# Report of the fifth WHO stakeholders meeting on gambiense and rhodesiense human African trypanosomiasis elimination

Geneva, 7–9 June 2023

World Health Organization

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# Contents

# Abbreviations and acronyms

| | |
|---|---|
| AAT | animal African trypanosomiasis |
| AU-IBAR | African Union-Interafrican bureau for animal resources |
| BMGF | Bill & Melinda Gates Foundation |
| 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'Elevage en zone Subhumide (International Centre for Research and Development of Livestock in the subhumid zone) |
| COCTU | Coordinating Office for Control of Trypanosomiasis in Uganda |
| COVID-19 | coronavirus disease |
| CSF | cerebrospinal fluid |
| DBS | dried blood spot |
| DRC | Democratic Republic of the Congo |
| DNDi | Drugs for Neglected Diseases initiative |
| DTAG | Diagnostic Technical Advisory Group |
| EDCTP | European and Developing Countries Clinical Trials Partnership |
| EMA | European Medicines Agency |
| EMA CHMP | European Medicines Agency Committee for Medicinal Products for Human Use |
| FAO | Food and Agriculture Organization of the United Nations |
| FIND | Foundation for Innovative New Diagnostics |
| GAP-f | Global Accelerator for Paediatric Formulations |
| HAT | human African trypanosomiasis |
| g-HAT | human African trypanosomiasis due to infection with Trypanosoma brucei gambiense |
| r-HAT | human African trypanosomiasis due to infection with Trypanosoma brucei rhodesiense |
| HAT-DTAG | HAT Diagnostic Technical Advisory Group |
| HAT-e-TAG | Technical Advisory Group for HAT elimination |
| IAEA | International Atomic Energy Agency |
| ICAReB | Clinical Investigation and Access to Research Bio-resources |
| iELISA | inhibition ELISA |
| IHMT | Institute of Hygiene and Tropical Medicine, Lisbon |

| | |
|---|---|
| INRB | Institut National de Recherche Biomédicale (National Institute for Biomedical Research), Kinshasa |
| IPR | Institut Pierre Richet, Bouaké, Côte d'Ivoire |
| IRD | Institut de Recherche pour le Développement (National Research Institute for Development) |
| ITM | Institute of Tropical Medicine, Antwerp, Belgium |
| LSTM | Liverpool School of Tropical Medicine |
| mAECT | mini-anion exchange centrifugation technique |
| MSF | Médecins Sans Frontières |
| NECT | nifurtimox–eflornithine combination therapy |
| NSSCP | national sleeping sickness control programme (PNLTHA in French) |
| NTD | neglected tropical disease |
| PAAT | Programme Against African Trypanosomiasis |
| PADO | PAediatric Drug Optimization |
| PNLTHA | Programme National de lutte contre la trypanosomiase humaine africaine (NSSCP in English) |
| RDT | rapid diagnostic test |
| Sherlock | specific high-sensitivity enzymatic reporter unLOCKing |
| SIT | sterile insect technique |
| SL-RNA | Spliced leader RNA |
| STPH | Swiss Tropical and Public Health Institute |
| STROGHAT | Stop Transmission of g-HAT study |
| TL | trypanolysis |
| TPP | target product profile |
| VSG | variant surface glycoprotein |
| WHO | World Health Organization |

# 1. Introduction

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 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 *(1)*.

National sleeping sickness control programmes (NSSCPs) are core to progressing in the control of the disease and in adapting to the different epidemiological situations. **The involvement of different partners, as well as t**he support and trust of long-term donors, has been crucial for these achievements. More than 20 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, the Bill & Melinda Gates Foundation (BMGF) and other research institutions in the Democratic Republic of the Congo (DRC) has also been essential.

WHO convened the fifth stakeholders meeting on the elimination of HAT due to infection with *Trypanosoma brucei gambiense* (g-HAT) and *Trypanosoma brucei rhodesiense* (r-HAT) in Geneva, Switzerland, on 7–9 June 2023. The meeting was held again in person after the coronavirus disease (COVID-19) pandemic and jointly for both forms of the disease. The previous meetings on g-HAT held in 2014 *(2)*, 2016 *(3)* and 2018 *(4)*, as well as on r-HAT in 2015 *(5)*, 2017 *(6)* and 2019 *(7)*, and jointly for g-HAT and r-HAT in 2021 *(8)* reinforced the partnership and commitment for HAT elimination and structured the mechanisms of collaboration within the WHO network for HAT elimination. The network includes NSSCPs, groups developing new tools, international and nongovernmental organizations involved in disease control, and donors.

Fewer than 1000 cases of HAT annually have been reported over the past 5 years, which is a historic achievement. The area at risk has been substantially reduced. The elimination of HAT as a public health problem at the global level has been achieved.

The new road map for neglected tropical diseases (NTDs) 2021–2030 (“the road map”) *(9)* with the target to interrupt the transmission of g-HAT requires the strengthened and sustained efforts of all stakeholders, national authorities and partners, under WHO coordination. It will take disproportionally high efforts and innovative strategies to find the last cases of g-HAT and neutralize its transmission. Given the limited resources and other competing public health priorities, this is a challenge that requires our joint commitment.

# 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 HAT;
- to sustain and strengthen the network for collaboration and coordination among stakeholders;
- to monitor progress towards the elimination of HAT as a public health problem and share achievements, challenges and perspectives among countries and implementing partners;
- to assess the status of critical technical aspects in research, development and implementation of therapeutic and diagnostic tools, epidemiology and vector control; and
- to discuss strategies for reinforcing control and surveillance of HAT in regard to the targets of the new road map.

# 3. Opening remarks

Dr José Ramón Franco Minguell (WHO Global Neglected Tropical Diseases Programme (WHO/NTD)) opened the meeting, welcomed all participants in person and online, and introduced them.

Professor Michael Barrett (University of Glasgow) was nominated to chair the meeting. He acknowledged this privilege and reminded the participants that this was an exciting time to work as a community towards the elimination of HAT and to have reached a stage that was not thought possible some years ago. Dr Andreas Lindner was appointed as rapporteur of the meeting.

Professor Jérôme Salomon (WHO Assistant Director-General, Universal Health Coverage, Communicable and Noncommunicable Diseases) welcomed (in his recorded speech) the directors of the NSSCPs and the representatives of institutions collaborating to eliminate HAT. He expressed his personal commitment to the fight against NTDs. He congratulated all the participants, together with the many health workers in the field, for the tremendous progress in HAT control that has been made. He pointed out the challenge to reaching the objective of zero cases: "*the last miles are always hard to achieve".* He thanked all participants representing the health ministries and institutions and encouraged all to maintain their efforts to stop the transmission of this disease: "*We are all here to ensure that our efforts are well coordinated with other pertinent efforts, functioning as a network and maximizing the impact*." These efforts will contribute to the attainment of universal health coverage by increasing access to good-quality essential health care, regardless of ethnicity, sex, geographical location and social or economic status. He acknowledged all the donors for their continued financial support, so that the current impressive landmarks could be sustained. He wished everyone a successful and fruitful meeting.

Dr Augustin Kadima Ebeja (Focal Point Human African Trypanosomiasis and Mycetoma, WHO Regional Office for Africa) on behalf of the Regional Director, Dr Matshidiso Moeti, and the Director of Communicable and Noncommunicable Diseases, Dr Benido Impouma, was pleased to welcome the participants. He congratulated all stakeholders on their joint efforts, which have contributed to the elimination of HAT as a public health problem at global level. He pointed out the opportunity provided by the meeting to strengthen the partnership and commitment and to structure the mechanisms for collaboration within the WHO network.

Dr Daniel Argaw Dagne (Unit Head Prevention, Treatment and Care, WHO/NTD) on behalf of Dr Socé Fall (Director, WHO/NTD), welcomed all participants. He described the HAT network with its diverse activities as a model for other NTD programmes. He recalled the significant progress that has been made towards eliminating HAT as a public health problem. He congratulated Benin, Côte d'Ivoire, Equatorial Guinea, Ghana, Togo and Uganda for the validation of g-HAT elimination and Rwanda for the validation of r-HAT elimination as a public health problem. He recalled the road map with its ambitious target to interrupt the transmission of g-HAT. He acknowledged the support and cooperation with the Food and Agriculture Organization of the United Nations (FAO), highlighting that efforts are needed to enhance synergies in the control of the human and animal forms of the disease in a One Health framework, He emphasized the important role of all stakeholders and thanked all the partners whose commitment is highly appreciated.

The meeting agenda is attached as Annex 1 and the participants are listed in Annex 2.

# 4. Situation report of gambiense and rhodesiense human African trypanosomiasis

The situation report was presented by the representatives of NSSCPs at the stakeholders meeting for the four regional groups of countries: West Africa, Central Africa, Democratic Republic of the Congo (all with g-HAT) and East Africa (r-HAT).

