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# **Report of the first meeting of the Paediatric medicines Regulators' Network**

**WHO headquarters, Geneva, Switzerland**  
15-17 February 2010

**This publication contains the Report of the first meeting of the Paediatric medicines Regulators' Network and does not necessarily represent the decisions or policies of the World Health Organization.**



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## List of abbreviations

ACT	Artemisinin Combination Therapy
AMANET	African Malaria Network Trust
CRO	Contract Research Organization
CT	Clinical Trial
DIA	Drug Information Association
ECs	Ethics Committees
EDCTP	European & Developing Countries Clinical Trials Partnership
EMA	European Medicines Agency
EMP	Essential Medicines and Pharmaceutical Policies
FAQs	Frequently Asked Questions
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
HQ	Headquarters
ICDRA	International Conference of Drug Regulatory Authorities
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IRBs	Institutional Review Boards
MAR	Medicine Access and Rational Use
NGO	Nongovernmental organization
NIH	National Institutes of Health
NMRA <sub>s</sub>	National Medicines Regulatory Authorities
PDP	Paediatric Development Plan
PK/PD	Pharmacokinetic/pharmacodynamic
PQP	Prequalification Programme
PmRN	Paediatric medicines Regulators' Network
QSM	Quality and Safety: Medicines
WHO	World Health Organization

## Executive summary

This report provides a brief summary of discussions at the first Paediatric medicines Regulators' Network meeting, held at the World Health Organization (WHO) headquarters, Geneva, from 15-17 February 2010. The meeting was held following a recommendation from the 13th International Conference of Drug Regulatory Authorities (ICDRA) 2008 and the objectives were to (1) discuss the development of a Network for regulators interested in paediatric medicines issues; (2) to review current regulatory, scientific and ethical standards for paediatric medicines (drugs, biological products and vaccines) and to determine their applicability to developing country settings; and (3) to define the role of the regulators' Network and WHO in the development of international recommendations in relation to medicines for children.

During the meeting three background documents concerning clinical trials, research ethics and international guidance on research in the paediatric population were presented and used as a basis for further discussion. Working groups discussed: (1) Common 'standards' for registration of paediatric medicines; (2) Mechanisms for information sharing; (3) capacity development. It was concluded that, with respect to paediatric medicines, there is a great need among National Medicines Regulatory Authorities (NMRAs) for information sharing between countries as well as for capacity development. Participants from developing countries highlighted their need to strengthen human resources, to set-up adequate information technology (IT) infrastructure and to improve expertise in the review of clinical trial and marketing applications through specific training activities. Besides possible further capacity development activities, it was agreed to fill existing knowledge gaps and to strengthen competencies through joint efforts within the Network.

The participants agreed:

- To support the establishment of the Paediatric medicines Regulators' Network (PmRN).
- With the following functions:
  - establish a fast and effective mechanism for communication among the Members, and with scientific or other regulatory bodies;
  - communicate its considerations and recommendations to WHO;
  - support WHO in enhancing and assisting NMRAs worldwide on matters to do with effective and efficient regulation of paediatric medicines, in the context of World Health Assembly Resolution 60.20, Better Medicines for Children.
- WHO should provide the Secretariat, support the infrastructure for the Network and arrange the meetings of the Network.

## **Introduction**

Following World Health Assembly Resolution WHA60.20, the Department of Essential Medicines and Pharmaceutical Policies (EMP) commenced work on activities to improve the availability of "better medicines for children". The 13th ICDRA held in Bern, Switzerland, in 2008 recommended that WHO convene a global paediatric working group. As part of the "Better Medicines for Children Project" funded by the Bill & Melinda Gates Foundation, WHO invited representatives from NMRAs to develop a consolidated approach to the development and review of medicines for children.

This meeting was proposed to bring together key NMRAs representing all regions to facilitate the development of a Paediatric medicines Regulators' Network. During the meeting, participants conducted a review of current regulatory, scientific and ethical standards, to identify areas where more work is required, especially with regard to the applicability of current standards to developing country settings. Regulatory experiences and processes used by developed countries to facilitate the registration of medicines for children that may be transferable to the developing country context were identified. Further, WHO's role in the harmonization of international recommendations in relation to paediatric medicines and NMRAs was discussed.

