



**WHO - ITI Joint
Research Agenda Meeting
for the Elimination of
Blinding Trachoma**

Geneva, Switzerland April 1-2, 2004

World Health Organization, 2004

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I. Introduction

The World Health Organization (WHO) and the International Trachoma Initiative (ITI) organized a joint research agenda meeting, held in WHO Headquarter, Geneva from April 1-2, 2004.

The meeting was timed to follow the 2nd Trachoma Scientific Informal Workshop (held March 26, 2004) and the Eighth Meeting of the WHO Alliance for the Global Elimination of Trachoma (held March 29-31, 2004), when the majority of trachoma researchers and interested parties would all be in Geneva.

The specific objectives of this WHO-ITI Joint Research Agenda Meeting for the Elimination of Blinding Trachoma were:

- To review recent findings on trachoma and their current/future impact on the implementation of the SAFE strategy;
- To identify and determine trachoma research areas requiring in-depth study for each of the four components of the SAFE strategy;
- To identify and determine new areas for trachoma research;
- To define the trachoma research agenda for the next two years;
- To design the strategy for disseminating and implementing the research agenda at the country level.

Participants in the meeting included Program Managers for National Trachoma Control Programs, scientists in the fields of eye diseases and public health, senior management of the WHO's Prevention of Blindness and Deafness team, and representatives from the International Trachoma Initiative.

Dr. Bjorn Thylefors was elected chairman, and Dr. Hans Limburg was elected as rapporteur.

Dr. Serge Resnikoff, Coordinator of the WHO Team for the Prevention of Blindness and Deafness, opened the meeting by emphasizing that since its creation, the

WHO Alliance for the Global Elimination of Trachoma (GET 2020) has supported operational research to inform best practices and improve Ministry of Health National Programs' efforts to eliminate blinding trachoma. He highlighted that prioritizing operational research issues would assist the managers of National Trachoma Programs to plan and implement essential disease control programs, and would permit members of the research community to focus on issues that would allow them to contribute to enhancing program effectiveness and efficiency.

Welcoming participants on behalf of the International Trachoma Initiative, an international agency dedicated to the elimination of blinding trachoma, Dr. Jacob Kumaresan reiterated the organization's commitment to applied research in the furtherance of the 2020 goal.

The Joint Research Agenda Meeting began with a series of presentations by preeminent trachoma experts in order to raise core issues in the field of trachoma research and to highlight some of the main discussions from the two meetings held earlier in the week (i.e., the 2nd Trachoma Scientific Informal Workshop and the 8th Meeting of the WHO Alliance for the Global Elimination of Trachoma).

The following table outlines the topics presented and main issues addressed:

Speaker	Topic Presented	Main Issues Addressed
Dr. Sheila West	Community-based surveillance systems	Developing surveillance systems in countries that are approaching elimination or starting and expanding their operations
Dr. Rajiv Khandekar	Trichiasis surgery	Service delivery, access, and recurrence
Dr. Hans Limburg	Tools and strategies for eliminating trachoma	Assessment of available tools and strategies; eventual need for new ones
Dr. Emily West	Trichiasis surgery	Needs in the training of surgeons; reasons for recurrence of trichiasis post-surgery
Dr. Thomas Lietman	Current understanding of antibiotic distribution	Outstanding issues needing more operational research

II. Surveillance Systems: Issues for Ongoing Programs and Issues for Elimination

Dr. Sheila West, Dana Center for Preventive Ophthalmology at Johns Hopkins University, Baltimore, MD

The primary question explored in this presentation was: “Is it possible to use a surveillance approach (surveillance defined for the purposes of the discussion as the ongoing monitoring of a population for disease, for the purposes of treatment or prevention) to increase community involvement and participation in trachoma control?” Also discussed were strategies for developing surveillance systems in countries that are approaching elimination and in those that are starting or expanding their operations.

