Summary report of a consultation on the eradication of yaws

5–7 March 2012, Morges, Switzerland

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In January 2012, the Director-General of the World Health Organization, Dr Margaret Chan, launched a roadmap for neglected tropical diseases[1] at a partners' meeting in London, United Kingdom. The roadmap was endorsed unanimously by the partners as the way of attaining the goals set for the control, elimination and eradication of various neglected tropical diseases.

The roadmap targeted yaws for eradication by 2020, the third disease after dracunculiasis and poliomyelitis. In response, the World Health Organization Department of Control of Neglected Tropical Diseases organized a consultation in Morges, Switzerland, on 5–7 March 2012 to prepare a strategy for yaws eradication. This report summarizes the outcome of the meeting and outlines a framework for national plans to eradicate yaws by 2020.

Participants at the WHO consultation on eradication of yaws, 5–7 March 2012, Morges, Switzerland

[1] World Health Organization. *Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation—executive summary.* Geneva, 2012 (WHO/HTM/NTD/2012.1).

1. Background

When the World Health Organization (WHO) was established in 1948, yaws and other endemic treponematoses (bejel and pinta) were some of the major public-health problems it addressed, as reflected in World Health Assembly resolution WHA2.36[2] adopted in 1949. During 1952–1964, mass treatment campaigns organized by WHO and the United Nations Children's Fund (UNICEF) led to treatment of 50 million cases and contacts. By the end of the campaign, the number of cases of these diseases had been reduced by 95% to 2.5 million. This success and the complacency that followed led to a gradual dismantling of the vertical programmes and premature integration of yaws control activities into primary health-care systems, which were either weak or nonexistent in the many places in which yaws occurred. The resources and commitment for yaws control also disappeared. By the late 1970s, the disease had begun to resurge, and World Health Assembly resolution WHA31.58 was adopted in 1978. Renewed control activities, particularly in West Africa in the 1980s, failed after a few years because of a lack of political will and resources.

Yaws has been neglected, but its devastating consequences still affect some marginalized populations, especially children aged under 15 years. It is caused by *Treponema pallidum* subspecies *pertunue*. Humans are the only source of infection, and it is transmitted mainly by direct skin contact with fluid from a lesion on an infected person. Minor scratches and abrasions of the skin facilitate transmission. The incubation period is 9–90 days, with an average of 21 days.

The last WHO estimate, in 1995,[3] was that there were 2.5 million cases of endemic treponematoses (mostly yaws) globally, including 460 000 infectious cases. Except in the WHO South-Asia Region, where yaws was kept on the agenda, the disease was not considered a priority, and surveillance and reporting have been sporadic in other regions. The epidemiological status of yaws globally today is unknown; however, there is growing evidence that the number of cases of yaws and other endemic treponematoses is increasing in some countries, while they have disappeared in other previously endemic countries.

In 2011 (Figure 1 and Table 1), the endemic countries in the WHO South-East Asia and Western Pacific regions were Indonesia, Papua New Guinea, the Solomon Islands, Timor-Leste and Vanuatu. In the African Region, the full extent of yaws is unknown, but the disease is present in Benin, Cameroon, the Central Africa Republic, Congo, Côte d'Ivoire, the Democratic Republic of the Congo, Ghana, Sierra Leone and Togo. In most of these countries, underreporting of cases may be considerable. There is no recent information on yaws in the Region of the Americas, except for a report in 2003 in Ecuador.[4] A review by Hopkins in 1977 indicated that yaws and pinta were no longer public-health problems in the Americas.[5]

[2] http://www.who.int/neglected_diseases/mediacentre/WHA_2.36_Eng.pdf.
[3] World Health Organization. *Report of an informal consultation on endemic treponematoses.* Geneva, 1995:1–10.
[4] Anselmi M et al. Community participation eliminates yaws in Ecuador. *Tropical Medicine and International Health*, 2003; 8:634–638.
[5] Hopkins DR. Yaws in the Americas 1950–1975. *Journal of Infectious Diseases*, 1977; 136:548–554.

Figure 1. Countries with reported yaws in 2011

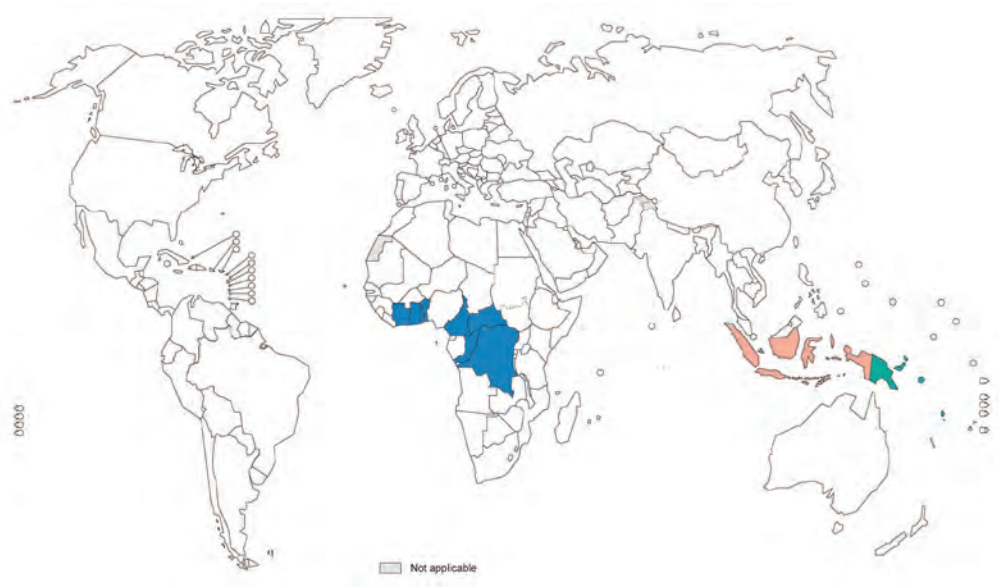


Table 1. Countries for which information on yaws was available, 2008–2011

Country (year of report)	Number of cases
African Region	
Benin[a,b]	No data
Cameroon (2010)	789
Central African Republic (2008)	243
Côte d'Ivoire (2010)	3 704
Democratic Republic of the Congo (2009)	383
Ghana (2010)	20 525
Republic of the Congo (2011)	167
Togo (2010)	15
South-East Asia Region	
India[c]	0
Indonesia (2011)	5 319
Timor-Leste[b]	No data
Western Pacific Region	
Papua New Guinea (2011)	34 628
Solomon Islands (2010)	20 635
Vanuatu (2010)	1 574

[a] Country known to be endemic.
[b] Country known to be endemic but with not data available.
[c] India interrupted transmission in 2004 and declared elimination in 2006. Since 2004, no new case has been reported.

2. The consultation on yaws

Rationale for the meeting

From 1996, India embarked on efforts to eliminate yaws. The final cases being reported in 2003. After 3 consecutive years in which no cases were reported, India declared interruption of yaws transmission in 2006. Up to 2011, zero cases have been reported, and careful serological surveys have revealed no evidence of transmission of yaws.

A recent publication in the *Lancet*[6] showing the effectiveness of a single dose of azithromycin in the treatment of yaws is a major advance in the history of the disease and could facilitate its eradication by large-scale treatment campaigns. Azithromycin has been used extensively in the elimination of trachoma, and its safety is well documented.

In 2012, WHO officially launched a roadmap to accelerate work in overcoming neglected tropical diseases (NTDs) in London, United Kingdom. In that document, yaws is targeted for eradication by 2020.[7] In March 2012, WHO organized a first consultation in Morges, Switzerland, to prepare a strategy for the eradication of yaws. The agenda, the list of participants and summaries of the presentations are given in annexes 1–3.

Objectives of the meeting

- to review the epidemiological situation of yaws in different regions and identify gaps in information;
- to set criteria and the process for yaws eradication and outline a plan for implementation;
- to analyse the implications of the Lancet article on use of azithromycin in yaws eradication;
- to identify potential donors and partners to support yaws eradication; and
- to explore collaboration with relevant NTD programmes, especially those for trachoma.

Expected outcomes

- update the epidemiological situation in different regions;
- define the criteria and process for eradicating yaws and plan implementation;
- agree on modalities for use of azithromycin in large-scale treatment campaigns to eradicate yaws;
- identify potential donors and partners; and
- identify possible areas for collaboration with other NTD programmes.

Opening remarks

Dr Jean Jannin, Coordinator, Innovative and Intensified Disease Management Unit, welcomed the participants on behalf of Dr Hiroki Nakatani, Assistant Director-General, HIV/AIDS, Tuberculosis, Malaria and Neglected Tropical Diseases, and Dr Lorenzo Savioli, Director of the Department of Control of Neglected Tropical Diseases. He referred to the roadmap endorsed in London at the end of January 2012, in which endemic treponematoses (yaws, bejel and pinta) were targeted for eradication by 2020. Dr Jannin urged the meeting to make concrete recommendations and propose strategies for achieving the eradication goal. He welcomed the news that azithromycin, which is given orally, would facilitate treatment in the field, although he warned that it would not by itself result in eradication of the disease. The political commitment of the governments of affected countries and the support of funding agencies would be necessary to deliver treatment to the remote communities in

[6] Mitjà O et al. Single-dose azithromycin versus benzathine benzylpenicillin for treatment of yaws in children in Papua New Guinea: an open-label, non-inferiority, randomised trial. *Lancet*, 2011; 379:342–347.