## 4.1 West Africa (gambiense HAT)

The current HAT situation was presented for the following countries in the West Africa region: Benin, Burkina Faso, Côte d'Ivoire, The Gambia, Ghana, Guinea, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo.

Guinea has the biggest HAT burden in this group, and therefore drives the trend in the region (Table 4.1.1 and Figures 4.1.1–4.1.3). The Ebola virus disease epidemic forced the interruption of HAT surveillance and control in Guinea by impeding 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 from 2016 to 2018. Since 2018 the number of reported cases has decreased with continued active screening efforts. Côte d'Ivoire continues to report a low number of cases. Active and passive screening activities, health facilities providing diagnostics, as well as information on treatment, are shown in Tables 4.1.2–4.1.4 for the West Africa region.

**Table 4.1.1.** Numbers of parasitologically confirmed (T+) and unconfirmed (T-) g-HAT cases declared by countries in the West Africa region, 2018–2022

| | Number of cases | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2018 | | | 2019 | | | 2020 | | | 2021 | | | 2022 | | |
| | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total |
| Benin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Burkina Faso | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Côte d'Ivoire | 1 | 1 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| Ghana | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Guinea | 74 | 0 | 74 | 60 | 9 | 69 | 35 | 1 | 36 | 28 | 0 | 28 | 30 | 0 | 30 |
| Liberia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mali | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Nigeria | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Senegal | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Togo | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total** | 75 | 1 | **76** | 61 | 9 | **70** | 35 | 1 | **36** | 29 | 0 | **29** | 30 | 0 | **30** |

**Figure 4.1.1.** Distribution of g-HAT cases (red) in the West Africa region, 2018–2022


**Figure 4.1.2.** Area at risk (high and very high, moderate, low and very low) for g-HAT in the West Africa region, 2018–2022

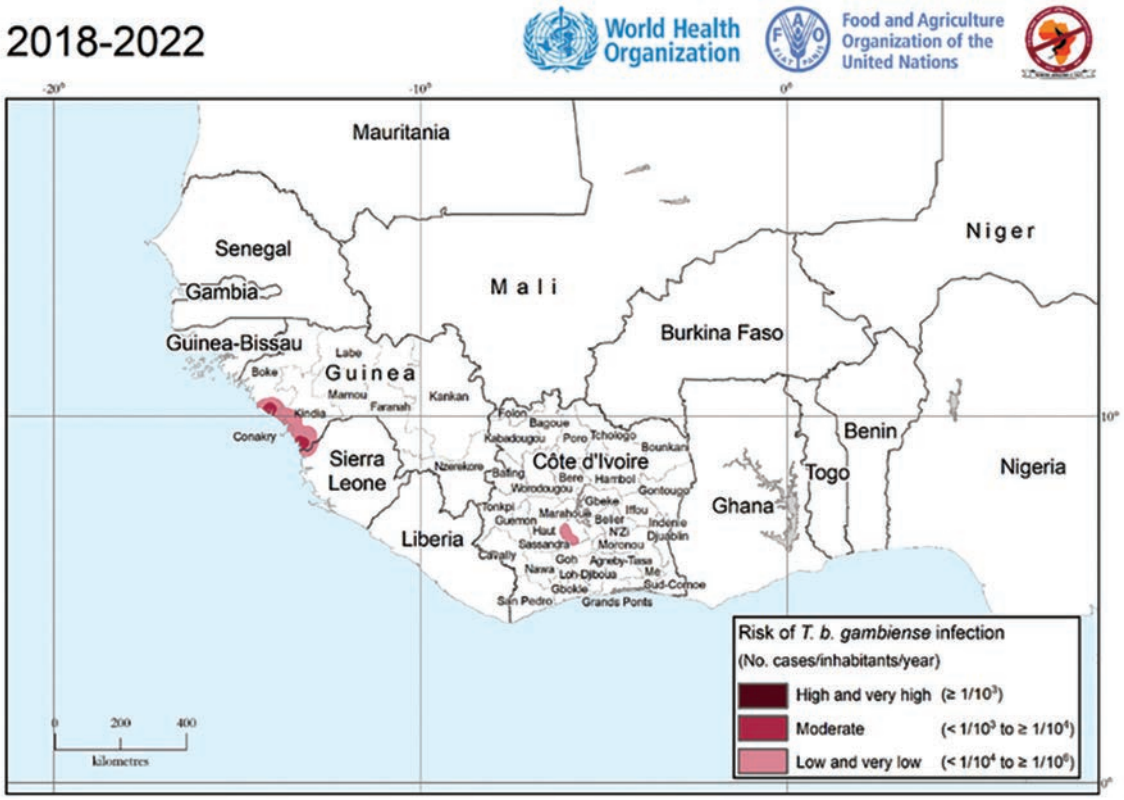


**Figure 4.1.3.** Numbers of g-HAT cases declared by countries in the West Africa region, 2013–2022

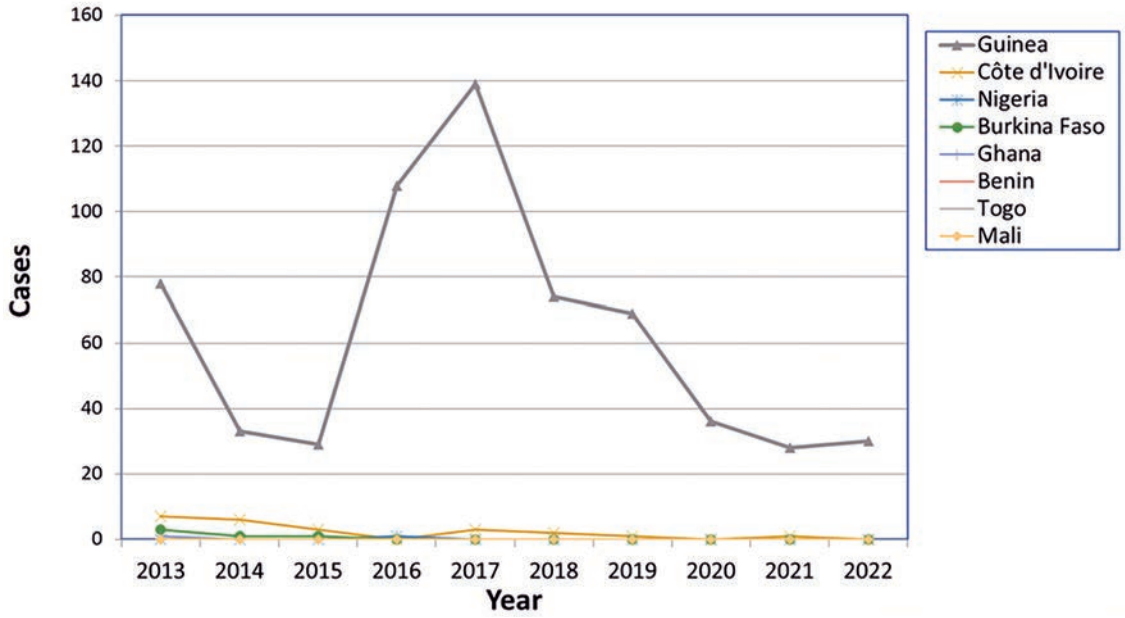



**Table 4.1.2.** Surveillance with active screening and numbers of HAT cases detected in the West Africa region, 2018–2022

| Active screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of countries with active screening | 2 | 2 | 2 | 1 | 1 |
| People screened | 35 082 | 21 866 | 20 421 | 11 388 | 15 311 |
| Detected cases | 43 | 41 | 15 | 10 | 11 |

**Table 4.1.3.** Surveillance with passive screening and number of HAT cases detected in the West Africa region, 2018–2022

| Passive screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of centres screening for HAT | 166 | 172 | 177 | 186 | 214 |
| People screened | 10 709 | 13 280 | 13 790 | 13 676 | 16 851 |
| Detected cases | 30 | 29 | 20 | 19 | 19 |

**Table 4.1.4.** Number of HAT cases treated in the West Africa region, 2018–2022

| Treatment of cases | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of centres treating HAT patients | 6 | 6 | 6 | 6 | 6 |
| Detected cases | 73 | 70 | 35 | 29 | 30 |
| Treated cases | 73 | 70 | 35 | 29 | 30 |
| (% of cases treated) | 100% | 100% | 100% | 100% | 100% |

Several countries practice **vector control** against HAT (Burkina Faso, Côte d'Ivoire, Guinea, Mali, Senegal). Insecticide-treated tiny targets, insecticide spraying and traditional traps (animal sector) are in use, especially in Côte d'Ivoire, Ghana and Guinea.

The group of West African countries pointed out the following **difficulties and challenges**:

- occurrence of pandemics and epidemics;
- political instability or socio-political crises;
- inadequate financial resources;
- lack of technical partners;
- lack of ownership of activities;
- staff turnover and insufficient staff assigned to the NSSCP;
- test shortages (expiry, insufficient stock);
- insufficient logistics for mobile interventions;
- no sentinel sites in some former endemic areas; and
- weak intersectoral collaboration (One Health).