Dr. West addressed the need to find a surveillance target that can be monitored after mass treatment in hyper-endemic areas. Three possible targets are:

1. Positivity to Laboratory Test for infection from Chlamydia, which is not practical for use in many settings, or with large numbers of individuals;
2. TF level, which is not a practical target due to the fact that levels may still be high following mass treatment, even when infection is no more present;
3. TI levels, which correlate better with the presence of disease, but are harder to grade and therefore monitor.

Dr. West noted that there are issues involved in ongoing surveillance programs that include:

- The need to determine the additional effect of surveillance over a longer period of time compared to the cumulative effect of mass treatment;
- The need to determine markers of trachoma for surveillance feasibility studies and area coverage;
- The need to determine a target for surveillance treatment.

In the second part of her presentation, Dr. West addressed the role of surveillance systems in villages close to the end of control efforts. She noted that the goal for activities in the A, F, and E components of the SAFE strategy is to reduce TF prevalence

to fewer than 5% of children aged 0-9 years old. Elimination of active trachoma could be considered as achieved when TF has decreased to less than 15% (+/- 5%) in children aged 0-9, because at this point very little *Chlamydia trachomatis* is found within the communities. Dr. West suggested that communities reaching this point prevalence level could “graduate” from mass treatment campaigns, and then starting a three-year surveillance program for TF. If prevalence remains less than 5%, the village can be turned over for management by the health system at this point. She noted that there are a number of key questions to consider:

- What is the appropriate TF cut-off for initial graduation?
- Who would be the target population for surveillance and treatment if TF in the community is less than the designated cut-off percentage?
- Who would undertake surveillance, and what kind of training would be required?
- What would be the frequency of surveillance?
- Does surveillance and treatment alone continue to reduce TF rates compared to mass treatment until TF is less than 10%?
- Is either approach more successful than allowing trachoma to run its own course?

III. Trachomatous Trichiasis:

Current Status and Scopes of Research

Dr. Rajiv Khandekar of the BC Centre for Epidemiologic and International Ophthalmology

Dr. Khandekar noted that the goals of care of individuals with Trachomatous Trichiasis (TT) are to:

1. Prevent visual disabilities due to TT;
2. Relieve symptoms due to TT and improve quality of life;
3. Prevent development of TT.

He pointed out that among countries where trachoma is endemic it is necessary to distinguish between two different types of countries, which have different objectives in addressing the disease. In countries that currently have high rates of active and blinding trachoma, the objective is to reduce the TT rate to less than 1% of TT in a small administrative area by 2020. In countries that have high rates of blinding trachoma due to active trachoma in the past, the objective is the elimination of blinding trachoma by 2020, with no more new cases of blindness due to TT. He stressed the important role that research could play in assisting those involved in the prevention of blindness to devise or refine policies that are evidence-based.

Dr.Khandekar mentioned that areas for research on Trachomatous Trichiasis can include pathophysiology of TT, clinical and public health intervention, health economy-related, genetic engineering, experimental surgery, and newer technologies. He concluded his presentation by making recommendations that research be conducted in the following areas:

- inter-country collaboration
- benefit to the country under trial
- freedom to choose resources
- publication
- data base and communication of research outcomes

IV. The 'S' Component: Trichiasis Surgery

Dr. Emily West of the Wilmer Institute of Johns Hopkins Medical Institutions

Dr. West noted that previously, trichiasis recurrence one-year post-surgery was 17%, but that recent studies have indicated that recurrence rates may be as high as 60% 3 years after surgery. There are several potential reasons for this recurrence, which include surgical factors (such as the skill level and training of the operating surgeons, and the surgical technique used); re-infection with *Chlamydia trachomatis*; and possibly other factors such as infection with other bacteria. Dr. West reviewed current studies of recurrence in Tanzania and Nepal, as well as ongoing clinical trials that seek to evaluate

the benefits of using Azithromycin at the time of surgery in Nepal, The Gambia, and Ethiopia. Surgical issues are being addressed through the development of a WHO manual that will be used to certify surgeons. The manual recommends that an outside monitor be used to perform certification, and it defines specific criteria for knowledge assessment and successful surgery. Dr. West concluded by listing the outstanding issues related to surgery:

- determining a ‘satisfactory’ training period for surgeons;
- implementing certification programs for surgeons in each country;
- monitoring surgeons after certification;
- integrating NGOs and government in the certification and follow-up;
- maintaining skill level in areas where few surgeries are done each year.

