SUMMARY OF THE FIRST MEETING OF THE ITFDE(II)
June 18, 2001

This International Task Force for Disease Eradication (ITFDE) was constituted with support provided by the Bill & Melinda Gates Foundation to The Carter Center. The main goals are to review progress in the field of disease eradication over the past decade since the previous ITFDE (1989-1992), review the status of selected diseases, and make recommendations regarding opportunities for eradication or better control of certain diseases (e.g., demonstration project, targeted research).

The Task Force members are: Sir George Alleyne, Pan American Health Organization; Dr. Yves Bergevin, UNICEF; Dr. David Heymann, World Health Organization; Dr. Jeffrey Koplan, Centers for Disease Control and Prevention; Mr. James Lovelace, The World Bank; Dr. Adetokunbo Lucas, Nigeria; 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. Dyann Wirth, Harvard School of Public Health; Dr. Yoichi Yamagata, Japan International Cooperation Agency, and Dr. Donald Hopkins, The Carter Center. Nine of the twelve members attended the first meeting, which was held at The Carter Center from 9:00am to 4:00pm on June 18, 2001. The other three Task Force members were represented by: Dr. David Brandling-Bennett, Pan American Health Organization; Dr. Daniel Colley, Centers for Disease Control and Prevention, and Ms. Vanessa Tobin, UNICEF. President Carter also participated in the first half of this meeting, which was chaired by Dr. Hopkins.

During this meeting, the Task Force reviewed the criteria that were developed by the predecessor ITFDE for assessing eradicability of diseases, as well as the definitions of **Eradication**, **Control**, and **Elimination** that were used by the previous ITFDE, and by recent international meetings on disease eradication that were convened in Berlin (1997) and Atlanta (1998). The Task Force agreed to use, at least for the time being, the criteria developed by the previous ITFDE. The Task Force also identified three issues for further deliberation at a future meeting: 1) use and varying definitions of the word "elimination" in regard to disease control; 2) how to assure equity among developed and developing countries in setting priorities for eradication initiatives, and 3) integration of eradication activities with other public health work.

The four diseases that were considered at this meeting were onchocerciasis (river blindness) in the Americas, leprosy (Hansen's disease), schistosomiasis, and Chagas' disease. Those deliberations and the resulting conclusions and recommendations are summarized below.

Onchocerciasis in the Americas

This presentation was made by Drs. Frank Richards (The Carter Center), Mauricio Sauerbrey (OEPA) and Richard Collins (consultant to OEPA).

Introduced into the Americas during the African slave trade, onchocerciasis officially exists in thirteen foci scattered over six countries: 4 in Guatemala, 3 each in Mexico and Venezuela, and 1 each in Brazil, Colombia and Ecuador. The number of people currently at risk of the disease is 544,009, of whom 429,920 are eligible for treatment, in 1,969 endemic communities, including 211 hyper-endemic communities. The overwhelming majority of persons at risk are in Mexico (39%), Guatemala (37%) and Venezuela (18%). The main vectors concerned are: in Mexico and Guatemala (Simulium ochraceum); in Colombia (S. exiguum); in Ecuador (S. exiguum, S. quadrivittatum), in Venezuela (S. metallicum, S. guianense, S. oyapockense); and in Brazil (S. oyapockense, S. guianense). S. exiguum is a highly efficient vector (similar to S. damnosum in Africa), whereas S. ochraceum is much less efficient and the other vectors mentioned are intermediate in their efficiency. The vectors in the Americas are relatively non-migratory, and transmission of onchocerciasis is highly seasonal.

The Onchocerciasis Elimination Program for the Americas (OEPA) is a regional initiative that began in 1990 with the support of the Pan American Health Organization (PAHO), the ministries of health of the six countries, the Mectizan Donation Program, USAID, the Inter-American Development Bank, the Centers for Disease Control and Prevention (CDC), and the River Blindness Foundation (replaced by the Global 2000 River Blindness Program of The Carter Center in 1996, with additional support provided by the Lions Clubs International Foundation beginning in 1999). The goals of OEPA are 1) to eliminate morbidity due to infection with O. volvulus in the six-country program by 2007, and 2) to eliminate transmission of the parasite in those countries or foci where feasible (no time limit specified). The intervention strategy being used is mainly mass distribution of Mectizan twice per year, although the beginning of mass treatments has been staggered over time in the different foci, and six-monthly administration has not been attained or maintained in all of the endemic foci. In addition, some mass nodulectomies are conducted in Mexico. Compliance with Mectizan treatment has been good, except when Mectizan distribution has been conducted simultaneously with nodulectomies. About US$17.5 million has been expended on the program between 1991-2000, including $10 million by the six countries themselves.