Table 4.1.5 categorizes the eligibility of the g-HAT endemic countries in the West Africa region – according to the national indicator (< 1 case/10 000 people per year in each health district, averaged over the previous 5-year period) and control/surveillance activities – to request the validation of elimination as a public health problem. By 2022, six countries (in green) are eligible in this region to request the validation of elimination, are in the process of doing so or have been already validated.

**Table 4.1.5.** Situation of countries in the West Africa region according to the criteria for claiming the validation of elimination as a public health problem, 2022

| **Two criteria** | **Epidemiological status (national indicator for elimination as a public health problem)** < 1 case/10 000 people per year, in each health district, averaged over the previous 5-year period | |
|---|---|---|
| **Control and surveillance activities** | **True in all districts** | **One or more noncompliant districts** |
| **Adequate** | Benin, Burkina Faso, Côte d'Ivoire, Ghana, Guinea, Togo | |
| **Insufficient** | Liberia, Mali, Nigeria, Senegal | |
| **Absent** | Gambia, Guinea-Bissau, Niger, Sierra Leone | |

Eligible to request validation
Need to reinforce surveillance before requesting validation
Need to set up a surveillance system
Non-eligible to request validation

Table 4.1.6 categorizes the eligibility of the g-HAT endemic countries in the West Africa region – according to the national indicator (zero g-HAT cases for at least 5 consecutive years) and appropriate control and surveillance activities – to request the verification of the interruption of transmission. By 2022, four countries are eligible to request the verification (in white).

**Table 4.1.6.** Situation of countries in the West Africa region according to the criteria for claiming the verification of elimination as a public health problem, 2022

| Two criteria | | National indicator for elimination of transmission. Zero human cases infected by *T. b. gambiense* for at least 5 consecutive years | |
|---|---|---|---|
| | | **True in the whole country** | **Non-compliant** |
| **Control and surveillance activities** | **Adequate** | Benin, Burkina Faso, Ghana, Togo | Côte d'Ivoire, Guinea |
| | **Insufficient** | Liberia, Mali, Nigeria, Senegal | |
| | **Absent** | Gambia, Guinea-Bissau, Niger, Sierra Leone | |

Eligible to request verification
Need to reinforce surveillance before requesting verification
Need to set up a surveillance system
Non-eligible to request verification

## 4.2 Central Africa (gambiense HAT)

The Central Africa group comprised nine countries (excluding DRC): Angola, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Uganda and South Sudan, and includes several transboundary HAT foci

Overall, the numbers of cases and areas at risk in this region have decreased significantly since 2013 (Table 4.2.1 and Figures 4.2.1–4.2.4).. During the period 2018–2022, the number of people who were actively or passively screened decreased and the number of patients slightly increased (Tables 4.2.2–4.2.3). Also in 2022, the number of people screened is still noticeably lower than before the COVID-19 pandemic. An increase in cases in Angola, Central African Republic and South Sudan in 2021 or 2022 is associated with an increase in active screenings. Treatment information is specified in Table 4.2.4.

**Table 4.2.1.** Numbers of parasitologically confirmed (T+) and unconfirmed (T-) g-HAT cases declared by countries in the Central Africa region (excluding DRC), 2018–2022

| | Number of cases | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2018 | | | 2019 | | | 2020 | | | 2021 | | | 2022 | | |
| | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total |
| Angola | 79 | 0 | 79 | 30 | 0 | 30 | 33 | 0 | 33 | 174 | 0 | 174 | 44 | 0 | 44 |
| Cameroon | 7 | 0 | 7 | 12 | 8 | 20 | 2 | 0 | 2 | 4 | 7 | 11 | 7 | 0 | 7 |
| Central African Republic | 43 | 14 | 57 | 46 | 40 | 86 | 16 | 23 | 39 | 26 | 19 | 45 | 73 | 37 | 110 |
| Chad | 11 | 1 | 12 | 8 | 8 | 16 | 5 | 12 | 17 | 3 | 12 | 15 | 6 | 12 | 18 |
| Congo | 14 | 10 | 24 | 9 | 8 | 17 | 6 | 9 | 15 | 5 | 13 | 18 | 5 | 5 | 10 |
| Equatorial Guinea | 3 | 1 | 4 | 3 | 0 | 3 | 1 | 0 | 1 | 3 | 0 | 3 | 11 | 2 | 13 |
| Gabon | 14 | 2 | 16 | 8 | 0 | 8 | 11 | 0 | 11 | 17 | 1 | 18 | 21 | 0 | 21 |
| South Sudan | 9 | 8 | 17 | 9 | 2 | 11 | 9 | 6 | 15 | 5 | 5 | 10 | 15 | 15 | 30 |
| Uganda | 1 | 0 | 1 | 2 | 0 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total** | 181 | 36 | **217** | 127 | 66 | **193** | 84 | 50 | **134** | 237 | 57 | **294** | 182 | 71 | **253** |

**Figure 4.2.1.** Distribution of g-HAT cases in the Central Africa region (excluding DRC), 2018–2022

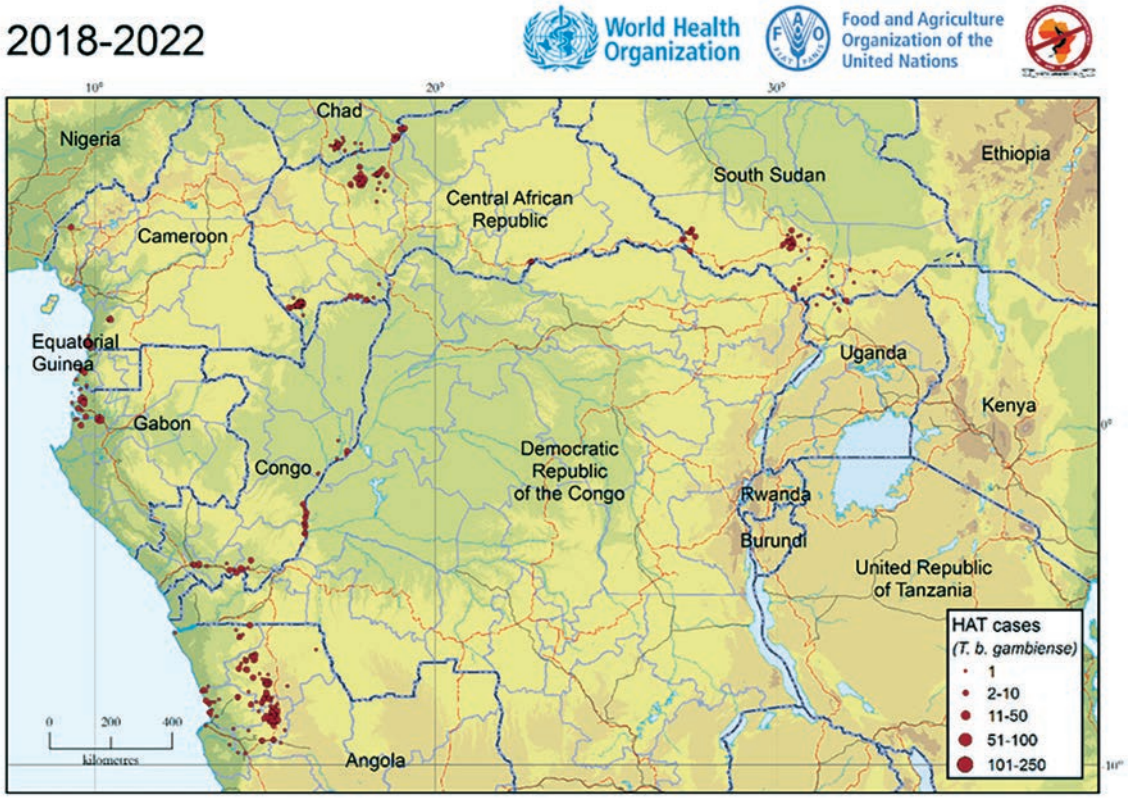



**Figure 4.2.2.** Area at risk (high and very high, moderate, low and very low) for g-HAT in the Central Africa region (excluding DRC), 2018–2022