V. Tools for the Field Assessment of Blinding Trachoma Prevalence

Dr. Hans Limburg, of the International Centre for Eye Health at the University College of London’s Institute of Ophthalmology

Dr. Limburg began by discussing the Trachoma Rapid Assessment (TRA) methodology, the objective of which is to provide a simple and quick method to identify communities with hyperendemic trachoma and to prioritize these affected communities for intervention activities. According to six reports that have been conducted so far, in comparison to prevalence surveys, TRA has been found to be quicker and easier, with a fair correlation for trichiasis, and a correlation for TF that varied from good to poor. However, results from TRA have been often incorrectly interpreted and presented as prevalence rates, leading to confusion.

Dr. Limburg introduced the concept of the Acceptance Sampling Trachoma Rapid Assessment (ASTRA) survey method. In utilizing sequential sampling, investigators count the number of cases of TF, and check whether the number of TF cases exceed the established threshold. There is no fixed sample size, and collection and analysis of data is combined in the sampling plan. Sequential sampling is indicated when classification of a population in terms of prevalence classes is useful, and when the emphasis of the

research is on making decisions as to whether or not to treat. The principal differences between classical and sequential sampling are summarized below:

Classical	Sequential
Fixed sample Size	Variable sample size
Hypothesis testing <ul style="list-style-type: none"> - accept null hypothesis - reject null hypothesis 	Hypothesis testing <ul style="list-style-type: none"> - accept null hypothesis - reject null hypothesis - unable to decide
Estimation (prevalence estimate with confidence interval)	Estimation not usually possible
Data analysis separated from data collection	Analysis and data collection simultaneous

Dr. Limburg stated that were mass treatment with Azithromycin becomes the preferred treatment for trachoma, both mapping of the prevalence of TF over wider areas and identification of clusters of hyperendemic communities are needed to assess which communities require treatment. ASTRA provides a reliable estimate of the prevalence category of TF in a community, but examination of all communities is not feasible. Prevalence surveys provide average prevalence rate of TF in a wider area, but no accurate estimate at the community level, and may ignore clustering. ASTRA and Centric Systematic Area Sampling (CSAS) can provide prevalence estimates over wide areas, as well as coarse mapping of TF prevalence, and CSAS has proven to be as accurate as stratified random sampling. Following CSAS, adaptive sampling will identify the clusters of hyper-endemic communities in low-prevalence areas, provide accurate wide-area estimates, and allow detailed mapping of areas.

VI. Antibiotic Distribution: current understanding and outstanding issues needing more operational research

Dr. Thomas Lietman, Director of the Center for Prevention of Blindness at the Francis I. Proctor Foundation for Research in Ophthalmology at the University of California

Dr. Lietman began his presentation by speaking about the rationale for mass antibiotic treatment, and by discussing studies currently underway in Ethiopia that seek to determine optimal timing of antibiotic distributions for local elimination. He noted several key research issues related to antibiotic distribution:

- Can we eliminate infection?
- How frequently should antibiotics be administered?
- For how long should antibiotics be administered?
- Who should the target population for antibiotic distributions be?

Dr. Lietman continued his presentation by commenting on whether repeat treatment of children alone would eliminate infection in an entire community. Research to date has shown that children are more likely than adults to be infected; infectious loads are much higher in young children; infections tend to be of longer duration in children; children have more contacts per day; mathematical models imply that repeat treatment of children could eliminate infection; and treating children seems to be effective in controlling infection in hypo-endemic areas

VII: Setting Priorities For Research

Following these five presentations on recent findings about trachoma and their effect on the implementation of the SAFE strategy, the participants proposed and discussed critical research areas for each of the components of the SAFE strategy, as well as identifying new frontiers for research of this disease. Participants generated a list of critical research issues and prioritized the research agenda to the following timeframe:

- a). To be developed immediately,
- b). To be developed within the next year,
- c). To be developed within the next two years,
- d). To be developed after two years.

