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Certification of elimination of human onchocerciasis:

criteria and procedures

Following a WHO meeting on
"Criteria for certification of interruption of transmission / elimination of human onchocerciasis"
Geneva, 28-29 September 2000
(document WHO/CDS/CPE/CEE/2001.18a)

GUIDELINES

World Health Organization
Communicable Diseases

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Onchocerciasis is still endemic in 34 countries, 26 in WHO's African Region, six in the Region of the Americas, and two in the Eastern Mediterranean Region. The epidemiology of onchocerciasis is that of a vector-borne disease, of which human beings are the only vertebrate host, showing coincidence between the degree of human infection and the intensity of exposure to infected vectors. However, the epidemiology of onchocerciasis is not uniform throughout its distribution because different disease patterns are associated with different variants or strains of the parasite, with differences in the vector competence and feeding characteristics of local blackfly populations, with the abundance of the vector, and with differences in the human host responses to the parasite. These factors, together with those related to environment, geographical, social and demographic influences, increase the complexity of the epidemiology of the disease in the different areas of its distribution.

The framework presented in this document is the result of a broad consultative process led by WHO, which was initially triggered by the wish of the Latin American Oncherciasis Elimination Programmes to describe the process, milestones and procedures needed to certify an eventual future elimination of onchocerciasis in its countries. In view of the relative few isolated foci in Latin America, this might be an ambitious but theoretically reachable goal on the American continent. These epidemiological settings might only be comparable to isolated foci in Yemen, and some few isolated foci in Africa. In contrast, the distribution of *O. volvulus* in the tropical belt of Africa, hosting about 99% of the worldwide-infected persons, does not show clearly defined boundaries. The epidemiological characteristics in Africa imply that the elaborated framework might not be technically and operationally feasible in most endemic areas of the African continent.

An account is given of previous efforts to control or eliminate onchocerciasis in various areas of Africa and of Latin America by the use of vector larvicidal control (which has proved successful in several areas), or by treatment with drugs unsuitable for large-scale use, or by nodulectomy (neither of which has been successful).

The advent of ivermectin (as Mectizan® provided free-of-charge under the Mectizan Donation Program of Merck & Co. Inc.), an effective microfilaricide *cum* temporary microfilarial suppressant that is suitable for large-scale rural use, has greatly improved the chances of controlling, or even eliminating onchocerciasis in many areas. Given as a single oral dose, once or twice a year, ivermectin can lower *Onchocerca volvulus* microfilarial skin loads to levels below those required for effective transmission by *Simulium spp.* (blackflies).

In Africa, annual distribution of ivermectin is being used to supplement or replace the larvicidal vector control activities of the Onchocerciasis Control Programme in West Africa (OCP); and, distributed annually in community-directed country programmes, it is the mainstay of the African Programme for Onchocerciasis Control (APOC), which covers all the non-OCP African countries wherein onchocerciasis is endemic.

In Latin America, semi-annual mass treatment with ivermectin in all endemic communities is now the strategy adopted by all endemic countries. In 1991, Resolution XIV of the XXXVth. Directing Council of the Pan American Health called for the elimination of morbidity due to onchocerciasis by the year 2007. The Onchocerciasis Elimination Program for the Americas (OEPA) was established in 1992 as a multi-national, multi-agency coalition aiming to eliminate morbidity due to infection with *O. volvulus* in the Americas by the year 2007, and to eliminate onchocerciasis in those countries or foci where feasible (no time limit was specified for this second goal).

In order to eliminate onchocerciasis through mass-community treatments with the temporary-microfilarial-suppressive drug ivermectin, parasite transmission must be continuously suppressed for a period longer than the maximum life span of adult female worms plus that of their last-produced microfilariae. If treatment is discontinued or interrupted, transmission can be re-established, and morbidity again develop in the human population. Thus, the expected period required to terminate both infection and parasite transmission, might be 14 to 18 years of sustained and uninterrupted interventions. The described framework and time horizon

INTRODUCTION

Onchocerciasis has long been recognized as disease of public health importance. In 1974, the first regional onchocerciasis control programme (OCP) was launched in west Africa, based on a vector control strategy and sponsored by the FAO, UNDP, World Bank and WHO as the executing agency. With the development of a safe drug for use in public health programmes, two other large programmes were launched subsequently in the Americas (OEPA) and in Africa (APOC).

After more that 25 years of onchocerciasis control, the World Health Organization convened a meeting in September 2000 to provide, in the light of progress so far achieved by the above mentioned programmes, guidance for the verification and the certification of interruption of transmission. This document is the outcome of this meeting and is meant to guide in a consistent manner, the work undertaken by International Certification Teams and the country approach to certification.

