

Second Informal Consultation on Long Term Studies (LTS) on Environmental Threats to the Health of Children in Developing Countries

**PAHO, Washington D.C., USA
23-25 August 2004
Report**

1. The Second Informal Consultation on Long Term Studies (LTS) on Environmental Threats to the Health of Children in Developing Countries was convened by the World Health Organization (WHO) on 23-25 August 2004, hosted in Washington, D.C. at the headquarters of the Pan American Health Organization (PAHO), which also serves as the WHO regional office for the Americas.
2. The purpose of the consultation was to discuss the implementation of long-term (longitudinal) cohort studies (LTS) on children's environmental health in developing countries, and to address specific issues, such as funding, networking, awareness-raising, and development of a core set of environmental health factors for inclusion in LTS. Specific objectives of the consultation were:
 - a. Review activities undertaken since the Glion/Montreux consultation (October 2003) and respond to issues raised in the resulting White Paper.
 - b. Review a draft paper on LTS.
 - c. Discuss the incorporation of a core set of environmental health factors into ongoing and new LTS.
 - d. Explore potential sources of funding.
 - e. Establish links with existing LTS, especially with the National Children's Study in the USA.
 - f. Make recommendations on a follow-up strategy.
3. Representatives from 13 countries conducting or embarking on LTS were present. (See participants list, Annex A, and agenda of the consultation, Annex B)
4. Dr. Stephen Corber, Area Manager for Disease Prevention and Control in PAHO, opened the conference by pointing out the importance of children's environmental health in the Americas, reminding the group that children have special vulnerabilities that need to be taken into consideration when working for the protection of their health. He mentioned the many activities that PAHO has undertaken on children's environmental health since first called to action by the *1997 Declaration of the Environment Leaders of the Eight on Children's Environmental Health*. Dr. Corber highlighted the national children's environmental health profiles that PAHO developed in 2003 to assess country readiness to undertake actions that promote policies, awareness, research and effort to improve children's environmental health. He noted the need for increased research and the

importance of international collaboration on research that leads to pooling resources and sharing findings.

5. Dr. Duane Alexander (Director, National Institute of Child Development and Health, NIH, USA), provided information about the National Children's Study (NCS) taking place in the United States and offered insight to its planning, goals and activities underway. (Martha to add in notes based on presentation file) Several questions were fielded by Dr. Alexander. Questions ranged from specifics on the population to be included in the NCS, participation of industry, and interventions based on findings of the NCS. Dr. Alexander reported that federal funding was sought for support of the full core study but that additional data collection or analyses may be supported by governmental agencies or non-public sector.
6. Dr. Jenny Pronczuk (WHO/PHE/PCS) provided background on international cohort studies and their importance to global programs to improve children's environmental health. She mentioned the strong relationship of certain environmental factors to leading killers of children worldwide, for example, acute respiratory infections, acute diarrheal disease, and malaria. She pointed out that environmental hazards can also lead to illness and disability, for example, malnutrition is an underlying factor of child morbidity and mortality and is strongly related to degraded environments. Dr. Pronczuk reported on many activities underway, supported by WHO (including the Healthy Environments for Children Alliance, HECA), to increase awareness of children's environmental health, develop policies to improve the protection of children's health from environmental hazards and conduct studies, such as the national profiles of children's environmental health around the world. Dr. Pronczuk presented the steering committee for the consultation, consisting of herself, Dr. Danuta Krotoski (NICHD/NIH), and Dr. Adolfo Correa (CDC). She then presented the objectives of the consultation (see Annex B), and informed the audience that the two abstracts on LTS submitted to the Global Forum on Health Research were accepted (one for full session, one as a poster).
7. Dr. Jean Golding (ALSPAC: Avon Longitudinal Study of Parents and Children - Children of the 90s) opened the first session of the consultation to review country activities undertaken since the first consultation on LTS, which took place in 2003 in Glion/Montreux. Each participant provided an update on activities. Participants from additional countries, not present in the first consultation, also informed the group of planned or ongoing LTS on children. Studies are underway in several countries, for example, Canada, China, India, Mexico, South Africa, Spain, Thailand, and the United Kingdom. Participants from other countries, such as Brazil and Uruguay, were either planning studies or were present to learn about LTS because of increased interest by their governments on children's environmental health. Reference was made to an important ALSPAC study that looked into the relationship between thiomerasol in vaccines and neurodevelopmental problems in children. (NB: on 23/9/04 Dr. Landrigan reported that this study proves the absence of such a relationship, and has been published in the September issue of Pediatrics (Pediatrics Vol. 114 No. 3 September 2004, pp. 577-583). This illustrates the point that LTS, once established, are uniquely well positioned to answer important questions that go beyond their initial scope.)

