Report of the third WHO stakeholders meeting on gambiense human African trypanosomiasis elimination

Geneva, Switzerland
18–20 April 2018
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Abbreviations and acronyms

CATT  card agglutination test for trypanosomiasis
CIRAD  Centre de coopération internationale en recherche agronomique pour le développement (Agricultural Research Centre for International Development)
CIRDES  Centre International de Recherche-Développement sur l’Élevage en zone Subhumide (International Centre for Research and Development of Livestock in the subhumid zone)
COCTU  Coordinating Office for Control of Trypanosomiasis in Uganda
CSF  cerebrospinal fluid
DiTECT-HAT  diagnostic tools for human African trypanosomiasis elimination and clinical trials
DNDi  Drugs for Neglected Diseases initiative
FAO  Food and Agriculture Organization of the United Nations
FIND  Foundation for Innovative New Diagnostics
GE Healthcare  General Electric Healthcare
HAT  human African trypanosomiasis
HAT-e-TAG  Technical Advisory Group for HAT elimination
HAT MEPP  HAT Modelling and Economic Predictions for Policy
IAEA  International Atomic Energy Agency
INRB  Institut National de Recherche Biomédicale (National Institute for Biomedical Research)
IPR  L’Institut Pierre Richet
IRD  Institut de Recherche pour le Développement (National Research Institute for Development)
ITM  Institute of Tropical Medicine of Antwerp
LAMP  loop-mediated isothermal amplification
LSTM  Liverpool School of Tropical Medicine
mAECT  mini anion exchange centrifugation technique
MSF  Médecins Sans Frontières (Doctors Without Borders)
NECT  nifurtimox–eflornithine combination therapy
PAAT  Programme Against African Trypanosomiasis
PATTEC  Pan-African Tsetse and Trypanosomiasis Eradication Campaign
PNETHA  Programme National d’élimination de la trypanosomiasis humaine africaine (national HAT elimination programme)
PNLTHA  Programme National de lutte contre la trypanosomiasis humaine africaine (national HAT control programme)
RDT  rapid diagnostic test
SSNCP  sleeping sickness national control programme (PNLTHA in French)
WBC  white blood cell
WHO  World Health Organization
# 1 Introduction

Since 2000, concerted efforts by national programmes, supported by public–private partnerships, nongovernmental organizations, donors and academia under the auspices and coordination of the World Health Organization (WHO), have produced important achievements in the control of human African trypanosomiasis (HAT). As a consequence, the disease was listed as a neglected tropical disease targeted for elimination as a public health problem by 2020. The Sixty-sixth World Health Assembly endorsed this goal in resolution WHA66.12 on neglected tropical diseases, adopted in 2013.

National sleeping sickness control programmes (NSSCPs) are core to progressing control of the disease and in adapting to the different epidemiological situations. The support and trust of long-term donors has been crucial for these achievements. The 16 years of partnership among WHO, Sanofi and Bayer have enabled WHO to strengthen and sustain financial, technical and material support for the implementation of control activities in countries where HAT is endemic. The long-term support from the Government of Belgium in the Democratic Republic of the Congo has also been essential. Other donors have committed themselves to sustaining the elimination effort.

WHO has now convened three stakeholders meetings on the elimination of gambiense HAT (g-HAT). During the two previous meetings in 2014\(^1\),\(^2\) and 2016\(^3\), commitment for HAT elimination was reinforced and structured mechanisms of collaboration were established in the network for g-HAT elimination. The network includes NSSCPs, groups developing new tools, international and nongovernmental organizations involved in disease control and donors. Meetings of the network are held biennially, and several specific working groups meet at other times to address the various aspects of elimination. A similar but simpler structure exists for rhodesiense HAT (r-HAT)\(^4\),\(^5\),\(^6\).

The third meeting of national programme coordinators and stakeholders discussed how to strengthen activities to achieve the elimination of HAT as a public health problem by 2020, how to achieve sustainable elimination of g-HAT by 2030 given the current challenges and how to renew commitment among stakeholders in order to plan beyond 2020.

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2 Meeting objectives

The objectives of the meeting were:

- to keep up the commitment of national authorities and technical and financial partners to WHO’s objectives for g-HAT;
- to review progress towards the elimination of HAT and share achievements, challenges and perspectives on the goal of elimination as a public health problem and beyond among countries and implementing partners;
- to discuss strategies for reinforcing control and surveillance of g-HAT;
- to assess the status of critical technical aspects in research, development and implementation of therapeutic and diagnostic tools, epidemiology and vector control; and
- to sustain and strengthen the network for collaboration and coordination among stakeholders.

3 Opening remarks

Dr Gautam Biswas, Acting Director, WHO Department of Control of Neglected Tropical Diseases, opened the meeting by thanking the various partners present for their commitment to fighting HAT. He recalled the significant progress that has been made towards eliminating HAT as a public health problem. He noted that some countries are eligible for validation of elimination while others still require additional efforts to reach the elimination goals. He stressed the challenges of the elimination process and the post-validation period. WHO’s new leadership is focused on the Sustainable Development Goals, including universal health coverage, and the elimination of HAT will contribute to achieving these goals.

Dr Didier Bakajika, on behalf of Dr Magda Robalo, Director, Communicable Diseases and Surveillance, WHO Regional Office for Africa, emphasized the importance of the meeting in creating and advancing solutions towards the elimination of HAT as a public health problem. He recalled the high-level commitment of African States to the Pan-African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC), as well as all the efforts made regionally to adopt HAT control strategies. Despite the important progress achieved, persistent challenges remain, including endemic foci that are difficult to access and inadequate financial and human resources for good coordination.

The meeting was chaired by Professor Michael Barrett, University of Glasgow. The meeting agenda is attached as Annex 1 and the list of participants as Annex 2.
4 Progress towards the elimination of gambiense human African trypanosomiasis

In 2012, WHO established the goal to eliminate HAT (g-HAT and r-HAT) as a public health problem by 2020. Beyond that, the goal for g-HAT is to interrupt transmission (sustainable elimination) by 2030.

The primary indicators are:
- the number of cases reported per year; and
- the area at risk reporting < 1 case/10,000 people per year.

The HAT elimination Technical Advisory Group (HAT-e-TAG) refined the original primary indicator of “number of foci reporting < 1 case/10,000 people per year” to “area at risk reporting < 1 case/10,000 people per year”. Foci are not objectively measurable, whereas the area at risk of HAT can be better measured in a standardized way.

The secondary indicators are to assess other aspects including the quality and intensity of activities, namely:
- the geographical extent of the disease;
- the populations at different levels of risk; and
- the proportion of the population at risk covered by control and surveillance.

4.1 Reported cases

The number of HAT cases reported annually reduced significantly from 26,872 in 2001 to 2,164 cases in 2016 (Figure 1). In 2017, for the first time, fewer than 2,000 cases were reported (the data for 2017 were under validation at the time of this meeting), most of which (98%) were g-HAT (r-HAT 2%).

Importantly, the sustained decrease in the numbers of reported cases is not a consequence of decreasing surveillance activities: rather, the numbers of people screened have been maintained at high levels (Figure 2). The numbers of health facilities with capacity to screen, diagnose and treat HAT have increased annually, improving access to diagnosis and treatment (see section 4.5).

It is considered therefore that such a decrease reflects the reality of transmission in the field that results from sustained active and passive screening in the g-HAT endemic countries.
The WHO road map on neglected tropical diseases (2012) set a benchmark for the elimination of HAT, with targets for the annual numbers of reported cases until 2020. In 2012 and 2013, higher numbers of cases were reported than the milestone figures. This increase was mainly due to the improvement of
security in Oriental Province (Democratic Republic of the Congo) and in the Ouham focus (Central African Republic), facilitating access to areas that had not been visited for some years, and to the detection of cumulated cases that had been infected for several years. At the same time, the case definition used in remote areas of Oriental Province was discordant with that used by the national programme of the Democratic Republic of the Congo (PNLTHA-RDC), producing a considerable over diagnosis of cases; however, the numbers of cases reported annually from 2014 onwards were well below the milestone figures (Figure 2).

### 4.2 Geographical distribution of cases

In 2016–2017, cases of HAT were reported from 17 endemic countries: Angola, Cameroon, Central African Republic, Chad, Côte d’Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Guinea, Malawi, Nigeria, Republic of the Congo, South Sudan, Uganda, United Republic of Tanzania, Zambia and Zimbabwe (Figure 3). Most (80%) cases were diagnosed in the Democratic Republic of the Congo.

**Figure 3.** Distribution of cases in HAT-endemic countries, 2016–2017

Cases of HAT have been mapped at the village level since 2000, with a total of 210 226 cases included in the HAT Atlas database up to 2016. The locations of active screening activities (with or without cases detected) are also included.

Figure 4 shows the distribution of cases cumulated by 5-year periods (2002–2006, 2007–2011, 2012–2016). The evolution of the distribution shows a progressive reduction in those areas presenting cases; the emergence of cases in new areas is extremely rare.
In West Africa, transmission of HAT continues in Guinea and Côte d’Ivoire. The marked decrease in the number of reported cases during 2014–2015 in Guinea reflects the reduction in case-finding activities during the outbreak of Ebola virus disease; however, case numbers increased as routine control and surveillance activities resumed in 2016.

In Benin, Ghana, Mali, Nigeria and Togo, no cases were detected, despite the operational surveillance system based on sentinel sites; however, an exported case from Nigeria was detected in the United Kingdom. In Guinea-Bissau, an assessment of the epidemiological situation was carried out and no cases were detected; however, the establishment of a surveillance system is recommended, as conditions for HAT transmission are present.
In Central Africa, the number of reported cases in Cameroon, Chad, Congo, Equatorial Guinea and Gabon shows a decreasing trend. As active and passive screening is ongoing in the transmission areas, the number of reported cases is believed to reflect the real disease trend. In the Central African Republic, the same trend is observed but its progression must be considered carefully as active screening activities have been weak due to security constraints.

In Uganda, the downward trend in the number of g-HAT cases continued, in a context of reinforced passive surveillance. Nevertheless, an important influx of refugees from South Sudan in the West Nile Region could represent an increased risk of HAT re-introduction.

In South Sudan, the number of reported cases has reduced dramatically, but the figures must be interpreted with caution because of the declining intensity of surveillance activities.

In Angola, there was a marked decreasing trend in the number of reported cases, but in the past 2 years active screening has been significantly weaker than before. The Democratic Republic of the Congo remains the country with the highest burden of the disease, but the number of reported cases continues to decrease steadily.

### 4.3 Population at risk

Both the population and the area at risk of HAT are assessed using geographical information systems (GIS) technology to collect and exploit consistent, comprehensive data on all reported HAT cases, including their geographical location at village level. The data have been maintained by WHO in collaboration with the Food and Agriculture Organization of the United Nations (FAO) since 2000.

The definition of HAT risk ($R$) is based on two variables:

- $D =$ average annual disease intensity; and
- $P =$ average annual population intensity.

Intensity surface $D$ is estimated through the “spatial smoothing” technique, using a search radius of 30 km. $P$ is obtained through commercially available population data by pixel.

Risk is defined as $D/P$ and is expressed in five different categories: very high, high, moderate, low, very low and marginal (Figure 5).

**Figure 5. Categories of population at risk of g-HAT**

<table>
<thead>
<tr>
<th>Category</th>
<th>$R = D/P$</th>
<th>HAT cases per annum</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high</td>
<td>$R &gt; 10^{-2}$</td>
<td>$\geq 1$ per $10^2$ people</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>$10^{-3} &lt; R &lt; 10^{-2}$</td>
<td>$\geq 1$ per $10^3$ people AND $&lt; 1$ per $10^2$ people</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>$10^{-4} &lt; R &lt; 10^{-3}$</td>
<td>$\geq 1$ per $10^4$ people AND $&lt; 1$ per $10^3$ people</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>$10^{-5} &lt; R &lt; 10^{-4}$</td>
<td>$\geq 1$ per $10^5$ people AND $&lt; 1$ per $10^4$ people</td>
<td></td>
</tr>
<tr>
<td>Very low</td>
<td>$10^{-6} &lt; R &lt; 10^{-5}$</td>
<td>$\geq 1$ per $10^6$ people AND $&lt; 1$ per $10^5$ people</td>
<td></td>
</tr>
<tr>
<td>Marginal</td>
<td>$R &lt; 10^{-6}$</td>
<td>$&lt; 1$ per $10^6$ people</td>
<td></td>
</tr>
</tbody>
</table>

During 2012–2016, some 53.1 million people at continental level were estimated to be at risk of infection: 0.75 million were at very high and high risk, and 7.49 million at moderate risk. Therefore,
8.24 million people lived in areas where g-HAT is still considered a public health problem. Compared with the former 5-year periods, substantial numbers of people have shifted from higher risk to lower risk categories. The number of people exposed to very high, high and moderate risk decreased by 7 million from 2010 to 2016. The most dramatic reduction was in the very high and high-risk category, which in the 12-year period from 2004 to 2016 decreased by 87%, from 5.66 million to 0.75 million people (Figure 6).


![Population at risk of g-HAT, by level of risk](image)

4.4 Area at risk

Figure 7 shows the total area at risk reporting ≥ 1 case/10 000 people per year – a primary indicator for the 2020 goal – and the associated milestones for 2000–2016 (g-HAT in red, r-HAT in blue). The area in all risk categories showed a marked and steady reduction, especially the areas at high and very high risk.

Figure 7. Total area at risk (very high, high and moderate) for g-HAT (red) and r-HAT (blue) reporting ≥ 1 case/10 000 people per year, 2000–2016; the green line is the set milestone

![Total area at risk](image)

TBG: Trypanosoma brucei gambiense; TBR: Trypanosoma brucei rhodesiense

Figure 8 shows the area at risk of HAT (number of cases/inhabitants per year) by risk categories (very high, high, moderate, low, very low) cumulated by 5-year periods (2012–2016).
4.5 Coverage of the population at risk

The numbers of health facilities with capacity to screen, diagnose and treat HAT have increased annually, thereby improving access to diagnosis and treatment. In 2017, some 1246 fixed health facilities provided diagnosis of HAT (with at least one method, including clinical and laboratory methods) and 642 fixed health facilities provided any treatment for HAT (253 nifurtimox–eflornithine combination therapy (NECT) than in 2013 (732 fixed health facilities provided diagnosis and 530 fixed health facilities provided treatment for HAT (180 NECT)). Compared with the February 2016 survey, the number of health facilities providing diagnosis increased by 41% and those providing treatment increased by 24%.

Table 1 lists the number of health facilities providing diagnosis and treatment in 2017, by country.

Table 1. Health facilities providing g-HAT diagnosis and treatment in 2017, and Δ(delta) compared with the February 2016 survey, by country

<table>
<thead>
<tr>
<th>Country</th>
<th>DxC</th>
<th>DxS</th>
<th>DxP</th>
<th>DxPh</th>
<th>Total Dx</th>
<th>Δ</th>
<th>Tx1P</th>
<th>Tx2M</th>
<th>Tx2E</th>
<th>Tx2N</th>
<th>Total Tx</th>
<th>Δ</th>
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<td>Burkina Faso</td>
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<td>1</td>
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<tr>
<td>Total</td>
<td>1,242</td>
<td>1,049</td>
<td>354</td>
<td>272</td>
<td>1,246</td>
<td>364</td>
<td>640</td>
<td>83</td>
<td>205</td>
<td>253</td>
<td>642</td>
<td>126</td>
</tr>
</tbody>
</table>

CAR: Central African Republic; DRC: Democratic Republic of the Congo
DxC: clinical  DxS: serological  DxP: parasitological  DxPh: disease staging
Tx1P: 1st stage – pentamidine  Tx2M: 2nd stage – melasoprol  Tx2E: 2nd stage – eflornithine  Tx2N: 2nd stage – NECT
In 2016, 47% of the population at very high and high risk of g-HAT lived less than 1 hour away from a health facility capable of diagnosis (92% < 5 h away); 42% of the population at moderate risk lived less than 1 hour away (87% < 5 h) and 45% of the population at low and very low risk lived less than 1 hour (86% < 5 h), while 44% of the total population at risk lived less than 1 hour (86% < 5 h) away from a facility that provides treatment.