1. HUMAN ONCHOCERCIASIS AS A DISEASE OF PUBLIC HEALTH IMPORTANCE

Human onchocerciasis is a vector-borne disease, endemic in parts of Africa, the Arabian Peninsula, and Latin America, and caused by a filarial nematode worm, *Onchocerca volvulus*. It produces eye lesions, which can lead on to blindness, and also itching and disfiguring lesions of the skin. Because the vectors (blackflies belonging to the genus *Simulium*) are insects which breed in fast-flowing rivers and streams and bite humans near these sites, the disease is often known as River Blindness. In Africa the blindness and the severity of the skin lesions can have severe socio-economic consequences and, in the past, River Blindness has led to the desertion of large areas of fertile land adjacent to *Simulium damnosum s.l.* breeding rivers, thus seriously impeding the economic development of the countries concerned. In Latin America the disease is sometimes referred to as Robles' Disease in honour of Dr Rodolfo Robles, the Guatemala physician who first recorded its existence in the New World.

Estimates of the prevalence of onchocerciasis made in the mid-1990s indicated that, world-wide, approximately 123 million persons were at risk of infection, and some 17.6 million were infected (WHO, 1995), the vast majority of them in Africa.

In Latin America, the at-risk population was estimated in the mid 1990s at 4.7 million, with 150,000-200,000 persons infected. More recently, the thorough epidemiological characterisations of northern Venezuela and the re-assessment of Guatemala have lowered the total population at risk in Latin America to approximately 660,000 persons living in 2773 villages, of which only 200 are considered to be hyperendemic with high risk of ocular disease (WHO, 1999b).

Adult *Onchocerca volvulus* worms (females 30-80 cm long; males 3-5 cm) are thin worms which live coiled up in fibrous nodules situated just under the skin or deep in the intermuscular and periarticular connective tissue. They live for some 9-14 years and the females produce very large numbers of microfilariae, 250-300 µm in length, which invade the skin and eye and cause the signs and symptoms of disease. The microfilariae live for 6-24 months in the human body. When they die they cause lesions in the skin or eye of the human host. Only those living microfilariae that are ingested by blood-feeding *Simulium* vectors will survive and develop in the fly over 6-12 days to become infective larvae or L3s. These, when they are inoculated into a new human host, usually at the next but one time that the fly feeds, will enter a new human host, develop into adult worms (without any multiplication) over a period of some 10-15 months, mate and start a new generation of the parasite. Thus, with this infection, prolonged and repeated exposure to the parasite is necessary before an intense infection can be established in the human host.

Definitions of some of the terms used in this document, together with information on the various methods used to stratify the endemicity levels of communities with onchocerciasis, are to be found in APPENDIX I.

In northern Venezuela, widespread campaigns with suramin were introduced and continued for some years. They were doubtless of value to the individuals who were treated but they did little towards reducing transmission. In the southern Venezuelan endemic area in the Amazons Region, which is contiguous with the foci in the Brazilian rain forest, the presence of the disease had only recently been revealed and virtually no effective control measures had been undertaken

Again, the advent of ivermectin and the establishment of the Mectizan Donation Program sparked widespread interest in the control of onchocerciasis in the various foci in Latin America. Indeed, beyond mere control, support for a regionally-coordinated campaign to eliminate human onchocerciasis in the Western Hemisphere developed and grew during the nineteen nineties. The Onchocerciasis Elimination Program for the Americas (OEPA), established in 1992, now provides the administrative structure and the technical co-ordination of a multi-national, multi-agency coalition aiming to eliminate onchocerciasis in Latin America by coordinating the campaigns in each of the six affected countries – Brazil, Colombia, Ecuador, Guatemala, Mexico and Venezuela (Blanks, et. al 1998). OEPA, with its head-quarters in Guatemala, is the technical and coordinating body of a multi-national, multi-agency coalition which acts under the 1991 Resolution XIV of the XXXVth. Directing Council of the Pan American Health Organization calling for the elimination of all onchocerciasis morbidity from the Americas by the year 2007.

3. CONTROL AND ELIMINATION STRATEGIES

3.1. AFRICA

In Africa the goals of the onchocerciasis control programmes are the elimination of eye disease, the reduction of skin disease, and the prevention of the severe socio-economic effects of onchocerciasis. In Africa, WHO used extensive and repeated aerial application of rapidly-biodegradable insecticides as the original basis of the Onchocerciasis Control Programme in the Volta River Basin and later, after the Western and Southern Extensions were taken on, of the Onchocerciasis Control Programme in West Africa (OCP). As a result of larviciding against *Simulium,* transmission was interrupted over large areas but the parasite population in humans was not immediately affected, except in so far as it became an ageing population that was not rejuvenated by newly transmitted parasites. Onchocercal punctuate keratitis (a reversible lesion) became less frequent but the serious skin and eye lesions of those persons already infected still progressed, although at a somewhat lower rate because their original parasite loads were slowly dying out and were no longer being reinforced by new infections. In addition children born after the larviciding programme started remained free of infection.