The overall aim of the proposed "Paediatric medicines Regulators' Network" is to promote availability of quality medicines (including biological medicines and vaccines) for children by facilitating communication, collaboration and regulatory harmonization across manufacturing, licensing and research.

## **Meeting objectives**

1. To discuss the development of a Network for regulators interested in paediatric medicines issues.
2. To review current regulatory, scientific and ethical standards for paediatric medicines (drugs, biological products and vaccines) and to ascertain their applicability to developing country settings.
3. To define the role of the regulators' Network and WHO in the development of international recommendations in relation to medicines for children.

## Summary of discussions

### 1. Introduction and overview

Dr Suzanne Hill provided an overview on the Better Medicines for Children project at WHO/EMP and reviewed the objectives of the present meeting. The role of NMRAs in the development, registration and post-marketing surveillance of paediatric medicines was discussed.

Activities that could enhance the availability of better medicines for children include, but are not limited to:

- Further develop the WHO Model List of Essential Medicines for Children.
- Update relevant treatment guidelines.
- Develop paediatric prescribing information as a formulary.
- Encourage appropriate drug development and approval processes in NMRAs.
- Identify appropriate paediatric dosage forms.
- Develop quality standards.
- Develop generic formulation protocols for paediatric medicines.
- Provide lists of safe and appropriate excipients for paediatric medicines.
- Develop a system for enhancing safety monitoring of medicines in children.
- Provide guidance on procurement and supply of paediatric medicines.
- Build capacity and develop guidelines for regulators on, e.g. the review of applications for clinical trial to register paediatric medicines.

It was noted that some of these activities are ongoing in the context of the programme of work on Better Medicines for Children.

Dr Lembit Rägo presented programmes in the area of the Quality and Safety: Medicines Unit (WHO/EMP/QSM) that relate to paediatric medicines. In particular the draft guideline "Development of paediatric medicines: pharmaceutical development. Points to consider" is of importance in this area and will be further discussed during an upcoming consultation to be held in Geneva from 29-30 April 2010. It was agreed that:

- Existing resources and relevant activities should be mapped. Results of the search should be published on the WHO web site. In some cases information already exists and can be collated.
- Repetition of existing relevant guidelines should be avoided.

- Information/advice published should as far as possible be evidence-based.

## **2. Discussion of background papers**

### **A. Report to WHO Concerning International Guidelines for Paediatric Medicines Dr Susan Walters, 2010**

The first background paper was presented by Dr Susan Walters. It was a review of regulatory guidelines that relate to the development and availability of paediatric medicines as they appear on web sites. Guidelines considered significant in the context of this review were summarized in tabular format. By far the majority of relevant documents were found on the European Medicines Agency (EMA) and US Food and Drug Agency (FDA) web sites. Both of these regions have enacted legislation in this area over the last decade. Further, the report suggests that suitable marketed paediatric dosage forms may be encouraged by developing suitable guidelines for manufacturers, for example:

- Review ICH, EMA and FDA guidelines for studies in paediatric populations. Either adopt these guidelines or modify them for WHO purposes.
- Prepare a list of excipients that should normally be avoided in paediatric medicines, giving reasons in each case.
- Prepare a list of excipients that are suitable for use in paediatric medicines, together with appropriate routes of administration and again giving reasons.
- Make information available about suitable dosage regimes for drugs that are safe and effective in the paediatric population as far as is known. Inter alia this will permit manufacturers to better predict the strengths that will be marketable.
- Formulate bioequivalence guidelines for generic versions of paediatric dosage forms.
- Consider including paediatric dosage forms in the WHO Prequalification Programme (PQP).

To support the development of paediatric medicines of appropriate dosage forms, the following additional topics were raised during the discussion of the first background paper:

- Guidelines should be developed for extemporaneous preparation of paediatric medicines.
- A protocol should be prepared for extemporaneous dilution of injectables with microbiological consequences in mind.