[7] World Health Organization. *Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation—executive summary. Geneva, 2012 (WHO/HTM/NTD/2012.1).*

which yaws and other endemic treponematoses occur. He stressed that, in an eradication programme, every effort and every approach should be used to identify, treat and report each case systematically.

Dr Kingsley Asiedu, head of the yaws eradication programme in the Department of Control of Neglected Tropical Diseases, listed the objectives of the meeting. He said that a new era of eradication of yaws and other endemic treponematoses was beginning, which this time should succeed. The meeting should propose pragmatic, new policies and strategies to achieve the eradication goal, taking advantage of the new tool represented by azithromycin.

3. Definitions

Two types of definition – clinical and operational – are provided to guide activities to eradicate yaws.

3.1 Clinical

Classification of yaws lesions

The classification of yaws lesions (Table 2) is described in the *Handbook on endemic treponematoses*.[8]

Table 2. Classification of yaws lesions

Clinically active yaws	
Infectious	Initial lesion(s) – papilloma Multiple papillomata Plantar and palmar papillomata Ulcers Other early skin lesions (macules, papules, micropapules, nodules, plaques)
Non-infectious	Hyperkeratosis Bone and joint lesions
Inactive yaws	Late active yaws: gummata, ulcers, gangosa, sabre tibia

Case definitions

Suspected case: a person with a history of residence in an endemic area (past or present) who presents with clinically active (visible) yaws.

Confirmed case: a suspected case with a positive serological test (rapid treponemal test or qualitative and quantitative rapid plasma reagin tests).

Imported case: a person who presents with clinically active serologically confirmed yaws in an area where yaws is not known to be endemic.

Index case: first case of yaws which is detected in a community.

A contact of a case of active infectious yaws: a person who has close, frequent contact with the infected person. A contact for the purpose of yaws eradication is the household, classmates or close playmates as identified by the contact.

[8] World Health Organization. *Handbook on endemic treponematoses*. Geneva, 1984:11. http://whqlibdoc.who.int/publications/1984/9241541768.pdf.

For practical and operational purposes, in areas where a case of yaws has been confirmed, all people without visible clinical yaws may be considered contacts.

Treatment success (cure): a person with clinically active yaws who has been treated with a single oral dose of azithromycin (or an injection of benzathine penicillin), and the lesion(s) was healed completely 4 weeks after treatment.

Treatment failure (non-response): a person with clinically active yaws who was treated with a single oral dose of azithromycin (or an injection of benzathine penicillin), and the lesion(s) had not healed or did not heal satisfactorily 4 weeks after treatment. (In such cases, it is important to request a serological test to confirm or exclude yaws. If the result is positive, swabs should be taken from the active lesion for PCR to detect any resistance. If the result is negative, an alternative diagnosis should be considered and the appropriate treatment given.)

3.2 Operational

Endemic area: community or village; district, region or country where yaws is constantly present, or at least one case of clinically and serologically confirmed yaws is present.

Unit of implementation of yaws eradication: the village or community. The GPS coordinates of each village should be available to allow mapping of endemic communities.

Passive case detection: patients are detected during regular health service activities in health centres and clinics. Health workers manage cases and notify the authorities at district level.

Active case detection: health workers or village health workers go to communities and screen the populations to find cases. This is an essential component of a yaws eradication strategy, especially after initial large-scale treatment. Two approaches can be used:

- house-to-house search: health workers visit every house in an endemic community and screen every household member for yaws.
- index-case approach: a focused search is conducted among all household members, schoolmates and close playmates of an index case. Total targeted treatment is recommended.

4. Eradication of yaws

The goal of the WHO roadmap is to eradicate yaws, **defined as the complete interruption of transmission (absence of new cases of yaws) globally, by 2020.** Endemic countries should aim at interrupting transmission of yaws by 2017 to allow 3 years of clinical and serological surveillance to confirm no further transmission.

4.1 Criteria for confirming interrupted transmission of yaws

The two criteria for confirming that there is no more transmission of yaws in an area are:

- *clinical:* absence of any report of the disease (case) for 3 consecutive years, supported by high coverage with active surveillance, and information, education and communication; and

- *serological:* continuous negative serological tests (rapid treponemal test; qualitative and quantitative rapid plasma reagin tests) for at least 3 consecutive years in all children aged under 5 years in the community.

4.2 Conditions favourable for yaws eradication

Some conditions that may favour the eradication of yaws are:

- new tools: single-dose oral azithromycin and simple, rapid, inexpensive serological tests;
- new treatment policies that ensure adequate treatment of populations at risk;
- the fact that humans are the only reservoir of infection;
- the fact that infection spreads only through close bodily contact;
- the fact that yaws is focalized (only a few countries have the disease);
- recent interruption of transmission in India; and
- current interest in and resources for the control, elimination and eradication of NTDs.

4.3 Possible operational challenges

The following aspects are critical to eradication of yaws and should be addressed before and during implementation of activities:

- complete epidemiological information on location of cases (all endemic communities and villages and their populations);
- complete, continuous access to the entire population at risk and endemic communities;
- clear, comprehensive follow-up plans for repeated surveys and retreatment after initial large-scale treatment, until zero cases are reported;
- clear plans for continuous health education and active surveillance as long as yaws has not been eradicated from an area;
- adequately trained human resources;
- necessary support from the community and national political authorities;
- committed financial support from the governments of affected countries and partners;
- available, affordable drugs (azithromycin or benzathine penicillin); and
- the necessary logistics (transport, information materials, recording forms, registers).

4.4. New treatment policies based on azithromycin

The meeting recommended two treatment policies to replace those that have been in existence since the 1950s. One of the failures of past eradication efforts was the large number of subclinical infections (contacts), which meant that treating cases alone was not sufficient to eradicate yaws. As there were no practical, cost-effective ways to determine the extent of subclinical infections, new infectious clinical cases continued to occur between treatment surveys.

The purpose of the new policies is to ensure a more pragmatic, aggressive approach to dealing with cases and all contacts, so that transmission can be interrupted in a reasonably short time, leading to eradication. As oral drugs are easier to administer than injection penicillin, it is recommended, if practicable, to undertake large-scale treatment once a community is identified as endemic.

The two new policies are:

- **total community treatment**, which is recommended to treat an entire endemic community initially, irrespective of the number of active clinical cases; and
- **total targeted treatment**, which is recommended to treat all active clinical cases and their contacts (household, school and playmates) during repeat surveys or retreatment or in response to a localized outbreak; also applicable for imported cases.

Both types of treatment should be flexibly adapted to the local situation (community characteristics and epidemiological situation of yaws); however, the ultimate aim should be rapid interruption of transmission. The meeting favoured use of total community treatment in the initial stages to reduce the need for frequent, costly follow-up visits to treat any new infectious cases.

Two drugs will be used in the eradication of yaws:

Azithromycin (Zithromax)[9]

Azithromycin given orally is preferred to benzathine penicillin. The recommended dosage is 30 mg/kg body weight (maximum, 2 g) as a single dose by mouth (Table 3). For children aged under 6 years, syrup is preferable; if this formulation is not available, a tablet should be crushed and mixed with water.

Table 3. Recommended dosages of azithromycin by age

Age (years)	Total dose (mg)	No. of tablets	Syrup (ml)
< 6	500	1	12.5
6–9	1000	2	
10–15	1500	3	
> 15	2000	4	

5 ml from a 15- or 30-ml bottle of Zithromax syrup contains 200 mg
Azithromycin is not recommended for children under 6 months

Benzathine penicillin

Benzathine penicillin is still effective and relevant in yaws treatment and eradication. Given the operational and logistic problems associated with its administration, however, it may be used as a back-up for people who cannot be treated with azithromycin, those who fail on azithromycin or in large-scale treatment in places where azithromycin is not available. The standard doses are 0.6 million units for children aged under 10 years and 1.2 million units for people aged over 10 years.

[9] International Trachoma Initiative. *Zithromax in the elimination of blinding trachoma: a programme manager's guide.* Decatur, Georgia, 2012 (also available at: http://www.trachoma.org/sites/default/files/guidesandmanuals/Zithromax%20manager's%20guide.pdf).

5. The eradication strategy

The eradication strategy will be based on a four-pronged approach:

Component 1. Large-scale treatment

Initially, treatment of the entire population of a known endemic community: the rationale is to cover as many as possible of active clinical cases and contacts (incubating and latent cases) that could develop into infectious cases later.

Repeat surveys at least every 3–6 months (depending on the population, communities and initial coverage) until no clinical cases are reported, with either total targeted treatment or total community treatment if coverage during initial total community treatment is <90%, if access to endemic communities is difficult, and to reduce the frequency of returning to treat any new cases.

Repeat surveys are systematically carried out in previously treated villages at intervals of 3 months when attendance was not maximal (low coverage); otherwise, 6-monthly intervals are considered adequate and practical. (This is based on the experience of the yaws eradication campaign in Nsukka, Nigeria, in the 1950s).[10]

Component 2. Health system approach (complementary to large-scale treatment)

Treatment after initial total community treatment and between repeat surveys. Health facilities in endemic areas (if they exist) will have stocks of azithromycin (or benzathine penicillin) to implement total targeted treatment, in order to respond to:

- cases diagnosed at consultation at health facilities (see Annex 4) and their contacts;
- cases identified in the community by village volunteers; and
- any outbreaks or cases missed during large-scale treatment.

