



# TARGET PRODUCT PROFILE

for the detection of a case  
of **yaws** and the detection of  
azithromycin resistance





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World Health  
Organization

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# Contents

Acknowledgements	iv
1. Epidemiology	1
2. Public health response	1
3. Available diagnostic tools	1
4. WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases	2
5. Purpose of the Target product profile (TPP)	2
6. Audiences engaged and external consultations to develop the TPP	2
References	3
Use case needs statements	4
Identify a single case of yaws	5
Azithromycin resistance	10

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Yaws is a bacterial infection that is found across the tropics. More than 80 countries/territories are known to have previously reported or currently report cases of yaws.

## 1. Epidemiology

Yaws is caused by infection with *Treponema pallidum* subsp. *pertenue*. The disease is now predominantly reported in West and Central Africa and the Pacific but has previously been endemic throughout the tropics (1, 2). Most cases of yaws are found in children. Transmission is believed to occur through skin-to-skin contact with infectious lesions of primary yaws. *T.p.* subsp. *pertenue* is closely related to *T.p.* subsp. *Pallidum*, the causative agent of syphilis, but unlike the latter is not transmitted through sexual contact or from mother to the developing fetus during pregnancy.

The clinical course of yaws starts with primary yaws, characterized by a single infectious lesion. If the individual is untreated, the initial lesion will heal but the infection will continue. This asymptomatic state is called latent yaws. The individual may then progress to develop secondary yaws, during which time new infectious lesions occur. The patient may alternate between asymptomatic latent yaws and further episodes of secondary yaws for several years. If the patient remains untreated for a long time (> 5–10 years), tertiary yaws may develop. The lesions of tertiary yaws are destructive and disfiguring but not infectious.

## 2. Public health response

Yaws has been targeted for eradication since the mid-20th century. Previous efforts focused on the use of mass or targeted treatment with penicillin. Although these efforts reduced the prevalence of yaws by > 90%, they were ultimately not successful at achieving eradication (1). In 2012, WHO launched a new strategy – the Morges strategy – based on mass treatment with azithromycin (3). Central to this strategy is the identification of all endemic communities, followed by community mass treatment. Small-scale pilot projects of this strategy have been implemented in several settings.

Once the number of yaws cases has fallen, ongoing case-finding and treatment is required to identify and treat remaining cases and their close contacts. Once no further cases of yaws are detected, the programme switches to surveillance, including serological surveillance of children aged < 5 years (4).

As the aim of the programme is eradication, detection of single cases is important. This detection occurs in two scenarios: (i) deciding whether to initiate a programme – in this setting, finding a single yaws case is sufficient to declare a community endemic and needing treatment; and (ii) surveillance after mass treatment – in this setting, it is important to exclude that even a single suspected case is truly yaws and therefore that interventions can stop.

A major concern has been the identification of a small number of cases of yaws in whom resistance to azithromycin has developed (5). Two mutations are known to confer resistance to azithromycin. Detection of phenotypic resistance is complicated by the inability to routinely culture *T. pallidum*, and therefore the focus of resistance detection is to identify (a) cases of clinical treatment failure, and (b) known mutations associated with resistance to azithromycin.

The new road map for neglected tropical diseases 2021–2030 has set a target of yaws eradication by 2030 (6).

## 3. Available diagnostic tools

To date, clinical examination combined with serological tests are the mainstay of yaws diagnosis. Serological tests can be performed either in a laboratory or in the field through lateral flow assays. Molecular diagnostic tests including polymerase chain reaction are commonly used in research and increasingly within programmes.

## 4. WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases

WHO's Department of Control of Neglected Tropical Diseases manages a diverse portfolio of 20 diseases and disease groups, each with its own unique epidemiological and diagnostic challenges. At its 12th meeting (Geneva, 29–30 April 2019), the Strategic and Technical Advisory Group (STAG), the principal advisory group to WHO on the control, elimination and eradication of NTDs, decided to establish a single WHO working group to ensure use of a unified approach to identify and prioritize diagnostic needs, and to inform WHO strategies and guidance on the subject (7).

At its inaugural meeting (Geneva, 30–31 October 2019), the Diagnostic Technical Advisory Group for Neglected Tropical Diseases (DTAG) discussed priorities for the year ahead as well as how to manage the complexity of supporting the diagnostics agenda across the entirety of WHO's NTD portfolio. Recommendations were made, based on the understanding that they would be reviewed at the next meeting, as it had been made clear that all NTDs had diagnostic needs that would have to be addressed in due course.

One of the recommendations was to prepare target product profiles (TPPs) for diagnostics to support emerging yaws control programmes.

## 5. Purpose of the TPP

The purpose of this TPP is to lead to development of new diagnostic tools for “detection of a case of yaws” and “detection of an azithromycin-resistant case of yaws”.

For detection of a case of yaws, the tool or tools must be able to detect a single case of active yaws infection.

For detection of a case of azithromycin resistant yaws, the tool or tools must be able to detect mutations known to be associated with azithromycin resistance in yaws.

## 6. Audiences engaged and external consultations to develop the TPP

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