Summary of the Tenth Meeting of the ITFDE (II)
January 11, 2007

The Tenth Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 3:30pm on January 11, 2007. The Task Force reviewed the status of evidence pertaining to the potential eradicability of onchocerciasis (river blindness), five years after the Conference on the Eradicability of Onchocerciasis met at The Carter Center in January 2002.

The Task Force members are Dr. Olusoji Adeyi, The World Bank; Sir George Alleyne, Johns Hopkins University; Dr. Julie Gerberding, Centers for Disease Control and Prevention (CDC); Dr. David Heymann, World Health Organization (WHO); Dr. Donald Hopkins, The Carter Center (Chair); Dr. Adetokunbo Lucas, Harvard University; Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Mark Rosenberg, Task Force for Child Survival and Development; Dr. Harrison Spencer, Association of Schools of Public Health; Dr. Pascal Villeneuve, UNICEF; Dr. Dyann Wirth, Harvard School of Public Health, and Dr. Yoichi Yamagata, Japan International Cooperation Agency (JICA). Five of the Task Force members (Hopkins, Lucas, Molyneux, Spencer, Wirth) attended this meeting, and four others were represented by an alternate (Dr. Ousmane Bangoura for Adeyi, Dr. Kayode Oyegbite for Villeneuve, Dr. Lorenzo Savioli for Heymann, Dr. Mike St. Louis for Gerberding).

Presenters at this meeting included Dr. Boakye Boatin of the World Health Organization; Dr. Ousmane Bangoura, The World Bank; Dr. Edward Cupp, Auburn University (retired); Dr. Achim Hoerauf, University Clinic Bonn; Dr. David Molyneux, Liverpool School of Tropical Medicine/ITFDE Member; Dr. Richard Ndyomugyenyi, Ministry of Health/Uganda; Dr. Eric Ottesen, Lymphatic Filariasis Support Center; Dr. Frank Richards, The Carter Center River Blindness Program, and Dr. Mauricio Sauerbrey, Onchocerciasis Elimination Program of the Americas.

Onchocerciasis

In January 2002, the Conference on the Eradicability of Onchocerciasis concluded that onchocerciasis was not eradicable in Africa, using available tools, but that the disease could be eliminated in the Americas.[1] The conference strongly recommended that everything be done to preserve the gains of the Onchocerciasis Control Program (which closed later that year) and that elimination efforts should be undertaken in Africa in isolated foci where it was technically feasible to do so. The conference also recommended further research into the impact of ivermectin, potential macrofilaricidal drugs, alternative delivery strategies, better diagnostic tools, and mathematical modeling.

Important developments since the previous conference include the realization that up to 37 or 40 million persons may be infected with onchocerciasis compared to the 18 million

[1] Dadzie Y, Neira M and Hopkins D. Final Report of the Conference on the Eradicability of Onchocerciasis. *Filarial Journal* 2003:2

estimated to have been infected earlier, as a result of studies in newly accessed areas of countries such as the Democratic Republic of Congo (DRC). Other notable improvements in the interim include political settlements and much less insecurity in Angola, Liberia, Sierra Leone, and southern Sudan. However, health systems are still very weak in the affected African countries.

The Onchocerciasis Control Program (OCP) ended in December 2002, having protected 40 million persons in 11 West African countries between 1974 and 2002. Vector control by aerial larviciding, and later mass administration of ivermectin (Mectizan®, donated by Merck & Co.) annually to populations in hyper- and meso-endemic villages interrupted transmission in many areas. However, transmission continues in certain Special Intervention Zones in parts of Guinea, Sierra Leone, Ghana, Togo and Benin, where Mectizan® is now being distributed annually or semi-annually, and with ground larviciding in a few of those areas. The current situation is uncertain in Cote d'Ivoire and Guinea Bissau, which have had no interventions since 2002 due to insecurity.