The number of people actively screened each year was maintained at high levels (Figure 2, section 4.1).

4.6 Challenges for elimination

The following challenges for elimination of HAT as a public health problem were discussed:

- the lack of a peaceful context and sociopolitical stability in which to develop control and surveillance activities (e.g. Central African Republic, Democratic Republic of the Congo (Kasai), South Sudan);
- the sustainable integration of control and surveillance activities in the context of weak general health services, unskilled staff, lack of resources and low attendance rates;
- the insufficient ownership by and commitment of national authorities in endemic countries to elimination;
- the progressive loss of expertise in NSSCPs, with lack of replacement;
- the importance of coordination among stakeholders with different agendas to avoid overlap and disruption of sustainable elimination;
- the fact that while access to treatment is guaranteed, access to screening and diagnostic tools must be ensured for the population at risk; the lack of funding mechanisms to support availability of diagnostic tools is worrisome; and
- the funding available to implement HAT elimination activities, which is far from sufficient.

Two questions must be addressed: (i) how can the engagement of national authorities and stakeholders be maintained beyond 2020? and (ii) how can the funding required to advance the elimination of HAT transmission be ensured until 2030?

The following technical aspects require special consideration:

- the need for better and simpler confirmatory tests and better performing screening tools;
- the need to estimate the proportion and location of undetected cases;
- the epidemiological role of asymptomatic human carriers and animal reservoirs in maintaining transmission and re-emergence of g-HAT;
- the need for surveillance tools for the elimination of HAT in order to detect the reemergence or reintroduction of the disease (sustainability); and
- the need for monitoring tools for the elimination of HAT as zero transmission.
5 Country status reports

The heads of g-HAT control programmes from endemic countries had convened their annual country coordination meeting before the stakeholders meeting in order to review the situation by country, identify weaknesses and gaps and prepare national action plans for the 12 months ahead.

The situation was presented by the representatives of national HAT programmes at the stakeholders meeting in four regional groups of countries, namely: West Africa, Central Africa, East Africa and the Democratic Republic of the Congo as a standalone country.

5.1 West Africa

The West Africa group included eight countries: Benin, Burkina Faso, Côte d'Ivoire, Ghana, Guinea, Mali, Nigeria and Togo. These countries can be grouped according to their surveillance activities as:

- countries without surveillance and information: Liberia, Guinea Bissau;
- countries without surveillance but occasional assessment activities: Gambia, Niger, Senegal and Sierra Leone;
- countries that have moved from active surveillance to passive surveillance: Benin, Burkina Faso, Ghana, Mali, Nigeria and Togo; and
- countries conducting both active and passive surveillance: Côte d'Ivoire and Guinea.

Guinea has the biggest HAT burden in this group, and therefore leads the trend in the region (Figures 9–10). The Ebola virus disease epidemic forced the complete interruption of HAT surveillance and control in Guinea and impeded access to diagnosis and treatment at that time. Consequently, the number of reported cases decreased in 2014 and 2015. The resumption of active screening led to an increase in the number of cases detected in 2016 and 2017. Côte d’Ivoire continues to report a low number of cases. In Nigeria, cases are occasionally reported despite limited surveillance. Active and passive screening activities, as well as information on treatment, are shown in Tables 2–4 cumulatively for the West Africa region.

Figure 9. Distribution of g-HAT cases in the West Africa region, 2012–2016
Table 2. Surveillance with active screening in the West Africa region, 2013–2017

<table>
<thead>
<tr>
<th>Active screening</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of countries</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>People screened</td>
<td>20867</td>
<td>7204</td>
<td>9606</td>
<td>10976</td>
<td>25419</td>
</tr>
<tr>
<td>Cases detected</td>
<td>50</td>
<td>0</td>
<td>0</td>
<td>67</td>
<td>93</td>
</tr>
</tbody>
</table>

Table 3. Surveillance with passive screening in the West Africa region, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of functioning centres</td>
<td>74</td>
<td>74</td>
<td>72</td>
<td>165</td>
<td>179</td>
</tr>
<tr>
<td>Cases detected</td>
<td>37</td>
<td>39</td>
<td>33</td>
<td>40</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 4. Number of treatment sites and cases treated in the West Africa region, 2013–2017

<table>
<thead>
<tr>
<th>Treatment of cases</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treatment sites</td>
<td>9</td>
<td>9</td>
<td>7</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Cases detected</td>
<td>85</td>
<td>39</td>
<td>33</td>
<td>104</td>
<td>143</td>
</tr>
<tr>
<td>(% of detected cases)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 5 categorizes the eligibility of the g-HAT endemic countries in the West Africa region to request validation of the elimination of HAT as a public health problem, according to national indicators and control and surveillance activities. Five countries are eligible to request validation (shown in green) and are encouraged to prepare the dossier and enter the validation process.
Table 5. Eligibility to claim validation of HAT elimination, according to the epidemiological situation and control and surveillance activities in the West Africa region, as of 2017

<table>
<thead>
<tr>
<th>Two criteria</th>
<th>Epidemiological situation (National Indicator for Elimination)</th>
<th>Activities of control and surveillance</th>
<th>Eligible for claiming the validation</th>
<th>Need for reinforce the surveillance before claiming the validation</th>
<th>Non eligible for the validation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 case / 10,000 persons / year, per health district, averaged over the previous 5-year period</td>
<td>True in all districts</td>
<td>Not true in one or more districts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>adequate</td>
<td>Benin, Burkina Faso, Cote d'Ivoire, Ghana, Togo</td>
<td>Guinea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>insufficient</td>
<td>Mali, Nigeria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>Liberia, Gambia, Niger, Sierra Leone, Senegal, Guinea Bissau</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For vector control, the following strategies are used in West Africa:
- basic entomological surveys;
- insecticides treated targets; and
- community awareness campaigns.

The working group of West African countries pointed out the following difficulties:
- lack of awareness of HAT by young clinicians;
- lack of motivation of actors;
- abandonment of HAT screening activities due to epidemics (Ebola virus disease, Lassa fever, epidemic meningitis);
- mistrust of health workers by the population;
- delays in case management and transport to treatment centres;
- insufficient financial, logistical and human resources; and
- vector control in some countries only in the context of research.

5.2 Central Africa

The Central Africa group comprised seven countries: Angola, Cameroon, Central African Republic, Chad, Equatorial Guinea, Gabon and the Republic of the Congo (see section 5.4 for the Democratic Republic of the Congo).

Active screening activities are routinely carried out but have been reduced in some countries (Angola); the system of passive case detection has been reinforced in most countries (Cameroon, Chad, Equatorial Guinea, Gabon, Republic of the Congo).

Overall, the numbers of cases in this region have decreased significantly from 2137 cases in 2008 to 145 cases in 2017 (Figures 11–12).
This decreasing trend is seen in all the countries of the region; however, in the Central African Republic it must be interpreted carefully as active screening activities have been erratic and even stopped in the Haut Mbomou and Ouham prefectures due to security constraints.

**Figure 11.** Distribution of g-HAT cases in the Central Africa region, 2012–2016

![Map of Central Africa region showing distribution of g-HAT cases](image)

RCA, République centrafricaine (Central African Republic)

**Figure 12.** Numbers of g-HAT cases declared by countries in the Central Africa region (excluding the Democratic Republic of the Congo), 2008–2017

![Graph showing number of g-HAT cases](image)

Tables 6–8 summarize active and passive screening activities as well as information on treatment for the Central Africa region (excluding the Democratic Republic of the Congo) from 2013 to 2017.
Table 6. Surveillance with active screening in the Central Africa region, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of countries</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>People screened</td>
<td>197,994</td>
<td>103,008</td>
<td>111,388</td>
<td>83,149</td>
<td>117,064</td>
</tr>
<tr>
<td>Detected cases</td>
<td>174</td>
<td>232</td>
<td>171</td>
<td>121</td>
<td>71</td>
</tr>
</tbody>
</table>

Table 7. Surveillance with passive screening in the Central Africa region, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of functioning centers</td>
<td>39</td>
<td>47</td>
<td>58</td>
<td>137</td>
<td>211</td>
</tr>
<tr>
<td>Detected cases</td>
<td>194</td>
<td>131</td>
<td>101</td>
<td>117</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 8. Number of treatment sites and cases treated in the Central Africa region, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treatment sites</td>
<td>35</td>
<td>35</td>
<td>38</td>
<td>39</td>
<td>87</td>
</tr>
<tr>
<td>Cases detected</td>
<td>360</td>
<td>359</td>
<td>298</td>
<td>233</td>
<td>142</td>
</tr>
<tr>
<td>(% of detected cases)</td>
<td>100%</td>
<td>98%</td>
<td>100%</td>
<td>100%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Table 9 categorizes the eligibility of the g-HAT endemic countries in the Central Africa region to request validation of the elimination of HAT as a public health problem, according to national indicators and control and surveillance activities. No country in the region was eligible to request validation of elimination in 2018.

Table 9. Eligibility to claim validation of HAT elimination, according to the epidemiological situation and control and surveillance activities in the Central Africa region (excluding the Democratic Republic of the Congo), as of 2017

<table>
<thead>
<tr>
<th>Activities of control and surveillance</th>
<th>Epidemiological situation (National Indicator for Elimination)</th>
<th>Two criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 case / 10,000 persons / year, per health district, averaged over the previous 5-year period</td>
<td></td>
</tr>
<tr>
<td>adequate</td>
<td>True in all districts</td>
<td>Not true in one or more districts</td>
</tr>
<tr>
<td>insufficient</td>
<td></td>
<td>Angola, Tchad, Congo</td>
</tr>
<tr>
<td>absent</td>
<td></td>
<td>Gabon, CAR, Cameroon, Equatorial Guinea</td>
</tr>
</tbody>
</table>

CAR: Central African Republic
For vector control, three of the seven countries perform activities (Angola, Gabon and Chad) using the following strategies:

- insecticide-treated targets (Angola, Gabon, Chad);
- traditional traps (Angola);
- ground spraying (Angola, Gabon); and
- involvement of the populations and awareness campaigns.

The working group of Central African countries identified the following difficulties:

- difficult access in insecure areas;
- underfunding, lack of logistical means, materials;
- low level of awareness among professionals and communities about HAT;
- shortage of skilled staff (retired or inexperienced);
- frequent transfer of trained laboratory technicians;
- refusal of patients to travel to treatment facilities;
- little involvement of traditional healers to raise suspicion and to refer patients;
- treatment costs in some countries;
- lack of expertise in vector control at country level;
- lack of partners for vector control;
- low ownership of HAT control activities by states; and
- delayed distribution of allocated funds.

### 5.3 East Africa

The East Africa group included two countries: South Sudan and Uganda. Figure 13 shows the distribution of reported cases in 2012–2016.

**Figure 13.** Distribution of g-HAT (red) in South Sudan and Uganda and of r-HAT (blue) cases in Uganda, 2012–2016
In both countries the number of reported cases has decreased considerably from 123 cases in 2013 to 12 cases in 2017 (Figure 14).

The decreasing trend in the number of cases in South Sudan, with only 10 reported cases in 2017, must be interpreted carefully as capacities for case detection have deteriorated. In South Sudan, HAT-endemic areas are highly insecure. There has been displacement of residents to refugee settlements across the borders with neighboring countries, and displacement also of non-residents into endemic areas. There are long distances between facilities with capacity for rapid diagnostic testing and those with confirmatory diagnostic services and treatment.

In South Sudan, there are no vector control activities. In Uganda, insecticide-treated tiny targets have been deployed as a vector control strategy along rivers and streams in Amuru, Arua, Koboko, Maracha, Moyo and Yumbe (by the Liverpool School of Tropical Medicine). Despite improved cross-border coordination, there is a lack of joint vector control activities.

Activities in both countries are especially hampered by insecurity and lack of funding. There is a shortage of skilled staff (retired, displaced or inexperienced). Poor remuneration is leading to high staff turnover. The level of awareness about HAT among professionals and communities is low, also in newly opened facilities in refugee settlements. There is reluctance among serologically positive suspects to do regular follow-up. Only a few treatment centres are operational. Population movements are hampering treatment provision and post-treatment follow-up. The refugee population, especially men, is not always stationary.

**Figure 14.** Numbers of g-HAT cases declared by South Sudan and Uganda, 2008–2017

Tables 10–12 summarize active and passive screening activities as well as information on treatment for South Sudan and Uganda from 2013 to 2017.
### Table 10. Surveillance with active screening in South Sudan and Uganda, 2013–2017

<table>
<thead>
<tr>
<th>Active screening</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of countries</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>People screened</td>
<td>18,575</td>
<td>0</td>
<td>13,668</td>
<td>10,993</td>
<td>13,359</td>
</tr>
<tr>
<td>Cases detected</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 11. Surveillance with passive screening in South Sudan and Uganda, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of functioning centers</td>
<td>91</td>
<td>218</td>
<td>131</td>
<td>305</td>
<td>189</td>
</tr>
<tr>
<td>Population screened</td>
<td>4,514</td>
<td>11,847</td>
<td>6,372</td>
<td>17,480</td>
<td>11,580</td>
</tr>
<tr>
<td>Cases detected</td>
<td>123</td>
<td>61</td>
<td>32</td>
<td>26</td>
<td>12</td>
</tr>
</tbody>
</table>

### Table 12. Number of treatment sites and cases treated in South Sudan and Uganda, 2013–2017

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treatment sites</td>
<td>12</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Cases treated</td>
<td>129</td>
<td>72</td>
<td>30</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>Case treated / cases detected (%)</td>
<td>97</td>
<td>99</td>
<td>87</td>
<td>97</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 13 shows the indicators for the elimination of HAT as a public health problem in South Sudan and Uganda, by health district. All districts should have an annual average of < 1 case/10,000 people during the previous 5 years (last column), to be eligible for validation of elimination as a public health problem. Uganda has reached this target.

Table 14 categorizes the eligibility of South Sudan and Uganda to request validation of elimination as a public health problem, according to national indicators and control and surveillance activities. Uganda needs to reinforce activities before being able to claim validation. South Sudan is non-eligible on both counts (number of cases and control and surveillance activities).