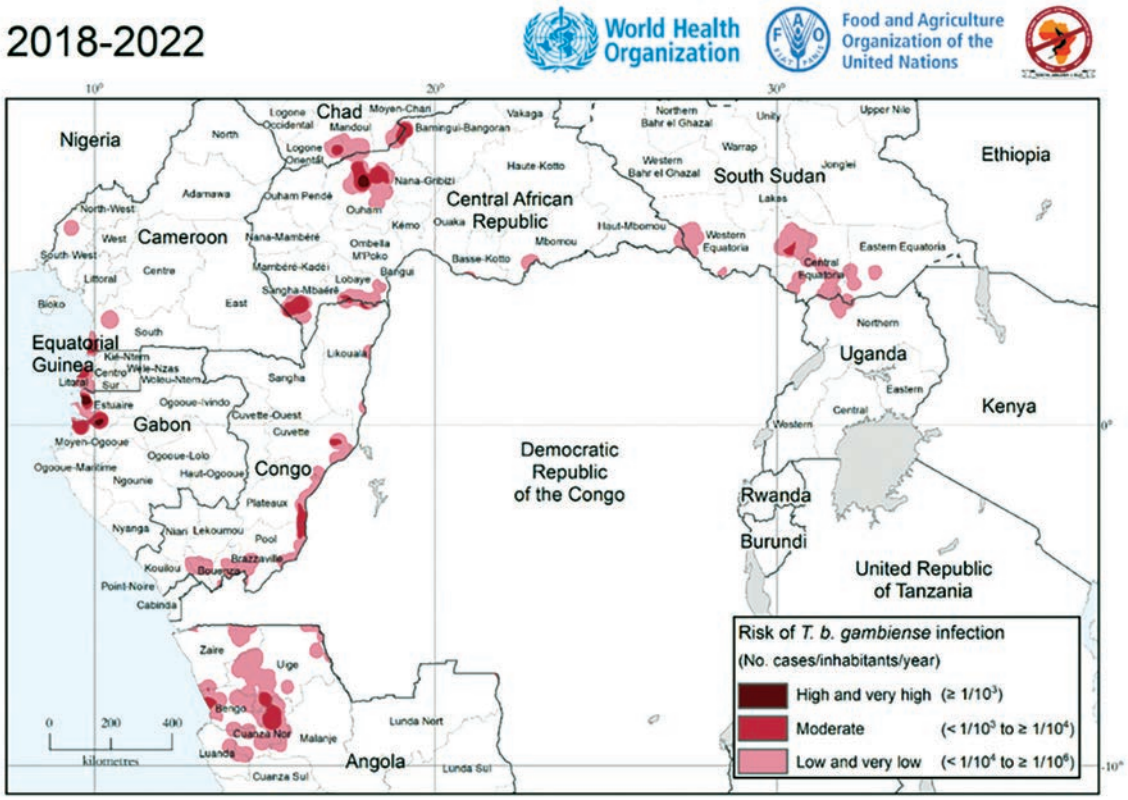


**Figure 4.2.3.** Numbers of g-HAT cases declared by countries in the Central Africa region (excluding DRC), 2013–2022

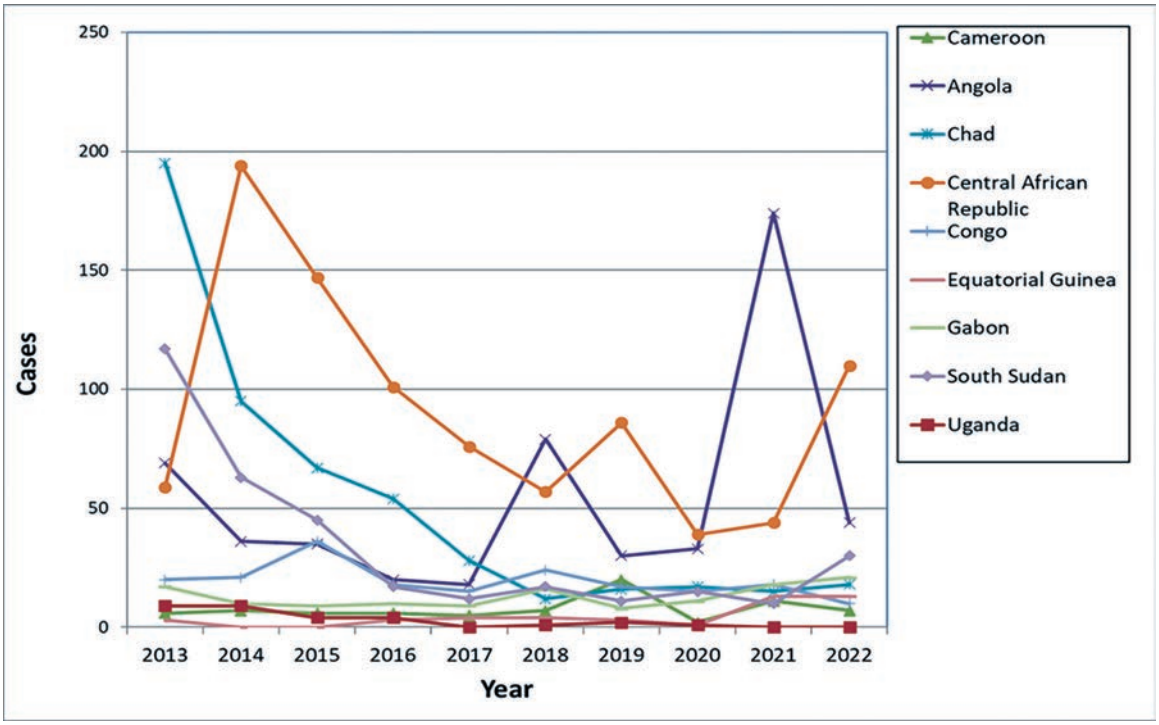



**Figure 4.2.4.** Proportional distribution of g-HAT cases declared by countries in the Central Africa region (excluding DRC), 2013–2022

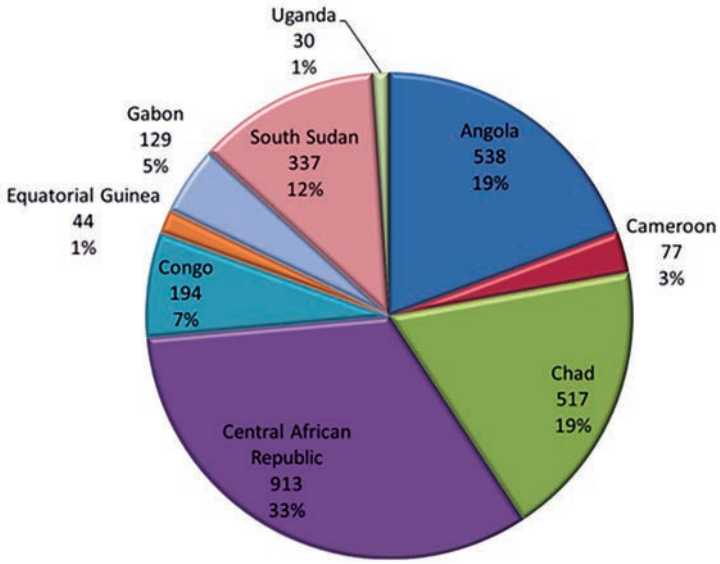


**Table 4.2.2.** Surveillance with active screening and number of HAT cases detected in the Central Africa region (excluding DRC), 2018–2022

| Active screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of countries with active screening | 9 | 9 | 6 | 8 | 9 |
| People screened | 226 201 | 226 180 | 54 491 | 119 344 | 123 471 |
| Detected cases | 118 | 122 | 52 | 223 | 123 |

**Table 4.2.3.** Surveillance with passive screening and numbers of HAT cases detected in the Central Africa region (excluding DRC), 2018–2022

| Passive screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of centres screening for HAT | 331 | 139 | 138 | 146 | 169 |
| People screened | 57 918 | 39 676 | 32 956 | 19 664 | 17 522 |
| Detected cases | 99 | 71 | 82 | 71 | 130 |

**Table 4.2.4.** Numbers of HAT cases treated in the Central Africa region (excluding DRC), 2018–2022

| Treatment of cases | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of centres treating HAT patients | 32 | 32 | 42 | 56 | 63 |
| Detected cases | 217 | 193 | 134 | 294 | 253 |
| Treated cases | 205 | 187 | 133 | 274 | 252 |
| (% of cases treated) | 94.5 | 96.9 | 99.3 | 93.2 | 99.6 |

**Vector control** activities are undertaken with tiny targets in Cameroon, South Sudan and Uganda, as well as in Angola and Chad with traditional traps and tiny targets. In the Central African Republic, Congo, Equatorial Guinea and Gabon, vector control has not been implemented for more than 10 years.

The group of Central African countries identified the following **difficulties and challenges**:

- insufficient funding of field activities;
- little involvement of political and administrative authorities;
- poor integration of passive HAT surveillance into health facilities;
- insufficient laboratory equipment;
- lack of vehicles to carry out field activities in certain countries;
- insufficient number of staff and turnover of staff trained in diagnosis and treatment of HAT;
- low population participation in active screening in certain communities;
- poor access to certain communities (crisis situations, road conditions, high mobility, etc.);
- insufficient financial resources to cover the costs of their care for people in rural areas; and
- lack of coordination of cross-border activities.

Table 4.2.5 categorizes the eligibility of countries endemic for g-HAT in the Central Africa region – according to the national indicator (<1 case/10 000 people per year in each health district, averaged over the previous 5-year period) and control/surveillance activities – to request the **validation** of elimination as a public health problem. By 2022, three countries are eligible to request the validation of elimination, are in the process of doing so or have been already validated (in green).