The idea of reaching a group consensus on the prioritization of the research issues was to involve all of the stake-holders in determining the research needs in the field of trachoma, as well as in determining the relative urgency of these priorities. It was agreed by participants that the list of priorities that had been elaborated was dynamic and would be revisited and updated annually if need be.

Surgery Component

- Intervention to reduce failure rate
 - Standardized training procedures and certifications for surgeons
 - Reassessment of surgeons so that their ocular surgery skills can be kept up to date
 - Long-term impact on visual function
 - Surgical uptake
 - Refusal management (incentives, quality, etc).
-
- Finalization and testing of ASTRA and CSAS
 - Prevalence categories in communities
 - Prevalence rate in wider areas
 - Identification of clusters of hyperendemic communities in hyperendemic areas
 - Certification
 - Relation between TF and CT infection
 - Time-span of stable reduction
 - No new incidence of TT
 - Evidence for $TT < 1/1000$
 - Surveillance data/registry
 - TT assessment in RACSS surveys
 - PHC report

Antibiotics, Face-washing and Environmental Improvement Components:

- Synergy of trachoma control with other community-based disease control/ elimination programs
- Frequency of treatment (once vs. twice per year) in hyperendemic areas; value of surveillance approaches
- Target population (treating entire population vs. treating children and mothers)
- Importance of coverage
- Importance of timing of treatment
- When to stop treatment
- Social anthropological studies for effective behavioral change (clean faces/ latrine use/water utilization)
 - Impact of health education in schools on the reduction of trachoma

It was agreed that all the listed research issues would deserve resources to be implemented, but in order to fund the most needed ones, a shorter list was needed.

Following prioritization by the researchers, the National Trachoma Program Managers in attendance were invited to recommend areas that, based on their own experience, were topics for immediate research.

As a result of the meeting, the following trachoma research agenda was established for the next two years (2004-2006):

- Interventions to reduce surgical failure rate
- Surgical training standardization/ certification
- Re- assessment of surgeons to ensure that their skills are kept up to date
- Long term impact of surgery on visual function
- Surgical uptake
- Refusal management (incentives, quality, etc.)
- Frequency of azithromycin treatment (annually or biannually) in hyperendemic areas
- When to stop treatment with antibiotics
- Development of simplified methods for epidemiological studies (ASTRA)
- Certification process for establishing that a country has eliminated blinding trachoma within its borders

International Trachoma Initiative's (ITI) Director of Research and Evaluation, Dr. Pina Balducci-Silano, reiterated ITI's commitment to pursuing and encouraging research.

She explained that ITI was potentially interested in funding future research, based on recommendations made by ITI's Trachoma Expert Committee and approved by its Board of Directors.

VIII. Closure of the Meeting

Dr. Serge Resnikoff, Coordinator of the WHO Team for the Prevention of Blindness and Deafness closed the meeting with thanks to all who had contributed to its smooth running and to all those who had so actively participated.

Annex 1: List of Participants



WORLD HEALTH ORGANIZATION
PREVENTION OF BLINDNESS &
DEAFNESS

**WHO/ITI JOINT RESEARCH AGENDA MEETING FOR
THE ELIMINATION OF BLINDING TRACHOMA**

Room X7, Geneva, Switzerland (1-2 April 2004)

LIST OF PARTICIPANTS

Dr. Amos ABBENYI, Director, Planning and Analysis, International Trachoma Initiative, 441 Lexington Avenue, 16th Floor, New York, New York, 100 17-3 91 0, USA. (Tel + 1 212 490 6460/ Fax: +1 212 490 64-61 - E mail: sabbenyi@trachoma.org)

Dr. Abdou AMZA, Coordinateur adjoint, Direction Generale des Etudes, Programme national de Lutte contre la Cecite, Ministere de la Sante publique, B.P. II347, Niamey, Niger/Niger (Tel./Fax + 227 75 29 06 - Fax: + 227 75 33 13 E.mail: pnlcc@intnet.ne)