### Table 13. Elimination indicator by health district in South Sudan and Uganda; for elimination, all districts should have an average of < 1 case/10,000 people during the previous 5 years

<table>
<thead>
<tr>
<th>Countries</th>
<th>Total Number of Cases</th>
<th>Annual mean of cases</th>
<th>Mean Population</th>
<th>n/10000/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Sudan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yei</td>
<td>32</td>
<td>6.6</td>
<td>288,172</td>
<td>0.2</td>
</tr>
<tr>
<td>Juba</td>
<td>1</td>
<td>1.2</td>
<td>525,953</td>
<td>0.0</td>
</tr>
<tr>
<td>Kajo Keji</td>
<td>15</td>
<td>3.2</td>
<td>280,299</td>
<td>0.1</td>
</tr>
<tr>
<td>Mundri-Lui</td>
<td>56</td>
<td>11.2</td>
<td>44,179</td>
<td>2.5</td>
</tr>
<tr>
<td>Maridi</td>
<td>6</td>
<td>1.2</td>
<td>106,834</td>
<td>0.1</td>
</tr>
<tr>
<td>Yambio</td>
<td>10</td>
<td>2</td>
<td>197,603</td>
<td>0.1</td>
</tr>
<tr>
<td>Magwi</td>
<td>45</td>
<td>9</td>
<td>170,000</td>
<td>0.5</td>
</tr>
<tr>
<td>Tambura</td>
<td>26</td>
<td>5.2</td>
<td>71,490</td>
<td>0.7</td>
</tr>
<tr>
<td>Ezo</td>
<td>0</td>
<td>0</td>
<td>105,228</td>
<td>0.0</td>
</tr>
<tr>
<td>Morobo</td>
<td>9</td>
<td>1.8</td>
<td>148,023</td>
<td>0.1</td>
</tr>
<tr>
<td>Source Yubu</td>
<td>1</td>
<td>0.2</td>
<td>30,000</td>
<td>0.1</td>
</tr>
<tr>
<td>Lainya</td>
<td>20</td>
<td>4</td>
<td>127,552</td>
<td>0.3</td>
</tr>
<tr>
<td>Terekoka</td>
<td>3</td>
<td>0.6</td>
<td>206,287</td>
<td>0.0</td>
</tr>
<tr>
<td>Nagero</td>
<td>1</td>
<td>0.2</td>
<td>12,852</td>
<td>0.2</td>
</tr>
<tr>
<td>Iba</td>
<td>0</td>
<td>0</td>
<td>54,622</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Table 14. Eligibility to claim validation of elimination according to the epidemiological situation, and control and surveillance activities in South Sudan and Uganda, 2017

<table>
<thead>
<tr>
<th>Countries</th>
<th>Total Number of Cases</th>
<th>Annual mean of cases</th>
<th>Mean Population</th>
<th>n/10000/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGANDA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjumani</td>
<td>5</td>
<td>1</td>
<td>229,500</td>
<td>0.0</td>
</tr>
<tr>
<td>Arua</td>
<td>4</td>
<td>0.8</td>
<td>229,500</td>
<td>0.0</td>
</tr>
<tr>
<td>Maracha</td>
<td>0</td>
<td>0</td>
<td>840,900</td>
<td>0.0</td>
</tr>
<tr>
<td>Koboko</td>
<td>3</td>
<td>0.6</td>
<td>229,200</td>
<td>0.0</td>
</tr>
<tr>
<td>Moyo</td>
<td>8</td>
<td>1.6</td>
<td>147,600</td>
<td>0.1</td>
</tr>
<tr>
<td>Yumbe</td>
<td>5</td>
<td>1</td>
<td>652,600</td>
<td>0.0</td>
</tr>
<tr>
<td>Amuru</td>
<td>0</td>
<td>0.2</td>
<td>199,900</td>
<td>0.0</td>
</tr>
</tbody>
</table>

5.4 Democratic Republic of the Congo

The Democratic Republic of the Congo has the highest number of cases of all the endemic countries and reported 82% of all HAT cases in 2016 (1769/2163); however, in 2008–2017 the number of reported cases decreased considerably from 7326 to 1100 cases (Figures 15–16, Table 15). The level of surveillance was maintained and even reinforced in some areas. In 2017, > 2,127,000 people were actively screened by 30 mobile teams, > 437,000 people were passively screened by 514 screening sites and 167 treatment sites were functional (Tables 15–17). In areas where the prevalence had decreased significantly, surveillance sentinel sites were set up.

Figure 15. Distribution of g-HAT cases in the Democratic Republic of the Congo, 2012–2016
Figure 16. Total number of g-HAT cases declared by the Democratic Republic of the Congo, 2008–2017

Table 15. Numbers of g-HAT cases by focus (foyer) declared by the Democratic Republic of the Congo, 2013–2017

<table>
<thead>
<tr>
<th>Foyers</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coordination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>provincial THA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nbrs ZSE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T+</td>
<td>T-</td>
<td>Total</td>
<td>T+</td>
<td>T-</td>
<td>Total</td>
</tr>
<tr>
<td>Bandundu mord</td>
<td>17</td>
<td>1585</td>
<td>0</td>
<td>1585</td>
<td>1335</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bandundu sud</td>
<td>18</td>
<td>5780</td>
<td>0</td>
<td>5780</td>
<td>550</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kongo central</td>
<td>14</td>
<td>130</td>
<td>0</td>
<td>130</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kasai occidental</td>
<td>13</td>
<td>132</td>
<td>0</td>
<td>132</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kasai oriental</td>
<td>29</td>
<td>502</td>
<td>0</td>
<td>502</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katanga/Katanga</td>
<td>8</td>
<td>234</td>
<td>0</td>
<td>234</td>
<td>127</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sankuru</td>
<td>5</td>
<td>196</td>
<td>0</td>
<td>196</td>
<td>113</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinshasa</td>
<td>10</td>
<td>166</td>
<td>0</td>
<td>166</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equateur Nord</td>
<td>20</td>
<td>50</td>
<td>0</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equateur Sud</td>
<td>22</td>
<td>21</td>
<td>0</td>
<td>21</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Province orientale</td>
<td>3</td>
<td>1971</td>
<td>0</td>
<td>1971</td>
<td>535</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total DRC</td>
<td>159</td>
<td>5817</td>
<td>0</td>
<td>5817</td>
<td>3206</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 16.** Surveillance with active screening in the Democratic Republic of the Congo, 2013–2017

<table>
<thead>
<tr>
<th>Active screening</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of mobile teams</td>
<td>31</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>People screened</td>
<td>1,864,216</td>
<td>1,585,539</td>
<td>1,858,695</td>
<td>2,243,518</td>
<td>2,127,754</td>
</tr>
<tr>
<td>Cases T+</td>
<td>3,931</td>
<td>1,781</td>
<td>1,241</td>
<td>1,027</td>
<td>505</td>
</tr>
<tr>
<td>Cases T-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Detected cases</td>
<td>3,931</td>
<td>1,781</td>
<td>1,241</td>
<td>1,027</td>
<td>505</td>
</tr>
</tbody>
</table>

**Table 17.** Surveillance with passive screening in the Democratic Republic of the Congo, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of functioning sites</td>
<td>317</td>
<td>317</td>
<td>242</td>
<td>198</td>
<td>514</td>
</tr>
<tr>
<td>People screened</td>
<td>275,369</td>
<td>271,436</td>
<td>277,538</td>
<td>410,035</td>
<td>437,402</td>
</tr>
<tr>
<td>Cases T+</td>
<td>1,693</td>
<td>1,425</td>
<td>1,112</td>
<td>742</td>
<td>595</td>
</tr>
<tr>
<td>Cases T-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Detected cases</td>
<td>1,693</td>
<td>1,425</td>
<td>1,112</td>
<td>742</td>
<td>595</td>
</tr>
</tbody>
</table>

**Table 18.** Number of treatment sites and cases treated in the Democratic Republic of the Congo, 2013–2017

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treatment sites</td>
<td>145</td>
<td>145</td>
<td>304</td>
<td>99</td>
<td>167</td>
</tr>
<tr>
<td>Cases treated</td>
<td>5,140</td>
<td>3,109</td>
<td>2,311</td>
<td>1,767</td>
<td>1,091</td>
</tr>
<tr>
<td>Case treated / cases detected (%)</td>
<td>91</td>
<td>97</td>
<td>98</td>
<td>100</td>
<td>99</td>
</tr>
</tbody>
</table>

Table 19 shows the indicators for the elimination of HAT as a public health problem in the Democratic Republic of the Congo, by province, for simplicity. Formally, the indicator is calculated for each health district (Zone de Santé). All districts should have an average of < 1 case/10 000 people during the previous 5 years. In the Democratic Republic of the Congo, this indicator was not reached in many endemic health districts.
Table 19. Elimination indicator by province in the Democratic Republic of the Congo, 2013–2017

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bandundu</td>
<td>1047961</td>
<td>2415</td>
<td>932964</td>
<td>1885</td>
<td>1084499</td>
<td>1575</td>
<td>1310203</td>
<td>1072</td>
<td>1312710</td>
<td>573</td>
<td>1504</td>
<td>4638169</td>
</tr>
<tr>
<td>Kongo central</td>
<td>91230</td>
<td>130</td>
<td>45365</td>
<td>70</td>
<td>55211</td>
<td>82</td>
<td>113312</td>
<td>125</td>
<td>99649</td>
<td>34</td>
<td>88,4</td>
<td>325047,8</td>
</tr>
<tr>
<td>Kasai Oriental</td>
<td>326163</td>
<td>502</td>
<td>276145</td>
<td>313</td>
<td>308057</td>
<td>266</td>
<td>378400</td>
<td>247</td>
<td>375120</td>
<td>172</td>
<td>300</td>
<td>1363789</td>
</tr>
<tr>
<td>Kasai occidental</td>
<td>181888</td>
<td>132</td>
<td>160208</td>
<td>98</td>
<td>236788</td>
<td>118</td>
<td>205355</td>
<td>69</td>
<td>171261</td>
<td>125</td>
<td>108,4</td>
<td>818491,2</td>
</tr>
<tr>
<td>Equateur</td>
<td>159818</td>
<td>71</td>
<td>133676</td>
<td>75</td>
<td>159964</td>
<td>47</td>
<td>334219</td>
<td>48</td>
<td>330158</td>
<td>30</td>
<td>54,2</td>
<td>8523728,6</td>
</tr>
<tr>
<td>Kinshasa</td>
<td>82719</td>
<td>166</td>
<td>45071</td>
<td>103</td>
<td>60169</td>
<td>83</td>
<td>70462</td>
<td>70</td>
<td>61403</td>
<td>64</td>
<td>97,2</td>
<td>270701,6</td>
</tr>
<tr>
<td>Province orient</td>
<td>155248</td>
<td>1971</td>
<td>153813</td>
<td>535</td>
<td>120361</td>
<td>75</td>
<td>84810</td>
<td>45</td>
<td>109467</td>
<td>18</td>
<td>528,8</td>
<td>536125,4</td>
</tr>
<tr>
<td>Maniema</td>
<td>39379</td>
<td>104</td>
<td>51220</td>
<td>63</td>
<td>54292</td>
<td>58</td>
<td>79339</td>
<td>43</td>
<td>47911</td>
<td>28</td>
<td>59,2</td>
<td>233812,2</td>
</tr>
<tr>
<td>Katanga</td>
<td>55179</td>
<td>133</td>
<td>58513</td>
<td>64</td>
<td>56872</td>
<td>48</td>
<td>76463</td>
<td>48</td>
<td>57477</td>
<td>56</td>
<td>69,8</td>
<td>258522,4</td>
</tr>
<tr>
<td>RDC</td>
<td>2139585</td>
<td>5624</td>
<td>1856975</td>
<td>3206</td>
<td>2136233</td>
<td>2353</td>
<td>2652563</td>
<td>1776</td>
<td>2565156</td>
<td>1100</td>
<td>2810</td>
<td>9298387,2</td>
</tr>
</tbody>
</table>

Table 20 categorizes the eligibility of the Democratic Republic of the Congo to request validation of the elimination of HAT as a public health problem, according to national indicators and control and surveillance activities. Currently, it is not eligible to claim validation.

Vector control activities are poorly implemented due to insufficient resources. Community-based selective vector control activities take place in certain areas depending on the availability of resources. In the pilot area of Yasa Bonga, the feasibility of vector control with tiny targets is being evaluated (vertical approach versus community approach).

Table 20. Eligibility to claim validation of elimination, according to the epidemiological situation and control and surveillance activities in the Democratic Republic of the Congo, as of 2017

<table>
<thead>
<tr>
<th>Two criteria</th>
<th>Epidemiological situation (National Indicator for Elimination)</th>
<th>Activities of control and surveillance</th>
<th>Eligible for claiming the validation</th>
<th>Need for reinforce the surveillance before claiming the validation</th>
<th>Non eligible for the validation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 case / 10,000 persons / year, per health district, averaged over the previous 5-year period</td>
<td>True in all districts</td>
<td>DRC, Democratic Republic of the Congo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The national programme (PNLTHA) reported the following difficulties and challenges:

- the availability of screening tests (card agglutination tests for trypanosomiasis, (CATT) and rapid diagnostic tests (RDTs)) in sufficient quantity due to increasing activities, the insufficient numbers of CATT tests and the time taken for customs clearance procedures;
- the reduction in the number of cases and the long distances teams have for case-finding, with limited resources;
- the significant number of endemic villages that are still not covered by active screening;
- the integration of HAT diagnostics in regular health facilities, in the context of decreasing number of cases, especially the training of laboratory technicians;
- the difficulties in maintaining the motivation of health care providers, as HAT care is free of charge and there is no financial gain for the health structure;
- the limited capacity to refer patients from screening sites (CATT/RDT positive cases) to diagnostic confirmation sites; and
- the long distances that second-stage patients are sometimes forced to travel to find second-stage treatment sites (for NECT) that are located only in specialized structures and general referral hospitals, and the difficulty of HAT treatment at the peripheral level.


Coordination among stakeholders is crucial as we advance towards elimination. Following the declaration of the first stakeholders’ meeting, the network established under WHO’s leadership (Figure 17) is working to coordinate, strengthen and sustain efforts to eliminate the disease.

**Figure 17. Configuration of the WHO Network for HAT elimination**

![Diagram of the WHO Network for HAT elimination](image)
At the first g-HAT stakeholders meeting (March 2014) at which a large number of NSSCPs, international organizations, donors, nongovernmental organizations and scientific institutions developing new tools participated, the g-HAT network was set up and a declaration was issued. During the second stakeholders meeting (March 2016), the commitment to eliminating the disease was reinforced and the mechanisms of collaboration were further structured.

The r-HAT network was set up and a declaration issued at the first meeting of rhodesiense HAT stakeholders (October 2014) and streamlined during its second meeting (April 2017).

Between 2014 and 2018, the different groups and subgroups of the network conducted various activities.

- Ad-hoc country coordination:
  - Côte d’Ivoire: workshop for the creation of a research and control network on trypanosomiasis and tsetse organized by the French National Institute for Research and Development (IRD) and the national HAT elimination programme (PNETHA) (February 2015).
  - Uganda: trypanosomiasis and tsetse partners harmonization meeting organized by WHO and the Coordinating Office for Control of Trypanosomiasis in Uganda (COCTU) (March 2015).
  - Benin and Togo: workshop to assess and plan surveillance in historical foci (Lomé, June 2017); three previous workshops (Cotonou, July 2012; Lomé, July 2013; Cotonou, December 2015).
  - Chad: trypanosomiasis and tsetse partners harmonization meeting (March 2017).
  - Guinea: HAT National Steering Committee meeting (December 2017).
- Subgroup “Development of new tools” meeting to update the methodological framework for HAT clinical trials (September 2014).
- Integration of new tools into national and global policies through several subgroup activities:
  - first meeting, to agree next steps after the phase III clinical trial of the new oral drug fexinidazole (December 2014);
  - second meeting, to advance HAT diagnostics (May 2015);
  - third meeting, to follow up on new oral drugs for HAT (June 2015);

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o fourth meeting, to follow up on new oral drugs for HAT (December 2015);
o fifth meeting, to advance HAT diagnostics (October 2016);
o sixth meeting, oral treatment for rhodesiense HAT; perspectives for a trial of fexinidazole (December 2016);
o seventh meeting, review of fexinidazole access plan for gambiense HAT (December 2016).

The Scientific Consultative Group includes:
o the Technical Advisory Group for HAT elimination (HAT-e-TAG), constituted in 2016 to establish criteria and procedures for assessing HAT elimination; first meeting (Geneva, November 2016), second meeting (Geneva, November 2017); and
o the Guideline Development Group, convened to update the WHO guidelines on HAT therapeutics (introduction of fexinidazole); first meeting (Geneva, 2018).

The network has conducted multiple activities involving all the different technical groups and NSSCP partners involved in g-HAT elimination. WHO will continue to follow this strategy of collaborative discussion and development of new strategies to overcome the anticipated obstacles. Two new thematic subgroups have been proposed and are under evaluation: vector control and socio-anthropology. These subgroups could bring new perspectives to the global understanding of g-HAT and, consequently, make a very positive contribution towards its elimination.

7 Reports from various organizations and institutions

7.1 Malteser International

Malteser International, the humanitarian wing of the 900-year old Sovereign Hospitaller Order of Malta, has 13 500 members, 42 000 staff and 80 000 volunteers worldwide. Founded on Christian values and humanitarian principles, its goal is to improve health, strengthen resilience, provide relief during emergencies and assist people to live healthy lives with dignity.