When ivermectin became available, WHO adopted annual treatments with ivermectin both to supplement the insecticidal programme in the OCP and also to form almost the sole basis of the interventions of the APOC, which now covers the remaining onchocerciasis-afflicted countries of Africa. Under APOC, the ivermectin distribution is Community-Directed and the treatments are also given annually. There is no vector control under APOC except in a few small isolated foci of transmission where vector eradication appears feasible. On the other hand there is an immediate benefit to the human population as a result of the rapid lowering of their microfilarial loads by ivermectin. In addition, a degree of reduction of transmission is achieved, which depends solely on the ivermectin-induced reduction in the human microfilarial reservoir. The duration of control based on ivermectin alone may thus have to be longer than that following *Simulium* larvicidal control. However, follow-up studies in the OCP have demonstrated that repeated ivermectin treatment does significantly affect the embryonic productivity of *O. volvulus* (Alley et al., 1998; Plaisier et al., 1995) and that this could result in a shortening of the control period (Plaisier et al., 1997). Hence the OCP has ceased larviciding after 14 years in areas with only vector control, but after 12 years in areas where there has been a combination of vector control and ivermectin treatment (Guillet et al., 1995). The incidence of new infections in the central OCP area has been zero or near zero for the past 11 years, despite the presence of potential *Simulium* vectors.

from other endemic foci. It was agreed that efforts towards elimination of onchocerciasis for individual countries would be continued until certification of elimination of the disease in the entire region has been achieved.

The most important requirement for attaining elimination is sustained, high-level coverage with ivermectin, and the 1998 IACO, held in Caracas, Venezuela, focused on strategies for sustaining high treatment coverage throughout the region (WHO, 1999b). The term "coverage", as used here, has two dimensions:

(1) **Extent of Coverage**, meaning endemic communities receiving ivermectin. The requirement being that all endemic (100%) communities be identified and receive regular mass distribution of ivermectin; and

(2) **Depth of Coverage**, meaning percentage of the eligible population treated. The requirement being that 85% of the eligible population in each community be treated at each treatment round.

Indeed, any country wishing to certify elimination of onchocerciasis must demonstrate that it has met these two prerequisites before the certification process can begin.

To carry out the process of certifying elimination, WHO in collaboration with its regional Office will designate a panel of specialists, whose members can be assigned to International Certification Teams (ICT). The ICT will operate under the auspices of WHO and will inform both WHO, its Regional Office and the respective regional Onchocerciasis Programme (OEPA in Latin America) regarding those countries that fulfil the requirements for certification as well as the criteria, procedures, and progress made towards verification of the absence of disease and parasite transmission in endemic areas.

In Latin America, OEPA will facilitate national preparations for certification by carrying out regular visits by staff or by consultants to the country or sub-region concerned. A register will be established of countries requesting certification and also of those countries where official certification of elimination is pending. Finally, WHO/PAHO in conjunction with OEPA will establish an official register of countries where onchocerciasis has been eliminated, based on evaluations made by the ICT and their review. Countries on this register will be classified as Post-endemic - Past history of onchocerciasis, but no current evidence of transmission or new clinical disease.

One of the aims of the present document is to describe the criteria and procedures for verifying the elimination of new and reversible onchocerciasis morbidity together with the transmission of, and infection with, *O. volvulus* in Latin America. In addition OEPA has developed programmatic guidelines for monitoring the impact of ivermectin distribution through in-depth epidemiological assessments that include the entomological evaluation of parasite transmission.

In Latin America, the elimination strategy is based on regular, 6-monthly mass distribution of ivermectin to all persons who are eligible to take the drug in all endemic communities. The aim is to make use of this drug to suppress greatly or, better still, to interrupt transmission of the parasite for longer than the maximum life span of the adult female worm. If this can be achieved, the adult worm population will gradually die out from old age and will not be replenished by new infections, thus leading to the elimination of the parasite from a defined geographical area.

The ivermectin should be given out to all persons at risk of infection and who are eligible to take ivermectin, regardless of whether or not they have positive skin biopsies, nodules or other evidence of infection. In fact, biopsies, nodulectomies and physical examinations should not be done during mass treatment because this has been shown to reduce participation by the communities.

established, and morbidity will again develop in the human population. Thus, the minimum time required to terminate new morbidity, infection and parasite transmission is 14-18 years, based on the observed longevity of adult worms in other control programmes (Duke, 1993). This variable time-schedule gives some flexibility should ivermectin prove effective against adult worms, or should a new and safe macrofilaricide be found. Also the periodic in-depth evaluations after 6, 10 and 14 years of 6-monthly treatments may help to determine the exact length of the necessary time frame.