Component 3. Essential supportive measures

- training of health workers to diagnose and treat cases, surveillance, health promotion and implementation of the new strategy;
- training of schoolteachers and village volunteers to recognize and refer cases, and assist in health promotion and treatment activities;
- information, education and communication, and health promotion in communities and schools;
- community engagement and involvement of chiefs and other opinion leaders; and
- a standard surveillance system (see annexes 4 and 5).

Component 4. Operational research

Serological tests: optimal use of treponemal and non-treponemal tests in yaws eradication.

[10] Zahra A. Yaws eradication campaign in Nsukka division, eastern Nigeria—a preliminary review. *Bulletin of the World Health Organization,* 1956; 15:911–935.

6. Implementing the eradication strategy

In planning and implementing the yaws eradication strategy, national yaws programmes may explore synergistic collaboration with other programmes on various aspects, including logistics. There is sufficient experience in planning mass drug administration and immunization campaigns in different countries, and yaws programmes should collaborate and learn from those programmes. Sometimes, such collaborations may be more appropriate at district or village level. At this stage, co-administration of azithromycin for yaws eradication with other mass drug administration is not recommended.

6.1 Identifying and mapping affected communities and villages

Affected villages should be identified (if not already known) on the basis of: data from the literature; a review of health facility records; reports from communities and districts; and geographical contiguity with a known endemic area. In every endemic village, the population should be stratified by age (0–4 years, 5–9 years, 10–14 years and ≥15 years) and its geographical coordinates taken by GPS, so that all endemic villages can be mapped for monitoring.

In villages for which there is limited information on yaws, baseline clinical and serological surveys of children aged <15 years should be carried out to determine the burden. Again, the geographical coordinates should be taken by GPS so that all endemic villages can be mapped.

6.2 Logistics and financial planning

Logistics and funding should be planned at the beginning. Programme managers should ensure that items such as transport means, drugs, serological tests and communication materials are secured in sufficient quantities to meet the planned activities. Forecasting and correct distribution of drugs are essential to the eradication strategy.

6.3 Advocacy with stakeholders

Advocacy is essential for gaining the attention and support of endemic communities, local political authorities, local and national government, funding bodies and other relevant sectors such as education and rural development. Various approaches should be used to gain such support, depending on the local and national context.

6.4 Capacity-building and training

Health workers should be trained in the clinical and public-health aspects of yaws eradication. The clinical aspects should include diagnosis and treatment of individual cases, serological tests, monitoring patients for any adverse events and curing lesions. The public-health aspects should include the programme objectives, planning, implementation, monitoring and evaluation of yaws eradication activities.

Village health workers and schoolteachers should also be trained to suspect and refer cases to health facilities for treatment. They should also be trained to support the activities of total community treatment. Depending on the country, village health workers or community drug distributors may be involved in community treatment with azithromycin, including following-up anyone who was missed during total community treatment so that they can be treated without delay.

6.5 Community mobilization and planning

Community education about the purpose of yaws eradication activities is essential to ensuring maximum coverage. During community meetings, the dates for implementing activities should be agreed upon, and the central role of the community, especially chiefs and other community leaders, should be clearly defined. It is important to emphasize that if everyone is treated once, the disease will be eradicated from the community, but, if some people are not treated, they pose a continuous risk to the community. Pictorial recognition cards, booklets and posters should be widely distributed in each community and schools to generate awareness. Local radios may be used to transmit information about yaws and the dates of community treatment.

6.6 Total community treatment

During total community treatment, 100% of the eligible population should be treated to ensure rapid interruption of transmission. Other approaches, such as use of village health workers or community drug distributors, should be adopted to provide treatment to people who are absent during the large-scale treatment.

Other common diseases encountered during large-scale treatment should be recorded separately, treated if possible and reported.

6.7 Detection and treatment of cases and contacts between treatment campaigns

Under component 2 of the eradication strategy, health workers should continue to detect and treat cases. Village volunteers (community drug distributors) will be crucial in ensuring prompt detection of any cases and alerting the nearest health facility. They should conduct house-to-house visits to educate people and detect suspected cases.

Other common diseases encountered during large-scale and follow-up treatments should be recorded separately and treated or reported.

6.8 Monitoring and surveillance of treatment

Although the safety of azithromycin used in large-scale treatment of trachoma is established, in yaws eradication activities, national programmes should document its effectiveness, evidence of treatment failure and antimicrobial resistance as well as any serious adverse events. This information should be transmitted regularly to WHO.

6.9 Standard and centralized surveillance systems

For eradication of yaws, a strict surveillance system is required, and every case must be reported. All data will be centralized at WHO headquarters and published online to make them accessible to all. Standard forms (see annexes 4 and 5 and www.who.int/yaws) will be used in all yaws-endemic countries to record and report yaws activities.

A strong village-based surveillance system should be in place to pick up and report every case.

Cross-border surveillance and rapid notification of cases to the health authorities is essential. In this regard, regular exchanges should also be in place, through inter-country or district border review and information-sharing meetings.

6.10 Intersectoral and inter-programme collaboration

Close coordination should be maintained between the health and other sectors, according to local and national conditions. The education sector is a natural partner for yaws control, as >75% of people affected are children aged <15 years. Collaboration with other disease control programmes should be explored on a case-by-case basis.

6.11 Supportive supervision and monitoring

The eradication of a disease requires close supervision and monitoring at all levels. District and sub-district health authorities should closely monitor activities in endemic villages. Programme activities should be monitored by:

- monthly reporting of cases from each endemic community (zero cases should also be reported),
- reports of active case searches,
- review meetings and
- independent appraisals by a national task force.

6.12 Structures for yaws eradication at country and global levels

At the national level, each endemic country may consider establishing:

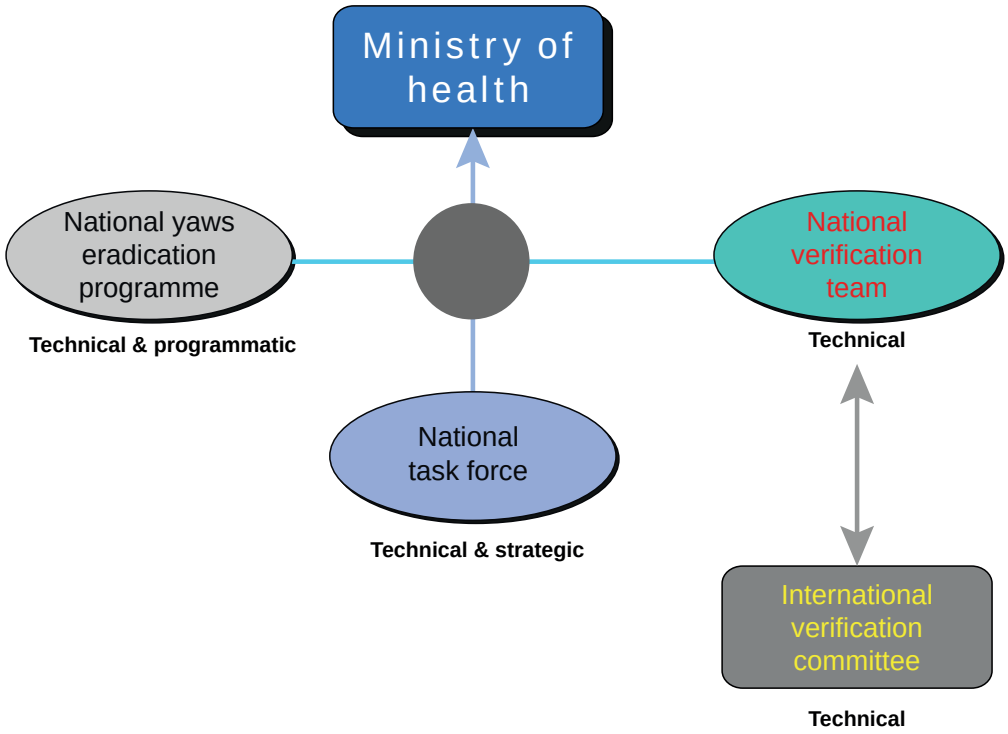
- a national yaws eradication programme as part of the national NTD programme,
- a national task force to give technical advice and strategic guidance for yaws eradication activities and
- a national verification team to verify local interruption of transmission initially.

A possible structure for yaws eradication at country level is shown in Figure 2.

At the global level, the WHO Yaws Eradication Programme will establish:

- an advisory committee to give technical advice and strategic guidance for yaws eradication activities and
- an international verification committee to certify that countries have met the criteria for interruption of transmission.

Figure 2. Possible structure for yaws eradication



6.13 Validation and certification at country level

The national task force should give technical advice and strategic guidance for yaws eradication. The national verification team, consisting of experts in areas such as dermatology, serology, sociology and public health, should validate the status of interruption of yaws once zero cases have been reported in a given village or district. Such assessment should be done every year for 3 consecutive years; if zero cases are found and serological tests in children aged <5 years prove negative, WHO should be contacted for the assistance of the International Verification Committee. The sero-survey protocol used in the Indian yaws eradication programme might be adapted for use (Annex 6 and www.who.int/yaws).

6.14 Key indicators

Yaws interventions can have a visible impact in communities within a relatively short time (about 6 months). Theoretically, if everyone in an endemic community (cases and contacts) is treated once with azithromycin, transmission should be interrupted.

The primary indicator is the number of new cases reported monthly from a community. **The secondary indicator** is coverage with treatment.