The number of persons at risk of onchocerciasis in the Americas has been refined from an estimated 4.7 million in 1995 to 544,009 in 2000, as a result of on-going assessments of endemic areas. The number of persons treated with Mectizan increased from less than 30,000 in 1990 to 367,619 in 2000. The Ultimate Treatment Goal (UTG), or number of eligible persons at risk who need to be treated is 429,920. In the Americas, however, the Ultimate Treatment Goal(2) is used to express the number of treatments that should be given in each country in order to treat each eligible person at risk twice annually. Of that number for the region (859,840), 73% were treated in 2000. The percentages of UTG(2) treatments achieved in each of the six countries in 2000 are: 99% of 2,202 (Colombia), 91% of 317,648 (Mexico), 74% of 320,000 (Guatemala), 56% of 13,588 (Brazil), 50% of 38,642 (Ecuador) and 41% of 167,760 (Venezuela).

With respect to impact on morbidity, data on reductions in prevalence of *microfilariae in the skin* are available from sentinel communities throughout the Americas (totaling over 5,000 persons examined). The data show dramatic reductions in prevalence in all study areas: Brazil (from 63% in 1995 to 28% in 1998), Colombia (40% in 1996, 7% in 1998), Ecuador (37% in 1991, 0.3% in 1996), Guatemala (52% in 1994, 20% in 1998), Mexico-Oaxaca (7% in 1993, 0% in

1996), Mexico-Chiapas (16% in 1995, 7% in 1997), and Venezuela-North (29% in 1998, 2% in 1999). Data from the baseline and first evaluation of sentinel communities regarding prevalence of *microfilariae in the anterior chamber of the eye* are available from Brazil (31.2% in 1995, 0.1% in 1998), Colombia (2.2% in 1996, 0.1% in 1998), Ecuador (9.8% in 1991, 0.0% in 2000), Mexico-Oaxaca (0.0% in 1995, 0.2% in 2000), and Mexico-Chiapas (1.5% in 1995, 1.0% in 2000). The prevalence of *nodules* in the Oaxaca-Mexico focus has fallen from about 3 per 1000 in 1991 to zero per thousand in 1996-2000.

Regarding impact on transmission of onchocerciasis, the thirteen foci in the Americas may be divided into three groups: four foci currently are suspected to have no known transmission, three foci are very close to ending transmission, and six foci are still significantly endemic. The suspected non-endemic foci include Huehuetenango, Guatemala; Escuintla, Guatemala; Santa Rosa, Guatemala; and Northern Chiapas, Mexico. Onchocerciasis immunochromatographic antibody tests (ICT) conducted on 448 persons (including 286 persons under 11 years old) in 12 communities of Huehuetenango, Guatemala in 2001 were all negative. This corroborates parasitological data from 2000 and entomological data from 2001. Other ICT tests conducted on 936 persons in 23 communities of Northern Chiapas, Mexico in 2001 were also all negative. No recent evaluations have been conducted in the Escuintla and Santa Rosa foci in Guatemala (more ICT test kits are needed in order to do so). These four foci have not yet been officially certified as having no transmission.

The three foci that are close to ending transmission are Oaxaca, Mexico; Lopez de Micay, Colombia; and Esmeraldes, Ecuador. In Esmeraldes, Ecuador, where mass treatments began in 1990-1991, 5 of 7 formerly endemic sentinel communities (6 hyper-endemic, 1 meso-endemic) had zero positive infections found in pooled heads of S. exiguum and S. quadrivittatum blackflies examined in 2000. In the two other endemic sentinel communities, the percentage entomological positivity rates averaged 0.020% (no pre-treatment data is available), and 0.105% (down from 1.188% in 1996) of examined S. exiguum in 2000, respectively. Of 430 persons examined by ICT test in these 7 communities in 2001, only 4 were positive: 3 in one of the two communities with positive entomological results in 2000, and 1 in one of the communities where no positive entomological evidence of residual infection was found. Earlier studies of children born in 1980-85 and in 1990-96 in one of the now negative areas of this focus documented reductions in prevalence of infection (from 64.3% to 0.0%), prevalence of microfilariae in the skin (from 4.5 mf/mg to 0.0 mf/mg), and prevalence of nodules (8.8% to 0.0%). Ecuador's program has not consistently achieved twice annual, high coverage treatments. In Oaxaca, Mexico, none of 210 ICT tests conducted in 2001were positive. No such recent studies have been conducted in Lopez de Micay, Colombia because of insecurity.