The level of 1 L3 of *O. volvulus* per 1'000 parous vector *Simulium,* which has been adopted by the OCP as a safe level at or below which transmission does not occur, is unlikely to be a useful index for Latin America, for two reasons. The first is that by using PCR there will not be data available on the parous ratios of biting populations. The second is that the OCP index is above the transmission threshold for *Simulium* spp with very high biting densities. For example at the *Finca* El Vesuvio in Guatemala (Porter et al., 1988), the biting density was 550'599 flies per year, with 49.2% parous. At the rate of 1 L3 per 1'000 flies this would give an estimated Annual Transmission Potential (ATP) of 271 L3s per person per year but, as the mean number of L3 per infective fly was 2.0, this would equate to an ATP of 542. However, the biting density obtained in this experiment was really a landing rate because it was necessary to collect the flies before they had had time to bite. Assuming that the biting rate would be one quarter of the landing rate, this results in an estimated ATP of 68-136, which could very well be above the transmission threshold for *S. ochraceum.* In Latin America it is considered that it is more useful to take the measure of the safe level of transmission (at or below which there is "suppression of infectivity") as being "*a minimum reduction of 99% of the Base-line ATP*".

4. CRITERIA FOR CERTIFICATION OF INTERRUPTION OF TRANSMISSION / ELIMINATION

Standard criteria for certification of elimination are needed for the following reasons.

A. To give national onchocerciasis elimination programmes the step-by-step accomplishments required eliminating reversible morbidity, parasite transmission and infection over a specified period of time.

B. To give national elimination programmes and external agencies a consistent and established mechanism for monitoring and evaluating programme achievement.

C. To insure international credibility for the expected future claim that onchocerciasis has been eliminated from a country or other area.

D. To insure that national programmes have ascertained and classified all endemic communities in their countries by the application of guidelines developed by the Task Force on Epidemiological Characterisation of Onchocerciasis.

Elimination should be considered as achieved in a country when **adequate surveillance** in all endemic regions in that country has shown the following.

4.1. Elimination of Morbidity

The absence of reversible lesions in the anterior segment of the eye (punctuate keratitis, microfilariae in the anterior chamber), which are here referred to as "new morbidity". A 5-year cumulative incidence rate of less than 1 new case per 1000 is acceptable (provided this size of the population is available)

It must be remembered that permanent eye lesions or onchocercal blindness, as well as some severe skin or lymphatic lesions, are irreversible and will persist after the person so affected ceases to be a source of transmissible microfilariae, until he or she dies. Such "old morbidity" cannot be eliminated except by death.

5.4. In-depth epidemiological surveys of sentinel communities after six years of treatment shows no infection (skin microfilariae, nodules) in untreated 5-year old children who are about to take their first dose of ivermectin. Antibody testing using specific *O. volvulus* antigens and finger-stick blood samples (Weil et al., 2000) may be used if skin snipping of young children is resisted by mothers and/or children. There should be a 5-year cumulative incidence of < 1 new case per 1000 persons.

5.5. Entomological assessments in sentinel communities after 12 years of thorough suppression or complete interruption of transmission indicate that infective stage larvae (L3s) are absent from the vector population, thus making the beginning of pre-certification period. As an intermediate step, and where resources are available, each country should carry out entomological evaluations of sentinel communities at 2-4 year intervals after initiating treatment, in order to ascertain whether adequate suppression or interruption of transmission is being sustained.

6. CERTIFICATION PROCEDURES

The Ministry of Health in the endemic country initiates the certification process by sending a letter to WHO, to the WHO Regional Office and to the Regional Onchocerciasis Programme, saying that it is preparing a country report and plans to apply for certification. WHO, after consultation with its Regional Office and with the health authorities of the country concerned, will appoint an International Certification Team (ICT). The ICT must be able to communicate and report in the official language of the country concerned, although this does not imply that all members of the ICT must be fluent in the relevant national language. The team will review the country report in detail, including data supporting the extent and depth of coverage obtained at each treatment cycle and the results of in-depth surveys in sentinel communities. Prior to the ICT nomination, visits by selected consultants can be arranged by WHO or the Regional Onchocerciasis Programme to help in the preparation of the country report and to recommend additional data analysis or surveys before the ICT begins its audit.

6.1. Operation of the International Certification Team

6.1.1. ICT Evaluation

The ICT will visit the applicant country to become acquainted with the operation and personnel of the control programme. The visit will take place before certification surveys are carried out. The principal aim of the first ICT visit will be to evaluate the reliability of the country report by interviewing health personnel and others, and by examining records at both central and peripheral levels. Good evidence of high treatment coverage is essential and certification should only be triggered if it is certain that the required coverage levels (at least 85% of the population eligible to take ivermectin in all endemic communities) have been reached during the indicated number of treatment rounds. At the end of this visit, the ICT will ascertain the likelihood that transmission of *O. volvulus* has been interrupted and that certification surveys are justified.