The Integrated HAT Strategy Project 2014–2017 aims to contribute to the elimination of HAT as a public health problem by 2020. The project focuses on three main activities:

(i) Passive screening using a new diagnostic algorithm. In South Sudan, RDTs are used in health posts for passive screening of HAT. Patients who test positive are referred to diagnostic centres. If the parasitological examinations are negative, a blood sample on filter paper is analysed by polymerase chain reaction (PCR) diagnostics loop-mediated isothermal amplification (LAMP) in two existing LAMP centres and the results reported via mobile devices (sms). During 2014–2017, about 20 161 HAT RDTs were conducted in 132 health facilities; 11 primary health care laboratories were upgraded and equipped; and 14 laboratory technicians and 150 healthcare workers were trained. Supervision and technical support were provided. A total of 19 new cases were reported.
(ii) **Communication strategy in South Sudan and in refugee settlements in Uganda.** Information, education and communication materials were developed from the results of KAP (knowledge, attitudes and practices) studies: flip charts, brochures, pamphlets, radio jingles, announcements and drama plays were disseminated in five languages for use in health facilities, schools and in the communities. Focal persons in Uganda and South Sudan were sensitized.

(iii) **Active screening among the internally displaced population in endemic foci bordering Uganda.** A total of 2223 internally displaced persons were screened and 118 suspects underwent confirmatory testing through use of haematocrit centrifugation technique and mini anion exchange centrifugation technique (mAECT). No cases were confirmed.

The protracted conflict in the endemic regions and the weakened health systems with scarce resources make activities challenging. There is cross-border movement of populations from endemic regions. Access to areas of risk is problematic.

The plans for 2018 are to:

- use radio for information, education and social mobilization;
- train village health teams on HAT in refugee settlements;
- conduct community mobilization and sensitization in refugee settlements;
- provide health education in schools in refugee settlements;
- sensitize health care workers and identify key persons to lead HAT activities;
- support the implementation of HAT activities by the Ministry of Health in South Sudan; and
- mobilize resources for additional activities.

Activities will be conducted in cooperation with the Government of South Sudan (national, state and county departments), the NSSCP of Uganda, the Foundation for Innovative New Diagnostics (FIND), Passion Africa, WHO and other implementing partners.

### 7.2 IRD and CIRAD

The French National Research Institute for Development (IRD) and the French Agricultural Research Centre for International Development (CIRAD) are science and technology research institutes under the joint authority of the French Ministry of Higher Education and Research and the French Ministry of Foreign Affairs. Their main missions are to foster research, support and training and provide expertise in ethical partnerships with developing countries. IRD focuses on humans and the environment, and CIRAD on agriculture and livestock.

A joint Research Unit “Host–Vector–Parasite–Environment Interactions in Neglected Tropical Diseases due to Trypanosomatids” (UMR Intertryp) develops methods to prevent and control trypanosomatid infections, tailored to the context of developing countries.

The main research and control activities of UMR Intertryp in the field and in the laboratory include:

- activities of the WHO Collaborating Centre, based in Bobo-Dioulasso (V. Jamonneau and colleagues);
- diagnosis (EU-EDCTP diagnostic tools for HAT elimination and clinical trials (DiTECT-HAT) project), 2016–2020: Burkina Faso, Côte d’Ivoire, Democratic Republic of the Congo and Guinea;
passive and active surveillance (FIND, WHO) plus tsetse control (Bill & Melinda Gates Foundation) with FIND, the Liverpool School of Tropical Medicine (LSTM), Vestergaard, the French International Centre for Research and Development of Livestock in the subhumid zone (CIRDES) for HAT (Côte d’Ivoire, Chad, Democratic Republic of the Congo, Guinea, Uganda) and “Trypa-no!” targeting tsetse “Tryp-elim” (ITM);

- laboratory research on tsetse (population genome with the International Atomic Energy Agency (IAEA) and Member States; larviposition behaviour (CIRAD), sterile insect technique (ERC Revolin) and symbionts (ITM; joint FAO/IAEA Coordinated Research Project);

- research on geography, environment and identification of villages at risk;

- research on asymptomatic cases and reservoirs of infection (Pasteur Institute, ITM), genetics of tolerance (University of Glasgow, Wellcome Trust H3Africa: TrypanoGEN), vaccines (Trypanovac) and atypical infections (Network on Atypical Infection by Animal Trypanosomes);

- modelling (NTD Modelling Consortium, University of Warwick);

- involvement in clinical trials (Guinea, coordinated by the Drugs for Neglected Tropical Diseases initiative, DNDi);

- dedicated partnership tools from IRD: LAMIVECT, JEAI, PhD grants and others; and

- training students and health agents (WHO, DNDi, PATTEC, regional structures).

In partner institutions in Burkina Faso, Cameroon and Côte d’Ivoire, IRD-CIRAD researchers have long been present. In Benin, Guinea-Bissau, Liberia, Mali, Niger, Senegal, Sierra Leone and Togo, HAT research and control activities and training with national partners are implemented.

The unit is mandated to conduct capacity-building and training in order to strengthen national capacities and empower the scientific communities of the South. Students from the South can obtain a third-cycle degree (Master, DEA or PhD thesis). Training and retraining of health workers in endemic countries are conducted: DiTECT-HAT project (Burkina Faso, Côte d’Ivoire, Democratic Republic of the Congo), WHO supervision training (Guinea), regional courses and workshops (ICAT, CIRDES, IAEA, etc.), hosting partners in Montpellier (Central African Republic, Democratic Republic of the Congo) or South–South exchanges.

IRD and CIRAD are part of the Francophone Network on Neglected Tropical Diseases, hosted by AVIESAN (Alliance pour les sciences de la vie et de la santé) with various partners in endemic and non-endemic countries, which was launched on 8 April 2016 in Montpellier.

### 7.3 FIND

The Foundation for Innovative New Diagnostics, or FIND, is a global non-profit organization that is dedicated to the development, evaluation and use of high-quality, affordable diagnostic tests for poverty-related diseases, including HAT, leishmaniasis, Chagas disease, Buruli ulcer, schistosomiasis, tuberculosis, malaria, HIV/AIDS, hepatitis C and febrile illnesses, as well as antimicrobial resistance and other emerging threats.

Fifteen of the 20 neglected tropical diseases listed by WHO, and seven of the 10 targeted in the London Declaration, lack diagnostic solutions. For HAT, FIND has partnered to deliver new diagnostic tools, such as the first- and second-generation RDTs, PCR techniques (LAMP) and the Primo Star iLED fluorescence microscope, together with a number of techniques for preparing and staining samples with acridine
orange. FIND-supported implementation projects on HAT diagnostics are ongoing in Angola, Chad, Congo, Democratic Republic of the Congo, Guinea, Côte d’Ivoire, Nigeria, South Sudan and Uganda; two projects have already ended in Malawi and Nigeria (Figure 18).

Figure 18. HAT diagnostic implementation projects supported by FIND

A new partnership, “Trypa-No!” was launched in 2016 and is a collaboration with FIND, IRD, LSTM and partners in Chad, Côte d’Ivoire, Guinea and Uganda. It works closely with an Industry Liaison Group led by Vestergaard and is funded by the Bill & Melinda Gates Foundation. The project will expand efforts to prevent transmission by integrating new tsetse fly control methods with intensive screening, diagnosis and treatment of HAT across Chad, Côte d’Ivoire, Guinea and Uganda.

8 Control and surveillance: innovations and challenges

8.1 Screening and diagnosis

8.1.1 Update on the development of new screening tools

The first-generation RDTs (SD BIOLINE HAT) with two native antigens (VSG LiTat 1.3 and VSG LiTat 1.5) have been commercially available since the fourth quarter of 2013. More than 900 000 tests had been supplied by the end of 2017. Packaging: 25 tests/kit; stability: 2 years at 40 °C; price: US$ 0.50/test.

Several challenges and limitations remain, notably:
1. Reliance on supply of native antigens
   - Native antigens are difficult to produce (laborious and dangerous).
   - Differences in quality control methods (between supplier and SD) that resulted in interrupted production of RDT for several months (2017).
   - Quantity could also become a challenge if demand increases.
   - Reliance on native antigens is the main reason for developing a second-generation RDT with recombinant antigens.

2. Sensitivity concerns
   - True sensitivity remains unclear, as estimates vary significantly between studies (probably because of different study designs, and other reasons).
   - Sensitivity could be very low in some settings (e.g. as low as 49.2% in the Democratic Republic of the Congo for active screening; Lumbala et al., 2018).

3. Specificity concerns
   - Relatively low positive predictive value (PPV) in the elimination context, even if specificity is rather high, for example:
     - PPV = 20% (68/344) in active screening in the Democratic Republic of the Congo (Lumbala et al., 2018).

4. Packaging volume
   - Volume is significantly larger for native antigens than for CATT, posing transport/storage issues for active screening.

The second-generation RDTs (SD BIOLINE HAT 2.0) are expected to be commercially available soon. They use two recombinant antigens (ISG65 and VSG LiTat 1.5), produced directly by Standard Diagnostics (Escherichia coli) and Abbott (baculovirus expression systems). Packaging: 25 tests/kit, 16% smaller than first-generation RDTs; stability: 2 years at 40 °C; price: US$ 0.50/test. Recombinant antigens are cheaper to produce and easier to standardize than the native antigens used for the first-generation test, which will drive down the price of testing while improving test quality.

A different format and packaging (SD BIOLINE HAT 2.0 Multi) with 100 tests per kit may be commercially available by July 2018. This kit is 52% less bulky than single RDTs. The price is expected to be at least 10% lower than that of single RDTs (needs to be confirmed).

A prototype of a combined RDT for diagnosis of malaria and screening for g-HAT (SD BIOLINE HAT/Malaria Duo RDT) has been developed for targeted use in regions reporting HAT cases recently, therefore not to replace malaria RDTs nationally. It could also be used as a surveillance test in the post-elimination context. The prototype was developed with Standard Diagnostics and Abbott. The HAT band includes two recombinant antigens of Trypanosoma brucei gambiense (ISG65 and VSG LiTat 1.5), the Pf band antibodies against HRP2 antigen of Plasmodium falciparum. The prototype was evaluated at Makerere University on stored samples from the Democratic Republic of the Congo and Uganda (250 HAT positive, 250 HAT negative, 500 P. falciparum positive, 250 P. falciparum negative). No difference in the diagnostic accuracy of either HAT or malaria between the HAT/Malaria Duo RDT and the individual tests (SD BIOLINE HAT 2.0 and SD BIOLINE Malaria Ag P.f) was observed. Prospective
evaluation studies are due to start in Uganda and in the Democratic Republic of the Congo during the third quarter of 2018, with registration planned (Korean FDA and CE mark) by mid-2019.

In the post-elimination context, the following questions remain:

- Would a screening test that could be missing 30–50% of cases be appropriate?
- Would a screening test with a specificity of 97–99% be acceptable in terms of cost–effectiveness and workload to confirm suspects?
- Would it be worth investing in the development of a different type of test?
- Should it be a serology test? Or a molecular test?

In 2018, FIND facilitated the development of a target product profile for a post-elimination surveillance test.

8.1.2 Innovations in tools and quality control for diagnosis

The ITM in Antwerp has a development agreement with Coris BioConcept to produce a rapid serodiagnostic test for g-HAT: **HAT Sero K-SeT** for fixed health centres and **HAT Sero Strip** for high-throughput screening by mobile teams. The 24-month project is financed by the Government of Belgium. The replacement of two native antigens by three recombinant proteins and the design of the RDT-reader are planned for 2018; a field evaluation is due in 2019.

A *T.b. gambiense* inhibition ELISA (**iELISA**) for serodiagnosis in post-elimination monitoring is under development. This collaboration among ITM, Icosagen, ApDia, the University of KwaZulu-Natal and the University of Warwick is financed by the Bill & Melinda Gates Foundation. The iELISA is intended as an alternative to immune trypanolysis with 100% specificity and is applicable on dried blood-spots.

For parasitological diagnosis, **mAECT** is still the most sensitive tool. It is produced with support from the Government of Belgium and GE Healthcare. Some recent improvements include: combining two gels to allow loading with 500 μL of blood and increase sensitivity; and modifying the collector tube to allow the use of the 20x objective and increase visibility under the microscope (a new stopper retains the upper filter in place). All these innovations may increase the price from €3.5 to €4. While the mAECT tubes are functionally stable up to 70 °C, the recommendation is still 4°C for long-term storage to prevent growth of bacteria or fungi. Investments are ongoing to increase the production capacity to 80 000 mAECT tubes/year at the National Institute for Biomedical Research (INRB) in Kinshasa. Alternatives for achieving higher availability and lower cost are sterilization by irradiation with γ-ray or X-ray instead of tyndallization and production by GE Healthcare or replacement of gels by surface modified hollow fiber filters.

**Viscoelastic focusing** is a method for detecting parasites directly with cell recognition software for trypanosome microfluidic detection (UMR Intertryp – CIRAD, IRD; deMello working group at Eidgenössische Technische Hochschule Zürich).

**Molecular diagnosis** is being investigated for improved sensitivity, particularly for specific targets of *T.b. gambiense*. Moving from conventional to quantitative PCR is faster, has less risk of contamination and higher specificity and allows multiplexing. New TBR primers can distinguish most *T.b. gambiense* strains from other Trypanozoon taxa. The search for other multicopy gambiense-specific sequences is ongoing. RNA detection can reach a higher analytical sensitivity than DNA detection.
For quality control, a HAT Diagnosis Quality Assessment System will be implemented in the Democratic Republic of the Congo in cooperation with PNLTCHA, LNRTHA at INRB and IRD and financed by the EU-EDCTP DiTECT-HAT and the Belgian Government. It includes the following components: control sera for quality control on RDTs; training toolkit; proficiency panel for assessing serological and parasitological performance of diagnostic centres; and digital image capturing of serological and parasitological test results.

8.1.3 The DiTECT-HAT project: research on screening, surveillance and test of cure

The Diagnostic Tools for Human African Trypanosomiasis Elimination and Clinical Trials project (abbreviated as DiTECT-HAT) is a new programme with various partners (IRD France, PNLTCHA Guinea, PNLTCHA-RDC, INRB-RDC, CIRDES Burkina Faso, IPR Côte d’Ivoire, ITM Belgium and the University of Liverpool, UK and in collaboration with DNDi), funded by the European & Developing Countries Clinical Trials Partnership.

The objectives of DiTECT-HAT are to evaluate the accuracy and feasibility of new, ready-to-use diagnostic tools and to propose algorithms for HAT diagnosis in three contexts: passive case detection in peripheral health centres (WP2); post-elimination surveillance for detection of disease re-emergence (WP3); and early test of cure in therapeutic trials (WP4).

WP2 on passive case detection strives to increase integration of case detection, which is essential to controlling HAT. The goal is to determine the diagnostic performance and cost–effectiveness of RDTs in peripheral health centres in low prevalence HAT foci and to establish diagnostic algorithms combining RDTs at point-of-care, and remote serological and/or molecular reference tests on blood impregnated filter paper. Individuals positive in at least one RDT, will undergo sensitive parasitological confirmation. Blood on filter paper is taken for remote testing in a reference centre using ELISA, trypanolysis, RT-PCR and LAMP.

WP3 on post-elimination monitoring seeks to propose cost–effective systems for early detection of disease re-emergence. It is based on a strategy whereby non-specialized health workers collect blood on filter paper in villages and send it to a regional reference centre for testing (ELISA, trypanolysis, RT-PCR and LAMP). In parallel, blood is tested with RDTs; one or more positive tests are revisited for parasitological examination.

WP4 aims to determine the accuracy of SL-RNA detection in the blood and cerebrospinal fluid (CSF), and of neopterin quantification in CSF, for assessing treatment outcomes and as an early test-of-cure. DNDi provides biological specimens, taken during the therapeutic trial with acoziborole, to DiTECT-HAT.