The six foci where onchocerciasis is still significantly endemic are Southern Chiapas, Mexico; Solola-Suchitepequez-Chimaltenango, Guatemala; the north-central, north-eastern and southern foci in Venezuela; and the Roraima, Amazonas focus in Brazil.

There is no evidence of Mectizan-resistant O. volvulus in the Americas, but specific surveillance for this has not been conducted.

ITFDE Conclusions and Recommendations:

1. The scientific feasibility of eliminating ocular morbidity and interrupting onchcocerciasis transmission in the Americas, using currently available tools, is clear.

2. The primary remaining concern is whether all six programs can reach and maintain at least 85% coverage of the UTG(2). This is particularly a concern in southern Venezuela, where access to the population at risk is an issue, but which contains only 1% of the persons at risk in the Americas.

3. The OEPA needs to address specific operational, political, and financial constraints in order to escalate its advocacy and help the endemic countries to intensify interventions against onchocerciasis in all remaining endemic foci. Consideration should be given to selective use of vector control, and to making nodulectomy available on a voluntary basis (separate from Mectizan distribution) when prevalence of onchocerciasis becomes low.

4. Priority research needs include an effective macrofilaricide, an antigen serological test for onchocercal infection, and better understanding of the significance of low transmission levels.

5. It is important that ICT antibody tests continue to be available in order to facilitate evaluation of onchocerciasis in the Americas.

Leprosy (Hansen's Disease)

This presentation was made by Dr. Robert Jacobson, former director of the (U.S.) National Hansen's Disease Center.

This ancient disease is caused by a bacterium, Mycobacterium leprae. Less than five percent of the general population is susceptible to the infection, apparently as a result of genetic and immunologic factors. It is still not known exactly how the disease is transmitted; respiratory and skin contact are the likeliest routes. Multi-bacillary cases are probably more infectious to other persons than the more common pauci-bacillary cases. The incubation period is long: 3-4 years or more. Leprosy disappeared in formerly endemic Europe, and is declining in some other countries (e.g., Japan, China, Korea) apparently as a result of increasing standards of living. The genome of M. leprae has been completely sequenced, showing 80% commonality with that of M. tuberculosis. Unlike tuberculosis, which is severely exacerbated by HIV infection, there is no evidence that HIV co-infection exacerbates leprosy, and M. leprae cannot be grown on artificial media in the laboratory. About 15-20% of wild armadillos in parts of Texas and Louisiana are naturally infected, but the epidemiological significance of this is not clear. Whether the microbe can exist in tropical soil is also uncertain.

Diagnosis is based primarily on clinical findings. There is no test for pre-clinical diagnosis. Treatment requires administration of 2-3 drugs (multi-drug therapy, MDT) for up to six months

for pauci-bacillary cases and one year for multi-bacillary cases. The frequency of Dapsone-resistant strains has increased. Relapse rates are usually less than one percent for multi-bacillary cases. A slightly larger percentage of treated persons will still harbor viable bacilli. No suitable preventive is available.

In 1991, the World Health Assembly adopted a resolution that called for the "elimination" of leprosy "as a public health problem", to a prevalence of "less than 1 case/10,000 population, by 2000". The intervention strategy calls for early diagnosis and treatment of cases at the community level, ideally integrated into the general health services. WHO began making MDT available free of charge in 1995. According to WHO, by the end of 2000, the number of cases of leprosy had been reduced from 5.4 million in 1985, to 753,000, and the number of countries with more than 1 case/10,000 population was reduced from 122 to six (Brazil, India, Madagascar, Mozambique, Myanmar, Nepal; countries with populations of less than one million persons or with fewer than 100 cases registered are not included). The current goal is to complete the campaign by 2005, for which period US$6 million per year as well as the required supplies of drugs for providing free treatments have been donated to WHO. Reduction in the length of chemotherapy from 24 to 12 months, and the ten year old campaign to "eliminate" the disease are the main advances since the review by the previous ITFDE.

