

**Meeting of the WHO Technical Advisory Group
on Buruli ulcer
3 April 2008, Geneva**

Summary Report

Members present	
Dr Edwin Ampadu (Ghana) Prof. Henri Assé (Côte d'Ivoire) Prof. Pierre Couppié (French Guiana) Prof. Jacques Grosset (USA) Dr Christian Johnson (Benin) Dr Paul Johnson (Australia) Ms Verónica Malda (Spain)	Prof. Richard Merritt (USA) Dr Gerd Pluschke (Switzerland) Prof. Françoise Portaels (Belgium) Dr Paul Saunderson (Norway) Prof. Pam Small (USA) Dr Tim Stinear (Australia, Rapporteur) Dr Alphonse Um Boock (Cameroon) Dr Mark Wansbrough-Jones (UK, Chair)
Members absent	Observers
Dr Gerald Mumma (Kenya). Unable to attend the meeting.	Dr Samuel Etuaful (USA) Dr Richard Phillips (Ghana) Dr Tjip van der Werf (Netherlands)

The purpose of the TAG meeting was to review issues arising from the annual meeting and provide recommendations on any actions required. The TAG discussed the implementation of the control strategy, research, the next annual meeting and TAG membership. Below is a summary of the discussions.

The TAG noted with interest, the progress made by different countries in implementing the Buruli ulcer strategy. It also took note of the logistics and financial constraints faced by some countries in implementing control activities.

Specific comments concerned the following countries:

Guinea

The necessity to improve on laboratory confirmation of cases during 2008; progress should be reported at the 2009 meeting.

Nigeria

Cases were confirmed in 2006 but there was no further information on the disease in 2007. The TAG requested WHO to check with Nigeria on the current status of Buruli ulcer activities. It also recommended that some support should be provided to ensure that activities continue, especially in states where the cases were identified during the 2006 assessment.

Benin and Ghana

The TAG welcomed the request by Benin to assist in evaluating the implementation of the current strategic plan which ends at the end of 2008. The lessons learnt in this review will be used in developing a new plan. A similar review was also suggested for Ghana which has implemented its programme since 2002.

Togo, Gabon, Congo and DRC

Good progress is being made in these countries. The TAG requested WHO and partners to increase their support to these countries in order to make further progress in 2008.

Prevention of disability (POD)

Noting that the correct implementation of the technical guidelines provided in the available documents on POD requires training, the TAG supported the recommendation arising from the side meeting on POD to organize in the second half of the year, a training of trainers from endemic countries. Country teams would include a technical resource person (physiotherapist), a nurse actively involved in wound care and care of BU patients and the national programme manager. WHO, American Leprosy Missions (ALM), ANESVAD and ALES will work out the details of this training.

Laboratory confirmation of cases

The TAG noted that the implementation and expansion of antibiotic treatment require optimal skills in clinical diagnosis supported by laboratory confirmation of cases. Recognizing the importance of laboratory confirmation of cases, the TAG recommended that countries should ensure that at **least 50%** of all cases are confirmed by PCR (best method). Many endemic countries now have access to laboratories (locally or externally) that can confirm cases by PCR and arrangements should be made with these laboratories to obtain transport media and devise the best ways to send samples to these labs. Countries will report case confirmation rate by PCR in future meetings and laboratories will also summarize the cases confirmed from countries during these meetings.

Guidelines for specimen collection

As part of the implementation of confirmation of cases, the TAG also noted the importance of good collection of specimens. In this regard, the TAG recommended the development of a simple, pictorial guide for field health workers to improve specimen collection. It was also recommended that a short video on specimen collection could be useful.

The TAG tasked Dr Richard Phillips and Professor Françoise Portaels to develop the draft guide to be shared with TAG members and other experts within the BU community for comments.

Definition of recurrence

With the use of antibiotics, the TAG reviewed the definition of recurrence. It strongly recommended that recurrent cases can only be declared after positive culture. Positive AFB smears or PCR are not evidence of recurrence. All recurrent cases should be closely reviewed and specimens collected for culture.

International monitoring teams

The idea of International Monitoring teams should continue as the visits carried out last year in Cameroon and Congo were very helpful. Other countries should benefit from these technical support visits.