**Table 4.2.5.** Situation of countries in the Central Africa region (excluding DRC) according to the criteria for claiming the validation of elimination as a public health problem, 2023

| **Two criteria** | **Epidemiological status (national indicator for elimination as a public health problem)** < 1 case/10 000 people per year, in each health district, averaged over the previous 5-year period | |
|---|---|---|
| **Control and surveillance activities** | **True in all districts** | **One or more non-compliant districts** |
| **Adequate** | Chad, Equatorial Guinea, Uganda | Angola |
| **Insufficient** | Cameroon | Central African Republic, Congo, Gabon, South Sudan |
| **Absent** | | |

Eligible to request validation
Need to reinforce surveillance before requesting validation
Need to set up a surveillance system
Non-eligible to request validation

## 4.3 Democratic Republic of the Congo (gambiense HAT)

The endemic country with the highest HAT burden is the DRC. The numbers of cases and areas at risk have decreased significantly since 2013, with 516 reported cases in 2022. Patients are predominantly found in Bandundu and Kasai provinces (Table 4.3.1 and Figures 4.3.1–4.3.3).

**Table 4.3.1.** Numbers of parasitologically confirmed (T+) and unconfirmed (T-) g-HAT cases declared in DRC, 2018–2022

| | **Number of cases** | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **2018** | | | **2019** | | | **2020** | | | **2021** | | | **2022** | | |
| | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total | T+ | T- | Total |
| Bandundu Nord | 142 | 0 | 142 | 139 | 0 | 139 | 82 | 0 | 82 | 82 | 0 | 82 | 62 | 0 | 62 |
| Bandundu Sud | 188 | 0 | 188 | 184 | 0 | 184 | 92 | 0 | 92 | 115 | 0 | 115 | 178 | 0 | 178 |
| Equateur Nord | 18 | 0 | 16 | 21 | 0 | 21 | 14 | 0 | 14 | 37 | 0 | 37 | 17 | 0 | 17 |
| Equateur Sud | 8 | 0 | 8 | 5 | 0 | 5 | 3 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 2 |
| Kasai Occidental | 105 | 0 | 105 | 90 | 0 | 90 | 66 | 0 | 66 | 38 | 0 | 38 | 59 | 0 | 59 |
| Kasai Oriental | 35 | 0 | 35 | 20 | 0 | 20 | 43 | 0 | 43 | 28 | 0 | 28 | 81 | 0 | 81 |
| Kinshasa | 30 | 0 | 30 | 14 | 0 | 14 | 11 | 0 | 11 | 21 | 0 | 21 | 14 | 0 | 14 |
| Kongo Central | 10 | 0 | 10 | 4 | 0 | 4 | 0 | 0 | 0 | 8 | 0 | 8 | 9 | 0 | 9 |
| Maniema/Katanga | 65 | 0 | 65 | 70 | 0 | 70 | 40 | 0 | 40 | 38 | 0 | 38 | 19 | 0 | 19 |
| Province Orientale | 8 | 0 | 8 | 16 | 0 | 16 | 13 | 0 | 13 | 26 | 0 | 26 | 25 | 0 | 25 |
| Sankuru | 51 | 0 | 51 | 50 | 0 | 50 | 25 | 0 | 25 | 32 | 0 | 32 | 50 | 0 | 50 |
| **Total** | **660** | **0** | **660** | **613** | **0** | **613** | **389** | **0** | **389** | **425** | **0** | **425** | **516** | **0** | **516** |