Some qualifiers to the progress of the campaign were discussed. The target prevalence rate of 1 case per 10,000 population is still relatively high. Much of the impressive reduction in the number of active cases is statistical, since patients who complete a course of MDT are considered cured (most are), and are removed from case registries. Thus, a case of leprosy is now defined as an infected person who requires, but has not yet received or completed a course of MDT. Despite the apparent reduction in prevalence, the number of new cases detected annually (incidence) has not yet declined: 738,000 new cases were diagnosed in 2000 (this probably reflects the long incubation period). The quality and reliability of surveillance and case detection are questionable in certain endemic countries that are not included among those known to have more than one case/10,000 population at the end of 2000.

ITFDE Conclusions and Recommendations:

1. Leprosy is not now eradicable, but commendable progress has been made in its control over the past decade.
2. Control measures will need to be continued indefinitely in endemic areas so long as the incidence of new infections is not reduced significantly.
3. The current campaign against this disease should seek to make maximal progress by 2005, given the unique combination of resources and public support that have been mobilized. The campaign would benefit from improved case detection and surveillance, to include all geographic areas where the disease is endemic.
4. Intensified research is badly needed, including a) development of a test for early diagnosis, b) improved and shorter chemotherapy, c) development of an effective vaccine, and d) epidemiologic studies to better understand how the infection is transmitted and the relevance, if any, of non-human reservoirs of M. leprae.

Schistosomiasis

This report was presented by Dr. Daniel Colley of the Centers for Disease Control and Prevention (CDC) and Dr. Michael Reich of Harvard School of Public Health.

WHO estimates that about 200 million persons are infected with schistosomes (about 170 of them in sub-Saharan Africa), of whom 120 million have symptoms, including 20 million persons with severe disease. Between 20,000 and 200,000 persons are estimated to die of this disease annually. Despite significant progress in controlling schistosomiasis over the past two decades, increases in population in some endemic countries have kept global prevalence about the same as it was when the previous ITFDE reviewed this disease. This infection is very focally distributed. Multiple points of attack on the parasite's life cycle are available, including health education to promote hygienic practices (hard to show efficacy), vector control (expensive), and mass chemotherapy (best current control measure), but implementing them is a challenge. Diagnosis of intestinal schistosomiasis (S. japonicum, S. mansoni) is still much more difficult than urinary schistosomiasis (S. hematobium). Reservoir hosts in some areas are a problem for the control of S. japonicum.

Several important positive developments have occurred since the previous ITFDE review:

- Increased recognition of the severity and extent of morbidity due to schistosomiasis
- Increased recognition of the ability to reduce schistosomiasis morbidity by mass chemotherapy (which became possible with the availability of safe, effective, affordable drugs)
- Establishment of the safety of drug combinations against several helminthic infections
- Reduction in the cost of praziquantel by more than 90% since the 1980s, to <US$0.10/tablet
- Demonstration of how control measures may be integrated with those against other diseases
- Development of the Schistosomiasis Control Initiative at Harvard School of Public Health
- Adoption of a resolution on schistosomiasis control by the World Health Assembly in May 2001 (WHA 54.19)

Because of the necessary longevity of control measures, attention to sustainability and opportunities for combining interventions against schistosomiasis with other interventions such as school-based programs or community-based programs, is especially important. The innovative project to demonstrate simultaneous mass chemotherapy and health education for urinary schistosomiasis, onchocerciasis and lymphatic filariasis in two states of Nigeria is a significant step. Unlike global programs against onchocerciasis and lymphatic filariasis, no drug company is yet willing to donate the amount of praziquantel that is needed for a global campaign against schistosomiasis.

The Schistosomiasis Control Initiative being developed at Harvard School of Public Health is funded by a one-year planning grant (October 2000-September 2001) from the Bill and Melinda Gates Foundation. It is seeking to assemble a coalition of partners to help mount a serious attack on schistosomiasis in 5-7 African countries initially, in order to demonstrate the feasibility of better control of the disease in Africa.

ITFDE Conclusions and Recommendations:

1. Schistosomiasis is not eradicable using currently available tools.

2. It is possible to achieve much better control of the vast morbidity from schistosomiasis now, and the Schistosomiasis Control Initiative could potentially become a significant step in that direction.

3. More research is needed. Priority targets include development of simpler diagnostic methods for intestinal schistosomiasis, rapid community assessment methods, studies to quickly establish the safety of simultaneous administration of praziquantel/ivermectin/albendazole, studies to establish parameters for praziquantel dosing based on height, and measurement of the economic costs and benefits associated with schistosomiasis control. It might be possible to develop an effective vaccine against schistosomes in the long term.

Chagas' Disease

This report was presented by Dr. Gabriel Schmunis, consultant to the Pan American Health Organization (PAHO).