- Manufacturers should be encouraged to include information concerning drug stability and physicochemical characteristics in the product leaflet (packet insert). A guideline should be developed for this purpose.
- Journals should be encouraged to require authors to provide information on dosage form, manufacturer and, as far as possible, formulation and method of manufacture in reports of studies using paediatric products.
- For tablets, suppositories and possibly other solid dosage forms, product information should state whether the product can safely be halved or crushed. The stability of diluted products (solid and liquid) in various media at suitable temperatures should be identified. For WHO purposes and in the context of less well-developed nations, suitable temperatures and humidities are likely to be those nominated in WHO's stability guidelines for climatic zones III and IV.
- What is the stability of the product when crushed or diluted etc., or further mixed with food and drink? Product information should highlight any food and drink that affect the stability of the product when mixed with it.
- For transdermal patches and possibly other dosage forms, product information should state whether they can safely be cut, and whether subsequent dose delivery will be uniform and reproducible.
- For injectables, nebulizing solutions and possibly other dosage forms, product information should provide information on pH, osmolality and irritancy of dilutions, in addition to stability.

**B. Review of Clinical Trial Ethical Standards for Inclusion of Children  
Dr Lisa Bero, 2010**

The summary of this paper was presented and during the discussion it was noted that:

Some ethical guidelines do not mention children at all.

Guidelines differ as to:

- Whether children should be included in research studies.
- Whether research in children is beneficial to the participants themselves.
- Healthy children may be subjected to clinical studies and, if so, Under what circumstances.
- The definition of the ages of 'children'. Neonates are rarely mentioned.

Common features included:

- Recommendations as to special safeguards for consent and assent.
- Conditions under which consent is necessary, procedures for assent and dissent of the child, and waiver of consent.
- That research conducted in children must be justified and relevant to the health needs of children included in the research.
- Pain management and facilities must be appropriate to children.
- Ethical review committees should contain paediatric expertise.
- Placebo controlled studies should be limited to those that are essential.

Questions arising include:

- Should less risk be tolerated in children, or should more benefit be demanded?
- Should large (above minimal) risks ever be tolerated?
- If a child has a fatal condition, should the child ever be given an experimental treatment that is a known risk?

Guidelines differed as to recommendations concerning:

- Whether participants may be paid and, if so, whether payment should be limited to reimbursement and compensation, or may include incentive payments.
- Whether research in children is acceptable only if it is necessary and beneficial to the children who participate.
- Whether an acceptable risk benefit ratio for children can be defined, including a clear distinction of how this might differ from an acceptable ratio in adults.
- Whether studies concerning diagnostic tests or preventive interventions be considered to directly benefit participating children.
- Whether the timing of clinical trials in children, relative to studies conducted in adults, be specified.
- Whether pharmacokinetic (including bioavailability/bioequivalence) studies may be conducted in children, including healthy children.
- How safety may be measured in children, and healthy children in particular.

The FDA offered to develop a process of discussion of questions raised on ethical standards and to provide written responses. It was noted that the question of guidelines for paediatric medicines may need to be re-opened with ICH with a view to further development of existing guidelines and preparation of new guidelines. Feedback from the Network to ICH would be useful.

Participants observed that it may not be possible to reach a global consensus as to the ethics of clinical studies in children. Opinions may be culturally based, with corresponding laws already in place. The Network could instead aim to make regulators aware of the issues to be considered and fill existing knowledge gaps on a technical basis.

**C. Survey of Current Guidance for Child Health Clinical Trials  
Florine Frakking, Hanneke van der Lee, Terry Klassen, Martin Offringa, for  
the StaR-Child Health Group, 2009**

This report provided a summary of current guidance for the conduct of clinical trials in children. The objectives of the review were: (1) systematic identification and review of all documents describing standards or guidelines for clinical trials in children; (2) an initial focus on 'scientific' standards; (3) identification of needs for additional guidance/guideline/standards.

The following topics were identified in the report as needing further development of guidance or standards:

- Ethics in the conduct of paediatric clinical trials.
- The design of paediatric clinical trials, including:
  - timing in relation to adult trials,
  - alternative study designs,
  - stratification of studies, and in particular across age groups,
  - extrapolation between patient groups,
  - eligibility criteria for inclusion in studies.
- Practical issues including:
  - sampling procedures,
  - costs.
- Pharmacokinetics studies.
- Statistical methods:
  - sparse sampling,
  - small populations.
- Study outcomes.
- Standards for reporting.

It was agreed that this review had identified gaps in information but it was not obvious what additional guidance would be helpful. The Network was asked to identify the areas where they would like more guidance.