Transmission

Based on the conclusions of the main meeting, the TAG supported the recommendations of the transmission session on future research to better understand transmission of *M. ulcerans* in nature:

1. blood meal analyses - identify what a suspected invertebrate vector feeds on in nature (e.g., mosquitoes, other biting insects);
2. vector competency studies - even though one finds *M. ulcerans* in or on an insect, it does not indicate it is capable of vectoring *M. ulcerans*;
3. search for potential reservoirs of the disease, indicating a potential zoonosis;
4. proving Koch's postulates from an environmental perspective;
5. improved methods for rapid and specific detection of the pathogen in environmental samples; and
6. integration of quantitative ecology with human behaviour and activity.

Antibiotic treatment

The TAG noted with satisfaction the results of Rifampicin and Streptomycin treatment, showing that this combination is highly effective. Even though studies are required to simplify antibiotic treatment, it suggested that the BU community should wait for results of the ongoing studies: 1) Randomised control trial in Ghana comparing R+S for four weeks followed by R+CLR for another 4 weeks with the standard treatment of R+S for 8 weeks and 2) a pilot study in Benin using a combination of R+CLR and 3) a pilot study in Ghana of R+S for 5 days per week.

The TAG also discussed the long time required for complete healing of lesions after antibiotic treatment. Realizing that timely surgery/grafting is necessary to reduce undue suffering by patients, it suggested that this issue be examined closely so that a clearer recommendation can be made regarding the timing of surgery/grafting. In the meantime, it also recommended rewording the WHO recommendations to provide better advice regarding the timing of surgery.

Basic science

The TAG noted with interest the excellent work presented on basic science. It supported further work on direct detection of mycolactone in tissues as a possible diagnostic test. It also discussed BCG vaccination in view of new data presented in the mouse model. A protocol developed 5 years ago for repeated BCG vaccination will be revisited.

BU and HIV

A case-control study in Benin has suggested that there may be a positive association with HIV. A larger case-control study could be conducted in Ivory Coast where BU and HIV rates are much higher.

Quality control and quality assurance of clinical and environmental diagnostic PCR

The TAG welcomed the suggestion that inter-laboratory comparison of PCR results on clinical and environmental samples be established. The WHO Collaborating Center for *M. ulcerans* at the Victorian Infectious Diseases Reference Laboratory in Melbourne will support environmental PCR and the WHO Collaborating Centre for the Diagnosis and Surveillance of *Mycobacterium ulcerans* Infection at the Institute of Tropical Medicine in Antwerp will focus on PCR in clinical samples.

Meeting in Benin 2009

In view of the commitment of the President and Government of Benin to host the next meeting, the TAG accepted the proposal to hold the next annual meeting in Cotonou, Benin as part of the 2nd International Conference on Buruli ulcer control and research. This conference is expected to attract high level participants including heads of state from some of the affected countries. It will also provide an opportunity for greater participation from endemic countries in Africa.

The TAG proposed 30 March – 3 April 2009 for consideration by the Benin authorities. Once the dates are confirmed, WHO will notify all potential participants via e-mail and on its website.

Technical Advisory Group (TAG) membership

The TAG discussed the nomination of new members in 2009, for a three-year term. The mandate of the current membership ends at the end of 2008. There is the possibility of a one-time renewal of membership but due care will be taken in implementing this policy to ensure continuity and maintenance of historic memory. Consideration may be given to increasing the total membership to 20, taking into consideration the need to maintain expertise in different areas, as well as gender and geographical balance. Calls for renewal of membership and nomination of new members will be made by the end of this year.

The TAG is a group of experts selected by WHO and approved by the office of the Director General.

Current terms of reference

1. To monitor the implementation of the intensified control strategy;
2. To promote research according to the agreed priorities;
3. To identify obstacles to the effective control of Buruli ulcer and recommend corrective actions;
4. To advise on and prioritize new research initiatives;
5. To ensure impartial reviews for new research proposals;
6. To promote awareness of Buruli ulcer in the context of neglected tropical diseases;
7. To assist in identifying funding to support the implementation of the above-mentioned activities.

Criteria for selection

1. Good knowledge of English;
2. Sound knowledge of Buruli ulcer and reasonable experience of Buruli ulcer in an endemic area;
3. Expertise in one or more of the control and research areas;
4. Actively involved in Buruli ulcer activities;
5. Willingness to contribute proactively towards the work of the group and the Global Buruli Ulcer Initiative;
6. Demonstrable ability to work with partners;
7. Willingness/availability to participate in scheduled meetings of the Group.