Proof of principle. In order to demonstrate in a real-life situation that a single dose of azithromycin works in large-scale treatment, the meeting agreed to conduct a proof-of-principle study, including intensive, careful monitoring, with implementation in selected places in six countries. The experience gained in this study will be used to adapt the proposed policies and strategies. The sites are Cameroon (Lomie District), Ghana (West Akim District), Indonesia (Timor Tengah Selatan District), Papua New Guinea (Lihir Island), the Solomon Islands and Vanuatu (Tafea Province).

7. Recommendations of the meeting

7.1 Endemic countries

1. Countries in which yaws is currently endemic should take the necessary steps to assess the full extent of the disease in order to plan and implement activities to interrupt transmission by 2020.
2. In pursuit of eradication, these countries may establish national task forces to guide activities.
3. The countries might explore collaborations with programmes against other NTDs in areas such as training, education, information, education and communication, and identification of populations at risk. Co-implementation of treatment is not recommended at this time.
4. Countries in which yaws was endemic in the 1950s and in which the current epidemiological status is unknown should assess the presence or absence of the disease and report their current status to WHO.

7.2 Financial partners

Donors and nongovernmental organizations should support WHO and ministries of health of endemic countries to implement the agreed plan to eradicate the disease.

7.3 Academic and research institutions

Academic and research institutions should support the research necessary to achieve the ultimate goal of yaws eradication.

7.4 World Health Organization

1. Publish and disseminate the recommendations of the meeting.
2. Take the lead and mobilize resources to eradicate yaws by 2020.
3. Support endemic countries in preparing or revising yaws eradication plans in accordance with the outcome of this meeting.
4. Provide technical guidance for implementation, monitoring and evaluation to interrupt transmission of yaws.
5. Prepare the necessary technical and information materials to support eradication activities in countries.
6. Convene annual regional or global meetings of countries in which yaws is endemic and partners to assess progress towards eradication.
7. Establish an independent body to monitor eradication efforts, including verification of interruption of transmission.

Annex 1. Agenda of the meeting

Day 1 Chair: David Mabey		
Time	Introduction	
09:00–10:30	Opening remarks	Jean Jannin
	Introduction of participants	
	Nomination of Chair and Rapporteurs	
	Background, objectives and expected outcomes	Kingsley Asiedu
10:30–11:00	Break	
11:00–12:00	Yaws situation in the WHO South-East Asia, Western Pacific and African regions (15 min each + 15 min discussions)	Regional representatives
12:00–13:00	Yaws situation in Ghana, Indonesia and Vanuatu (15 min each + 15 min discussion)	National focal points
13:00–14:00	Break	
14:00–15:30	Yaws situation in Cameroon, Central African Republic and Congo (15 min each +15 min discussion)	National focal points
	Azithromycin study in Lihir, Papua New Guinea, and plans for the island (20 min + 10 min discussion)	Oriol Mitja
15:30–16:00	Break	
16:00–17:00	Azithromycin study in Ghana: progress report (20 min + 10 min discussion)	Cynthia Kwakye

Day 2 Chair: Lasse Vestergaard		
09:00–10:30	Serological tests in support of yaws control (20 min + 10 min discussion)	Yaw Adu-Sarkodie
	Yaws in India: process to eradication (20 min + 10 min discussion)	Rajendra Panda
10:30–11:00	Break	
11:00–12:30	Definition of terms: Eradication Treatment failure Large-scale treatment Historical policy and proposal for a new policy Coverage Frequency When to stop large-scale treatment Criteria and process for confirming Clinical Serological	André Meheus
12:30–14:00	Break	
14:00–15:30	Discussions on implementation Identification of endemic foci Regular large-scale treatment of affected populations Post large-scale treatment impact assessment surveys Drug safety and resistance monitoring Training, information, education and communication Data collection system and reporting Operational research Co-implementation with other mass drug administration for NTDs	All
15:30–16:00	Break	
16:30–17:00	Discussions on implementation (continued)	

Day 3 Chair: Yaw Adu-Sarkodie		
09:00–10:30	Logistics Azithromycin Serological tests Information, education and communication; training documents Transport	All
	Areas of collaboration with other programmes/network Trachoma	Silvio Mariotti
10:30–11:00	Break	
11:00–12:00	Potential donors and partners for yaws Global Regional Country	All
12:00–13:00	Break	
13:00–15:00	Conclusions, recommendations and next steps Closure	

Annex 2. List of participants

Professor Yaw Adu-Sarkodie
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Annex 3. Summaries of presentations made

WHO regional offices

WHO Regional Office for South-East Asia

Dr A.P. Dash, Regional Advisor for Vector Borne Diseases, presented an overview of the yaws situation in the South-East Asia Region. Since India achieved elimination of the disease in 2006, the only countries in which yaws is endemic are Indonesia and Timor-Leste. India's achievement was the result of high-level government commitment. Indonesia reported 6000 cases in 2011, but the situation of yaws is not clear in Timor-Leste, where an estimated 500–1000 cases are expected to occur annually. Timor-Leste is a new country, where the public-health system is still weak. The regional goal to eliminate yaws by 2012 was revised at a meeting held in Timor-Leste in late 2011, and the new regional target is 2020.

WHO Regional Office for the Western Pacific

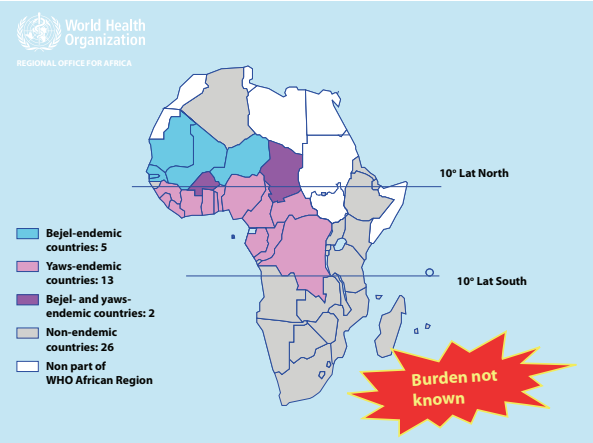
Figure A3.1. Distribution of yaws in the Western Pacific Region, 1990s to present

Dr Lasse Vestergaard presented the past and current situation of yaws in the region. Before the campaigns in the 1950s, there was a high burden of yaws. The campaigns led to the elimination of yaws in many countries, and for a long time it was thought that the disease was no longer present in the region. In the 1970s, however, cases began to be reported in Papua New Guinea, the Solomon Islands and Vanuatu, and these countries are still endemic today.[11] The exact numbers of cases in these countries (Figure A3.1) are unknown, as the data are based on routine surveillance and informal reports. Yaws is not a notifiable disease in the region. Furthermore, knowledge about yaws among health workers is weak, and training is needed as part of the new global eradication efforts. Some countries and donors do not like the mass treatment concept, and a way should be found to use health systems (where they exist) effectively to achieve the eradication goal. The Regional Director, Dr Dr Shin Young-soo, is committed to eradicating yaws from the region.

[11] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3253475/pdf/JTM2011-642832.pdf.

WHO Regional Office for Africa

Figure A3.2. Distribution of yaws and bejel in Africa



Dr Issa Sanou, Research Officer for Neglected Tropical Diseases (NTDs) at the WHO Regional Office for Africa, gave an overview of NTDs in the region and the current situation of yaws. A total of 11 NTDs occur in the Region, including endemic treponematoses (yaws and bejel)

(Figure A3.2), which are dealt with by case management. The goal is to eliminate these diseases, which cause disability, disfigurement and stigma among poor populations, mainly in West and Central Africa. Although the full extent of yaws is not known, it is endemic in nine countries: Benin, Cameroon, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Ghana, Sierra Leone and Togo. Burkina Faso and Chad are endemic for endemic syphilis (bejel).

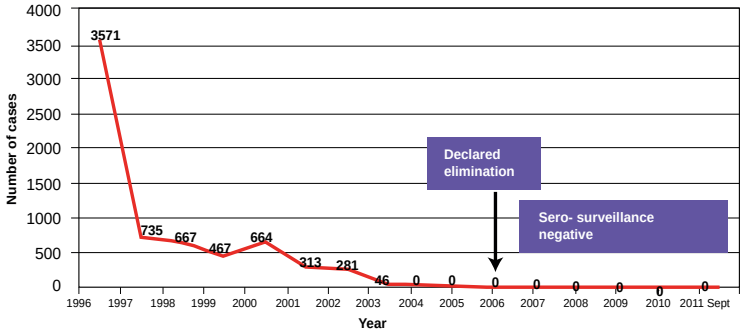
Ghana appears to be the most endemic country, reporting more than 20 000 cases annually. Three countries (Cameroon, Congo and Ghana) have national programmes to fight yaws. Dr Sanou described the opportunities for enhancing elimination of these diseases in the region: political and donor interest in NTDs; progress in other parts of the world; and new treatment (azithromycin which can be used in preventive chemotherapy). He presented the regional strategic plan for NTDs for 2011–2015 and remarked that it was important for WHO to provide guidelines for mass treatment of yaws and bejel.