8. A draft manuscript on the opportunities posed by LTS cohort studies was presented for discussion by Dr. Danuta Krotoski and Dr. Thea de Wet (Associate Professor in Anthropology, RAU University/Medical Research Council, South Africa). Participants reviewed the draft in advance and offered many suggestions and comments. The group agreed in general that it was a good idea to use this draft manuscript as a basis to jointly author a paper for publication in a peer reviewed journal. They agreed to provide comments and continue reviewing drafts as a writers group developed them. There was a consensus that two separate papers or a paper with two distinct parts would be helpful, (i) one aimed at policy-makers and donors, (ii) the other targeted to scientists.

9. Dr. Adolfo Correa (Medical Epidemiologist, CDC) opened the third session on incorporating environmental factors into LTS. He introduced Dr. Philip Landrigan (Chairman, Dept of Community Medicine and Preventative Medicine, Mount Sinai School of Medicine, NYC) who presented lessons learned from the US research centers on children's environmental health. Dr. Landrigan reported that five centers have established seven prospective children's cohort studies focusing on indices of physical growth and neurobehavioral outcomes. He had several insights to offer regarding the design and implementation of LTS and shared his observation that the best results were from research that focused on the outcome from the start and were linked to specific exposures. He pointed out the key parameters for incorporation in LTS design:
 - a. good biomarkers of exposure
 - b. good biomarkers or genetic susceptibility
 - c. hypothesis-driven studies (as they provide the best results)
 - d. well validated outcomes
 - e. limited timeframe
 - f. repeated measures design
 - g. secure repositories for biological samples
 - h. community partnership

10. Based on his experience with studies in Mexico, Dr. Carlos Santos-Burgoa (Ministry of Health, Mexico), proposed some factors for consideration when designing LTS. He advised that the benefits of collaborative LTS children's studies must be highlighted and considered in terms of their excellent contribution to capacity building of scientists and experts, and increased access to technology transfer that they offer. Also, cross-sectoral participation is crucial and has shown success in programs, such as growth out of poverty and vector control successes without use of DDT or other pesticides. He made suggestions on reflecting the reality of the pool of people studied, for example, do they migrate back and forth from rural to urban, from a country and back? Also, he suggested some environmental factors for consideration by the group, emphasizing the need to consider routes and patterns of exposure. Dr. Santos Burgoa pointed out a need to focus on poverty and determine how to incorporate indicators or descriptors of poverty and economics.