After arrival, national control programme personnel and other health authorities will brief the ICT on the country report. Of particular importance are (1) the accuracy and completeness with which the programme has investigated and stratified all endemic communities, and (2) the extent and level of coverage obtained throughout the various treatment cycles. While negative results from the in-depth epidemiological surveys of sentinel communities (paragraphs 5.4 and 5.5 above) are useful indicators of possible elimination throughout the country or focus, sustained, high-level coverage of all endemic communities (paragraphs 5.2, 5.3, above) is crucial. Indeed, if for some reason (economic, civil unrest, natural disasters) the in-depth evaluations of sentinel communities have not been completed, and yet high coverage has been maintained, the certification process could still go forward.

The ICT should be able to visit any epidemiologically important areas identified in the country report. These could be (i) areas identified as potentially having been missed in the original assessment, (ii) areas contiguous with neighbouring countries affected by onchocerciasis,

Flow chart 1 shows the time frame and steps leading to the cessation of control operations, the pre-certification period and final certification.

FLOW CHART 1

FLOW CHART OF ACTIVITIES LEADING TO CERTIFICATION OF INTERRUPTION OF TRANSMISSION / ELIMINATION OF ONCHOCERCIASIS

PRE-TREATMENT PHASE

STEP

1. Identify and stratify all endemic communities
2. Identify sentinel communities and carry out in-depth surveys therein for base-line data.

↓

TREATMENT PHASE

1. **Year 1.** Initiate (yearly or 6-monthly) ivermectin treatment of all endemic communities (at 85% coverage of eligible population).
2. **Year 2–14 or 16.** Establish and maintain yearly or 6-monthly ivermectin treatment (at 85% coverage of eligible population).
3. **Year 3.** In-depth survey of sentinel communities.
4. **Year 3-4.** Check vector population for suppression or interruption of transmission.
5. **Year 5.** Check population for disappearance of reversible morbidity. Check that 5-year-old children are not infected.
6. **Year 6-14 or 16.** Maintain Steps 2-5 above.

↓

PRE-CERTIFICATION PHASE

1. **Year 14-16.** Ascertain that transmission is interrupted.
2. **Year 15-17 or 17-19.** Stop ivermectin treatment for the 3-year pre-certification period. Maintain heightened surveillance activities. Carry out ICT verification surveys.

↓

POST-ENDEMIC PHASE

1. **Year 19.** Certificate of Elimination granted. Enter Post-endemic period. Maintain "post-endemic" surveys and surveillance.

Figure 1 (on next page) shows the time-scale for the theoretical fall-off of the Annual Transmission Potential or ATP to zero (or near zero), together with the theoretical fall-off of the dying and unreplenished adult worm population, both in relation to the timing of the various interventions and certifications.

The fall-off of the ATP is shown here as taking place over a period of four years of 6-monthly ivermectin treatment (*i.e.* eight treatment rounds). In fact the 'zero' target for the ATP may well be achieved after two years of 6-monthly treatments (*i.e.* four treatment rounds), in which case the date for pre-certification may be advanced from year 17 to year 15.

6.1.4. Conclusions of the ICT

At the end of the verification surveys, the ICT will be asked to reach one of two possible conclusions: either (1) they are satisfied that elimination has been achieved and recommend that treatment be stopped, or (2) they are not satisfied to this effect. ICT reports must spell out the reasons for their conclusion. If the ICT decides it is not satisfied, then it must indicate what additional actions are required. These might be additional data analyses, additional surveys, more complete coverage or extended treatments.

6.2. Post-endemic Surveillance for Parasite Transmission

If elimination is certified, the applicant country will establish a surveillance system to detect possible renewal of parasite transmission, both in previously endemic areas and in areas where imported cases might be expected to occur. Entomological evaluation, using PCR to detect parasite larvae in vector populations, is recommended because of the long prepatent period in human infection. Both heads and bodies of flies should be tested because a positive test indicates contact with a microfilarial carrier. If positive flies are detected, epidemiological surveys should be carried out to identify and treat both infected people and the at-risk population. This post endemic surveillance should be carried out until elimination of onchocerciasis is declared for the Region.

6.3. Selection of ICT Members

Persons selected as team members should be able to be critical in their assessments and their views as experts should be respected both nationally and internationally. Potential conflicts of interest, such as nomination of a national from a country under review as a member of the ICT, should be avoided. Members should be chosen from different areas of the world so that the nature and extent of the efforts made to document the interruption of transmission might become widely known. Scientists working on onchocerciasis and countries with elimination programmes should both be represented on ICTs so that technical expertise can be exchanged and applied to the certification process.

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APPENDIX I

DEFINITIONS RELEVANT TO ONCHOCERCIASIS ELIMINATION

An onchocerciasis case is defined as an individual with evidence of current infection with *Onchocerca volvulus*.

Incidence is the rate at which new cases arise in a population within a defined interval of time.