## Discussion of key topics

The working groups' discussions on the topics of (1) common standards for registration of paediatric medicines; (2) mechanisms for information sharing; and (3) needs for capacity development in regulation of paediatric medicines were reported in plenary to the entire meeting. The following tables summarize these discussions with key items and possible actions for the Network listed for each topic.

### 1. Common “standards” for registration of paediatric medicines

Key topic	Possible action
Harmonization of terminology	<ul style="list-style-type: none"> <li>Seek consensus between regulators to facilitate discussion</li> </ul>
Paediatric Development Plan (PDP)	<ul style="list-style-type: none"> <li>Develop guidance on content and evaluation of the PDP</li> <li>Provide capacity building/training</li> <li>Develop guidance on safe, efficient, and effective</li> <li>Develop generic advice on dosage forms</li> <li>Provide technical advice on age bands, specific diseases, dosage forms of paediatric medicines, aspects of research in developing countries</li> </ul>
Application for Conduct of Clinical Trials	<ul style="list-style-type: none"> <li>Collect FAQs on the conduct of clinical trials with special emphasis on developing countries; provide answers/references from already existing documentation (e.g. from EMA or FDA)</li> <li>Develop a reference document</li> <li>Develop practical FAQs/answers guide</li> </ul>
Marketing Authorization	<ul style="list-style-type: none"> <li>Develop guidance on content and evaluation of the application dossier</li> <li>Define the documents which should accompany the Marketing Authorization Application when the paediatric plan/data have already been assessed by another NMRA</li> <li>Develop capacity building/training activities for NMRAs</li> </ul>
Pharmacovigilance	<ul style="list-style-type: none"> <li>Identification of stakeholders and resources (existing data bases, networks)</li> <li>Development of relevant reference documents</li> </ul>



Key topic	Possible action
Advocacy for research on and development	<ul style="list-style-type: none"> <li>• Report Network activities internationally (e.g. WHO to reserve timeslot in 2010 ICDRA meeting)</li> <li>• Report Network activities (e.g. to Ministries of Health)</li> <li>• Identification of national focal point for paediatric topics</li> </ul>
Transparency of the Network's activities	<ul style="list-style-type: none"> <li>• Use WHO web site for exchange of information (e.g. regulatory documents from countries)</li> <li>• Circulate Network Newsletter on a 6-months basis</li> <li>• Conduct Network meetings on a 12-months basis</li> </ul>

## 2. Mechanisms for information sharing

Key topic	Possible owner/Tools for information sharing
Regulatory Policies and Ethical Guidelines	<ul style="list-style-type: none"> <li>• NMRAs, NGOs, ICH, WHO</li> <li>• WHO web site, share point, catalogue of resources</li> </ul>
Information on clinical trials (e.g. suspended trials, rejected CT applications)	<ul style="list-style-type: none"> <li>• NGOs, Universities, Governments, CROs, IRBs</li> <li>• WHO web site, share point, electronic Newsletter</li> </ul>
Product information (e.g. specification on dosage form, excipients, stability, label information, marketing authorization, counterfeiting efforts, negative assessments, withdrawals)	<ul style="list-style-type: none"> <li>• NMRAs, Pharmaceutical Industry</li> <li>• WHO web site, share point, electronic Newsletter</li> <li>• WHO, International Clinical Trials Registry Platform (ICTRP)</li> </ul>
Safety information about paediatric medicines	<ul style="list-style-type: none"> <li>• NMRAs, Pharmaceutical Industry, WHO (the Uppsala Monitoring Centre)</li> <li>• WHO web site, share point, electronic Newsletter</li> </ul>
Knowledge on age-appropriate dosage forms	<ul style="list-style-type: none"> <li>• NMRAs, Pharmaceutical Industry, Universities</li> <li>• WHO web site, share point, electronic Newsletter</li> </ul>