11. Dr. Correa provided a draft list of environmental factors and health outcomes to consider in the design of LTS and opened Session 3 for discussion. The group discussed and revised the list of factors presented. The purpose of this was to work toward defining a core set of environmental factors and a core set of health outcomes that would be interesting for a country LTS or a multi-national LTS. The group then discussed prioritization of these factors. As follow-up, the group was asked to review the examples of environmental factors in the context of the list of health outcomes and to provide comments to Dr. Correa for developing a prioritized list of environmental factors. Some criteria were shared to suggest how to reach a prioritized list. This session was successful in that it offered a chance for all participants to give input on key factors and outcomes of importance, contributing to a mutual understanding of interests, potential hypotheses and areas of interest (see Annex C).
12. Dr. Correa noted interest in a potential multi-national children's LTS and suggested the group consider the hypothesis for such a study. In addition, advantages and challenges of such a study were discussed. Participants who had prior experience in conducting LTS offered insights into the importance of laboratory standardization for the study, how to manage samples, crucial issues of particular countries or areas (e.g., water and sanitation in developing countries), need for training, need to collaborate with partners that could offer experience in planning and conducting LTS, and political and financial support over the long term. The group then reviewed and commented upon the WHO "green page" (see Annex D) for clinical history taking and discussed this and other health statistics collection tools and their potential use for data collection and analysis.
13. Dr. Chanpen Choprapawon (Director, Prospective Cohort Study of Thai Children, Ministry of Public Health, Thailand) and Ms. Cathy Allen (Environmental Protection Agency, USA) opened Session 4, with the purpose to review two outreach products: a draft brochure and a video on LTS. Several comments were offered on the idea of outreach, mainly on assessing the target audience and speaking to those audiences. Suggestions were made to coordinate within WHO with public relations experts and writing in order to target the message to the audience for the brochure. The group recommended that not only the one-page document be slightly modified and then published and circulated, but also that an additional brochure be developed, targeted to policy officials and potential donor organizations, answering key questions on why LTS should be funded and otherwise supported. Dr. Thea de Wet presented the draft video created to provide basic information about the importance of LTS to long-term protection of children around the world. This video was developed by the RAU University/Medical Research Council and supported by WHO. It targets academics, policy officials and donor organizations interested in CEH. The group applauded this well-done draft video, offered some comments and recommendations for final edits and suggested using this video in upcoming national and international meetings to raise interest and support for LTS.
14. Dr. Danuta Krotoski and Dr. Jean Golding chaired Session 5 on seeking funding to support LTS in developing countries. Dr. Krotoski presented a chart that averaged costs of LTS from around the world and discussed cost effectiveness of LTS. She presented a

strategy for obtaining funding which included components such as partnering across countries and gaining the interest of international aid and donor organizations. Dr. Golding offered lessons learned on obtaining and maintaining funding for a cohort study, including the crucial central coordination function needed for multi-national studies.

15. The Round Table on International Collaboration on Long Term Studies on Environmental Threats to the health of Children in Developing Countries was convened in the afternoon of August 24. Invited to this roundtable were the consultation participants as well as special invitees from donor and international organizations, including the World Bank, the Inter-American Development Bank, the Organization of American States, the Physicians for Social Responsibility, the March of Dimes and the United Nations Foundation. This session was chaired by Dr. Peter Scheidt (Director of the NCS Program Office, NIH, USA) and Dr. Jenny Pronczuk (See agenda for the Roundtable, Annex C). Dr. Scheidt opened the session with initial remarks on why LTS on children were timely, useful and cost-effective. Dr. Pronczuk provided background on the international LTS workgroup, outcome of the first and second consultations, and goals of the working group. The draft video on LTS was then played, followed by a presentation by Dr. Adolfo Correa, summarizing the work to date and presenting the next steps.
16. Dr. Chanpen Choprapawon presented the Thai LTS on children. Based on a survey of families, Thailand had found disturbing facts about children in some parts of the country, with a mean intelligence quotient of 92, and markers such as height and weight significantly lower than those of children in the United States. With the goal of offering the highest possible potential for future to Thai children, the government supported an LTS on children, their environment and health status, as a way to begin to find answers to questions arising from the survey of families. The study follows over 4000 children, all born in the study year, in five districts of Thailand, whose families were willing to volunteer participation. It will follow the children from the mother's 28th week of pregnancy through the child's 24th year. Already, results from the study have caught the attention of the Thai Prime Minister and other policy makers. Communities have come together to take actions to improve children's environmental health. The next phase of this study is currently in the planning stage and will incorporate additional environmental exposures.
17. Dr. Thea de Wet presented the *Birth to Twenty* cohort study of South Africa. Beginning in 1990, this study tracks children from birth to age twenty. At fourteen years into the study, it continues to enjoy a 73% participation by the original cohort. Community involvement, while difficult in a big city, was an important facet of this study. Research assistants from the areas where the study is being conducted were employed to broker the relationship between the participants and the researchers, and modern technologies, such as cell phones and internet were employed as means of communication. Dr. de Wet presented a video that described the study, explained how it was run and demonstrated how results were already affecting policy change. This spurred on discussion and questions regarding how science can affect policy and create change to improve children's lives. The presenter was applauded for the success in telling a story about this

research project that, while complex, could still tell an important story that could capture the interest of policy-makers.