Prevalence is the proportion of the host population infected at a particular point in time.

Morbidity is defined as the presence of disease manifestations caused by onchocerciasis.

Basic reproductive ratio (Ro) is a measure of the reproductive success of the parasite population. It encapsulates all the process rates that determine the flow of the parasite through its life cycle, and defines a theoretical threshold between extinction (Ro continuously less than 1), and persistence of infection (Ro continuously equal to or greater than 1) (Basáñez and Boussinesq, 1999).

Transmission threshold occurs for a parasite when the basic reproductive rate is equal to 1.0. Below this threshold level the parasite is unable to maintain itself in the host population.

Suppression of infectivity (or conditional interruption of transmission) means the absence of infective larvae (L3s) in the *Simulium* vector population as determined by polymerase chain reaction (PCR) or any other valid method, coupled with a 5-year cumulative incidence of <1 new case per 1000 persons. Suppression of infectivity can be achieved through drug (ivermectin) pressure despite the fact that there can still be a population of adult worms capable of reinitiating transmission if the drug pressure is removed.

Interruption of transmission means the permanent interruption of transmission in a clearly-defined area after all the adult worms in the human population in that area have either died out from old age or been exterminated by some other intervention. This should occur within 15 years of the establishment of sustained interruption of infectivity.

Transmission breakpoint is a critical average worm burden below which the mating frequency of the parasites is too low to maintain the parasite population.

Sentinel Communities are pre-selected hyperendemic communities where in-depth epidemiological evaluations take place at regular intervals; first before treatment starts, then again after two years, and finally at 4-year intervals thereafter. The evaluations include parasitological (mf and nodules), ophthalmological, and entomological indicators. [It should be noted that the use of *sentinel communities* in this way has two disadvantages. First, the community populations may become tired of these repeated examinations and refuse to co-operate. Second, it will soon become known by those working in the programme which are the designated sentinel communities and they may reserve their best efforts for these communities at the expense of others. A possible way round this difficulty is to have a larger number of *potential sentinel communities* and just before each round of examinations to pick at random a smaller number of them that will be examined.] The International Certification Team is encouraged to use other villages for monitoring, pre-certification or certification activities.

Elimination *(literally "casting out over the threshold")* of the parasite population from a defined geographical area means the sustained absence of transmission until the adult parasite population within that area has died out naturally or has been exterminated by some other intervention. This should occur within 15 years after interruption of transmission. When elimination of the parasite is certified, the endemic area moves into the 'post-endemic' phase.

40-50% are included, then the two groups will account for nearly all the blindness due to onchocerciasis. Therefore the treatment strategy is as follows: large-scale ivermectin treatment is a "must" where the microfilarial prevalence is greater than 60% and highly desirable where it is 40-59%. No attempt was made to define the threshold below which mass treatment with ivermectin was not indicated, as such a lower limit depends primarily on the locally available resources.

Because it was found that a good 2.1 relationship exists between classification of onchocerciasis levels of endemicity based on skin-snip data and those based on nodule palpation, a rapid epidemiological assessment method (REA), based on the proportion of nodule carriers in a sample of 30-50 adult males, who have been resident in the community for at least five years and who are engaged in rural activities was developed and tested (Taylor et al., 1992). This method is now widely used as being more practical and faster than skin snip surveys for making the decision on whether to undertake mass treatment or not (see equivalence table attached).

Assessment method	**Large scale treatment**	
	Treatment is a "must"	**Treatment is highly desirable**
Parasitological assessment		
Prevalence of mf in skin snips		
- Males and females of all age	60% and over	40 – 59%
- Males over 20 years	90% and over	70 – 89%
Rapid assessment methods		
Prevalence of nodules in males over 20 years	40% and over	20 – 39%
Prevalence of leopard skin in males over 20 years	20% and over	Not useful

2.3. Latin America. In Latin America, the levels of endemicity are defined as follows:

Hypoendemic is a term used to mean an area with little transmission. It corresponds to communities where the microfilarial biopsy positive rate is 20% or less in 30 adult males who have lived in the community for at least 5 years.

Mesoendemic means an area of moderate parasite transmission where the microfilarial biopsy positive rate is greater than 20% and less than 60 %.

Hyperendemic means an area of high parasite transmission where the microfilarial biopsy positive rate is 60% or more. In Latin America, most eye disease is found in hyperendemic communities (Brandling-Bennett et al., 1981).

APPENDIX II

GUIDELINES FOR THE PREPARATION OF A COUNTRY REPORT

To initiate the certification process, each country will submit a comprehensive written report to WHO. The length and detail of this report will vary widely from a brief document for those countries that have few foci, to highly detailed documents with supporting data needed from those countries applying with many foci and a large population at risk. The report will be examined by the ICT for records to substantiate the extent and depth of coverage obtained over the life of the elimination programme. Extent of coverage means that all endemic communities have been discovered and treated; depth of coverage means that at least 85% of the population eligible to take ivermectin and living in these communities were treated at each round of treatment. In addition, methods and results of in-depth epidemiological and entomological surveys should be given. Countries are encouraged to set up a National Review Committee to compile and review the report as an internal programme review before starting the certification process. The format of the report is optional but should contain the following common elements.