### 3. Needs for capacity development

Key topic	Results and comments
Which topics should be addressed through capacity building - in the short term (1-2 years)?	<ul style="list-style-type: none"> <li>• Assessment of dossiers submitted to NMRAs for marketing authorization; GMP issues</li> <li>• Evaluation of scientific and ethical aspects of CT protocols</li> <li>• Paediatric-specific registration requirements</li> <li>• Training for ECs/IRBs to review paediatric applications</li> <li>• Data analysis, including statistics</li> <li>• Evaluation of bioequivalence data for generic products</li> <li>• Adverse event reporting and evaluation</li> <li>• Inspection and monitoring of CTs and GCP issues</li> </ul>
Which topics should be addressed through capacity building - in the long term (5 years)?	<ul style="list-style-type: none"> <li>• Assessment of electronic dossiers</li> <li>• Clinical trial methodology for investigators</li> <li>• Training in drug recall procedure</li> <li>• Training in investigation of counterfeit</li> <li>• PDP, especially formulation development</li> <li>• Developing guidelines for paediatric research</li> <li>• Formation of expert committees</li> <li>• Development of IT infrastructure</li> </ul>
Who needs what in terms of capacity ? NMRAs	<ul style="list-style-type: none"> <li>• Qualified personnel for evaluation and appropriate training</li> <li>• International accepted guidelines and procedure</li> <li>• Transparency in registration requirements and procedures</li> </ul>
Who needs what in terms of capacity building? ECs/IRBs	<ul style="list-style-type: none"> <li>• In the short term, training on registration requirements</li> <li>• In the long term, training in clinical trial methodology</li> </ul>
Who needs what in terms of capacity building? Manufacturers/Pharmaceutical industry	<ul style="list-style-type: none"> <li>• Most of the items listed above</li> </ul>
Which types of capacity building and from whom is available?	<ul style="list-style-type: none"> <li>• WHO Prequalification programme</li> <li>• QSM at WHO</li> <li>• DIA or equivalent (workshops, online courses; <a href="http://www.diahome.org/DIAHome/Home.aspx">http://www.diahome.org/DIAHome/Home.aspx</a>)</li> <li>• AMANET (specific programmes on malaria; <a href="http://www.amanet-trust.org/">http://www.amanet-trust.org/</a>)</li> <li>• Swiss Tropical and Public Health Institute (clinical trials, protocol development; expertise in developing countries; <a href="http://www.swisstph.ch/en.html">http://www.swisstph.ch/en.html</a>)</li> </ul>



Key topic	Results and comments
	<ul style="list-style-type: none"> <li>• Eudipharm (<a href="http://www.eudipharm.net/">http://www.eudipharm.net/</a>)</li> <li>• Family Health International (conduct of clinical trials, expertise in developing countries; <a href="http://www.fhi.org/en/index.htm">http://www.fhi.org/en/index.htm</a>)</li> <li>• University programmes (The London School of Hygiene and Tropical Medicine, The Royal Tropical Institute (Amsterdam))</li> <li>• Vienna School of Clinical Research (GCP-training, protocol development, statistics)</li> <li>• EDCTP (e.g. GCP courses, linked to CTs; <a href="http://www.edctp.org/">http://www.edctp.org/</a>)</li> <li>• EU initiatives for capacity building; e.g. training of Assessors)</li> </ul>
How can capacity building be delivered?	<ul style="list-style-type: none"> <li>• Through experts in a specific field (e.g. statistics, epidemiology, paediatrics, PK/PD)</li> <li>• One on one training with experienced regulators</li> <li>• Exchange programmes with other RAs, learning on the job</li> <li>• Promote capacity building and training to relevant authorities</li> <li>• Tap into existing international meetings and initiatives</li> </ul>
What can the Network do with regard to capacity development?	<ul style="list-style-type: none"> <li>• Function as a forum and a catalyst</li> <li>• Collaboration with international groups</li> <li>• Promote the inclusion of paediatric topics in meeting agenda</li> <li>• Function as a resource for information</li> <li>• Function as an advocate for training and capacity building</li> </ul>
What can WHO do?	<ul style="list-style-type: none"> <li>• Provide training and content</li> <li>• Coordinate</li> <li>• Provide guidance documents</li> <li>• Establish Prequalification programmes for paediatric medicines</li> </ul>
Which resources are needed?	<ul style="list-style-type: none"> <li>• Regulators with expertise in the understanding of paediatric drug development and evaluation</li> <li>• Funding to set-up capacity development activities provided by external experts</li> </ul>

## Proposed next steps

The meeting participants agreed on the proposed next steps in the development of the activities of the Network:

- WHO should establish a web site for the Paediatric medicines Regulators' Network. The web site should have an open/public domain section, and a section that is confined to members.
- WHO/Network should prepare and circulate a Newsletter on a 6-months basis.
- WHO should provide expertise for guideline development and review.
- WHO should perform an in-depth review of the needs for capacity building at NMRA; the following needs were highlighted by the participants as most urgent:
  - review of clinical trial applications,
  - review of application dossiers for marketing authorization,
  - ethical aspects of research in the paediatric populations.
- The group agreed that the forthcoming meeting of ICDRA (Singapore, Nov. 2010) could usefully incorporate a satellite meeting on paediatric medicines.
- A list of Frequently asked questions (FAQs) concerning paediatric medicines and their regulation should be developed and presented on WHO webpage. This list should be discussed within the Network, and used as a reference for further activities.
- Based on the list of FAQs, WHO will collect answers and references from already established guidance documents (e.g. EMA, FDA or ICH) to develop a technical working document on the conduct of clinical trials in children, with an emphasis on the special circumstances in developing countries.
- From the Network members, a Steering Committee will be set-up to oversee the further development of the proposed activities and the Network.
- The participants have discussed various possible names and acronyms for the Network. A final decision will be made shortly.
- National Institutes of Health (NIH) offered to provide two existing documents on how to review clinical trial protocols.
- FDA offered to provide existing templates for reviewing drugs in certain diseases and the results from a review of paediatric drug labels.
- Canada offered to provide its existing list of FAQs to be used as a starting point for the PmRN list.

## **Conclusion**

The participants reviewed a draft set of terms reference and operating principles (Annex 1). It was agreed that these would be circulated for final approval with the meeting report and that NMRAs would then be approached for formal agreement to participate in the Network. A Steering Committee would be established with the aim of developing a work plan for the Network, to report to ICDRA in December 2010.

## **Annex 1**

### **DRAFT Paediatric medicines Regulators' Network Terms of Reference**

#### **Background**

A Paediatric medicines Regulators' Network has been convened by WHO to promote the availability of quality medicines for children. This effort is the result of a recommendation from the 2008 13th ICDRA meeting. Notwithstanding differences in the needs and challenges faced by NMRAs in responding to their domestic and regional requirements, there is a pressing need to support the global availability of safe, effective and affordable medicines for children. The overall objective of the proposed Paediatric medicines Regulators' Network is to support availability of quality medicines for children through facilitation of communication, collaboration and regulatory harmonization across manufacturing, licensing and research. All regulators are free to join the Network and contribute to discussions.

It is envisaged that the establishment of a Network of NMRAs could provide an effective and flexible forum for enabling dialogue and fostering development of international consensus on effective regulatory approaches for increasing the availability of paediatric medicines. Accordingly, the Network is established as a group of NMRAs. The aim of the Network is to promote the availability of safe, effective and affordable medicines for children, by enhancing information sharing between NMRAs, improving the transparency of the decision-making process, promoting appropriate ethical and clinical research standards for children, strengthening paediatric pharmacovigilance and contributing to capacity building for the licensing of paediatric medicines.

#### **A. Objectives**

The Paediatric medicines Regulators' Network will focus on:

1. Provide a forum for discussion between NMRAs to build awareness on paediatric medicines regulatory considerations.
2. Facilitate the collaboration, discussion and work towards consensus on regulatory 'standards' for paediatric medicines.
3. Promote capacity for development of paediatric medicines, including formulations, with attention to identifying the special needs of children in developing countries and other vulnerable paediatric populations.

4. Promote appropriate conduct of paediatric clinical trials, including establishing links with existing networks, as well as work on scientific and ethical review of clinical trials for the development of paediatric medicines.
5. Strengthen licensing (approval) systems for paediatric medicines by increasing regulatory cooperation, information sharing and training.
6. Identify the need for, promote the generation of, and make available, evidence-based recommendations and advice on all aspects of medicines for children, including dosage forms, excipients and delivery devices for medicines.
7. Provide a forum for promoting and strengthening paediatric pharmacovigilance, including identifying needs for methodological development and complementing existing information sharing mechanisms.
8. Encourage expansion of the membership of the Network to include all NMRAs.
9. Collaborate with other networks and NGOs on research and development of paediatric medicines, licensing procedures, pharmacovigilance, and capacity building, and to foster interaction with industry, health-care professionals, patients and consumers.