Country presentations

India

Dr Rajendra Panda, Assistant Director (Medical), National Centre for Disease Control, Ministry of Health and Family Welfare, presented the results of the detailed serological and clinical surveillance that has been in place since India declared elimination of yaws on 19 September 2006. A cash reward system, which is sometimes introduced during the last phases of an eradication programme, is designed to encourage voluntary reporting of any suspected case. In India, Rs 5000 (approximately US$ 100) is given to health workers for a confirmed case and Rs 500 (approximately US$ 10) to the first informer of the confirmed case. Up to September 2011, there had been no case of yaws, and serological tests in children aged <5 years had also shown no evidence of transmission (Figure A3.3). A full report of India's achievement was published in the *Weekly Epidemiological Report* in 2008.[12]

Figure A3.3. New cases of yaws in India between 1996 and 2011



[12] http://www.who.int/wer/2008/wer8315.pdf

Indonesia

Dr Christina Widaningrum, National Programme Manager for leprosy and yaws at the Ministry of Health, presented the situation of yaws and the efforts being made to eliminate it. In Indonesia, leprosy and yaws are addressed in one programme, allowing efficient use of resources to tackle these two diseases, which occur in remote rural areas. The numbers of cases detected in 2001–2011 are shown in Figure A3.4 and the geographical distribution in Figure A3.5. Most cases are found in the eastern part of Indonesia. The strategies for yaws elimination are advocacy, strengthened surveillance (including serological surveys), capacity-building, information, education and communication, case detection, treatment of cases and contacts, and monitoring and evaluation. Some of the problems faced by the programme include difficulty in reaching the endemic communities, which are scattered over many small islands, use of injected benzathine penicillin, which is difficult to administer to children in some areas, and weak political support.

Figure A3.4. Trends in reported numbers of yaws cases in Indonesia, 2001–2011

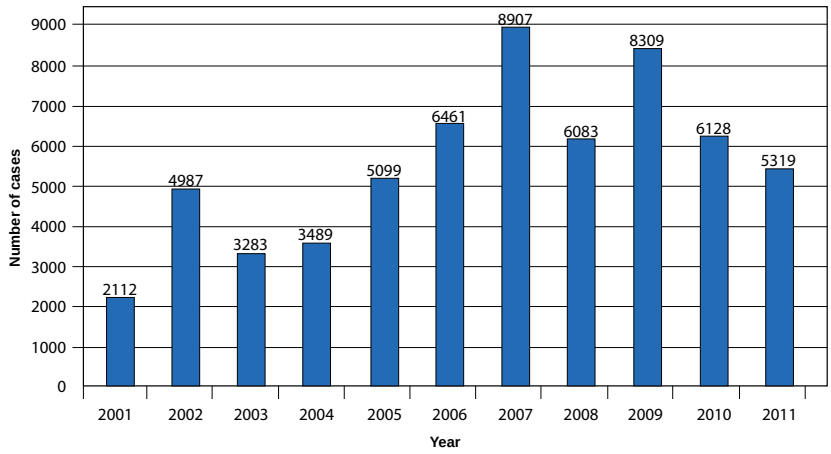
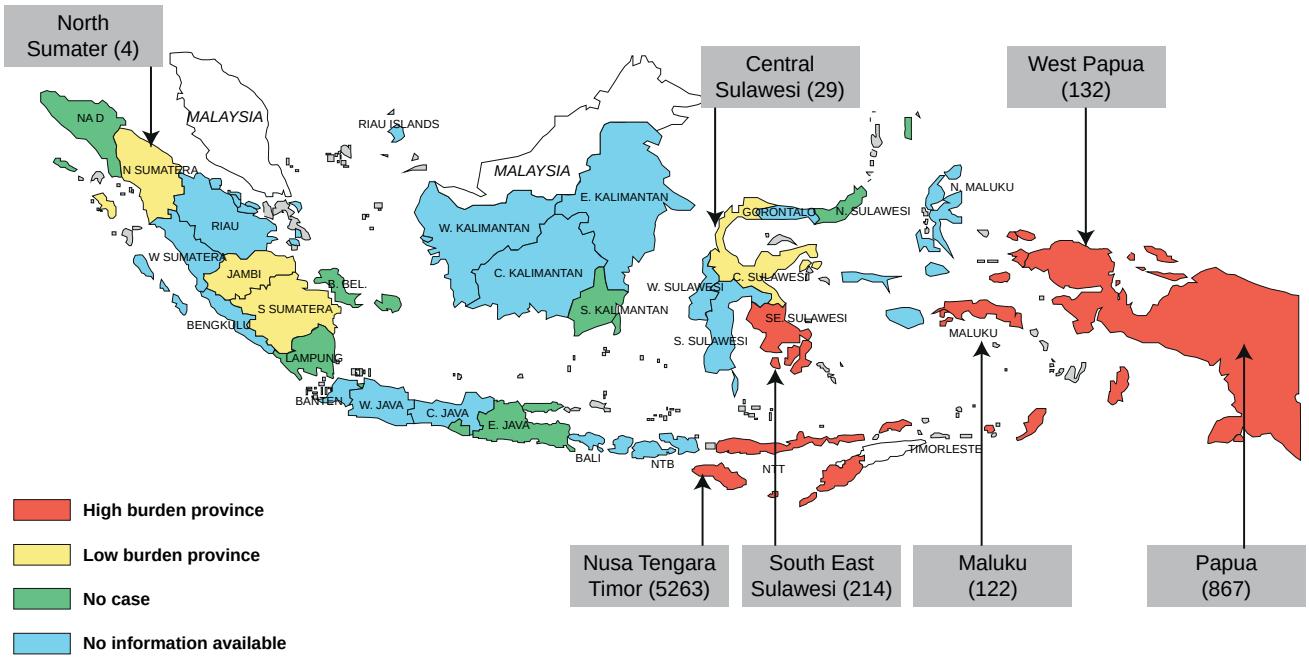
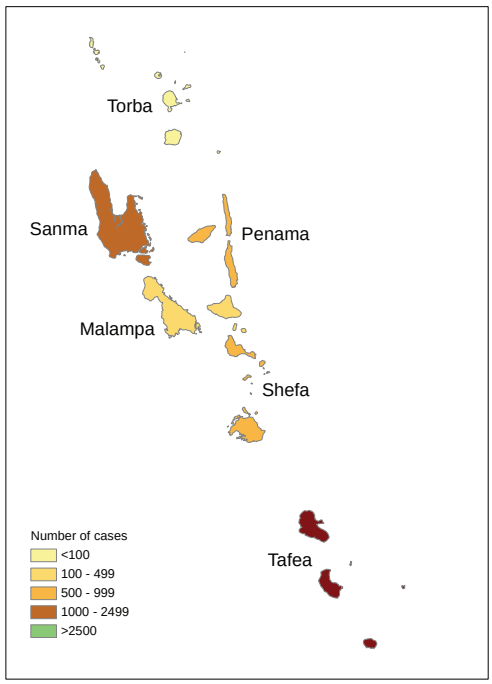


Figure A3.5. Geographical distribution of yaws in Indonesia



Vanuatu

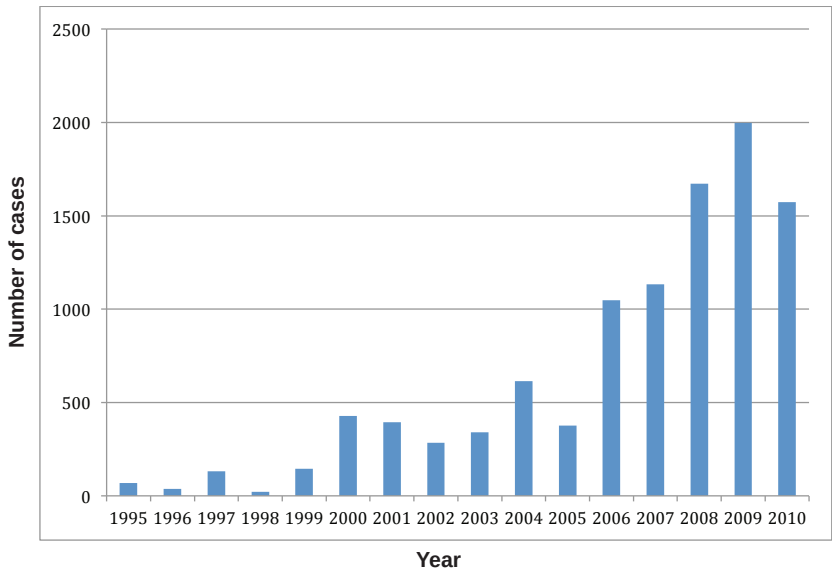
Figure A3.6 Distribution of yaws by province in Vanuatu, 1995-2010



Mrs Marie Woleg, National Focal Person for Yaws and Coordinator of the National IMCI Program of the Ministry of Health, presented the yaws situation in Vanuatu. Clinical cases of yaws are routinely reported through the national health information system, showing an increase in the number of cases over the past five years (Figure A3.7). All six provinces report cases, but prevalence varies widely between provinces and Tafea Province is the most affected area (Figure A3.6). Mass treatment campaigns were implemented in Tafea Province (1989) and in Sanma Province (2001), but despite the high treatment coverage achieved (>90%), cases have resurged in both provinces because surveillance or other follow-up activities were not implemented.