Chagas' disease is caused by the parasite Trypanosoma cruzi. About 10-12 million persons are infected in Central and South America and parts of Mexico. Following a few weeks of acute inflammatory symptoms, the infection often has a long period (years) without symptoms, but an estimated 10-30% of victims develop chronic enlargement of the heart and/or other internal organs. About 23,000-43,000 persons, often young adults, die of the disease annually. In Latin America, Chagas' disease causes the fourth-highest disease burden (measured in Disability Adjusted Life Years-DALYs) among infectious diseases, after acute respiratory infections, diarrhea, and HIV/AIDS. The economic costs of the disease are very large: an estimated US$158 million per year in Argentina for hospitalization of cardiac cases alone; an estimated US$120 million in Bolivia in 1992. In Brazil, costs for pacemakers and surgeries, and for lost man-hours of work were estimated at US$250 million and US$625 million, respectively, in 1987.

Chagas' disease is transmitted to humans mostly by several species of triatomine bugs; and less commonly by blood transfusion, or to fetuses through the placenta. It is closely associated with poverty and poor housing, since the triatomine bugs live in the cracks of adobe walls and in thatched roofs. Many different domestic and wild animals also harbor the infection.

The infection is diagnosed by serological tests. Two drugs are effective for treating children during the acute stage. Despite a vast base of scientific knowledge about this parasite, no drug development research is being conducted. The main control measures are spraying residual insecticide in homes, health education, improvements in housing, and screening of blood donors.

An insecticidal paint has also been developed. A cost benefit analysis of the vector control program in Brazil in 1995 estimated savings of US$2.01 (from prevented hospitalizations, early retirement, disability and premature death) for each US$1.00 invested in the program. Of 17 countries for which information was available to PAHO in 2000, 5 screened all blood donors, 4 screened over 90% of donors; the others screened less.

In 1991, the Ministries of Health of Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay launched the Southern Cone Initiative, with the assistance and coordination of PAHO. Argentina and Brazil had begun nationwide programs in the 1960s, and Chile and Uruguay in the 1970s. The aim of the Southern Cone Initiative is to interrupt transmission of Chagas' Disease by eliminating the vector (mainly Triatoma infestans in that subregion), which lives exclusively in houses and peri-domiciliary structures (e.g., chicken coops, corrals) there. The main intervention is spraying of houses. The results have been dramatic in four of the countries. In Argentina, the serological prevalence rate among men joining the military services declined from 5.8% in 1982 to 1.2% in 1994. In Brazil, serological prevalence rates in 7-14 year olds declined by 96% between 1979/80 and 1994/98, while the total number of vector triatomine bugs captured inside of houses by field workers in the entire country declined from 84,334 in 1983 to only 295 in 2000. Chile reduced its house infection rates by 90% between 1982 and 1993, while its sero-prevalence rates in children under 15 years declined from 20.3% to 4.2% between 1986 and 1992. Uruguay reduced its house infection rates by 99% and sero-prevalence rates among children under 12 from 5.2% to 0.5% between 1985 and 1999. Progress in Bolivia and Paraguay has been much less dramatic so far, because of late starts and/or inadequate funding.

An International Commission of experts declared that vector borne transmission of Chagas' disease was interrupted in Uruguay in 1996 and in Chile in 1999. It is also believed that transmission of Chagas' disease has been interrupted in six of Brazil's nine formerly endemic states, as of 2000.

Studies conducted in Guatemala, Honduras and Nicaragua show that some of the vectors of T. cruzi there are also closely associated with human habitations and surrounding areas, but others are not. Attempts are now being made to investigate ways to control the vectors in those endemic Central American countries. The estimated number of houses that need to be sprayed in these three Central American countries are 300,000; 90,000; and 30,000, respectively.

ITFDE Conclusions and Recommendations:

1. Although Chagas' disease cannot be eradicated, because of the extensive reservoir of infection in domestic and wild animals, the possibility of stopping vector borne transmission of the disease to humans in areas where the vector is found exclusively in peri-domestic settings, has now been well demonstrated in three of the "Southern Cone" countries.

2. The net economic benefits of controlling Chagas' disease by vector control appear to be substantial.

3. Additional external support is needed to help control this disease in endemic areas where the vectors are vulnerable, and for research on how to control non-domiciliary vectors.

4. In the absence of a means to treat the infection in the 10-12million persons who are already infected, the most urgent research need now is to develop a drug to cure the infection in the chronic stages. Better and cheaper reagents for diagnosing this infection are also needed.