1. Historical account and background information on onchocerciasis in the country concerned

- How the disease was discovered and/or imported into the country or focus concerned.
- Demographic information, including population distribution by geographical region of the country and indicating the populations in onchocerciasis endemic areas.
- Ethnographic information on the populations affected by onchocerciasis.
- Economic activities of the affected regions - agriculture, mining, forestry, etc.
- Migration patterns within the country and between adjacent countries, especially those where onchocerciasis is also endemic.
- Information on primary and secondary vectors of *O. volvulus* (including their parous biting cycles) and with their distribution shown on maps.
- Bibliography of published literature on onchocerciasis in the affected country.
- Health cares infrastructure of the endemic areas.

2. Methodology and findings of original assessments of the extent of onchocerciasis

- Methods used and data obtained from any epidemiological, ophthalmological, and entomological surveys.
- Maps delineating the endemic regions and areas investigated for onchocerciasis. These maps should be topographical and locate communities by name.
- Lists of communities surveyed for onchocerciasis, giving the rationale for including them as well as reasons for not surveying adjacent communities.
- Lists of any communities where onchocerciasis is suspected but not at present confirmed.
- Pre-treatment results of REA, used to stratify endemic communities and to select sentinel communities.
- Results of in-depth pre-treatment epidemiological surveys carried out in sentinel communities.

APPENDIX III

SUMMARY OF GUIDELINES FOR IN-DEPTH EPIDEMIOLOGICAL EVALUATIONS

1. Inventory of communities

A. Identification of all permanent communities located within or in close proximity to the known endemic foci.

B. This identification and an inventory of communities is entered in a database using geographic information system (G.I.S.) technology to map communities.

C. Basic epidemiological information on onchocerciasis gathered from current field surveys and from historical registers must be included.

D. Communities are characterised by:

1. Name;
2. Political/administrative classification (e.g. municipality, district, state, etc);
3. Total population from census (with date of last census) preferably from a recent house-to-house census conducted by the programme staff;
4. Economic base (e.g. coffee production);
5. Geographic location (altitude, map co-ordinates, etc);
6. Source of information on community and its reliability;
7. A permanent identification number.

2. Initial classification and stratification of the community

Risk factors, historical record or other information suggests classification as an endemic community and its level of endemicity, such as:

1. Hyperendemic, mesoendemic, hypoendemic;
2. Suspected endemic for onchocerciasis;
3. Non-endemic.

3. Rapid Epidemiological Assessment (REA)

Procedure:

1. Evaluation carried out rapidly, no more than 1 day per community;
2. Test group is 30 adult males with a minimum of 5 years residence in the zone and employed in rural tasks;
3. Should be carried out in all suspected and known endemic communities (the latter to detect any change in endemic status);
4. Obtain and process skin biopsies and process them according to standard criteria (incubation time, media, mf counts, etc);
5. Palpation of test subjects to nodules.

APPENDIX IV

GUIDELINES FOR THE ENTOMOLOGICAL EVALUATION OF THE IMPACT OF COMMUNITY-WIDE IVERMECTIN DISTRIBUTION ON ONCHOCERCIASIS TRANSMISSION

1. General remarks

The effects of ivermectin distribution on parasite transmission can be evaluated by monitoring infection rates of vector blackflies with larvae of *Onchocerca volvulus*. This method has several advantages over parasitological evaluation of the human population, especially when children are involved, for the following reasons:

- Infection rates in blackflies are rapid and sensitive indicators of the change in community microfilarial load that results from ivermectin distribution.
- Changes in vector infection rates correlate well with the percentage coverage of the human population with ivermectin.
- Absence of infective stage larvae in the vector population during the transmission season is the first indicator of having achieved interruption of parasite transmission. By contrast, the prepatent period for the appearance of nodules or skin microfilariae is about 10-24 months.
- Monitoring very low vector infection rates with polymerase chain reaction and DNA technology is easier and less expensive than monitoring very low levels of infection in children.
- Use of a *0. Volvulus-specific* DNA probes guarantees absolute specificity and allows for processing large numbers of flies, thus increasing reliability of the results.
- Vector collection teams working in the community can deliver health messages about ivermectin, thereby increasing coverage.
- It is completely non-invasive and well accepted by the community.