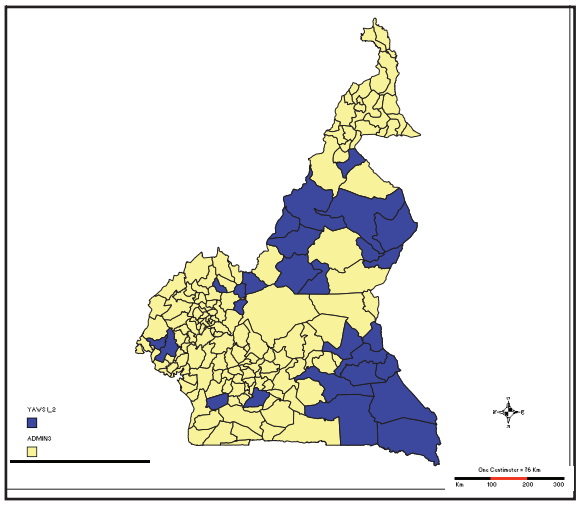
The Ministry of Health of Vanuatu is committed to fighting the increasing problem of yaws in the country. To better understand the extent of the disease, a national yaws situation analysis was conducted in 2011, comprising rapid national household surveys and health worker interviews piggy-backed onto a national malaria indicator survey. The household surveys involved clinical screening of yaws-like skin lesions based on pictorial cards, serological testing using a commercial syphilis (anti-treponemal antibody) rapid test in children aged <15 years, and interviews of heads of households about yaws treatment history in the past12 months. The assessment confirmed that yaws is widely prevalent in parts of Tafea Province and also focally present in other provinces at lower levels of endemicity. While further surveys may be required to guide yaws interventions outside Tafea, the Ministry of Health is considering the best strategy to tackle the urgent problem of the disease. This strategy will likely involve a combination of mass treatment campaigns supported by ongoing surveillance and case-finding, strengthening of primary health care services including integrated training of community health workers, improving water and sanitation standards, and increasing public awareness.

Figure A3.7. Number of cases of yaws reported in Vanuatu, 1995-2010



Cameroon

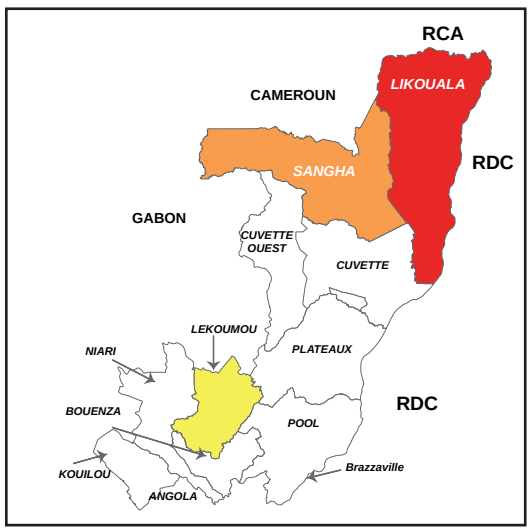
Figure A3.8. Geographical distribution of yaws in Cameroon, 2010–2011



Dr Earnest Njih, National Programme Manager for Leprosy, Yaws, Leishmaniasis and Buruli Ulcer at the Ministry of Public Health, described recent efforts to map the geographical distribution of yaws in Cameroon. As in many countries, yaws is not a health priority in Cameroon, and routine reporting is not required. Mass treatment campaigns in the 1950s reduced the disease to such an extent that it was thought that yaws no longer occurred in the country. In 2007 and 2008, however, outbreaks of yaws were reported among the indigenous population (pygmies) in Lomie health district. This prompted the Ministry of Health to include yaws in the leprosy, leishmaniasis and Buruli ulcer control programme in 2009. The activities carried out so far include capacity-building, rapid assessment surveys, mapping, screening, and treatment of cases and contacts. Further activity identified 789 suspected cases of yaws in 2010 and 130 cases in 2011. All cases were treated. Between 2007 and 2011, 1973 cases of yaws were reported in Cameroon. The geographical distribution is shown in Figure A3.8.

Congo

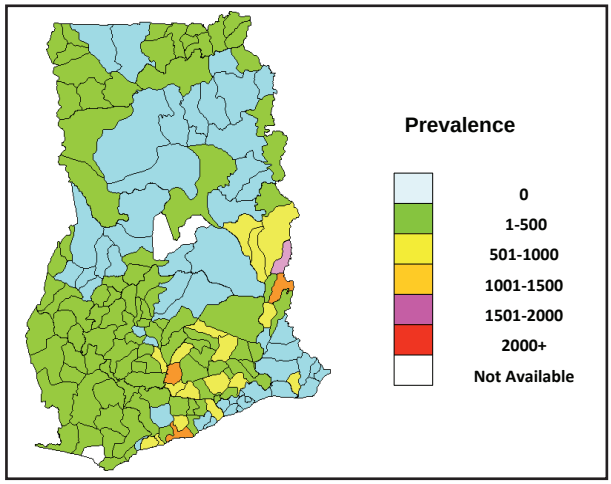
Figure A3.9. Distribution of yaws in the Congo



Dr Damas Obvala, National Programme Manager for Leprosy, Yaws, and Buruli Ulcer at the Ministry of Health and Population, had to leave the meeting because of an emergency. The presentation he had prepared is summarized here. There are three endemic regions (Lékoumou, Likouala and Sangha; Figure A3.9), but Likouala is the most severely affected. The population group most heavily affected is the indigenous people (pygmies and babengas), who live in the Likouala and Sangha regions. These regions are contiguous with endemic foci in Cameroon, the Central African Republic and the Democratic Republic of the Congo in which the pygmies live. In general, the pygmies live in poor areas with little or no access to health care and schooling. They are migrant populations who live in the forest. Screening and treatment of yaws are included in leprosy and immunization activities. In 2011, 197 cases were identified and treated during screening and treatment campaigns; 36% were in children and 64% in adults. This is contrary to the age distribution in other countries, where children are the most affected. The challenges to bringing health care to the pygmy population are the difficult access to communities, the high cost of medical missions to communities, lack of health services to integrate activities, and unhygienic and crowded living conditions in the deep humid forest, which is favourable for yaws.

Ghana

Figure A3.10. Distribution of yaws in Ghana in 2009, based on routine data



Dr Nsiire Agana, National Programme Manager for Yaws, presented the epidemiological situation in Ghana. Surveys carried out in 2008 showed a national prevalence of 0.681% among schoolchildren, the prevalence in some rural communities rising to 20%. The annual case notification rates in 2002–2010 are shown in Table A3.1. The Eastern, Central, Western, Volta and Ashanti regions are the worst affected, but all 10 regions report yaws annually (Figure A3.10). During routine reporting, only 19 of the 170 districts did not report yaws cases between 2008 and 2011 (Table A3.2). No cases are seen in the large metropolitan areas of Accra and Kumasi or in the many districts in the Northern Region, either because of annual mass distribution of azithromycin for trachoma during 2005–2010 or because cases are not being reported. The Ministry of Health is now scaling up active surveillance and containment for early detection and treatment of cases and contacts. A total of 28 000 cases were reported in 2008 and 25 000 in 2010.

Table A3.1. Case notification rates per 100 000 population, Ghana, 2002–2010

District	2002	2003	2004	2005	2006	2007	2008	2009	2010
Western	157	293	581	224	153	153	136	191	98
Central	628	501	665	172	211	194	145	368	383
Greater Accra	----	12	169	13	7	10	11	20	5
Eastern	931	516	393	141	228	415	610	376	188
Volta	67	360	----	584	88	283	33	301	54
Ashanti	79	71	134	55	55	47	50	85	32
Brong Ahafo	205	133	202	69	84	63	92	54	50
Northern	----	----	60	55	4	5	30	16	18
Upper West	24	5	7	4	2	7	34	6	14
Upper East	517	14	30	10	60	41	68	37	65
All	241	189	229	120	87	113	118	150	84

Table A3.2. Numbers of districts in Ghana that reported yaws between 2008 and 2011

Region	No. of districts	No. of districts that reported cases of yaws
Ashanti	27	26
Brong Ahafo	22	22
Central	17	16
Eastern	21	21
Greater Accra	10	1
Northern	20	14
Upper East	9	9
Upper West	9	9
Volta	18	16
Western	17	17

Other presentations

Trachoma

Dr Silvio Mariotti, Medical Officer in charge of the elimination of blinding trachoma at WHO headquarters, gave an overview of the trachoma programme and the SAFE strategy, and described areas in which collaboration was possible. The first step is to examine the geographical overlap of the two diseases. Mapping of trachoma is advanced; the maps for a number of countries can be accessed on the WHO web site http://apps.who.int/neglected_diseases/ntddata/trachoma/trachoma.html. Further mapping for trachoma is planned, which could provide an opportunity to assess the situation of yaws.

Trachoma programme (Pfizer)

Dr Charles Knirsch, Head of Clinical Affairs, Pfizer Inc., presented his company's involvement in the trachoma elimination programme, and suggested that yaws and trachoma programmes could learn from each other. Large mass treatment programmes were conducted for both diseases in the early days of antibiotics. Towards the end of a vertical programme, however, the horizontal component must be given more importance or the disease will resurge and drug resistance may appear. The programme went from a highly vertical approach to a more integrated one in the Task Force for Child Survival, and now includes continuous innovation as well as continuous monitoring of microbiological and clinical safety.