18. Dr. Terry Dwyer (National Children' Study, NIH, USA) gave a presentation about the Tasmanian Children's Study, which tracked 100 thousand children from 1984 through 1998. Three important publications came from this study, on asthma, bone density and metabolism. Dr. Dwyer summarized that not only do prospective cohort studies offer opportunities to share knowledge but they also allow for scientists to pool data in order to examine relatively rare childhood illnesses, such as cancer and diabetes. In this case, working across country cohort studies could allow the study of leukemia and testing hypotheses cancer causalities. He stressed that the next steps were to look more carefully at comparability of exposure data, an activity that is just being initiated.. Dr. Dwyer believes this is a worthwhile effort to better understand relatively rare child health outcomes. He strongly endorsed the need for international research collaboration and to identify additional studies to include in such data pooling investigations. The beauty of this, he maintains, is that existing data from existing studies can be used to another purpose so that the cost is very low in comparison to starting up large, long-term studies. A commenter reminded the group that these rare diseases, such as childhood leukemia, are catastrophic diseases in developing countries where parents are faced with either no treatment, leading to certain child death, or treatment that is so costly to the families that they become impoverished. Health sectors in developing countries are very interested in international studies that will contribute to knowledge and prevention about these rare diseases.
19. Dr. Luiz Galvao (Area Manager for Sustainable Development and Environment, PAHO) joined the consultation for its summary session, taking place the morning after the Roundtable (25 August). One topic resultant of the consultation was the necessity of cross-country collaboration on LTS to pool data, giving WHO a unique position to coordinate research across the countries. A motion was made by Dr. Carlos Santos Burgoa to engage in a multi-national LTS on children, sharing protocols, embarking on similar research, and standardizing sampling and laboratory procedures. Dr. Philip Landrigan suggested that instead of a multi-national study, there be a set of national studies that are linked for coordination at the international level, but that the country studies be funded, supported, developed and reported at the national level. Dr. Danuta Krotoski suggested that the agreed to common core studies were important for obtaining comparable data across countries and that donor organizations could be encouraged to fund the development of the core protocols across countries. Dr. Thea de Wet offered a compromise - stating that while it is interesting to have studies, new national LTS are hard to get national support for - but as part of an international study, countries would likely get funding to be a part, in particular because they leverage data, expertise, knowledge and other forms of capacity building across the countries. Dr. Jean Golding reported her experience with a European pregnancy LTS which had only limited success because of lack of a central coordination body.
20. Dr. P.K. Abeytungga (Canadian Center for Occupational Health and Safety, Canada) offered insights on the necessity to consider informatics design as a core part of the

planning and central coordination of the study, to incorporate protocols and information bases that will allow for pooling of data, to build in flexibility for change of protocols and technologies, and to build in multi-lingual needs inherent in a multi-national cohort LTS. Dr. Nuria Ribas-Fito (Municipal Institute of Medical Investigation, Spain) emphasized using what is available in ongoing and past LTS, starting there to develop protocols and thereby automatically incorporating ongoing studies into new studies and increasing collaboration among existing studies as well as new international LTS.