## **B. Functions of the Network**

The Network shall have the following functions for the purpose of furthering its objectives:

1. Establish a fast and effective mechanism for communication among the Members, and with scientific or other regulatory bodies;
2. Communicate its considerations and recommendations to WHO; and
3. Support WHO in enhancing and assisting NMRAs worldwide, as well as the regional Networks of NMRAs which are to be further developed in all WHO regions.

## **C. Members**

1. The Network will be comprised of a group of NMRAs (also referred to as "Members") that have responsibility for the regulation of paediatric medicines.
2. The Members will each designate a Representative to participate in the Network. The Representatives will themselves have expertise in the areas of regulation, standard-setting, licensing or pharmacovigilance of medicines. Every Representative should act as a contact person, and should be responsible for communication within the Network and with their NMRA. An alternative expert should be designated by each NMRA as a substitute Representative, in case the principal Representative is not available.

3. A Chair will be appointed by the Members of the Network. The Chair shall be rotated every two years by consensus of the Members and will work closely with the WHO Secretariat.
4. A Steering Committee, consisting of up to eight members of the Network, will be formed. The Steering Committee will work in collaboration with the appointed Chair and the WHO Secretariat to further the aims and objectives of the Network.

#### **D. Invited Experts**

At the request of the Network, WHO may invite individual relevant experts ("Invited Experts") to participate in certain meetings of the Network, to share information and/or advise the Network on matters within the sphere of their competence. "Invited experts" will not, however, be considered as Members.

#### **E. Operations**

1. The Network provides the Members and other participants with the opportunity to discuss matters and formulate proposals and recommendations which fall within the Terms of Reference.
2. The Network may establish ad hoc Working Groups composed of "Invited Experts" to support specific areas of expertise, as necessary. A Member of the Network will be elected as a Chair of each Working Group. The Chair of the Working Group will appoint the "Invited Experts" of the Working Group after consultation with the Chair of the Network and the WHO Secretariat. The Chair of the Working Group will report to the Network the conclusions reached by the Working Group.
3. The considerations and recommendations of the Network will be made by consensus of the Members. Considerations and recommendations of the Network will not legally commit WHO or the participating NMRAs and will not override the authority of the respective governing bodies of the Members. They will constitute expert advice which the Members, other NMRAs and WHO may use.
4. The Network is not an independent legal entity, but a collaborative mechanism between the Members. Whereas the Members may freely share the issues discussed and the consensus considerations and recommendations of meetings of the Network, the Network cannot be formally represented by individual participants at any other fora. The Chair of the Network, could however report on the activities of the Network with the agreement of a majority of the Members and the WHO Secretariat.
5. The Network shall conduct its activities by any method of communication that is efficient and appropriate to discharge its objectives, including in-person meetings, videoconference, exchange of written reports and communications, e-mail communications and telephonically.

6. It is understood that Members of the Network have to comply with the rules of their respective authorities regarding confidentiality of privileged information and conflict of interest. It is further understood that the Network will operate under the rules and regulations of WHO applicable to technical advisory groups.

#### **F. Secretariat support**

1. Secretariat support for the Network will be provided by WHO, acting through the Department of Essential Medicines and Pharmaceutical Policies (EMP) and the Team Medicine Access and Rational Use (MAR) at WHO headquarters in Geneva. In this connection, WHO will: (a) coordinate the organization of the meetings and other communications of the Network, and of any Working Groups, (b) prepare and distribute, in consultation with the Chair, draft agendas, meeting reports, progress reports, etc (c) receive and submit applications to the Members for membership in the Network, and (d) receive and inform the Members of notices of termination.
2. In addition, WHO will, as part of its secretariat support for the Network: act as a central repository of information and documentation relevant to the Network (including in particular reports of the Network and Working Groups), and disseminate and distribute such information and documentation to the NMRAs of WHO Member States and the public as appropriate, including through the WHO web site.
3. The Network's products will be disseminated with appropriate disclaimers, including that the content does not necessarily reflect the views or stated policy of the participating NMRAs, organizations, agencies and institutions (including WHO, acting as the secretariat for the Network). A clarification of the nature of the proposals/recommendations put forward in such Network documents, will be included along the following lines: "The name of the Network, including its Members and other participants may not be used for or in connection with commercial or promotional purposes".