Dr. B.P. ADHIKARI, Fatch Bal Eye Hospital, NJ. Fultekra, Nepalgunj, Nepal/Nepal (Tel. + 815 20598 - Fax + 81 5 22 737 - E.mail: drbpa@npj.wlinl.com.np)

Dr. Pina L. BALDUCCI-SILANO, Director, Evaluation and Research, International Trachoma Initiative, 441 Lexington Avenue, 16'h Floor, New York, New York, 10017 - 3910, USA
(Tel + 1 212 490 6460 ext. 12/ Fax: +1 212 490 64-61 - E mail: pbalducci@kachoma.org)

Dr. Youssef CHAMIKRAZRAJI, Chef de la Division des Maladies Transmissibles, Dir. de l'Epidemiologie et de la Lutte contre les Maladies, Service des Maladies Oculaires et Otologiques, Ministere de la Sante, 71 avenue Ibn Sina, Agdal, Rabat 10 000, Maroc/Morocco (Tel. +212 37 67 1332/ 212 37 67 1244 - Fax + 212 37 67 1298 - email: yhami@sante.gov.ma)

Dr Allen FOSTER, Medical Director, Christoffel Blindenmission e.V., Clinical Research Unit, London School of Hygiene and Tropical Medicine (LSHTD), Keppel Street, London, WC1E 7HT, United Kingdom
(Tel. 44 207 612 78 03 - Fax. 44 207 612 78 14 - E.mail: allenfoster@compuserve.com)

Dr Rajiv KHANDEKAR, Ophthalmologist and Epidemiologist, Eye & Ear Health Care Ministry of Health, Muscat, OMAN (Tel:00968607524/696187 - Fax:00968601832 - Email:rajshpp@omantel.net.om)

Dr Kazuichi KONYAMA, Department of Ophthalmology, Juntendo University School of Medicine 3-1-3 Hongo Bunkyo-ku, Tokyo, Japan (Fax: + 81338170260; kkon@interlink.or.jp)

Dr Charles KNIRSCH, Senior Medical Director, **Pfizer Inc**, 235 East 42nd Str., MS: 18-A, New York, N.Y., USA (Tel + 1 212 733 4231-Fax + 1 212 973 7379-E.mail: Charles.knirsch@pfizer.com;

Dr Thomas LIETMAN, Director, WHO Collaborating Center for Prevention of Blindness, Francis Proctor Foundation for Research in Ophthalmology, 95 Kirkham Street, University of California, Room 307, San Francisco, CA 94143-0944, USA (Tel. +1 415 502 2662 - Fax +1 415 476 0527 - E.mail: tml@itsa.ucsf.edu)

Dr Hans LIMBURG, Senior Research Fellow, International Centre for Eye Health, Institute of Ophthalmology, University College London, UK Private: BourgondiZweg 63, 1611 WC Bovenkarspeel The Netherlands (Tel. +31 228 515 481 - Fax +31 228 523 853 - E.mail: h.limburg@worldonline.nl)

Dr Qingjun LU, Department of Ophthalmology, Tong Ren Eye Centre, Beijing Tong Ren Hospital, No. 2 Chong Nei Street, Beijing, People's Republic of China/Republique populaire de Chine (Tel/Fax + 8610 8511 0023 - E.mail: qglu@trhos.com; Wningli@trhos.com)

Dr Andre'-Dominique NEGREL, Directeur des Programmes, Organisation pour la Prevention de la Cecite (OPC), 17 villa D'Alesia, 75014 Paris, France (Tel. +33 144124193 - Fax + 33 144122301 / E.mail: d.negrel@opc.asso.fr)

Dr. Eric A. OTTESEN, Director, Lymphatic Filariasis Support Center, Department of International Health, 1518 Clifton Road, NE, Atlanta, Georgia 30322, USA (Tel. + 1 404.712.9263 / Fax: + 1 404.727.5530 - E mail: eottese@sph.ernorv.edu)