Elimination of yaws in Lihir, Papua New Guinea

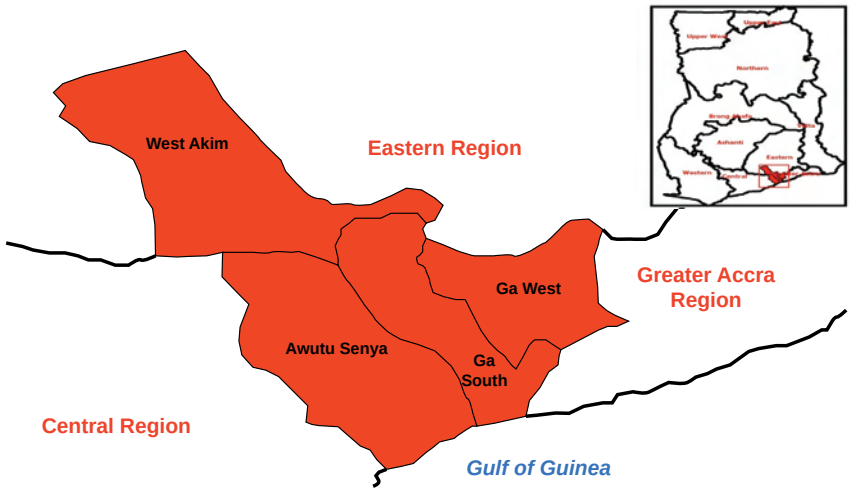
Dr Oriol Mitja, infectious diseases specialist and the principal investigator of the randomized trial in Lihir, Papua New Guinea, summarized the study and its main findings. He also proposed a pilot study to eliminate yaws from a limited geographical area with azithromycin used for large-scale treatment. Phase III of the trial involves large numbers of patients in order to show convincing, statistically significant evidence of efficacy. The objectives of the proposed open-label trial for mass treatment are to reach 80% of the population in each 6-monthly round of treatment for 2 years, with strict follow-up surveys, monitoring of drug resistance and the impact on other infections.

Randomized trial in Ghana

Dr Cynthia Kwakye, District Director of Ga West Municipal Directorate and the principal investigator of a randomized trial in Ghana, presented the preliminary results. Patients are being recruited from four adjacent districts (Figure A3.11), and 420 patients are expected to be enrolled. The preliminary results are encouraging and appear to be in line with the results from Papua New Guinea. Observations relevant for yaws eradication include:

- the importance of community participation and the involvement of village health workers;
- the expectation of the population that they will receive treatment for other conditions;
- excellent knowledge about yaws among parents, who often consider it a childhood disease that will resolve by itself;
- use of children to identify other cases of yaws; and
- the number of children who are not in school because of social problems (lack of money for lunches and uniforms).

Figure A3.11. Recruitment sites for the clinical trial in Ghana



Professor Yaw Adu-Sarkodie, Dean and Head of the Department of Clinical Microbiology at the School of Medical Sciences, Kwame Nkrumah University of Science and Technology, briefly presented the blinded serological results: 85% of patients had a lower titre after 3 months; 15/160 patients had titres that were two or four times higher; and 20/160 had unchanged titres. Preliminary incomplete results at 6 months showed that 65% had lower titres, 6/62 had increased titres and 6/62 were unchanged. There is no serological test to distinguish between venereal syphilis and non-venereal syphilis (yaws, bejel and pinta). Serological surveys could be conducted to establish the burden of disease, to confirm no new cases in children (in order to validate absence of transmission) and to confirm yaws in secondary cases. There are two types of test:[13]

- *Non-treponemal tests.* Treponemal infections lead to the production of nonspecific antibodies (reagin antibodies) that react to cardiolipin. Tests to detect reagin antibodies include rapid plasma reagin (RPR) tests, VDRL and TRUST. Rapid plasma reagin tests can be both qualitative and quantitative. Non-treponemal tests become unreactive in end-stage

[13]World Health Organization. *The use of rapid syphilis tests.* Geneva, 2011. http://www.who.int/tdr/publications/tdr-research-publications/use-rapid-syphilis-tests/en/index.html.

disease and in successfully treated cases. Rapid plasma reagin tests require refrigeration, however, and therefore present logistic problems for field use.

- *Treponemal tests.* Treponemal antibody detection tests include TPHA, TPPA and FTA-ABS. They remain positive even after successful treatment or cure.
- Some companies make combinations of rapid *non-treponemal* and *treponemal* tests. A positive result with a non-treponemal test and a negative result with a treponemal test indicate a false-positive, whereas a negative result in a non-treponomal test and a positive result in a treponomal test indicate an old or treated case. The cost of the new tests is not yet known.

The costs of current serological tests, according to prices obtained from WHO procurement in February 2012, are:

- syphilis fast disposal test card: 500 pieces = EUR 15.4; unit cost = EUR 0.0308
- syphilis fast reagents: 200 pieces = EUR 41.3; unit cost = EUR 0.2065
- SD Bioline syphilis 3.0, multi-device test kit: 100 pieces = US$ 45; unit cost US$ 0.45

Concepts of eradication, and policies and strategies for yaws control

Professor André Meheus, University of Antwerp, Belgium, made a detailed presentation of the definitions and principles for elimination and eradication. He presented the old treatment policies and strategies for yaws, and proposed new policies and strategies for renewed efforts. The presentation was discussed at length, and the outcomes form the basis for the technical part of this report.

Annex 4. Registration of yaws cases treated at health facilities

No.	Date (dd/mm/yyyy)	Name	Age (years)	Sex (M/F)	Village	District	Treatment		Comments (No. of contacts treated)
							Syrup	Tablets	
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									
18									
19									
20									

This form must be submitted to the district health authorities at the end of every month.

Annex 5. Registration from large-scale treatment

Name of community:_____	Date of large-scale treatment (dd/mm/yyyy) : ___/____/____
District:_____	Region/province_____

No.	Name	Age (years)	Sex (M/F)	Skin lesion (Yes/No)	Treatment given		Comments (including absences, refusal to take medicines, alternative treatment given, any side-effects)
					Syrup	Tablets	
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

Annex 6. Summary of large-scale treatment for years

Form A. Village- or community-based treatment

No	Name of village/household	Total population (based on the last census) = A	Population seen and treated (eligible population) = B		Coverage (B/A) x 100	Active suspected clinical cases found (aged 0-15 years)	Active suspected clinical cases found (aged > 15 years)
			M	F			
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							
16							
17							
18							
19							
20							

Form B. School-based treatment

No	Name of School	Total population (based on school register) = A	Population seen and treated (eligible population) = B		Coverage (B/A) x 100	Active suspected clinical cases found (aged 0-15 years)	Active suspected clinical cases found (aged > 15 years)
			M	F			
1							
2							
3							
4							
5							
6							
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19							
20							

Annex 7. Protocol of sero-surveys in India (www.who.int/yaws)

Sero-survey under Yaws Eradication Programme

Guidelines for Medical **Officers**

Department of Parasitic Diseases
(Centre for Epidemiology and Parasitic Diseases)
National Institute of Communicable Diseases
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(Tel: 23913028, Fax: 23912961)
April 2008

Contents

1. Introduction

Yaws is a disfiguring, debilitating non-venereal treponemal infection. It is a contagious disease transmitted by direct (person-to-person) contact with an infectious yaws lesion.

The organism responsible for Yaws is *Treponema pallidum* sub-species *pertenue*. It is identical in appearance to *T.pallidum pallidum* (the organism that causes venereal syphilis). Early yaws is primarily a disease of children and adolescents in the endemic situation. Man is the only reservoir of infection. The cases of early yaws serve as the source of infection. Incubation period is 9-90 days (average 21 days). Yaws also exhibits latency. After initial yaws which lasts for few months, the infection may remain for many months to years. However, lesions which reappear within 5 years may be infectious.

Early lesions of this disease manifest in the form of skin lesions, which on healing show little scarring. The disease can be progressive wherein bone and cartilage are affected leading to disability. The disease can be cured and prevented by a single injection of long acting (benzathine benzyl) penicillin.

Yaws is amenable to eradication as it does not have any extra human reservoir of infection, organism is sensitive to a single dose of long acting penicillin and yaws infection is limited to a small pocket.

As per available records, the disease has been reported from 10 states of the country viz., Andhra Pradesh, Assam, Chhattishgarh, Gujarat, Jharkhand, Madhya Pradesh, Maharashtra, Orissa, Tamil Nadu, and Uttar Pradesh. The problem perpetuated in remote, inaccessible, hilly and forest tribal areas.

Govt. of India approved Yaws Eradication Programme as a central sector health scheme as a Pilot Project for undivided Koraput district, Orissa during the year 1996-97. Subsequently, in March 1999, the Standing Finance Committee of Government of India approved extension of the scheme to cover all the endemic states.

2. Programme objectives and strategy:

The objectives include:

2.1. Yaws Elimination

Nil reporting of early yaws cases on the basis of good quality search, supported by laboratory investigations in all endemic areas of the country and validated by independent appraisals.

2.2. Yaws Eradication

Absence of new cases for a continuous period of three years, supported by absence of evidence of transmission with sero-survey among 1-5 years children (i.e. no sero reactivity to RPR/VDRL in <5 yr children).

2.3. The Programme Strategy includes

- Manpower development,
- Case finding & treatment of cases and contacts simultaneously; &
- IEC activities harnessing multisectoral approach.

Once elimination is achieved, sero-surveillance would be initiated.

2.4. Justification for sero-survey

- Elimination by definition means absence of new/early cases, likewise, eradication means absence of evidence of transmission of infection
- Thus validation of eradication rests on the demonstration of absence of transmission in the community, through sero-surveys.
- Once infected the serological positivity persist for long time. Hence, it is possible that, due to old infection, some adult persons may be found positive for yaws infection by serological test.
- On the other hand sero-positivity in young children will reasonably indicate a recent infection as they are new entrants in the potential pool of infection. Hence, no sero-reactivity to RPR test among 1-5 years children will be indicative of absence of transmission i.e., Eradication.