21. Participants from around the world stated interest and indicated consensus on forward movement to plan and design a multi-national children's LTS. They emphasized the support for national studies that would be given by participation in an international study. All participating countries would have the opportunity to share their experience and knowledge, as well as learn from other studies and experiences, maintained the participants. Dr. J. Ponzo (Ministry of Health, Uruguay) stated that such a study on environmental health of children would also be a challenge for epidemiologists, requiring new protocols and statistical capabilities. Experience from some techniques such as geographical information systems were suggested as potential valuable inputs. Seeking support from national governments, international organizations (specifically the World Health Organization), and finding opportunities at international research meetings or international ministerial meetings was considered crucial to obtaining support for creating and conducting a multi-national LTS on children and environment.
22. Dr. Pronczuk summarized the consultation and pointed out challenges and next steps. She was pleased with the outcome of the consultation, the increased awareness of many good efforts underway around the world, and the overall interest in developing a multi-national LTS. She summarized her understanding that participants recommend a multi-national study that has national components, belonging to individual countries, and an international component ("core study") that would be based on commonly developed protocols and three to four hypotheses developed and agreed by all participants. Following Dr. Landrigan's suggestions, the areas for the international component may include:
 - a) Respiratory diseases
 - b) Endocrine, sexual and reproductive effects
 - c) Neurobehavioural effects
 - d) Pregnancy outcome
 - e) Physical growth
23. For each of these areas, the organization of working groups was suggested. Dr. Pronczuk pointed out that such a multi-national research project could not become a WHO project because both the capability and expertise exists in the scientists of the country. However, WHO is in a position to offer some "loose" coordination through its ability to promote country, regional and global activities, organize meetings and bring together participants. Dr. Pronczuk stated that with the support of Dr. Krostoski, this multi-national study effort can be linked with the United States NCS (which may, in fact, involve Canada and Mexico in the future Dr. Krostoski offered to register participants of the consultation who

are not yet part of the NCS International Interest Group in order to utilize the NCS data sharing portal which would enable participants to communicate, share documents, and even manage working groups. Dr. Pronczuk also mentioned that WHO can help by strategizing fundraising and contacting the donor organizations.

24. The specific follow-up steps were the following:

- a. Dr. Krostoski will refine the draft manuscript discussed in the consultation and prepare it for a peer reviewed journal publication.
- b. Dr. Correa will receive input from participants on specific environmental factors and health outcomes and complete this chart.
- c. Dr. Ribas-Fito will send Dr. Correa the list of health outcomes and associated hypotheses developed for the Spanish study.
- d. All participants will propose hypotheses on one (or more) of the five areas (see para 21), submitting them to Drs. Correa, cc Pronczuk by September 10, 2004.
- e. Dr. Pronczuk will convene a teleconference meeting to discuss the hypotheses on September 14, 2004.
- f. Dr. Pronczuk will prepare a fundraising strategy, including one-page brochure, completed video, plan for central coordination of a study and budget.
- g. Dr. Pronczuk will send letters to donor and international organizations that participated in the roundtable with appropriate information, e.g. brochure, consultation report, one-pager. attached.
- h. Dr. de Wet will complete the LTS video, incorporating changes suggested by participants as practicable.
- i. All participants will seek to attend the Global Forum on Research Collaboration, 16-20 November, 2004 (Mexico City, Mexico), and participate in discussions on joint research on children's environmental health on 17 November, 2004, from 16:00-18:00.
- j. Dr. Pronczuk will convene a working group meeting (3rd Informal Consultation) after the Global Forum meeting in November 2004, in coordination with Dr. Santos-Burgoa (Mexico) and Drs. Krotoski and Correa.
- k. Drs. Pronczuk and Santos-Burgoa, will request PAHO assistance in planning to bring the multi-national children's LTS to the attention of health and environment ministers at the June 2005 Mar del Plata ministerial meeting.
- l. All working group members will continue to develop next steps for implementation after the November 2004 global forum.

25. Dr. Pronczuk adjourned the consultation, offering her thanks to Dr. Galvao for hosting the consultation at PAHO and to Ms. Shimkin for providing the support to the meeting and, especially for acting as Rapporteur. Dr. Krotoski seconded this appreciation, stating that the consultation had offered excellent results, both coalescing the workgroup and outlining clear steps for the next months in the planning and design of potential multi-national children's LTS.