to enhance and facilitate the use of the WHO Certification Scheme in countries of the EMR.

12. Collaboration between DRAs is urgently recommended, likewise, collaboration between DRAs and WHO.

13. WHO/EMRO in collaboration with WHO/HQ should regularly inform Member States in the EMR of the outcome of the ICH.

14. WHO/EMRO should initiate regional activities to promote harmonization of drug registration requirements at regional level. Priority can be given to registration requirements for stability, bioavailability, bioequivalence, vaccines, and other biological products.

15. WHO/EMRO should organize an intercountry meeting to develop the national plan on the ADR monitoring system in Member States of the Region. Such a system can consider reporting any lack of efficacy of drug therapy.

16. Ministries of health should identify focal persons and make facilities available for establishing a national system for ADR monitoring.
WHO Collaborating Centre on ADR can regularly provide some of the reports published by the Centre to DRAs in the Region.

17. Collaboration between DRAs in the EMR and the WHO Collaborating Centre in areas of training and exchange of information should be strengthened.

18. WHO and Member States should develop national programmes to strengthen national capabilities in areas of quality assurance of vaccines and other biological products. Stepwise development should be planned and monitored.

19. WHO/EMRO can consider supporting the idea of the establishment of a regional quality control laboratory for vaccines and other biological products. This should ensure compliance of regional vaccine production to appropriate standards and assure the quality of imported and regionally-produced vaccines and other biological products.

21. PREPARATION FOR ICDRA-7 AND EMDRAC-3

ICDRA Meetings

1. Member States in the EMR should prepare, as early as possible, for active participation in ICDRA-7.

2. WHO/EMRO and Member States should exchange views to prepare country and regional contributions to be included in ICDRA-7 agenda.

3. Member States can forward a proposal to WHO/EMRO on topics to be discussed during the coming ICDRAs.

EMDRAC Meetings

1. National responsible officers should provide WHO/EMRO with six-monthly reports on follow up of EMDRAC-2 recommendations.

2. WHO/EMRO will distribute, at regional level, a six-monthly report on follow-up reports received from EMR Member States.

3. DRAs can identify and conduct operational studies on areas of special interest. The results of these studies can be presented to EMDRAC-3. These areas can include:
   - Assurance of product efficacy
   - ADR monitoring activities
   - Drug availability at various health care levels
   - Drug pricing policies

4. WHO/EMRO should organize an intercountry meeting on topics of regional importance, e.g. ADR monitoring, risk/benefit and cost/benefit evaluation.
AGENDA

1. Opening session
2. Presentation by host country
3. Looking back at ICDRA-6 and EMDRAC-1
4. Looking forward to ICDRA-7
5. National drug policy: importance for drug control, presentation of newly developed indicators
6. Overview of drug control related activities
   - by WHO/DAP
   - by WHO/DMP
7. Drug regulatory authority (DRA) structure/organogramme: short plenary update on existing DRA guidelines; short presentation of a country example (participant); three working groups on organogramme, structure and tasks of DRA
8. DRA management: DRA inspection quality control laboratory; finances; human resources
9. DRA training needs
10. Poster session with country presentations
11. Regional quality control laboratories: existing experiences
12. Ethical criteria: short plenary update; working groups to discuss possible implementation; evaluation of promotional material; plenary debate
13. Harmonization of drug registration: plenary update from recent ICH-2 meeting; discussion of consequences for EMR
14. EMC directives: plenary update (vacancy) and discussion
15. Intercountry collaboration (participants)
16. WHO Certification System: short plenary update on new system; practical use in country
17. WHO model software package for DRAs; visit to Tunisian DRA; practical exercises; a visit to a drug manufacturer or pharmacy
19. Registration and control of herbal remedies: plenary presentation, regional experiences

20. Drug information sources

21. Adverse drug reactions (ADR): activities of the WHO ADR Collaborating Centre; perspectives for developing countries and information flows: relevance for the Region; a country example