**Figure 4.3.1.** Distribution of g-HAT cases in DRC, 2018–2022

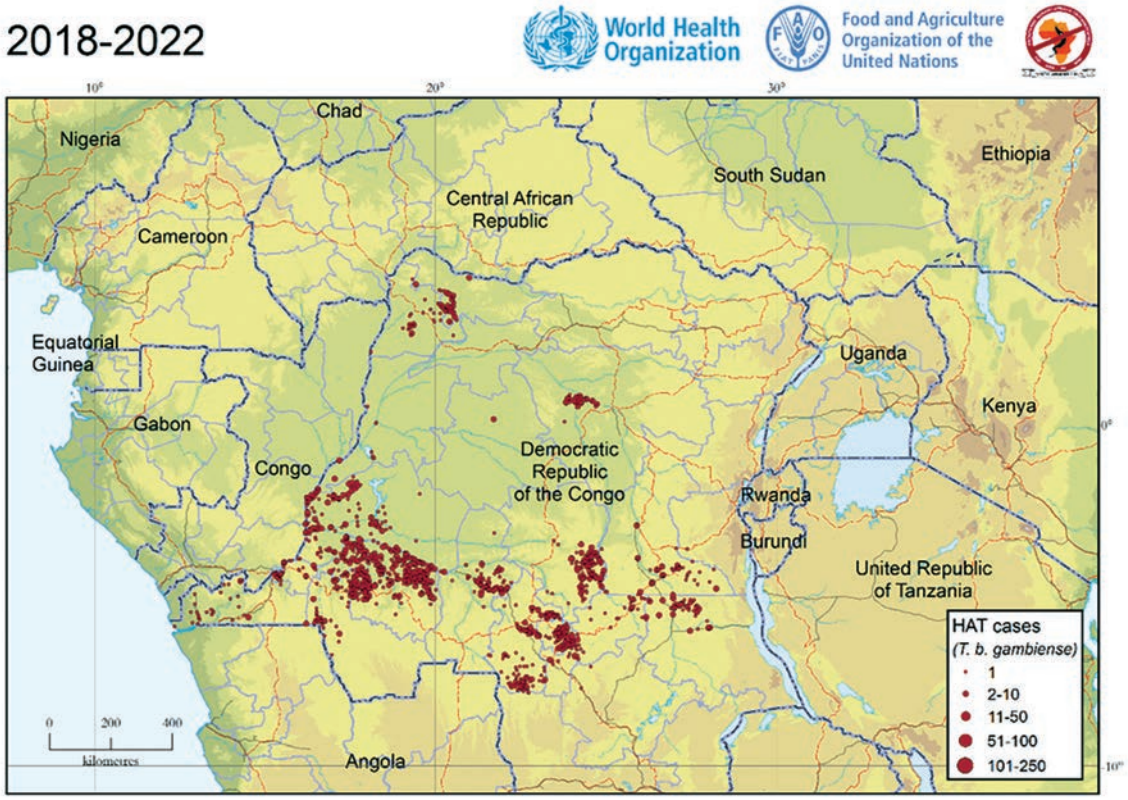



**Figure 4.3.2.** Area at risk (high and very high, moderate, low and very low) for g-HAT in DRC, 2018–2022

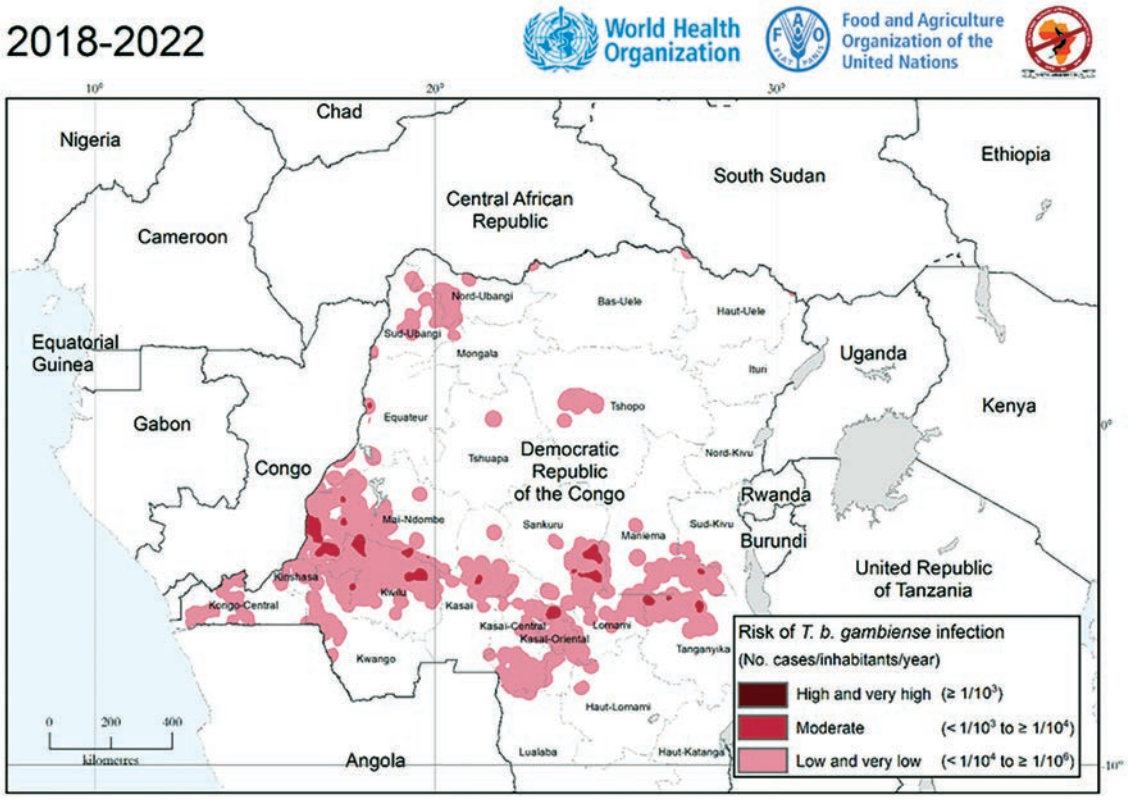
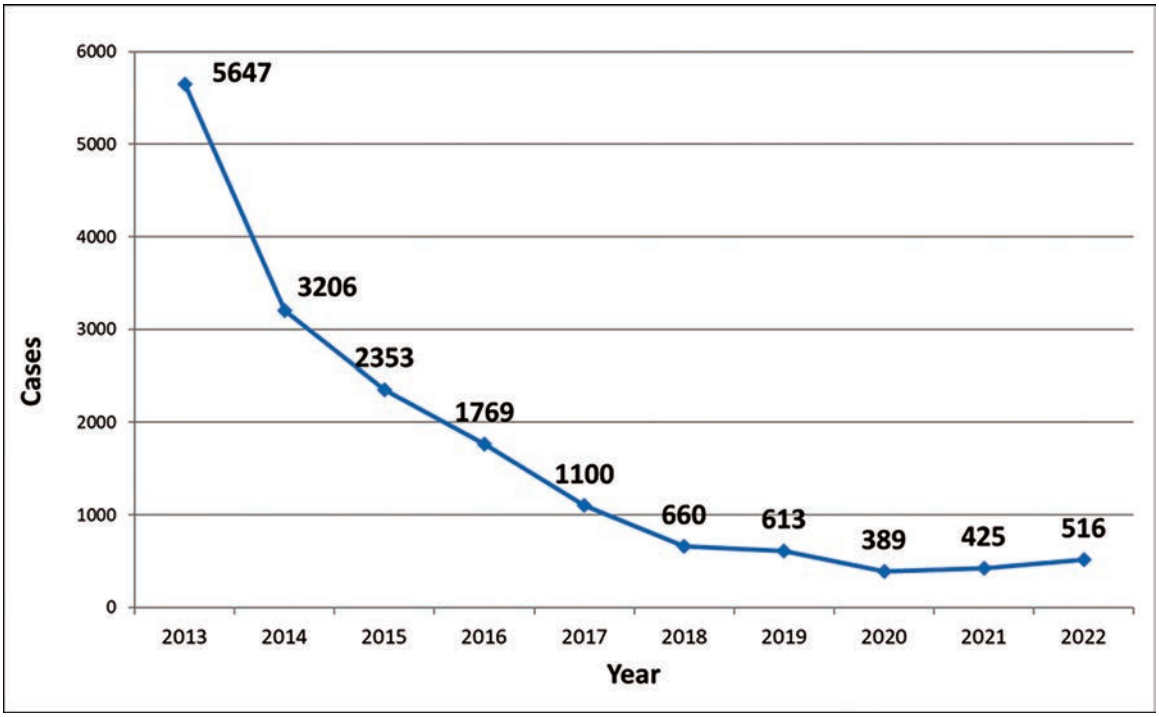


**Figure 4.3.3.** Numbers of g-HAT cases declared in DRC, 2013–2022




Since 2018, the number of people who have been actively and passively screened has decreased considerably (Tables 4.3.2–4.3.3). In 2022, a slightly higher number of cases were found despite the lower number of people actively screened. Lassitude among permanent staff due to lack of financial support and inadequate monitoring of drug stocks (with certain drugs out of stock) were problematic in 2022.

Treatment information is specified in Table 4.3.4 and the vector control activities summarized in Table 4.3.5.

**Table 4.3.2.** Surveillance with active screening and numbers of HAT cases detected in DRC, 2018–2022

| Active screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of mobile teams | 30 | 30 | 30 | 30 | 27 |
| No. of mini-mobile teams | 18 | 18 | 18 | 14 | 19 |
| People screened | 2 426 098 | 2 591 143 | 1 568 414 | 1 904 551 | 1 424 462 |
| Detected cases | 118 | 122 | 52 | 223 | 123 |

**Table 4.3.3.** Surveillance with passive screening and numbers of HAT cases detected in DRC, 2018–2022

| Passive screening | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|
| No. of centres screening for HAT (screening and diagnostic) | 203 | 234 | 234 | 270 | 270 |
| No. of centres screening for HAT (diagnostic) | 166 | 358 | 358 | 376 | 376 |
| People screened | 438 344 | 426 271 | 467 729 | 435 987 | 209 732 |
| Detected cases | 326 | 280 | 216 | 177 | 171 |

**Table 4.3.4.** Numbers of HAT cases treated and medicines used in DC, 2018–2022

| Treatment of cases | | 2018 | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|---|---|
| No. of centres treating HAT patients | | 460 | 546 | 546 | 573 | **573** |
| Treated cases | | 660 | 566 | 372 | 361 | **484** |
| (% of cases treated) | | **100%** | **92%** | **96%** | **85%** | **94%** |
| Treatment used | Pentamidine | 298 | 342 | 123 | 84 | **34** |
| | NECT | 338 | 174 | 161 | 142 | **132** |
| | Fexinidazole | 24 | 50 | 88 | 135 | **309** |
| | Melarsoprol | 0 | 0 | 0 | 0 | **0** |
| | Other | 0 | 0 | 0 | 0 | **9** |

NECT: nifurtimox–eflornithine combination therapy.

**Table 4.3.5.** Current vector control activities in DRC

| Strategy used | Location | Coverage ($km^2$) | Period |
|---|---|---|---|
| **Vertical deployment of tiny targets** | Provinces Kwilu and Mai Ndombe | 12.349 | 2015–2022 |
| **Community-based deployment of tiny targets** | Provinces Kwilu, Mai Ndombe and Kwango | 525 villages 93 861 households | 2015–2022 |

According to national indicators and control and surveillance activities, by 2022 the DRC is not eligible to claim the validation of elimination as a public health problem.

## 4.4 East Africa (rhodesiense HAT)

The East Africa group included eight countries endemic for r-HAT: Ethiopia, Kenya, Malawi, Rwanda, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

In the past 10 years (2013–2022), 85% of all cases were reported from Malawi and Uganda (Tables 4.4.1–4.4.3 and Figures 4.4.1–4.4.3).

**Table 4.4.1.** Numbers of r-HAT cases declared by countries in the East Africa region, 2018–2022

| | Number of cases | | | | |
|---|---|---|---|---|---|
| | 2018 | 2019 | 2020 | 2021 | 2022 |
| Ethiopia | – | – | – | – | 6 |
| Kenya | 0 | 0 | 0 | 0 | 0 |
| Malawi | 15 | 91 | 89 | 49 | 24 |
| Uganda | 4 | 5 | 2 | 2 | 0 |
| United Republic of Tanzania | 0 | 3 | 1 | 1 | 1 |
| Zambia | 5 | 15 | 6 | 3 | 7 |
| Zimbabwe | 0 | 2 | 0 | 0 | 0 |
| **Total** | **24** | **116** | **98** | **55** | **38** |