The regional HAT reference laboratories are CIRDES in Burkina Faso and INRB in the Democratic Republic of the Congo.

The following results are expected:

For passive case detection:

- cost–effective diagnostic algorithms for improved case management; and
- test-and-treat scenarios without parasitological confirmation.
For post-elimination surveillance:
- appropriate threshold to trigger active case-finding, avoid re-emergence of HAT and minimize false alarms; and

For early test of cure:
- earlier assessment of treatment outcomes to speed up drug development and improve routine detection and management of relapse cases.

8.1.4 Detection of trypanosomes in the skin

The skin as an anatomical reservoir for vector-borne African trypanosomes has been the object of new research interest lately. The activities of the Institute Pasteur in France, the University of Glasgow, the PNLTHA Guinea, IRD and the University of Kinshasa and of funding partners were presented.

A significant population of live, motile, extravascular *T. brucei* in the dermis and subcutis of animal models infected by artificial routes or by vector transmission was demonstrated. Retrospectively, 1121 archived skin snip biopsies taken as part of an onchocerciasis elimination programme in a HAT-endemic area of the Democratic Republic of the Congo were examined for trypanosomes by microscopy. Among these, six individuals with trypanosomes in their skin not previously diagnosed with HAT could be identified.

In a clinical study conducted in Guinea (Forecariah district) all confirmed g-HAT patients, as well as all seropositive untreated individuals, had trypanosomes in the dermis. The question was raised whether this could be the missing link that explains the maintenance of transmission? Several other questions were raised: Is it the norm in all *T. b. gambiense* transmission foci? What is the real prevalence of latent infections? Are latent cases hindering the elimination programme? Are current treatments efficient against skin-dwelling parasites? How could dermal trypanosomes be detected?

To detect trypanosomes in the skin, the following objectives were put forward:
- increased diagnostic sensitivity by including dermal trypanosomes;
- increased efficiency by using a simple, affordable, user-friendly, rapid, reproducible, sensitive and specific, possibly non-invasive, method; and
- an algorithm possibly combining clinical, serological and immuno-dermatological aspects.

Different approaches were explored: skin biopsies (touchprep, culture, molecular biology), scanning methods (skin inflammation monitoring, Raman spectrometry) and xenodiagnosis.

TrypaDerm is a collaboration of multiple partners that aims to understand the biological significance of skin parasites, especially their impact on our current view of transmission, diagnosis and treatment.

8.1.5 Challenges in access to screening and diagnostic tests

The diagnosis of HAT requires a significant amount of materials (Table 21).

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Table 21. Overview of the required materials for HAT diagnosis

<table>
<thead>
<tr>
<th>Clinical suspicion</th>
<th>Equipment</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CATT</td>
<td>Cold chain, agitator</td>
<td>CATT reagent + accessories</td>
</tr>
<tr>
<td>RDT</td>
<td>–</td>
<td>Individual tests</td>
</tr>
<tr>
<td><strong>Confirmation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillary tube centrifugation</td>
<td>Tubes, centrifuge, microscope</td>
<td>–</td>
</tr>
<tr>
<td>mAECT</td>
<td>Centrifuge, microscope</td>
<td>mAECT kits</td>
</tr>
<tr>
<td><strong>Staging</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF exam</td>
<td>Tubes, counting chamber, centrifuge, microscope</td>
<td>–</td>
</tr>
<tr>
<td><strong>Epidemiological evaluation</strong></td>
<td>Specialized laboratory</td>
<td>–</td>
</tr>
</tbody>
</table>

CATT: card agglutination test for trypanosomiasis; mAECT: mini-anion exchange centrifugation technique; RDT: rapid diagnostic test

The availability of tests depends on the following elements:

The **CATT test** is produced by a research institute (ITM-Antwerp), on a non-profit basis. Continuity of production therefore depends on the goodwill of the institute’s administration.

**RDTs** are manufactured by industry (SD Bioline, by Standard Diagnostics, South Korea). The price is 25% subsidized by the Bill & Melinda Gates Foundation and 25% by the manufacturer. A limited quantity is donated to WHO.

The **Sero K-Set** (by Coris, Belgium) is not subsidized. Production is only on-demand; in practice the test is not used.

**mAECT** is produced by research institutes. Its production at INRB in Kinshasa depends on technical and material assistance from ITM-Antwerp. Commercial materials are required. The production capacity is 40,000 tests per year. The “Projet de Recherches Cliniques sur la trypanosomiase” (PRCT) in Daloa, Côte d’Ivoire discontinued production for several years but it is now resuming gradually. Resins (an essential component) are donated by GE Healthcare, through WHO, which reduces costs by about 50%. The donation covers production for 3 years. Commitment to renewing the donation has been expressed, including the amount needed for production at both INRB and PRCT.

The **immune trypanolysis** test, a reference serological test with high specificity, still requires a sophisticated laboratory setting to be executed, and is available only in research institutes (ITM-Antwerp, CIRDES-Bobo-Dioulasso, INRB-Kinshasa).

Reactives for HAT diagnosis are specific and demand is limited (e.g. compared with that for HIV and malaria). Production is of little commercial interest and therefore depends on good will (scientific institutes), external subsidies (Bill & Melinda Gates Foundation) and donated materials (GE Healthcare). A shutdown would jeopardize the entire HAT elimination process.
To eliminate HAT, continued universal access to diagnosis is an absolute condition. With a decreasing number of patients, the needs for screening and diagnosis are increasing. Access to diagnosis cannot be ensured without the commitment of the manufacturers. A paradigm shift in the industry is needed, from marketing logic to social responsibility logic.

The quality of HAT diagnosis depends on trained personnel. Currently, there is a loss of capacity as skilled staff are retiring. Training programmes must be maintained. Manuals and digital media are required and must be updated periodically. Quality assurance systems are also important in HAT diagnostics. Clinicians must be sensitized to raise the suspicion of HAT. Frequently occurring shortages could be avoided by improved coordination along the production chain. A better forecast of the tests required, involving all actors, would facilitate their commercial production. Research is needed to develop new tools and to optimize the use of existing ones.

8.2 Treatment

8.2.1 Results from the fexinidazole trials

Fexinidazole is the first effective oral monotherapy against both stages of g-HAT.

Three major clinical trials on fexinidazole have been conducted.

- Study FEX004, a randomized, open-label, multi-centre, non-inferiority clinical trial in adults with stage 2 g-HAT, compared fexinidazole versus NECT; the fexinidazole regimen consisted of a single daily dose administered with food for 10 days as inpatient treatment. The study included 394 patients in the Central African Republic and the Democratic Republic of the Congo.

- Study FEX005, an open-label, single arm, multi-centre, cohort study in adults with stage 1 and early stage 2 g-HAT, which gave fexinidazole in the same regimen as in FEX004 as inpatient treatment. The study included 230 patients in the Democratic Republic of the Congo.

- Study FEX006, an open-label, single-arm, multi-centre, cohort study involved children aged 6–14 years and weighing > 20 kg, with stage 1 and stage 2 g-HAT, as inpatient treatment. The study included 125 patients in the Democratic Republic of the Congo.

The established dosage for treatment with fexinidazole is a single daily dose, taken with food as follow:

- for adults and children ≥ 35 kg body weight: 3 tablets of 600 mg (days 1–4) followed by 2 tablets of 600 mg (days 5–10); and

- for children aged ≥ 6 years and 20–34 kg body weight: 2 tablets of 600 mg (days 1–4) followed by 1 tablet of 600 mg (days 5–10).

In FEX004, efficacy based on the success rate at 18 months was recorded in 91.2% of the patients treated with fexinidazole and in 97.6% of patients treated with NECT. The difference (effect size) was −6.61% (Confidence interval −11.2% to −1.61%; p=0.0029), within a predefined non-inferiority margin of −13%. The success rates of FEX005 and FEX006 were 98.7% and 97.6% respectively (Figure 19).

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Safety data from the pooled analysis of the three main studies, including a total of 619 patients with g-HAT, was presented. Gastrointestinal disorders, mainly vomiting and nausea, and disorders related to the central nervous system (headache, insomnia, tremors) were the most commonly reported adverse events. The incidence of vomiting was higher in the paediatric study (FEX006) and was particularly high in the loading phase of the treatment. Most patients vomited 2 h after drug administration, likely triggered at CNS level; however, with the exception of two patients, no severe events of vomiting occurred, and treatment could be continued.

**FEX009**, an ongoing study (started in November 2016) will provide additional information on the effectiveness and safety of fexinidazole and assess its feasibility as close as possible to real-life conditions. Patients are treated either as out-patients or in hospital settings, depending on their clinical status and other factors.

Fexinidazole is a joint development between DNDi (responsible for preclinical, clinical and pharmaceutical development) and Sanofi (responsible for its industrial development, registration and production) with multiple partners. For the trials, more than 2 million people were screened. DNDi/Sanofi proposed the indication for the treatment of stage 1 and stage 2 g-HAT in adults and children aged ≥ 6 years and weighing ≥ 20 kg. Registration (Sanofi), therapeutic policy development (WHO), training (NSSCP/WHO), roll-out and pharmacovigilance will follow next. It was concluded that coupled with screening and diagnostic tools, fexinidazole represents a promising treatment that could contribute to reaching the last mile of the elimination goals.

The planned clinical trial **FEX007** aims to evaluate the efficacy and safety of fexinidazole against r-HAT. Currently, the only treatment available for stage 2 r-HAT is melarsoprol, which is highly toxic.
8.2.2 Fexinidazole supply and regulatory aspects

Sanofi has been engaged in fighting HAT since 2001 with an ongoing partnership with WHO for donated melarsoprol, eflornithine and pentamidine and by providing funds for programme implementation, capacity-building and HAT screening. Sanofi signed the London Declaration in 2012 and has a partnership with DNDi to develop fexinidazole.

The fexinidazole drug substance (active pharmaceutical ingredient) is produced by Sanofi Chinoin in Budapest, Hungary. The finished product, Fexinidazole Winthrop (600 mg tablets), is produced by Alcami (ex AAI Pharma) in Wilmington, NC, USA. Fexinidazole is provided in blister packs, with distinct packaging for adult and paediatric formulations, to enhance adherence to treatment (Figure 20).

Figure 20. Fexinidazole is provided in blister packs, with distinct packaging for adult and paediatric formulations

The current drugs for treatment of HAT are not registered in all endemic countries but are registered in at least one stringent regulatory authority (SRA). A letter of acceptance by national authorities, managed by WHO, allows import and distribution.

To register fexinidazole, Sanofi submitted the final dossier in December 2017 to the European Medicines Agency (EMA) under the “Article 58 pathway”. This novel approach, in cooperation with WHO, does not provide a market authorization but a scientific opinion intended for markets outside the European Union. The dossier was validated by EMA in January 2018 and then sent to WHO experts and national regulatory authority (NRA) observers of the Democratic Republic of the Congo and Uganda. A list of questions from EMA is awaited in April 2018.

Article 58, with the EMA’s CHMP (Committee for Human Medicinal Products) opinion has been chosen as the most efficient first step of the regulatory pathway. The CHMP opinion will allow the product to be registered in specific countries. Registration in one country will allow distribution by WHO also in other countries via a letter of acceptance. In agreement with WHO, the Democratic Republic of the Congo and Uganda have been chosen as targeted countries for registration following the CHMP opinion. Experts from both countries were appointed by WHO to participate in the EMA review of the dossier. A WHO facilitated procedure (Collaborative Procedure for products with Stringent Regulatory Approval) is being considered as an accompaniment for the registration pathway of fexinidazole in the Democratic Republic of the Congo and Uganda.
8.2.3 Update on WHO treatment guidelines

The standard therapy for gambiense HAT includes four drugs:15

- first-stage: pentamidine
- second-stage: nifurtimox–eflornithine combination (NECT), eflornithine, melarsoprol

For rhodesiense HAT the drugs are:

- first-stage: suramin and pentamidine
- second-stage: melarsoprol

With fexinidazole, a new therapeutic tool has emerged from clinical research that may receive regulatory authorization in the coming months. The oral administration and the possibility to treat both stages may call for significant modifications in the management of g-HAT. Therefore, the therapeutic protocol for g-HAT will need to be revised.

Health authorities will need guidance for the particular context in which the treatment can be administered. WHO guidance will help policy-makers to decide whether and how fexinidazole should be included in national protocols. Consecutively, the new drug should be submitted for inclusion in the WHO Model List of Essential Medicines (EML). As a condition for EML inclusion, the use should be recommended in WHO guidelines.

The guidelines are developed in accordance with the recommendations of the WHO Guidelines Review Committee16 It ensures that WHO guidelines meet the highest international standards, contain implementable recommendations, are based on an optimal use of evidence and adhere to WHO’s conflict of interest policy.

The WHO Guideline Review Committee approves the Guideline Development Plan and reviews the process and the guidelines. A WHO Steering Group took up activities. A Guideline Development Group with a balanced composition of experts and with a guideline methodologist was created and a meeting is planned. A specialized team was externally commissioned to conduct a systematic review of the published and unpublished evidence. An external review group was created.

The new treatment guideline will be an interim guideline, as new elements may emerge within 3 years (new evidence on the safety and efficacy of fexinidazole, on therapeutic alternatives with acoziborole, on application of fexinidazole for rhodesiense HAT). The foreseen timeframe for the publication of the interim guideline is late 2018 to early 2019.

8.2.4 Ensuring access to fexinidazole: distribution and pharmacovigilance

WHO is responsible for distributing the medicines to endemic countries via NSSCPs. There have been no major changes in the production and distribution of existing medicines or to the donation agreements between Sanofi (for eflornithine, melarsoprol and pentamidine), Bayer (for suramin and nifurtimox) and WHO. All the logistics related to storage, assembly of kits and international shipment are ensured by MSF-Logistique under a contract with WHO. The medicines are imported and distributed free of

charge by WHO, according to country needs. Fexinidazole will follow the current supply chain (Figures 21–22) and be distributed exclusively by WHO.

**Figure 21.** Current HAT drugs supply chain

**Figure 22.** Responsibilities in the supply chain and distribution process of HAT drugs

<table>
<thead>
<tr>
<th>National HAT programs</th>
<th>WHO Country Office</th>
<th>MSF Logistique</th>
<th>Manufacturers</th>
<th>WHO Geneva</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate needs and request to WHO</td>
<td>Reception &amp; process requests</td>
<td>Stock management</td>
<td>Drugs production on time and in required quantities</td>
<td>Monitor use of drugs &amp; forecast of needs</td>
</tr>
<tr>
<td>Monitor stocks at country level</td>
<td>Reception of shipments</td>
<td>Assembling kits (e.g. NECT)</td>
<td>Donation to WHO</td>
<td>Process orders from countries and NGO’s (to MSF-Log)</td>
</tr>
<tr>
<td>Delivery to treatment sites</td>
<td>Customs clearance</td>
<td>Shipment</td>
<td>Monitor supply process</td>
<td>Cover distribution to countries</td>
</tr>
<tr>
<td>Report of use &amp; stock</td>
<td>Covering administrative procedures</td>
<td></td>
<td></td>
<td>Supply to non-endemic countries worldwide (emergency or prepositioned stocks)</td>
</tr>
</tbody>
</table>
This procedure is based on the experience of 16 years and ensures access to the best available treatment for all HAT patients. From 2001 to 2016, more than 225 000 treatments were supplied (pentamidine: 684 751 vials; suramin: 18 378 vials; eflornithine: 633 122 vials; nifurtimox 1 851 100 tablets; melarsoprol: 620 935 vials).

Since 2009, an effective system has been in place with quarterly meetings between manufacturers and WHO to forecast the needs for HAT drugs. For fexinidazole, the needed amounts are expected to be low (low number of HAT cases) and, given the small volume of packaging, will simplify logistics (e.g. 2000–3000 treatments/year x 24 tablets = 48 000–72 000 tablets/year).