22. Vaccine quality assurance systems

23. National drug policies: development of a national drug policy masterplan

24. Working groups on national drug policy

26. Control and quality assurance of biologicals

27. Intercountry collaboration, planning for ICDRA-7 and CMDRAC-3; formulation of recommendations

28. Adoption of report; recommendations

29. Closing session
Annex 2
PROGRAMME

Tuesday, 2 November 1993

09:00 - 10:00 Opening session
- Address by Mr R. Merchert, DSE
- Message of Dr Hussein Gomairy, Regional Director, WHO/EMRO
- Welcome address by H.E. Dr El-Hedi M'henni, Minister of Public Health, Tunisia

10:00 - 11:00 Presentation by host country (Dr A. Toumi, Ministry of Health, Tunisia)

11:15 - 12:15 Looking back at ICDRA-6 (Mr B. Rowsell, DSE) and EMDRAC-1 (Dr A. Saleh, WHO/EMRO)
Looking forward to ICDRA-7 (Ms A. Wehrli, WHO/HQ and Dr W. Bannenberg, DSE); plenary discussion

12:15 - 13:00 National drug policy: importance for drug control, presentation of newly-developed indicators (Ms M. Helling-Borda, WHO/HQ)

15:00 - 15:20 Overview of drug control related activities (Ms Helling-Borda)

15:20 - 15:40 Overview of drug control related activities (Ms Wehrli)

16:00 - 18:00 Drug regulatory authority structure/organogramme: short plenary update on existing DRA guidelines (Ms Wehrli/Ms Helling-Borda); short presentation of a country example (participant); three working groups on organogramme, structure and tasks of DRA; plenary presentation of results and discussion

Wednesday, 3 November 1993

08:30 - 10:15 DRA management: relation of DRA to inspection, quality control laboratory, finances, human resources (Mr Rowsell)

10:45 - 11:30 DRA training needs (Dr Saleh); plenary discussion

11:30 - 13:00 Poster session with country presentations
Regional collaboration among DRAs: existing experiences (Ms Wehrli, Dr Saleh)

Ethical criteria: short plenary update (Ms Wehrli); working groups to discuss possible implementation, evaluation of promotional material; plenary debate

Thursday, 4 November 1993

08:30 - 10:15
WHO Certification System: short plenary update on new system (Ms Wehrli); practical use in country (Dr Saleh); group discussions; plenary debate

10:45 - 13:00
EEC directives: plenary update (Dr R. Grase, DSE) and discussion

15:00 - 15:45
Intercountry collaboration (participants)

16:15 - 18:00
Harmonization of drug registration: plenary update from recent ICH-2 meeting (Dr M. Ten Ham, WHO/HQ); discussion of consequences for EMR

Friday, 5 November 1993

08:30 - 13:00
WHO model software package for DRAs; visit to Tunisian DRA (Dr Toumi); practical exercises; a visit to a drug manufacturer or pharmacy

15:00 - 18:00
Visit to Carthage ruins and Sidi Bou Said (optional)

Saturday, 6 November 1993

08:30 - 12:00
Registration and control of herbal remedies: plenary presentation (Prof R. Anton, DSE); regional experiences (participant); working group discussion; plenary debate

12:00 - 13:00
Drug information sources (Dr Ten Ham)

15:00 - 18:00
Adverse drug reactions (ADR): activities of the WHO ADR Collaborating Centre (Dr S. Olsen, DSE); perspectives for developing countries and information flows (Dr Ten Ham); relevance for the region (Dr Saleh); a country example (participant); discussion
Sunday, 7 November 1993

08:30 - 10:15 Vaccine quality assurance systems (Dr M. Corbel, DSE)

10:45 - 13:00 National drug policies: development of a national drug policy masterplan (Dr Saleh, Dr Bannenberg)

15:00 - 18:00 Working groups on national drug policy

Monday, 8 November 1993

08:30 - 10:15 Control and quality assurance of biologicals (Dr Corbel)

10:45 - 13:00 Intercountry collaboration; planning for ICDRA-7 and EMDRAC-3; formulation of recommendations (working groups)

15:00 - 17:00 Adoption of report; recommendations (plenary)

17:00 - 18:00 Closing session
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