**Figure 4.4.1.** Distribution of r-HAT cases (blue), 2018–2022

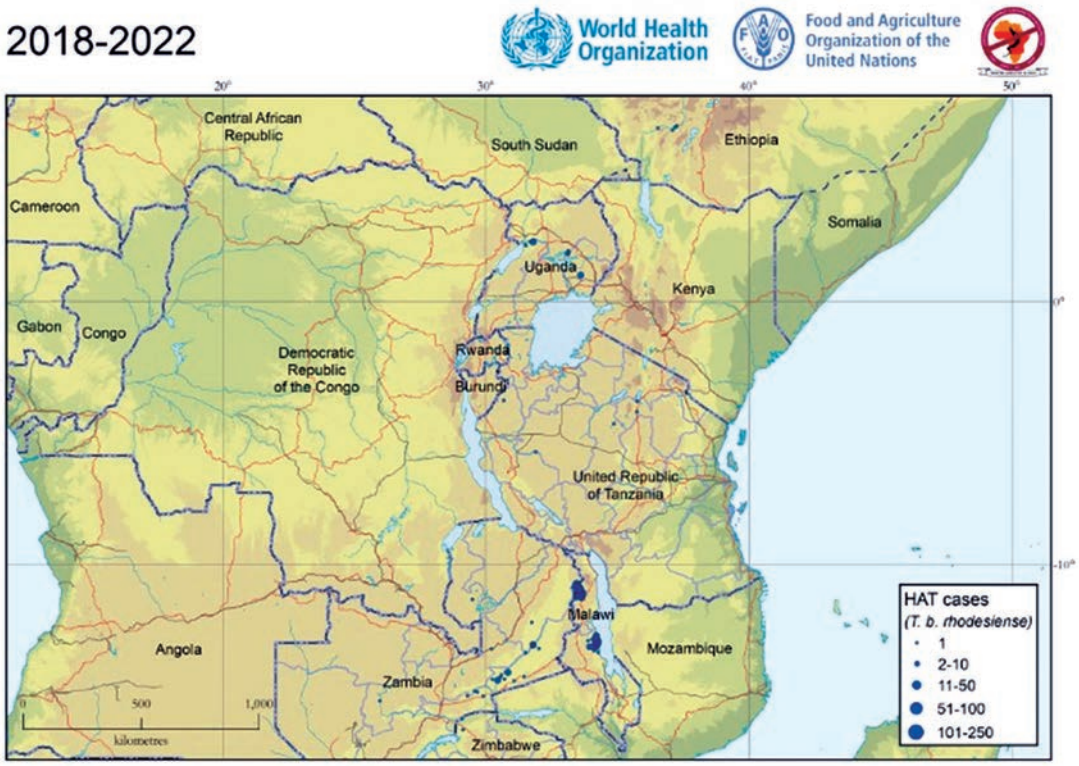



**Figure 4.4.2.** Numbers of r-HAT cases declared by Ethiopia, Kenya, Malawi, Rwanda, Uganda, United Republic of Tanzania, Zambia and Zimbabwe, 2013–2022

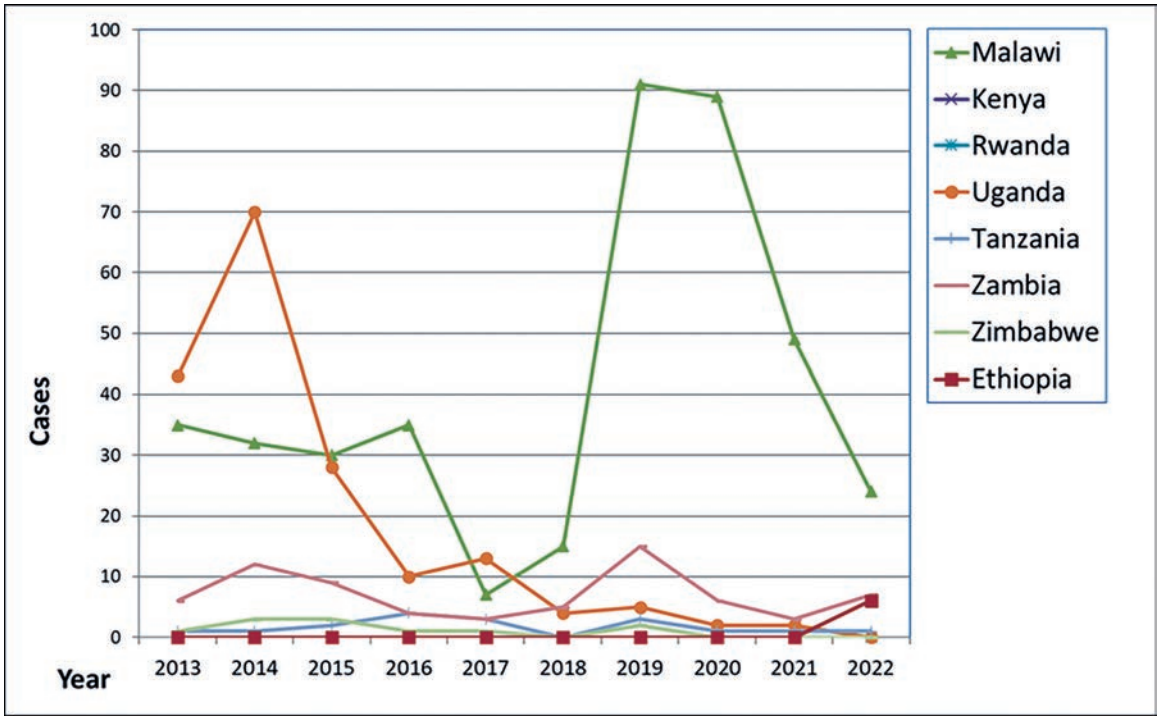


**Figure 4.4.3.** Distribution of r-HAT cases by country in the East Africa region, 2013–2022

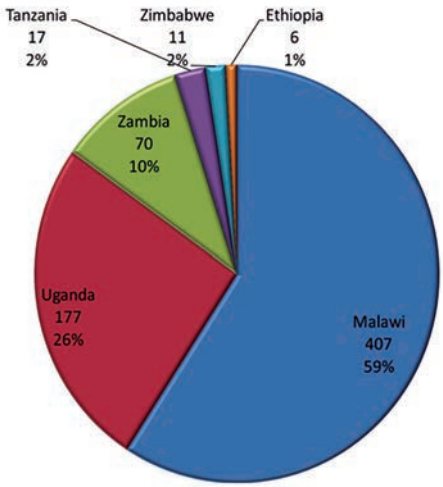
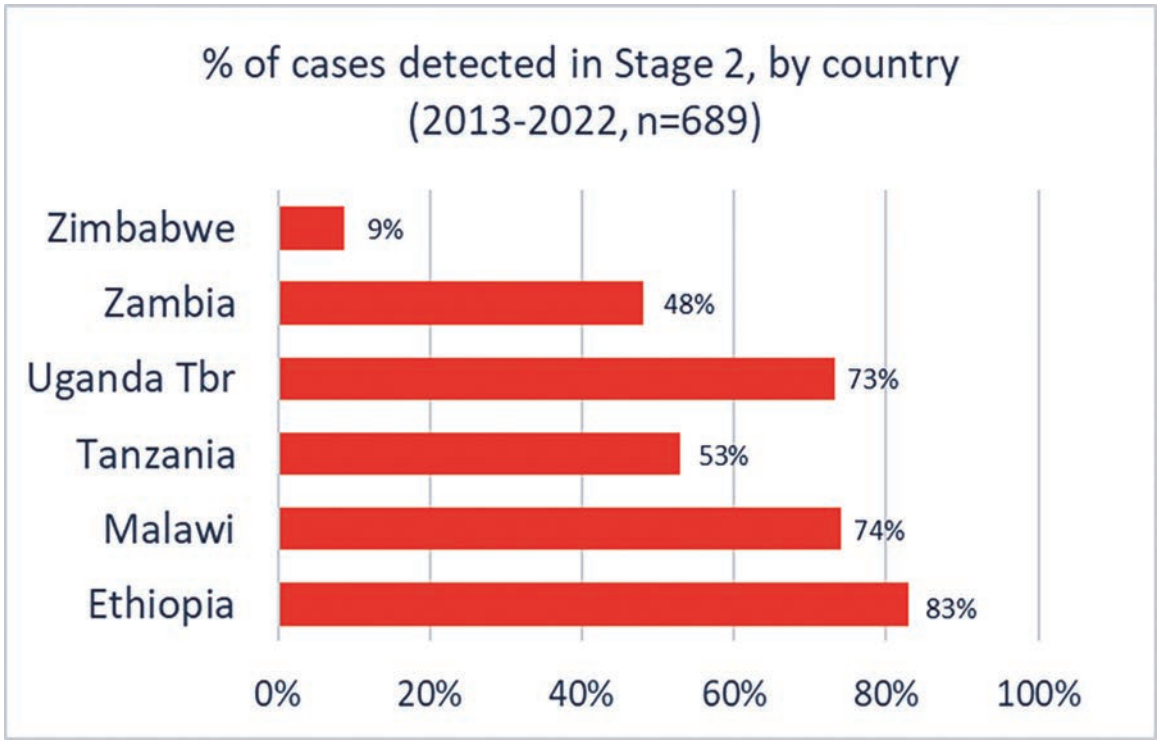



**Table 4.4.2.** Numbers of r-HAT cases by disease stage in the East Africa region, 2013–2022

| Disease stage | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Stage 1** | 17 | 22 | 27 | 15 | 4 | 14 | 46 | 33 | 13 | 13 | **204** |
| **Stage 2** | 64 | 94 | 45 | 39 | 22 | 10 | 66 | 65 | 41 | 25 | **471** |
| **Stage unknown** | 6 | 2 | 0 | 0 | 1 | 0 | 4 | 0 | 1 | 0 | **14** |
| **Total** | **87** | **118** | **72** | **54** | **27** | **24** | **116** | **98** | **55** | **38** | **689** |