Fexinidazole is a new drug for which there are limited data in real-life conditions. Since fexinidazole will be deployed in areas that are poorly served by standard pharmacovigilance systems, proactive data collection is required, and data collection will need to be adapted to the realities of the field. A specific system will be developed for fexinidazole based on well-defined sentinel sites with proactive declaration of adverse events and with training for drug management. WHO will organize and coordinate the system. The data collected will be transmitted to Sanofi. The system for fexinidazole will be based on previous WHO–Sanofi joint experience with NECT. Potentially, about 500 HAT treatment sites could be included progressively for the treatment with fexinidazole and for the pharmacovigilance system.

Training on fexinidazole treatment is an essential part of the implementation, which will enable an understanding of drug management and its particularities, such as the interaction with food, the need for compliance with treatment and the possibility of side-effects. The training will include how to identify, classify and report side-effects and relapses for the pharmacovigilance system. Local skilled staff will be used as facilitators (e.g. staff who participated in the clinical trials), following the concept of “training of trainers” and cascade training.

8.2.5 Update on the acoziborole clinical programme

Acoziborole (SCYX-7158), the first oxaborole-based candidate for the treatment of g-HAT, is administered as a single oral dose, with a proposed indication for both disease stages.

The study protocol OXA002 is a phase II/III, open-label, multi-centre trial assessing efficacy and safety in adults (aged ≥ 15 years) with late-stage g-HAT as the primary objective. The assessment will compare acoziborole with NECT historical controls. Recruitment started in October 2016. After a futility analysis during the fourth quarter of 2016, patients with early-stage could also be included. Follow up is planned for 18 months, if possible with evaluation after 12 months. The number of planned study patients has been reduced from 210 to 155. The continuously declining number of HAT patients is making recruitment more difficult. Figure 23 shows the recruitment status as of April 2018, with 81 patients in late stage and 19 patients in early or intermediate stage, all treated with acoziborole.
Figure 23. OXA002 study recruitment status as of 17 April 2018, with initial forecast (orange), new forecast (yellow), recruited late-stage patients (blue) and recruited early or intermediate patients (grey)

<table>
<thead>
<tr>
<th>Screened patients</th>
<th>Screen Failures</th>
<th>On Screening</th>
<th>Treated patients</th>
<th>M3 FU</th>
<th>M6 FU</th>
<th>M12 FU</th>
<th>M18 FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>132</td>
<td>31</td>
<td>1</td>
<td>100*</td>
<td>78</td>
<td>64</td>
<td>29</td>
<td>1</td>
</tr>
</tbody>
</table>

All late-stage patients are parasitologically confirmed and have > 20 WBC/μL in CSF. The diagnosis is documented by photograph (white blood cells (WBC) in CSF) and by video of the trypanosomes. So far there has been no loss to follow up; one patient reached the 18 months of follow up. Until now no rescue treatment has been needed. Figure 24 shows the high-level schedule for the clinical programme of acoziborole.

Figure 24. High-level schedule for the clinical programme of acoziborole, 2016–2022

This study also includes an assessment of new tests for treatment outcome (DiTECT HAT): detection of SL-RNA in blood and CSF, as well as quantification of neopterin in CSF.
Acoziborole could represent a treatment tool for sustainable elimination. Treatment of both disease stages with a single oral dose ensures compliance. It could be used in politically unstable regions or very remote areas. Combined with a field-adapted diagnostic tool, acoziborole could transform HAT into an easily manageable disease.

### 8.3 Epidemiological tools

#### 8.3.1 Deploying light mobile units: the Trypelim project

The “Trypelim project” by ITM and PNLTHA-RDC adapts active case-finding to epidemiological status using light mobile teams. The project involves door-to-door screening by mini teams on motorcycles. A mini-team includes three people to screen and one person to confirm the diagnosis. CATT and RDTs are performed as screening tests. Electronic data are collected with tablets (GPS, demographic data) and a list of suspects recorded. A few days later microscopic diagnostics are performed at the village level. With digital mobile devices pictures and videos of test results are recorded for quality control.

The data from android tablets are synchronized with a central database and stored in an electronic data collection system. A dashboard decision support system is accessible from a website. This system automatically generates epidemiological reports showing trends (statistics), monitors the system’s performance and produces maps with a planning tool for active screening by mini-teams and larger conventional teams. The dashboard menu contains a module for micro-planning, based on an interactive map for scheduling the villages to be screened. The buffer option allows variable perimeters to be applied around villages for adapting the target population based on the capacity of the mobile teams.

WHO recommends that each village where a case is detected should be screened annually for 3 consecutive years and again after 5 years before being considered as non-endemic. The project complies with this recommendation. Furthermore, the project systematically increases the coverage of populations at risk. Mini-teams were added to the conventional teams to include villages within a certain radius of an endemic village.

The model of this pilot project was used in Yasa Bonga and Mosango to plan one mobile team and three mini-teams for 3 consecutive years (2016–2018). A significant number of cases were found in the villages surrounding villages where cases had been declared originally. The cost–effectiveness of this strategy will be measured after the third year of screening and compared against the strict application of the WHO guideline for active screening based on village units.

In parallel with the pilot project, this approach is used throughout the former Bandundu Province, which accounts for the majority of cases reported by PNLTHA-RDC.

The project has different phases:

- **Phase 1 (2013–2014), HAT case**: Development and field testing of tools in health areas (sub-districts) in Bandundu and Bas Congo
- **Phase 2 (2015–2017), Trypelim pilot project**: Implementation in two health districts (Yasa Bonga and Mosango)
- **Phase 3 (2017–2020), Trypelim Bandundu**: Expansion to (former) Bandundu province
In 2017, the Trypelim pilot project used one large team to screen > 64,000 people and identify 34 cases, and 3 small teams to screen > 184,000 people and identify 22 further cases. Also in 2017, the Trypelim Bandundu project used six large teams to screen > 403,000 people and identify 178 cases, and 8 small teams to screen > 97,000 people and identify 17 further cases.

There are logistical challenges with functional materials and delays in training. The availability of screening tests is challenging, due to the production limits of RDTs and the long customs clearance of CATT and RDTs. There is also delay in the development of digital mobile tools.

8.3.2 Detecting sleeping sickness in low-prevalence settings in Côte d’Ivoire: a targeted door-to-door strategy

Concerted efforts to control HAT over the past three decades have resulted in a marked reduction of prevalence in Côte d’Ivoire. The “Projet d’élimination de la Trypanosomiase Humaine Africaine en Côte d’Ivoire: ElimTrypCI (2016–2020)” was created by various national and international partners.

With decreasing HAT prevalence, active mass screening is less cost–effective. Moreover, with decreasing prevalence, the population no longer perceives HAT as a threat and participates less in active screenings. Bonon, the last epidemic focus in Côte d’Ivoire, was contained at the beginning of the 2000s. No HAT cases were detected in 2012 during an active mass screening. Nevertheless, 7 HAT cases in second stage were diagnosed passively in 2010–2011.

An alternative active screening strategy consisting of visiting former patients at their home and testing the people living in their close neighborhood was investigated (targeted door-to-door strategy, TDD). Using the national database, 109 former HAT cases diagnosed since 2000 were referenced and 72 successfully localized. Subjects living in the same house, living in immediate vicinities and sharing the same daily activities were sensitized. A door-to-door medical survey (TDD) with a reduced mobile team (CATT, parasitology and trypanolysis) was conducted in 2012. The results were compared with a classical active mass screening survey conducted 2 months earlier in the same area. TDD detected significantly more cases (4 cases among 1058 people surveyed). By active screening no cases were identified among 3919 people. In addition, with TDD significantly more serological positives by trypanolysis test were identified. Door-to-door screening yielded a 3.5 times higher HAT prevalence than a mass screening in Forecariah focus.

The TDD provides a friendlier environment, by inviting inhabitants to participate in and gain awareness of the disease. It also appears to be more effective than classical active screening in detecting cases in a low prevalence context, where highly localized transmission cycles may persist. The TDD appears to be a useful complementary alternative for maintaining targeted active screening across the population at risk (early diagnosis).

In Côte d’Ivoire, through the ElimTrypCI project, immediate HAT screening and vector control in the neighborhood begins once a HAT case or a positive trypanolysis test is identified.

8.3.3 Intensifying surveillance for passive case-finding

FIND has been working on novel strategies to intensify passive surveillance. The development of new diagnostic and screening technologies offers the potential to integrate g-HAT surveillance and control into primary healthcare systems.

In Uganda, a novel strategy has been established to expand passive screening to the entire population at risk. Patients who are clinically suspected of having g-HAT and show persistent fever after malaria treatment are screened with an RDT at primary health facilities. For RDT-positive patients, parasitological confirmation follows at strategically located microscopy centres. For patients who are positive with the RDT and negative by microscopy, dried blood-spots undergo further molecular testing using LAMP at certain facilities. LAMP-positive patients are considered strong suspects and are reevaluated by microscopy. Facilities have been upgraded accordingly to perform RDTs, microscopy and LAMP. In 2017, 174 health facilities were able to perform HAT screening with RDTs and 12 facilities to perform confirmatory diagnosis. This enhanced passive screening strategy for g-HAT in Uganda is being replicated in other g-HAT endemic countries (Angola and Democratic Republic of the Congo, Central Province). The screening capacity can be adjusted to the epidemiological situation and also scaled-back as absence of disease is verified. A structured scale-back according to certain criteria may be more cost–effective and sustainable.

Novel intensified screening strategies have several advantages:

- the chances of patients being screened at the first facility where they seek health care are increased;
- the population to be screened is selected based on clinical signs, unlike in active screening where this could be influenced by various factors, such as economic activities;
- the screening is conducted as part of routine health care delivery and therefore at low cost; and
- the distance travelled by referred patients is reduced through up-grading of strategic facilities to perform microscopy, and referral of samples.

The data generated from passive screening can be used to identify sites for reactive screening (active screening in villages reporting cases by passive screening) or targeted active screening (active screening in villages considered to be at high risk).

In Uganda, an SMS-based data transfer system (Mango platform by Greenmash) is used to track HAT test results and to alert health centres and patients with information on the test results and appointments. For example, serological suspects are reminded by SMS for follow up testing. Real-time reports can be generated via Internet connection. It is planned to use this system also in Chad and Guinea in 2018.

8.3.4 Developing sero-surveillance for HAT in historic foci and integrating control of HAT with other neglected tropical diseases

A Health Demographic Surveillance System (HDSS) is under development in the health zone of Kimpese, Democratic Republic of the Congo, including in 11 rural areas, to follow up 60 000 inhabitants demographically.

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The objective of the Kimpese TRYP-WATCH project (in cooperation with ITM Antwerp) is to develop a sero-surveillance model for use in extinct HAT foci. Whole-blood is collected on filter paper and analysed by ELISA. All ELISA-positive samples are analysed by immune trypanolysis and, if positive, the person is re-visited. Parasitological diagnosis is confirmed according to PNLTHA guidelines, and a questionnaire on working and migration habits is completed.

Three phases are planned:

- **Phase I:** Pilot project in Kimpese (HDSS population) in three Aires de Santé (Malanga, an endemic focus, with reported cases in 2016; Lovo, a historic focus with no reported cases for > 10 years; and Adra41, Lubumbashi, a focus that never reported HAT cases, as control)
- **Phase 2:** Analysis for the development of the surveillance model
- **Phase 3:** Expansion in two other provinces

A kick-off workshop was held in Kimpese in May 2017. Some 6000 filter paper samples were collected in Kimpese. ELISA analysis was established in Kimpese in March 2018. Out of 833 dried blood samples, three from Malanga were ELISA positive. The collection of samples on filter paper in Lubumbashi is planned for June 2018.

Workshops with training packages on the integration of HAT control with other skin-related neglected tropical diseases (Buruli ulcer, leprosy, lymphatic filariasis, yaws) were held on central, intermediate and operational levels (Kimpese, Nsona Mpangu, Boma-Bungu and UM THA Congo Central). During two screening rounds in November and December 2017, the mobile HAT teams referred 17 suspects with other skin-related NTDs. Integrated campaigns for active screening of Buruli ulcer and leprosy at health zone level are planned during the first quarter of 2018.

### 8.3.5 Implementing integrated reactive sentinel surveillance

The question remains whether HAT has been eliminated in countries or regions that stopped reporting cases. WHO has set up integrated passive sentinel surveillance, with a pilot phase from 2010 to 2013 in Benin and Togo. From 2014 onwards, the approach entered a second phase of extension in countries or areas with low endemicity in West Africa (Côte d’Ivoire, Guinea, Mali, Burkina Faso, Niger, Ghana), Central Africa (Cameroon, Chad, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon) and East Africa (Rwanda).

The principle is to integrate HAT screening into existing health services using existing capacities, as sentinel surveillance sites in well-identified foci (active or historical). The choice of surveillance sites is the responsibility of the national coordinator, with WHO technical support. The choice depends on location in the transmission area, attendance rate of the population, number of staff, existence of laboratory activities, previous experience in the diagnosis and management of HAT and communication means with the central level.

Sensitization materials are available to raise awareness of HAT and strengthen the clinical suspicion among health personnel. In case of a clinical suspicion, a systematic serological screening (e.g. RDTs) is performed to establish a serological suspicion. Testing for a parasitological confirmation may not be available in countries or areas with low transmission. WHO may refer experienced technicians from other countries for temporary support.
If the parasitological testing is negative or not available, blood samples on filter paper are sent to specialized laboratories (WHO Collaborating Centres) through the national coordinator, for immune trypanolysis testing. This highly specific serology rules out the suspicion or reinforces it. If trypanolysis is negative the patient is followed up every 6 months. If it is positive, parasitological testing is performed again. If a positive trypanolysis is not parasitologically confirmed, the patient is followed up every 3 months. If parasitologically confirmed, the patient is staged and treated. An reactive screening survey is then started in the suspected transmission area with the support of WHO. The national coordinator is responsible for the register of sent specimens and results received. A report of activities is sent monthly by surveillance site. Regular supervision visits take place.

A total of 118 sentinel surveillance sites are operational in 15 countries: > 8000 clinical suspects were tested (serological test); the system detected one autochthonous HAT case in Burkina Faso, after years without cases. Through this system, countries are building the evidence to claim the elimination of HAT. The integrated reactive sentinel surveillance increases ownership of HAT surveillance by the national health system.

8.3.6 Understanding the role of animals and healthy human carriers in maintaining g-HAT transmission

Latent human infections and possible animal reservoirs may challenge the g-HAT elimination goals.19 It remains largely unknown whether, and to what extent, they have a role in g-HAT transmission. A better understanding of the contribution of human and putative animal reservoirs to g-HAT epidemiology may be mandatory to inform elimination strategies.

Van Hoof stated already in 1947 that: “The animal reservoir of T.b. gambiense acquires a special importance when one wants to obtain complete and final eradication of human trypanosomiasis.” Koffi et al. (2006) concluded that the results of their study on aparasitaemic serological suspects with positive PCR support the notion of a long-lasting human reservoir that may contribute to the maintenance or periodic resurgences of HAT in endemic foci.

The parasite reservoir must fulfill the following characteristics: susceptible to infection, long-term carrier and capable of transmitting infection to another host.

For T.b. gambiense (type I) the epidemiological role of cryptic reservoirs is not fully understood. For example, in Ghana 2013 a 9-year-old child was diagnosed with g-HAT, 13 years after the last reported case. It is unclear whether an animal or human reservoir, or vertical transmission were responsible.

Pigs, cattle, goats, sheep and dogs are susceptible domestic animals with experimentally proven potential to transmit g-HAT. Relatively high proportions of T.b. gambiense infection in domestic animals were seen in extinct HAT foci. Susceptible wild animals with experimentally proven potential to transmit g-HAT are Agama agama, Cricetomys gambianus, Reduncaredunca, Tragelaphus scriptus, Cephalophus dorsalis, Erythrocebus patas and Pan troglodytes.