Dr. Mohamed SAMNA, ITI Country Representative, B. P. 13670, Niamey - NIGER (Tel. +227 (-75) -47-90; (443) 644-0447 (efax); +227 (-75) -47-90; E mail: itinis@eraintnet.ne)

Dr Bjorn THYLEFORS, Director, Mectizan Donation Program, 750 Commerce Drive, suite 400, Decatur, Georgia 30030, USA (Tel. +1 404.687.56.16 / Fax +1 404.371.11.38, Email: btylefors@taskforce.org)

Professor Rasik B. VAJPAYEE MBBS, MS, FRCSEd, Clinical Professor of Ophthalmology, Head, Cornea and Refractive Surgery Services, RP Centre for Ophthalmic Sciences, ALL India Institute of Medical Sciences, New Delhi 110029, **India/Inde**

(Tel. + 9111 26 59 31 92. + 9111 26 58 98 22 / Fax: -91112658 8919
E.mail: rasikvajpayee@rediffmail.com and rbvajpay@medinst.ernet.in.)

Dr Emily WEST, Dana Center, The Wilmer Institute, **Johns Hopkins Medical Institutions**,

600 North Wolfe Street, Baltimore, Maryland, 21205, USA

(Tel. +1 410 955 2606/Fax +1 410 955 0096/E.mail: swest@dcpom.med.jhu.edu)

Prof. (Ms) Sheila WEST, El-Maghraby Professor of Preventive Ophthalmology, The Wilmer Institute, Rm 129, **Johns Hopkins Medical Institutions**, 600 North Wolfe Street, Baltimore, Maryland, 21205, USA (Tel. +1 410 955 2606 / Fax +1 410 955 0096 / E.mail: swest@dcpom.med.jhu.edu)

Secretariat

Dr Serge RESNIKOFF, Coordinator, Prevention of Blindness and Deafness, Management of Noncommunicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland (Tel +41 22 791 2652 - Fax +41 22 791 4772 - E.mail: resnikoffs@who.int)

Dr Silvio P. MARIOTTI, Medical Officer, Prevention of Blindness and Deafness, Management of Noncommunicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland (Tel +41 22 791 3491 - Fax +41 22 791 4772 - E.mail: mariottis@who.int)

Ms. Gladys PENA-MEDINA, Secretary, Prevention of Blindness and Deafness, Management of Noncommunicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland (Tel +41 22 791 2606 - Fax +41 22 791 4772 - E.mail: penag@who.int)

Annex 2: Scope and Purpose



WORLD HEALTH ORGANIZATION
PREVENTION OF BLINDNESS &
DEAFNESS

<p>WHO/ITI JOINT RESEARCH AGENDA MEETING FOR THE ELIMINATION OF BLINDING TRACHOMA</p>
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Room X7, Geneva, Switzerland (1-2 April 2004)

SCOPE AND PURPOSE

Since its inception, the WHO Alliance for Global Elimination of Trachoma (GET 2020) has addressed the need for operational research to inform best practice and improve MOH National Programmes' efforts to eliminate blinding trachoma.

Such research is supported and carried over by a number of organizations, and there is the need to review and redefine operational research priorities and opportunities.

Identification of operational research priorities will assist National Programmes managers in planning and implementation of national control programs and will help ensure that members of the research community focus on questions that will improve program effectiveness and efficiency.

The purpose of the meeting will be to review ongoing need for trachoma research, to identify promising research opportunities not currently addressed, and to ensure that a sound and widely supported strategic plan for trachoma research is developed.

The specific objectives of this meeting are:

- To review the recent findings on trachoma and their current/future impact in the implementation of the SAFE strategy;
- To identify and determine trachoma research areas in need of in-depth study for each of the four component of the SAFE strategy;
- To identify and determine new areas for trachoma research;
- To define the ITI supported trachoma research agenda for the next two years;
- To design the strategy for disseminating and implementing the research agenda at country level.