The African Program for Onchocerciasis Control (APOC), which began in 1995, treated 40 million persons with Mectizan® in hyper- and meso-endemic villages in 16 countries in 2005, and aims to treat 90 million persons annually in 19 countries by 2015. Progress is satisfactory in 9 countries, unsatisfactory in 7 countries, and

Since 1993, the Onchocericasis Elimination Program of the Americas (OEPA) has coordinated and helped support semi-annual mass administration of Mectizan® in 13 foci of 6 countries (Brazil, Colombia, Ecuador, Guatemala, Mexico, and Venezuela). As of 2006, it appears that new cases of blindness caused by onchocerciasis are no longer occurring and 8 of the 13 foci are believed to have interrupted transmission of *Onchocerca volvulus*, and one (Guatemala's Santa Rosa focus) has eliminated the parasite and will become the first to halt mass treatments in 2007. Others, including Colombia's single focus in Naiciona, may follow the Santa Rosa example in 2007 or 2008. In foci where transmission continues, the focus in southern Venezuela achieved >85% coverage for the first time, thus becoming the last of the foci to achieve that important milestone (the 12 other foci each have had 7-11 treatment rounds >85%). The South Chiapas focus in Mexico has administered Mectizan® four times per year in 50 of its highest endemic communities since 2003, as part of a trial aimed at hastening interruption of transmission by killing adult worms. The Rio Cayapas sector of the Ecuadorian focus, where *Simulium exigium* is similarly as efficient as a vector as *S. damnosum* in Africa, began with annual mass treatments but switched to semi-annual mass treatments in 1998, and now appears close to interrupting transmission.

A review of the macrofilaricidal effects of Mectizan® on *Onchocerca volvulus*, based on re-analysis of peer-reviewed literature describing results from Africa and Latin America, noted the importance of measuring Mectizan® macrofilaricidal impact in the settings where transmission generally is interrupted (a 'closed system'). The evidence suggests that Mectizan®, 150ug/kg twice per year would eliminate adult female worms in 6.5 years, and four times per year treatment would eliminate the adult female worms in about 5 years. It thus appears that multiple mass treatments each year accelerate the deaths of adult male and female *O.volvulus* in comparison with their natural rates of death when vector control eliminates new infections. WHO/TDR is also investigating the impact of treatment with Mectizan® given annually, semi-annually or at 3 month intervals without concomitant vector control, for 16 years in three foci in Senegal and Mali (former OCP areas). These studies have shown dramatic impact on prevalence of infection in humans and vectors. Data analysis is ongoing with particular interest in ascertaining whether mass treatment can be stopped in these foci without resumption of transmission in the coming one to two years.

Research is also ongoing on other potential macrofilaricides. Daily doxycycline (200 mg/dose) given orally for 6 weeks leads to a complete sterilization of adult *O.volvulus* female worms, and most recent data suggest that it also kills up to 70% after 27 months. The mode of action is by killing endosymbiont *Wolbachia* bacteria. Six weeks of treatment with doxycycline and Mectizan® (ivermectin) is superior to treatment with Mectizan alone in reducing microfilariae over a 21 month period. Moxidectin, an avermectin in the same class as ivermectin but with a longer half life, is now in Phase II trials, with community trials expected to be completed by 2011. It is hoped that it may have a more sustained microfilaricidal effect compared to ivermectin, or that it may even show macrofilaricidal affects. The Bill & Melinda Gates Foundation is funding research at WHO and via the Liverpool School of Tropical Medicine to screen and develop other potentially macrofilaricidal drugs.

Existing diagnostic tests include skin snip PCR to detect parasite DNA, detection of serum antibodies against species-specific antigen (OV-16) to identify past or current exposure to *O.volvulus* infection, and PCR to detect parasite DNA in pools of blackflies as a tool for assessing transmission. None of these is being produced commercially or readily available in laboratories, but if they were (especially the OV-16 antibody test), it would greatly facilitate monitoring of the transmission-interruption efforts. Mr. John Moores, Sr. is supporting research by the new WIRM initiative at the Scripps Institute in San Diego to develop a simple reliable test for detecting living adult

in Itwara and Mpamba-Nkusi. Six other foci are now targeted for interruption of transmission using a strategy of semi-annual mass distribution of Mectizan® and/or selective ground-based larviciding. Four foci require further epidemiological investigation. *S. neavei* is the vector in the 6 foci targeted for elimination. External support for this elimination initiative is being provided by The Carter Center, Merck (via the NGDO Group for Onchocerciasis Control)

7. The Task Force acknowledged the magnitude of the contribution to onchocerciasis control and elimination by the late Dr. Brian Duke, and requested the chair to convey to his widow its condolences on his recent demise as well as its appreciation and gratitude for his extraordinary work and dedicated commitment to this field.