Open questions are:

- Which species (domestic, wild) act as epidemiological reservoirs?
- What is the duration of carrier status (self-cure)?

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What effect does control of animal African trypanosomiasis have on HAT prevalence?

How could “spontaneous” extinction of HAT foci where tsetse flies are still transmitting AAT be explained?

The challenges are how to improve detection of \textit{T.b. gambiense} in animals and discriminate among \textit{T.b. brucei}, \textit{T. congolense}, \textit{T. vivax}, \textit{T. simiae}, \textit{T. theileri} and others; how to test the specificity of immune trypanolysis in animals and develop more sensitive gambiense-specific molecular tests; and how to protect (domestic) animals against \textit{T.b. gambiense} infection, with preventive methods and curative treatment of infected pigs.

Jamonneau et al. (2012) showed that untreated human infections by \textit{T.b. gambiense} are not 100% fatal. Latent infections are only described in West Africa (Congo, Côte d’Ivoire, Guinea, Sierra Leone). The relative frequency of latent infections and self-cure is low (Garcia et al., 2000, Kagbadouno et al., 2012). The outcome of a g-HAT infection is most probably related to human factors (Kaboré et al., 2011). The maximum duration of latent infection described is 29 years (Sudarshi et al., 2014). Non-confirmed serological suspects can infect tsetse flies (Frézil, 1971; positive xenodiagnosis on serological suspect). Rodents with trypanosomes in the skin but not in the blood can infect tsetse flies (Capewell et al., 2016; Caljon et al. 2016).

Open questions are:

- Do latent infections also occur in Central Africa?
- Are there prognostic markers for outcome of infection that can be turned into a diagnostic test? (Ilboudo et al., 2016)
- Should unconfirmed, trypanolysis positive patients receive treatment? (Simarro et al., 1999).

The challenges are to provide a 100% gambiense-specific test allowing treatment without confirmation and to develop very safe drugs allowing treatment of persons with unconfirmed infection.

Finally, atypical human infections with “animal” trypanosomes will continue to occur but may be missed by typical gambiense-HAT diagnostics (\textit{T. congolense}, \textit{T.b. gambiense} type II, \textit{T. lewisi}, \textit{T. evansi}).

8.3.7 Modelling to assess the role of cryptic reservoirs in the transmission of g-HAT

The University of Warwick is supporting ongoing HAT interventions through mathematical modelling under two projects:

The NTD Modelling Consortium

- with the second NTD modelling programme: quantitative tools for the study of elimination and re-invasion; and
- with projections: combining prevalence maps with predictive models

The HAT Modelling and Economic Predictions for Policy (HAT MEPP)

- with predictive models and economic evaluation to assist local control problems and to underpin the elimination investment case.
Modelling g-HAT transmission considers the known epidemiology and entomology, the heterogeneous risk of tsetse bites, the potential animal reservoir and the two different disease stages with different detection probabilities.

The modelling g-HAT dynamics (Warwick Model) is a compartmental model, fitted to data from former Bandundu province, Democratic Republic of the Congo and Mandoul focus, Chad. There is no clear support for or against an animal reservoir. Models require some type of “cryptic” reservoir to match data (risk heterogeneity).

Linking data from reported cases to models can help to estimate the disease burden and the extent of transmission and underreporting, with uncertainties in demography, spatial information and timing of detections. It gives estimates for intervention strategies (e.g. impact of the current strategy on transmission).

Models have been developed (by the University of Warwick and other groups) to test the hypothesis of an animal reservoir. Funk et al. (2013), using a specific set of assumptions, found that gambiense HAT in a Cameroon focus could not be maintained without the contribution of animals. Pandey et al. (2015) found insufficient information to determine either way in Boffa, Guinea. Rock et al. (2015) found that the presence of animals makes little difference since they make only a small contribution in Bandundu, Democratic Republic of the Congo. Mahamat et al. (2017) found that animals are an unlikely maintenance host in Mandoul, Chad.

Models of potential animal reservoirs predict that if animals are maintenance hosts, medical intervention alone cannot stop transmission. The role of animals may be regionally- and habitat-specific. The co-location of humans, reservoir animals and tsetse flies are the key variables. Animal prevalence data (ideally longitudinal), tsetse feeding preferences and fine-scale focus-specific data can help to better inform future models.

For the human reservoir, in order to match data in models there must be systematic non-detections. These could be from latent (asymptomatic) infections, non-participation in active screening or imperfect sensitivity of diagnostics.

For human trypanotolerance there are currently no published models (fitted to data) that have assessed the role of latent infections. There are many unknowns, such as infectivity towards tsetse flies, parasitaemia, duration of infection and diagnostic accuracy.

Future modelling goals are:

- Stochastic models
  - to better understand persistence and local-scale dynamics
- Minimizing and capturing uncertainty
  - in vector and host epidemiology
  - impact of reservoir or asymptomatic infected people
- Impact and economics of different strategies
  - can we define an “optimal” control in different regions?
New diagnostics/tools/drugs
- roll-out of new tools and help to define target product profiles for end-game diagnostics

Specific policy-relevant support for NSSCPs
- HAT MEPP’s goal is to provide robust predictions addressing local policy questions
- seeking strong interaction with country policy-makers.

8.4 Vector control

Historically, vector control has played a minor role in HAT control, as it was too expensive and logistically complex.

With funding from the Bill & Melinda Gates Foundation and the European Union, a partnership of African and European scientists, working with industrial partners, developed “tiny targets” (small insecticide-impregnated fabric screens, attractive to tsetse flies).

Tiny targets are twice as effective, 10 times cheaper, longer lasting (6 months) and easier to deploy than traditional traps. Inexperienced field technicians earn competency already after a short training.

Tiny targets are deployed along the banks of rivers and lakes where tsetse flies and people meet. Trials in different types of environment were conducted: linear habitat in West Nile focus, Uganda (Tirados et al., 2015); mangrove forest in Boffa focus, Guinea (Courtin et al., 2015); and swamp area in Mandoul focus, Chad (Mahamet et al., 2017). In each focus the numbers of tsetse flies decreased dramatically, by 60% to more than 90%. The greatest impact was seen in isolated foci such as the Mandoul focus in Chad. At each site, the annual incidence of cases declined. In Uganda, a combination of medical screening and vector control contributed to the continued decrease in case numbers. In Guinea’s Boffa focus, after a combined vector control and active case detection campaign, the incidence of g-HAT decreased to 0.07%, compared with 1.09% in an adjacent area where no targets were deployed. Following deployment of tiny targets combined with sustained medical control activities in Chad in Mandoul focus, the annual number of cases has fallen from 177 in 2013 to 45 in 2015.

The impact of tiny targets was investigated in Côte d’Ivoire in the Bonon focus (1997 targets deployed in 2016–2018) and in the Sinfra focus (736 targets deployed in 2017). The ADT (Apparent Density per day and per Trap) rapidly decreased in sentinel traps. The high efficacy of the combination of screening and vector control was also shown in the Democratic Republic of the Congo (Bandundu), where about 8000 targets were deployed biannually.

During the Ebola virus disease outbreak in Guinea, HAT active screening activities were postponed or impaired. However, tsetse control using tiny targets could be maintained in the Boffa focus, where a pilot project had been launched in 2012. While the disruption of screening activities over 2 years led to a dramatic increase of HAT prevalence, HAT remained under control in areas with tsetse targets (Kagabadouno et al., 2018).

Costs of vector control have been reduced more than 80%. The analysis of tsetse control operations in Uganda suggests that costs have declined from US$ 441–1145/km² per year with traditional traps to US$ 85/km² with tiny targets (Shaw et al., 2013; Shaw et al. 2015).

Vector control operations with tiny targets have been expanded in the Maro focus on the border of Chad and the Central African Republic (led by IRED and PNLTHA), in the Bonon focus of Côte d’Ivoire.
(led by IPR), across Bandundu Province in the Democratic Republic of the Congo (led by PNLTHA) and in the West Nile focus in Uganda (led by COCTU). In addition to the relatively low costs with tiny targets, little training is required. The technology can be carried out by local control programmes with limited external support.

A collaboration in vector control consists of international partners (LSTM, IRD, FIND, CIRDES, ITM, Vestergard-Frandsen) and national partners (PNLTHA-RDC, PNLTHA Guinée, UTCC and COCTU Uganda, IRED and PNLTHA Chad, IPR Côte d’Ivoire).

8.5 Capacity strengthening

In August 2017, the Seventh International Course on African Trypanosomiasis (ICAT) was carried out in Kampala, following courses held successively during 2000–2014 in Marseille, Lyon, Lisbon, Tunis, Nairobi and Kinshasa. The Course was organized in collaboration with the Association against Trypanosomiasis in Africa (ATA), WHO and Makerere University, Uganda. It lasted 3 weeks and covered key aspects of the skills required to diagnose, treat and control trypanosomiasis.

There were 19 participants, from Angola, Central African Republic, Chad, Congo, Côte d’Ivoire, Democratic Republic of the Congo, Guinea, Malawi, Uganda and South Sudan, and 13 facilitators coordinated and lectured. The ICAT should evolve towards an online training course, perhaps combined with a shorter face to face session.

9 Assessment of elimination

9.1 HAT-e-TAG

In 2016, the HAT elimination Technical Advisory Group (HAT-e-TAG) was convened to assist WHO in defining the criteria and procedures of the road map targets for HAT elimination. Elimination as a public health problem in a country requires validation. Elimination of transmission (zero cases) requires verification. Elimination also requires that the country status is assessed against objective criteria and that the achievement is formally recorded.

The HAT-e-TAG

- reviews the indicators to assess HAT elimination;
- defines the requirements to evidence low level or absence of transmission;
- defines the requirements for a functional surveillance system;
- establishes templates for national dossiers of validation or verification;
- establishes the procedures to review the national dossier;
- defines the procedures for post-elimination surveillance;
- revises the national status; and
- reviews the process periodically, according to scientific advances and tools.
The group consists of seven members, with no conflict of interests, who are appointed for 2 years in their personal capacity (not representing institutions) and 6 advisors, who represent their organizations. The advisors do not participate in final decisions. Meetings are held annually on the invitation of WHO.

A main outcome of the first HAT-e-TAG meeting in 2016 was the refinement of the target/indicator for elimination of HAT as public health problem. The global target was originally defined as: < 1 new reported case per 10 000 inhabitants per year in at least 90% of foci, with < 2000 reported cases per year at continental level. As foci are not objectively measurable and as the area at risk of HAT can be better measured in a standardized way, HAT-e-TAG refined the target for 2020 as: a 90% reduction of the area at risk reporting ≥ 1 case/10 000 people per year. The primary indicators are thus the number of cases (as before), and the area at risk reporting ≥ 1 case/10 000 people per year. This new indicator was endorsed by the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases in 2017 and is now the official metric. The 90% reduction refers to a baseline area at risk calculated during 2000–2004.

A subgroup was created to clarify how the global indicators should be adapted to national indicators of HAT elimination. As an outcome of the second HAT-e-TAG meeting in 2017, national-level indicators of HAT elimination as public health problem were defined.

### 9.2 Global and national indicators

The global target for elimination of HAT as a public health problem by 2020 is defined as follows:

- < 2000 cases reported annually at continental level; and
- 90% reduction of the total area at risk reporting ≥ 1 case/10 000 people per year from 2004 baseline levels.

The primary indicators should be interpreted in association with the secondary indicators, which include distribution of cases, population at risk and coverage of the exposed population by control and surveillance activities.

The first global indicator (number of cases) is not directly applicable at country level. The second global indicator (areas at risk) is not easily calculable as it requires relatively sophisticated analytical tools which are not easily accessible and not directly applicable by NSSCPs. The targets and indicators must be simple and easy to measure in the national context.

The target at country level for the elimination of HAT as a public health problem by 2020 was defined by the HAT-e-TAG as follows:

- < 1 case/10 000 people, as a mean over the previous 5-year period, in all health districts of the country.

For the calculation of the national indicators, the numerator is the yearly mean of cases reported during the previous 5 years in a district. The 5-year period is used to account for the frequent variations of coverage and reporting from one year to another. Cases are notified by the NSSCP in the health district according to the national case definition. Generally, this means parasitologically confirmed cases (T+); some countries include serological cases (T0). The differences of case definitions should be stated in the reporting.
The denominator is the health district population in the mid-period (same 5 years) if available or calculated as a yearly mean over the 5 years. The sources for estimating the health district population could vary (census, data collected by SSNCP or by the health system, data from geospatial datasets, etc.) and therefore should be specified in the reporting.

This indicator is calculated for each health district. All districts of the country should have an annual average of < 1 case/10 000 people during the previous 5 years. There is no overall calculation for the country. This indicator keeps the idea of the global indicator, but it greatly simplifies the calculation of the denominator for the NSSCPs. The threshold must be reached by means of control activities, and not due to the absence of surveillance.

A health district is an internationally accepted health administrative and operational division (health measures implementation unit). This geographical area includes all components of a health system required for community health care.

Figure 25 summarizes the pros and cons of this national indicator as compared with the global indicator.

**Figure 25. Pros and cons of transitioning from global to national indicators**

<table>
<thead>
<tr>
<th>PROS:</th>
<th>CONS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Simple, easy to calculate</td>
<td>• It does not take into account the focal nature of HAT</td>
</tr>
<tr>
<td>• Aligned with the second global indicator, but the spatial area and population estimated by a GIS analysis is replaced by the health district</td>
<td>• It can include in the denominator (population of the district) non-endemic populations. It can dilute a meaningful cluster of cases in a whole district when the area of transmission could be located just in a specific area of the district.</td>
</tr>
<tr>
<td>• Aligned with similar indicators used for measuring elimination in other diseases (e.g. leishmaniais, leprosy, onchocerciasis). It is based on a very well established threshold (&gt;1 case/10 000/year)</td>
<td>• An area of transmission can spread over two or more parts of different health districts.</td>
</tr>
<tr>
<td>• The health district is used also for operational and planning purposes.</td>
<td>• The health districts are heterogeneous in the different countries (in terms of surface area and population), and sometimes within countries, so the significance of elimination is not exactly the same everywhere</td>
</tr>
<tr>
<td>• Facilitates the assessment of silent historical transmission areas, where different approaches to calculating a denominator would be difficult to apply.</td>
<td>• People robust health district population data (in general available) but sometimes this information is not fully reliable</td>
</tr>
<tr>
<td>• Used by the well-established Integrated Disease Surveillance and Response Program</td>
<td></td>
</tr>
</tbody>
</table>
1. Description of the country and its capabilities
   1.1 General information of the country
   1.2 The country’s health system

2. Historical data and description of endemic areas
   2.1 Historical HAT data (essential)
   2.2 Description/demarcation of current endemic areas (essential)

3. HAT surveillance and control activities
   3.1 Structure and capabilities to combat HAT (essential)
   3.2 Active screening strategy (essential)
   3.3 Passive screening strategy (essential)
   3.4 Response to suspected/confirmed cases (essential)

4. HAT epidemiological data
   4.1 Current data, national level (essential)
   4.2 Data during the past 5 years, by health district (essential)
   4.3 Data following the national indicator of elimination (essential)
   4.4 HAT in neighbouring countries

5. Vector control
   5.1 Vector control strategy
   5.2 Results of vector control activities linked to HAT

6. African animal trypanosomiasis (AAT)
   6.1 Structure and capabilities to combat AAT
   6.2 Data on AAT

7. Plan of post-validation surveillance (essential)
   - Elimination status must be monitored
     - surveillance and response activities
   - Plan of surveillance for the next 5 years
     - resources available, involved partners
   - Maintenance of the acquired status
   - Move towards the elimination of HAT transmission

With this dossier the Ministries of Health can formally claim elimination of HAT as a public health problem and submit the claim to WHO. Eligible countries are encouraged to apply for validation, and also to express criticism in order to improve the process.
9.4 Validation process

A reviewing validation team is constituted to evaluate the completeness, accuracy and reliability of the country dossier and to ascertain the likelihood that HAT is no longer a public health problem in the country. The validation team determines whether the surveillance system proposed for the post-validation period is adequate and able to detect any re-emergence of the disease before reaching epidemic levels. The team consists of 1–2 experts identified from a panel of experts selected by the WHO Regional Office for Africa, 1–2 experts from the HAT e-TAG and members of the WHO secretariat (WHO Regional Office for Africa and WHO Department of Control of Neglected Tropical Diseases). Using a template, each team member prepares a report to be shared. The process is coordinated by the WHO secretariat and a final report is produced and agreed, then submitted to the WHO Regional Office for Africa. If the report is positive, it is approved by the Regional Director. Finally, the WHO Director-General sends a letter of notification to the Ministry of Health, and the information is published in the Weekly Epidemiological Record and the Global Health Observatory. A reassessment is foreseen after 5 years. Figure 26 details the pathway for the validation process.