#### **G. Financing of, and fundraising for operation of the Network (including the Secretariat support)**

1. Members and "Invited Experts" will, in principle, be responsible for meeting their own expenses in relation to the Network (including, but not limited to, travel and subsistence for the attendance of meetings). Subject to the availability of funds, the Members may decide to support the participation of other country organizations or agencies, individuals, and/or of "Invited Experts".

2. The secretariat support and related day to day operation of the Network will be financed by WHO. In addition, WHO may raise funds from other sources to support the work of the Network, in accordance with WHO's established policies and principles.
3. The acceptance by WHO of any contributions for the Network from the Members, as well as from other sources will be subject to WHO's established policies and principles and to WHO's financial rules and regulations, administrative procedures and practices.

## **H. Miscellaneous**

### **Membership**

1. The Members of the Network and WHO can propose new candidates for membership. Applications to become a Member will be addressed to the WHO Secretariat which, after consultation with the Members of the Network, will inform the applicant of the decision.
2. Termination. Any Member may decide to terminate his/her involvement in the Network by providing written notice to WHO. WHO shall remove the Member in question from the list of Members and inform other Members of the Network accordingly.
3. Amendments. These Terms of Reference may be modified in writing by consensus of all Members and with the endorsement of WHO.

## List of participants

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Dr Hermann Garden, EMP/MAR

Dr Suzanne Hill, EMP/MAR

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Dr Sabine Kopp, EMP/QSM



Dr Clive Ondari, Coordinator, EMP/MAR

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## Meeting agenda

Paediatric medicines Regulators' Network Meeting  
Salle D, WHO headquarters, Geneva  
15 - 17 February 2010

### PROVISIONAL AGENDA

#### Monday, 15 February 2010

08.30	Registration
09.00	Welcome & Introduction ADG/HSS or Director, EMP
09.15	Introduction of participants
09.45	Objectives and proposed meeting agenda Review of TORs for the Network Better Medicines for Children project (Dr Suzanne Hill)
10.15	Questions/comments from the group
10.30	Coffee
11.00	QSM presentation (Dr Lembit Rago)
11.15	Presentation of 1st background paper: Regulatory Guidelines for Paediatric Medicines (Dr Susan Walters)
11.45-12.30	Questions/comments/discussion
12.30-14.00	Lunch
14.00	Presentation of 2nd background paper: Clinical Trial Ethical Standards for Inclusion of Children (Dr Lisa Bero)
14.15	Questions/comments/discussion
15.00	Presentation of 3rd background paper: Current Guidance for Child Health Clinical Trials (Dr Suzanne Hill)
15.30	Coffee
16.00	Questions/comments/discussion
17.00-17.30	Summary & close
17.30-19.00	Reception, WHO Restaurant

## **Tuesday, 16 February 2010**

09.00-09.30	Brief recap of Monday Proposal for group work
09.30	Group work topic 1: Common standards
11.00	Coffee
11.30 - 12.00	Group work continued
12.00-13.00	Feedback from groups & discussion (Group Rapporteur)
13.00-14.00	Lunch
14.00-16.30	Group work topic 2: Information sharing (Coffee in groups)
16.30-17.30	Feedback from groups & discussion (Group Rapporteur)

## **Wednesday, 17 February 2010**

09.00-09.30	Brief recap of Tuesday
09.30	Group work topic 3: Capacity development
11.00	Coffee
11.30 - 12.00	Group work continued
12.00-13.00	Feedback from groups & discussion (Group Rapporteur)
13.00-14.00	Lunch
14.00-15.30	Plenary Next steps & workplans
15.30-16.00	Coffee
16.00-17.00	Summary & Close

## **Web links**

- WHO Essential Medicines:  
<http://www.who.int/medicines/en/>
- WHO Make Medicines Child Size:  
<http://www.who.int/childmedicines/en/index.html>
- WHO Selection of Essential Medicines:  
[http://www.who.int/selection\\_medicines/en/](http://www.who.int/selection_medicines/en/)
- WHO Quality, Safety and Efficacy of Medicines:  
[http://www.who.int/medicines/areas/quality\\_safety/en/](http://www.who.int/medicines/areas/quality_safety/en/)