For pre-treatment baseline data, vector infection rates are ideally measured over a complete year, or at least a complete transmission season. This provides baseline data for comparison with post-treatment evaluations. At present, such information is available only for *Simulium dannosum complex* in Africa, for *Simulium ochraceum areas* in Mexico and Guatemala, and to a lesser extent for *Simulium exiguum* in Ecuador (hyperendemic areas only). As of 1999, however, studies are under way in northern and southern Venezuela to obtain pre-treatment data on other vector species (M.-G. Basáñez, *personal communication*).

The methodology outlined here for the collection of vectors is based on studies of biting behaviour by Porter, CH, and RC Collins, 1988 (Am J Trop Hyg 38:142-152), and was used to evaluate community-based ivermectin trials in Guatemala (Cupp et al., 1992. Am J Trop Med Hyg 47: 178-180). Therefore, the described schedules for blackfly collection are for *S. ochraceum*. For other vectors, some modifications will have to be made because of differences in transmission season and vector biting behaviour.

The collection methodology can also be used to investigate areas that might be susceptible to introduction of the parasite. The systematic collections will determine if a competent vector is present, and if the biting density is sufficiently high to support a transmission cycle.

PCR technology vs dissection of flies. To monitor the effects of ivermectin in the WHO-sponsored community trials in Guatemala, the annual transmission potential (ATP) and infective biting density (IBD) were determined by individual dissection of over 110,000 flies

2.7. Hourly collection schedule. Each hour of collection for each team is divided into 50 minutes of collecting followed by 10 minutes of rest, during which time the collection can be labelled and stored. Each 50-minute collection unit must be maintained separately and labelled with the date, community, collection site, time of collection (e.g. 08:00-08:50, etc.), and collector team. Each 50-minute collection must be preserved in 100% isopropanol for PCR testing. This is most conveniently done in the evening after the daily catch is made.

2.8. Determination of the Biting Rate. Data analysis requires a biting rate as well as an infection rate. The biting rate is calculated as the geometric mean number of flies per 50-minute collection period, with 95% confidence intervals. These data can be used to estimate the biting rate per hour, per day, or per transmission season. The infection rate when applied to the biting rate yields the number of infective stage larvae potentially transmitted per unit time, and is a measure of the transmission potential. The biting rate and the infection rate are also required in order to estimate the basic reproductive ratio *(Ro)* for that community. Therefore, when the flies are processed for PCR testing, the number of flies collected during each 50-minute period must be counted and recorded.

2.9. Processing of flies for PCR. In the laboratory, flies from each 50-minute collection unit are examined under a stereomicroscope, identified as to species, and any flies containing ingested blood are discarded. Flies are then counted into "pools" of 50 each by species. The heads are separated from the bodies and tested separately, because most infective stage larvae are found in the head. If resources are available, testing the bodies as well is recommended. For example, if elimination has been certified for a focus and the purpose of testing flies is surveillance for renewed transmission, then it is important to test the bodies because a positive indicates previous contact with a microfilaria-positive person.

2.10. Data reporting and analysis. Three statistics can be reported. The minimum requirements are the infection rate, which is the proportion of flies infective based on heads alone *(Proporción de Infectividad, PI)* and the biting rate *(Tasa de Picadura, TP)*. The proportion of flies infected based on the flies' bodies *(Proporción de Infección Parasitaria, PIP)* can be calculated if the flies' bodies are processed. **PIP** is calculated from fly bodies only because if pools of heads and bodies both test positives, it impossible to know whether the positives were caused by the same fly or different flies. Having infective stage larvae in the head with first and second stage larvae in the bodies simultaneously (asynchronous parasite development) is more frequent in vectors without cibarial armature, for examples in *S. metallicum, S. exiguum* (Collins, RC. 1979. Am J Trop Med Hyg 28: 491-495; Vieira, JC. 1995. Master of Science Thesis, Univ AZ, Tucson). The "Poolscreen" programme calculates an infection rate plus or minus 95% confidence intervals. **TP** is the total number of flies collected divided by the total number of 50-minute collection units. However, the number of flies collected during each collection unit should also be reported separately in order to calculate the geometric mean biting rate with confidence intervals.

2.11. Transmission potential. Infectivity rate **(PI)** and biting rate **(TP)** are used to calculate a minimum transmission potential. The following example is taken from data presented by Juan Carlos Vieira from an entomological evaluation using PCR on flies collected from a hypoendemic, treated village in Ecuador.

- Geometric mean biting rate **(TP)** per 50-minute collection unit during June and July = 11.03 flies per period (95% c.i. = 8.38 – 13.68). 50 minutes = 0.833 of one hour; 11.03/0.833 = 13.24 flies per hour (95% c.i. = 10.06 – 16.42).

- Total biting density estimated for two months is 13.24 x 10 hr x 61 days = 8077 flies

- Infectivity rate **(PI)** from 1 positive pool of heads in 215 pools of 50 flies each calculated by the Poolscreen program is 0.000093 (95% confidence interval of 0.0000024 to 0.00052).