Figure 26. Pathway for the validation process of HAT elimination in a country

9.5 Country status

Figure 27 categorizes the g-HAT endemic countries according to their eligibility for claiming validation of elimination of HAT as a public health problem. The categorization depends on two criteria: the epidemiological situation (national indicators for elimination) and the status of control and surveillance activities.
Figure 27. Eligibility of g-HAT endemic countries to claim validation, as of 2018

<table>
<thead>
<tr>
<th>Two criteria</th>
<th>Epidemiological situation (National Indicator for Elimination)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 case / 10,000 persons / year, per health district, averaged over the previous 5-year period</td>
</tr>
<tr>
<td>Activities of control and surveillance</td>
<td>True in all districts</td>
</tr>
<tr>
<td>adequate</td>
<td>Benin, Burkina Faso, Cameroon, Cote d’Ivoire, Ghana, Togo, Uganda</td>
</tr>
<tr>
<td>insufficient</td>
<td>Mali, Nigeria</td>
</tr>
<tr>
<td>absent</td>
<td>Gambia, Guinea Bissau, Liberia, Niger, Senegal, Sierra Leona</td>
</tr>
</tbody>
</table>

Eligible countries are encouraged to prepare the dossier for validation of elimination and to submit it to WHO. This validation process can be a tool for raising awareness among local authorities and staff. WHO will give support in the elaboration and submission of the dossier.

9.6 Challenges and plan of action

The challenging components of a plan of action to reach the validation of elimination are:

1. Establishing surveillance in areas of HAT potential
   - evaluation, choice of sites
   - training and equipment

2. Maintaining surveillance for 5 years
   - supplying tests and other consumables
o shipping samples to the reference laboratory
o testing samples with trypanalysis
o supervision
o meetings
o collecting and analysing data

3. Building the country validation dossier
   o technical accompaniment (consultants)

4. Assessing the dossier and eventual validation
   o acceptance of the dossier upon initial check
   o set up of validation committee
   o meetings of validation experts

5. Maintaining post-validation surveillance
   o eventual re-training
   o supply consumables
   o supervision

Different country scenarios depending on the epidemiological situation are shown in Figure 28 with the components of the proposed plan of action to apply.

Figure 28. Different country scenarios according to the epidemiological situation and components of the proposed plan of action to apply

<table>
<thead>
<tr>
<th>Countries that:</th>
<th>E.g.</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>meet the epidemiological indicators, and have surveillance for a number of</td>
<td>Benin, Togo, Ghana, Cameroon, Cote d’Ivoire, etc</td>
<td>3-4-5</td>
</tr>
<tr>
<td>years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>do not meet the epidemiological indicators, but are progressing in that</td>
<td>Congo, Ecuatorial Guinea</td>
<td>2-3-4-5</td>
</tr>
<tr>
<td>direction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>meet the epidemiological indicators, but have conducted insufficient</td>
<td>Nigeria</td>
<td>1-2-3-4-5</td>
</tr>
<tr>
<td>surveillance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>report no cases (meet the epidemiological indicators), and have conducted no</td>
<td>Guinea Bissau, Liberia</td>
<td>1-2-3-4-5</td>
</tr>
<tr>
<td>surveillance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Countries where the epidemiological indicators must be taken with caution</td>
<td>CAR, South Sudan, Angola</td>
<td>1-2-3-4-5 or 2-3-4-5</td>
</tr>
</tbody>
</table>

CAR: Central African Republic

The validation process is currently at the beginning and will require resources. Estimations are needed for the required human and financial resources.
10 Conclusions

1. Progress has continued since the second stakeholders meeting (March 2016), and the downwards trajectory of case numbers in many countries indicates that gambiense HAT is on track to meet the goal of elimination as a public health problem by 2020. Strategies to advance towards the 2030 goal of eliminating transmission should therefore be considered.

2. The notional global target of < 2000 reported cases worldwide by 2020 has already been met in preliminary figures collated for 2017. This extraordinary success is raising the gambiense HAT elimination programme to the levels of some of the more celebrated programmes, such as those on dracunculiasis and poliomyelitis. It is therefore timely to bring this success story to the world’s attention. A high-profile Ambassador appointed to disseminate information regarding the campaign may bring great benefits.

3. Nevertheless, HAT remains a public health problem in a number of countries where various factors are limiting progress. Appropriate funding, ownership by endemic countries and civil stability in all endemic areas remain key requirements to ensure further progress and avoid setbacks. Addressing the problem of refugees moving from endemic to non-endemic areas also requires attention.

4. The network for g-HAT elimination, led by WHO, provides a framework in which activities conducted by its members are coordinated, facilitating implementation of novel practices and tools required to fulfill the disease elimination aims.

5. The success of many countries in bringing case numbers to a low level comes with the risk of stifling the resources required to sustain elimination. Endemic countries and the international community must therefore be galvanized to maintain their commitment to the elimination goals. To reach the 2020 and 2030 goals, more efforts from countries are needed to: ensure continued staff training and motivation; integrate control and surveillance into strengthened national health systems; enhance cross-border collaboration; and increase the level of commitment to support HAT control and surveillance.

6. The evolution of the International Course on African Trypanosomiasis (ICAT) towards an online training course, covering key aspects of the skills required to diagnose, treat and control trypanosomiasis, will provide a key resource to underpin the capacity of the programmes.

7. Case-finding is central not only to elimination but also to conduct trials on new tools to intervene against the disease. Access to the best screening and diagnostic tools must therefore be assured. However, the dependence upon external funders to purchase existing diagnostic tools and the shortage of companies willing to engage in their production at costs compatible with available resources is of concern. Consequently, efforts and contributions to emulate the previous success in assuring access to medicines, for diagnostic tools, offer a potential way forward.

8. Improved methods to enhance active and passive case-finding strategies are still required, and better understanding of the coverage of the populations screened is desired to help focus on the populations at highest risk. The use of data management and case mapping tools can critically help to better target case-finding activities. Enhanced community awareness in disease transmission areas is required to facilitate referrals of suspected cases to passive screening facilities, especially if active screening campaigns are scaled-back and focused increasingly on the highest risk areas.

9. Programmes including the European Union funded DiTECT HAT initiative through IRD, FIND’s programme of testing and other initiatives through ITM and IRD on screening are helping in the
evaluation of new tools and screening protocols. Continued independent, multi-centre evaluation is important and all future initiatives in this regard are encouraged.

10. Progress in the development of new oral drugs capable of curing both stages of the disease has continued and DNDi has completed successful clinical trials with fexinidazole. An industrial partner (Sanofi) is engaged and has submitted a dossier for regulatory evaluation to allow the drug’s registration in endemic countries. WHO will convene a working group to prepare guidelines on use of fexinidazole. A trial on a second oral treatment (acoziborole), this time available as a single-day dosing, is under way with DNDi.

11. Existing and innovative tools for vector control have demonstrated utility in decreasing vector abundance and are contributing to reduced disease transmission when strategically deployed and coordinated with medical intervention. These tools also interface with control of animal African trypanosomosis; possible synergy at the One Health interface between human and animal African trypanosomiasis is desired.

12. The roles of asymptomatic human carriers and animal reservoirs of the disease in epidemiology also require further attention. Epidemiological modelling could help to frame these roles. The skin may be a hitherto underappreciated site of trypanosome infection and may have a role to play in diagnosis.

13. WHO has established a formal protocol to enable any gambiense HAT endemic country having considered and wishing to declare elimination of the disease as a public health problem to claim to and receive validation from WHO.
### Annex 1: Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Organizers/Speakers</th>
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<tbody>
<tr>
<td>09:00–09:30</td>
<td><strong>Introduction and welcome: opening</strong></td>
<td>ADG CDS/Director CDS AFRO/Director NTD/Coordinator IDM</td>
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<tr>
<td>09:30–10:00</td>
<td><strong>Progress on gambiense-HAT elimination</strong></td>
<td>J.R. Franco (WHO)</td>
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<td>10:00–10:15</td>
<td>Coffee break</td>
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<tr>
<td>10:15–11:00</td>
<td><strong>Sub-region epidemiological report: West Africa</strong></td>
<td>National sleeping sickness programme focal points</td>
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<td></td>
<td>Benin, Côte d’Ivoire, Guinea, Ghana, Burkina Faso, Mali, Togo, Nigeria</td>
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<tr>
<td>11:00–11:45</td>
<td><strong>Sub-region epidemiological report: East Africa</strong></td>
<td>National sleeping sickness programme focal points</td>
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<td>Republic of South Sudan, Uganda</td>
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<td>11:45–12:15</td>
<td><strong>Sub-region epidemiological report: Central Africa (I)</strong></td>
<td>National sleeping sickness programme focal points</td>
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<td>Democratic Republic of the Congo</td>
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<td>12:15–13:30</td>
<td>Lunch break</td>
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<tr>
<td>13:30–14:15</td>
<td><strong>Sub-region epidemiological report: Central Africa (II)</strong></td>
<td>National sleeping sickness programme focal points</td>
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<td>Angola, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon</td>
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<td>14:15–14:30</td>
<td><strong>Report from nongovernmental organizations</strong></td>
<td>MSF focal point</td>
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<td>14:30–15:00</td>
<td><strong>WHO Network for g-HAT elimination: report 2016–2017</strong></td>
<td>G. Priotto (WHO)</td>
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<td><strong>WHO support and coordination to country activities</strong></td>
<td>A. Diarra (WHO)</td>
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<td>15:00–15:15</td>
<td>Coffee break</td>
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<tr>
<td>15:15–16:15</td>
<td><strong>Open floor to statement from donors</strong></td>
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<td></td>
<td>Sanofi</td>
<td>L. Kuykens (Sanofi)</td>
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<td>Bayer</td>
<td>U. Madeja (Bayer)</td>
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<td>Bill &amp; Melinda Gates Foundation (BMGF)</td>
<td>M. Steele (BMGF)</td>
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<td>Government of Belgium</td>
<td>M. Heirman/P. Verle (ENABEL)</td>
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<td>General Electrics</td>
<td>S. Stille (GE)</td>
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<td>Vestergaard</td>
<td>A. Mortensen (Veestergaard)</td>
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<td>Standard Diagnostics</td>
<td>Mijung Ji (SD)</td>
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<td>Others (JICA, KOICA, SIDA, DFID, SDC, NORAD, Wellcome Trust...)</td>
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<tr>
<td>Time</td>
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<td>Presentations</td>
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| 16:15–17:15| **Open floor to statements from institutions and academia**             | Institute of Tropical Medicine, Antwerp (ITM)  
Institut pour la recherche et le développement (IRD)  
Drugs for Neglected Diseases initiative (DNDi)  
The Foundation for Innovative New Diagnostics (FIND)  
Liverpool School of Tropical Medicine (LSTM)  
Institut National de Recherche Biomédicale (INRB)  
University of Glasgow  
University of Makerere  
University of Warwick  
Swiss Tropical & Public Health Institute (STPH)  
Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC)  
Programme Against African Trypanosomosis (PAAT)  
International Atomic Energy Agency (IAEA)  
Medecins Sans Frontieres (MSF)  
Malteser International  
PATH  
Others |
| Thursday, 19 April 2018 | **Innovation on screening and diagnosis of gambiense HAT** | FIND: Update on development of new screening tools  
ITM: Update on development of new screening tools; innovation for quality control  
IRD: Research on screening and surveillance; research on test of cure  
Institut Pasteur / University of Glasgow: Detection of trypanosomes in the skin  
Challenges on the access to screening and diagnostic tests |
| 09:00–10:45 | **Innovation on screening and diagnosis of gambiense HAT** | FIND: Update on development of new screening tools  
ITM: Update on development of new screening tools; innovation for quality control  
IRD: Research on screening and surveillance; research on test of cure  
Institut Pasteur / University of Glasgow: Detection of trypanosomes in the skin  
Challenges on the access to screening and diagnostic tests |
| 10:45–11:00 | Coffee break | |
| 11:00–12:45 | **Innovation on treatment of gambiense HAT: New oral drugs** | Results from fexinidazole clinical trials.  
Road to ensure access to fexinidazole  
- availability and affordability: regulatory and registration process, production, donation  
- update of WHO treatment guidelines  
- distribution, and pharmacovigilance  
Update of clinical trial on acoziborole  
- update on the acoziborole development and timeframe |
<p>| 12:45–14:00 | Lunch break | |</p>
<table>
<thead>
<tr>
<th>Time</th>
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<th>Presenters</th>
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<tbody>
<tr>
<td>14:00–14:30</td>
<td><strong>Innovation in vector control</strong></td>
<td>I Tirados (LSTM)/ P. Solano (IRD)</td>
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<tr>
<td>14:30–16:15</td>
<td><strong>Innovation in epidemiological tools:</strong> Rationalizing case-finding efforts</td>
<td>M. Boelaert (ITM)</td>
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<td>New approaches for active case detection: Light mobile units</td>
<td>V. Jamonneau (IRD)</td>
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<td>Door-to-door screening</td>
<td>J. Ndung’u (FIND)</td>
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<td>Intensifying passive case-finding</td>
<td>M. Boelaert (ITM)</td>
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<td>HAT sero-surveillance integrated with other diseases</td>
<td>G. Priotto/A. Diarra (WHO)</td>
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<td>Integrated reactive sentinel surveillance</td>
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<td>16:15–16:30</td>
<td>Coffee break</td>
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<td>16:30–17:00</td>
<td><strong>Improving epidemiological knowledge:</strong></td>
<td>P. Buscher (ITM)</td>
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<td>Roles of animal reservoir and healthy human carriers to maintain gambiense-HAT transmission</td>
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<td><strong>Friday, 20 April 2018</strong></td>
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<tr>
<td>09:00–10:30</td>
<td><strong>Assessing gambiense-HAT elimination (I)</strong></td>
<td>V. Lejon (chair of HAT-e-TAG)</td>
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<td></td>
<td>Genesis and roles of the Technical Advisory Group for HAT elimination (HAT-e-TAG)</td>
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<td>Validation of elimination of gambiense-HAT at country level:</td>
<td>J.R. Franco (WHO)</td>
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<td></td>
<td>- Indicators of elimination of gambiense-HAT as public health problem at country level</td>
<td>G. Priotto (WHO)</td>
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<td>- Country dossier: Objective and structure</td>
<td>A. Diarra (WHO)</td>
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<td>- Procedures for validation: From claim to validation</td>
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<td>10:30–10:45</td>
<td>Coffee break</td>
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<tr>
<td>10:45–11:30</td>
<td><strong>Assessing gambiense-HAT elimination (II)</strong></td>
<td>J.R. Franco (WHO)</td>
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<td>Status of gambiense HAT endemic countries with regards to the elimination as public health problem</td>
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<td>Challenges for the validation of elimination</td>
<td>G. Priotto (WHO)</td>
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<tr>
<td>11:30–12:30</td>
<td><strong>Conclusions and way forward</strong></td>
<td>Chairperson</td>
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<tr>
<td>12:30–13:00</td>
<td><strong>Closing</strong></td>
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</table>
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