3. Sero-survey under YEP:

3.1. Methodology: Selection of villages and Planning

- Cover all children of 1-5 years age-group from yaws and non-yaws villages.
- In case of non-yaws big villages (defined as having a population of >500 persons),cover two randomly selected natural segments traditionally known as tola, pada, falia, etc., from the village and collect blood samples from all children of 1-5 years in these two segments only.
- Information to the villagers about the activity specifying time of visit should be given in advance, in particular to Panchayat Raj Institutions (PRI).
- Village Health sanitation & nutrition committee should also be informed.
- Repeat the sero-surveys annually for three consecutive years.
- Sero-surveys should be carried out once a year coinciding with the two active case searches. However, any areas left un-surveyed due to any unavoidable reason/operational problems should be covered promptly at the earliest within the same year.

3.2. Sample collection and transportation

3.2.1. Collection of blood samples & processing

- Prepare the field kit as per check list(Annexure-I)
- Record details of the child as per sero- survey proforma (annexure- II)
- Collect blood sample by finger/heel prick ensuring all aseptic measures using a lancet or hypodermic needle.
- Press the finger/heel below the pricked area by applying adequate pressure to express the blood.
- Take 0.2 ml clean micro centrifuge (MC) tube (Eppendorf) containing a pinch of EDTA as anticoagulant (for carrying out RPR test, plasma sample obtained from anti-coagulated blood is required).
- Collect blood by touching the rim of the vial against the drop of blood from the punctured finger and applying pressure intermittently, till the tube is at least 3/4th full. (in case full face of the vial is put against drop of blood, it may lead to air bubble formation causing blockage of blood flow inside the vial)
- The tube should be labeled with patient's identification number (corresponding with the entry in the proforma).
- Ensure thorough mixing of the blood with EDTA by rolling/turning the tube upside down several times. This is essential failing which blood is liable to clot thereby rendering the sample unfit for testing.
- Separate plasma immediately by centrifuging at 1500-2000 rpm for 5-10 minutes to avoid haemolysis. In case of non-availability of centrifuge, allow the blood sample to stand at room temperature for 3-4 hours, the time needed for separation of plasma. Ensure that plasma is separated at the earliest.
- Separate the overlying plasma with Pasteur/ micro pipette and carry out the RPR test.
- In case it is not feasible to test the sample on the same day, store the plasma sample at 4-80C if proposed to be tested within a week or else keep at -200C or in the freezer compartment of the ordinary refrigerator for longer storage.

3.2.2. Sample Transportation:

3.2.2.1. From collection site to PHC/CHC/district laboratory:

- The MC tube containing the samples should be placed in tightly fitting tube racks/thermocol sheets.
- Ensure that specimen tube does not have cracks/leakage.
- Place some cotton or absorbent material between the tubes to ensure that they don't move or rattle during transport and put inside the vaccine carrier/thermocol box. Arrange for an adequate amount of refrigeration (minimum 3-4 ice packs will maintain refrigeration for 2-3 days) in case of delay in transportation.

- Securely fasten transport boxes in the transport vehicle; avoid excessive vibration of samples during transport as this can haemolyse samples, rendering them useless.
- The requisition slip should be placed in a plastic zip lock bag inside the vaccine carrier.

3.2.2.2. From District lab to NICD/Central Lab:

- Cover the rack containing plasma samples with a layer of cotton or any other absorbent material to ensure that there is no spillage. Place the rack in another container/plastic bag and then place in the vaccine carrier/thermocol box. Ensure triple packaging for biosafety purposes. Place ice packs below and on sides of the sample box and seal/secure the lid of the cool box. The requisition slip should be kept inside the zip locker in the transport box.
- A biohazard mark should be pasted on the visible outer surface of the cool box with 'This side up mark (↑)' clearly mentioned on it.
- Samples should be transported to the testing laboratory with prior intimation to the laboratory in-charge, ensuring that the transit period is minimal.

Note: RPR test kits should be stocked at district and distributed in such a way that the concerned PHC/CHC at any point of time has an adequate number of test kits available with them.

3.3. Sample testing by RPR test:

The RPR (Rapid Plasma Reagin) is a slide agglutination test to detect antibodies against syphilis/yaws. The test is reliable, economical, reproducible, rapid and easy to perform even under field conditions and is easily readable with naked eye. The specificity and sensitivity of the test is similar to that of VDRL test.

3.3.1. Principle of test:

RPR antigen suspension is a carbon coated non-treponemal cardiolipid antigen which detects reaginic antibodies present in serum/plasma of patients suffering from treponemal infections. Flocculation occurs in specimens containing antibodies against treponemal antigen due to co-agglutination of the carbon particles of the RPR antigen, which appear as black clumps against the white background of the card. False positive reactions (around1%) can be seen occasionally in sera of persons with other non- treponemal conditions like malaria, kala-azar, rheumatoid arthritis, tuberculosis, etc.

3.3.2. Test procedure:

Follow the instruction manual provided with the test kits. Briefly, the procedure is as follows:

- Bring all reagents as well as samples to room temperature before performing the test.
- Wear gloves before performing the test.
- The test card provided with the kit should be appropriately labeled using permanent marker.
- Positive and negative controls should be tested with each run.

- Place one drop of serum or plasma (50 µl) on the card with the help of a dropper provided with the kit for this purpose.
- After thoroughly mixing RPR antigen suspension, place one drop (15-20 µl) of the same alongside the drop of plasma on the card, using another dropper provided with the kit.
- Mix these drops well, and spread out the pool of liquid uniformly within the entire area of the circle by using the applicator stick provided with the kit. Use separate stick for each sample.
- Shake the card gently using a rotatory movement up to 5 minutes and observe for clumping under a good light source. In case a VDRL shaker is available, it can be used for shaking of the cards.
- Results should be read in comparison with those of +ve and –ve controls provided with the kit.

3.3.3. Interpretation of test results: Positive result

Black aggregates/clumps are formed within 5 minutes.

Negative result:

Absence of black aggregates/clumps at the end of 5 minutes.

3.4. Quality Control:

- All samples positive by RPR and 5% of randomly selected negative sera should be sent to NICD/designated central laboratory for cross checking by RPR and TPHA.
- Details as per sero-survey proforma and RPR test results should accompany the samples.
- Results of cross checking/QA by the central laboratory should be communicated at the earliest to the laboratories that have sent these samples.

3.5. Bio-safety measures during sample collection/transportation/ testing:

- Use clean and well lighted place for sample collection.
- Avoid crowding and make the child sit comfortably.
- Always use disposable gloves during collection and testing of blood sample and change on tearing /when soiled with blood.
- Wash hands thoroughly before and after the sample collection/testing.

- Discard the lancet and hypodermic needles after use in puncture proof containers; autoclave or handover to nearest central treatment facility (if not available, then dispose in burial pit/landfill as per the biosafety manual).
- Discard the used spirit swabs in the waste disposal bag as per guidelines.
- Transport samples following triple packaging system to ensure biosafety; wash and reuse after sterilization.
- Sample vials with residual blood/plasma to be discarde in buckets/waste disposal containers with 1% sodium hypochlorite solution.

Refer to IDSP biosafety manual for details. Also available at www.nicd.nic.in

Annexure I

Check List of kit contents during sero-survey:

- 0.2 ml EDTA microcentrifuge/eppendrof vials
- Lancets
- Spirit swabs
- Vial tray /thermocol sheets for placing the sample vials
- Needles & syringes
- 5ml screw cap vials
- Permanent water proof marker
- Vaccine carrier/ Thermocol box along with ice packs for packaging and transportation of samples.
- Waste disposal bags for used swabs
- Puncture proof container with 1% sodium hypochlorite for used needles and sharps.
- Bottle with concentrated sodium hypochlorite
- Disposable gloves
- Leucoplast/stickers
- Scissors/blade
- Medicines :
    - Paracetamol
    - ORS
    - B complex
    - Albendazole
    - Perinorm (Metoclopramide)
    - Cetrizine
    - Iron & Folic acid
    - Dressing material
    - Betadine lotion
    - Benzyl benzoate
- Anti-septic solution/ soap
- Hand towels/Tissue paper roll
- Proforma for sero-survey

Annexure-II

Performa for Sero-survey under YEP

Date of Sample Collection: _____

Village_____

PHC_____ Block_____District: _____

Population of Village: _____

Population of 1-5 year old children_____

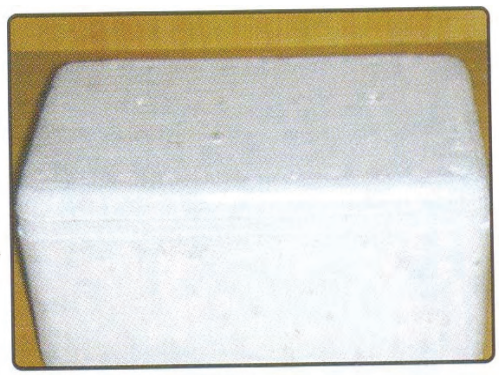
(As per available record)

S. No	Name	Age /sex	Father/ Head of the Family	RPR test result	Remarks

Annexure-III

Materials for Sample Collection & Transportation

Disposable Sterile Gloves



Thermocol Box

Ice Pack

Microcetrifuge (MC) Tube

Vaccine Carrier

Ziploc Bag

Cryo-vial Box

Lancets

Microcentrifuge vial tray

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World Health Organization
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http://www.who.int/yaws/en

WHO/HTM/NTD/IDM/2012.2