**Figure 4.4.4.** Percentage of cases detected in stage 2, by country in the East Africa region, 2013-2022 (*n*=689)



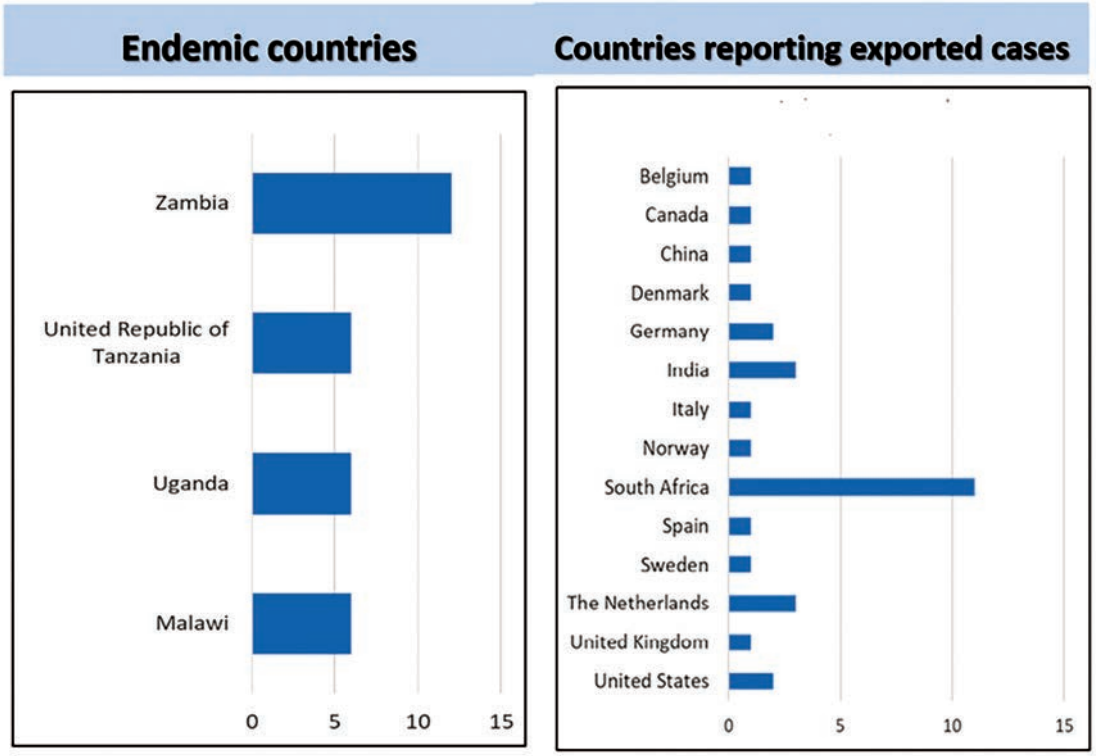

Tanzania: United Republic of Tanzania; Tbr: *Trypanosoma brucei rhodesiense*.

**Table 4.4.3.** Numbers of r-HAT cases treated, with number of deaths and case-fatality rate, East Africa region, 20162020

| Treatment of cases | 2016 | 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|---|---|
| Cases treated | 54 | 27 | 24 | 116 | 98 |
| % of cases treated | 100% | 100% | 100% | 100% | 100% |
| Deaths | 2 | 1 | 2 | 7 | 9 |
| Case-fatality rate | 3.7% | 3.7% | 8.3% | 6.0% | 9.2% |

During the period 2013–2022, the country exporting the most r-HAT cases was Zambia (12), followed by Malawi, Uganda and the United Republic of Tanzania (6 cases each). Most exported r-HAT cases were diagnosed in South Africa (11), a frequent destination for medical evacuation flights from south and east African countries, but also from various other countries (Figure 4.4.5).

**Figure 4.4.5.** Numbers of cases of r-HAT exported by country (left) and non-endemic countries reporting the cases (right), East Africa region, 2013–2022




The various **vector control** activities with locations and coverage are specified for Kenya, Rwanda, Uganda and Zimbabwe, as well as control strategies involving animals for Uganda (Table 4.4.4).

The group of East African countries identified the following **difficulties and challenges**:

- inadequate funding for capacity-building, surveillance and supervision;
- inaDequate clinical diagnosis of animal trypanosomiasis at district level;
- weak multisectoral engagement in One Health approach;
- low index of suspicion among health workers;
- preference for malaria rapid diagnostic tests (RDTs) by laboratory professionals instead of microscopy;
- high attrition rates of trained health professionals;
- low disease awareness in the communities;

- no cross-border collaboration for control activities;
- difficult access; and
- low community involvement for vector control activities.

**Table 4.4.4.** Vector control activities used in different countries of the East Africa region

| Country | Strategy used | Location | Coverage km$^2$) | Time period |
|---|---|---|---|---|
| **Kenya** | Deployment of biconical and Ngu traps | Busia, Bungoma, Homa Bay, Siaya, Migori and Narok counties | 357 | 2018 to date |
| | Deployment of insecticide-treated targets and insecticide-treated tiny targets | Busia, Bungoma, Homa Bay, Siaya, Migori and Narok counties | 357 | 2018 to date |
| | Insecticide-treated cattle | Busia, Bungoma, Homa Bay, Siaya, Migori and Narok counties | 1710 | 2018 to date |
| | Installation of livestock protective fence | Busia, Bungoma, Homa Bay, Siaya, Migori and Narok counties | 208 | 2018 to date |
| **Rwanda** | Use of traps and targets | Eastern Rwanda (Nyagatare, Gatsibo, Kayonza, and Kirehe districts) | | 2012 to date |
| | Target screens in the national park (along the roads frequented by tourists) | Akagera National Park | | 2012-to date |
| | Bush clearing is coupled with pasture management and fencing of individual farms | Eastern Rwanda (Nyagatare, Gatsibo, Kayonza, and Kirehe districts) | | 2012 to date |
| | Media engagement to increase community awareness of HAT | Eastern Rwanda (Nyagatare, Gatsibo, Kayonza, and Kirehe districts) | | 2022 to date |
| **Uganda** | Treated trap deployment | West Nile, Nwoya, Buvuma, Kalangala | | 2018–2022 |
| | Cattle mass treatment with trypanocides | Lango, Teso, Busoga, West Nile, Ankole, Buganda, Rwenzori, Buvuma, Kalangala, Karamoja | | 2018–2022 |
| | Vector surveillance | Lango, Teso, Busoga, West Nile, Ankole, Buganda, Rwenzori, Buvuma, Kalangala, Karamoja | | 2018–2022 |
| | Community engagement (awareness to encourage them to participate in control) | Lango, Teso, Busoga, West Nile, Ankole, Buganda, Rwenzori, Buvuma, Kalangala, Karamoja | | 2018–2022 |
| | Live bait technology | Lango, Teso, Busoga, West Nile, Ankole, Buganda, Rwenzori, Buvuma, Kalangala, Karamoja | | 2018–2022 |
| | Animal disease surveillance | Lango, Teso, Busoga, West Nile, Ankole, Buganda, Rwenzori, Buvuma, Kalangala, Karamoja | | 2018–2022 |
| **Zimbabwe** | Insecticide-impregnated targets | Makuti catchment area | 2000 | 2021 to date |
| | Ground and aerial spraying | Cattle-ranching areas | | 2018–2022 |
| | Mosquito nets (long-lasting insecticidal nets) | | | 2021 to date |

Table 4.4.5 categorizes the eligibility of countries endemic for r-HAT in the East Africa region – according to the national indicator (< 1 case/10 000 people per year in each health district averaged over the previous 5-year period) and control/surveillance activities – to request the validation of elimination as a public health problem. By 2021, three countries are eligible to request the validation of elimination, are in the process of doing so or have been already validated (in green).

**Table 4.4.5.** Situation of r-HAT endemic countries according to the criteria for claiming the validation of elimination as a public health problem, East Africa region, 2022

| **Two criteria** | **Epidemiological status (national indicator national for elimination as a public health problem)**<br>< 1 case/10 000 people per year, in each health district, averaged over the previous 5-year period | |
|---|---|---|
| **Control and surveillance activities** | **True in all districts** | **One or more non-compliant districts** |
| **Adequate** | Kenya, Rwanda, Uganda | Malawi |
| **Insufficient** | Ethiopia, United Republic of Tanzania, Zambia, Zimbabwe | |
| **Absent** | Burundi, Botswana, Eswatini, Namibia, Mozambique | |

Eligible to request validation
Need to reinforce surveillance before requesting validation
Need to set up a surveillance system
Non-eligible to request validation

# 5. Update on the global epidemiological situation

In 2012, WHO established the global target for elimination of HAT (g-HAT and r-HAT) as a public health problem by 2020, which was 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 the 2004 baseline level.

The primary indicators were the number of cases reported per year and the area at risk reporting ≥ 1 case/10 000 people per year.

In 2020, WHO published a new road map *(9)*, with the following different goals for g-HAT and r-HAT. For g-HAT, "to interrupt transmission of g-HAT (sustainable elimination) by 2030", and for r-HAT, "to keep r-HAT eliminated as a public health problem by 2030".

The indicators and the global targets set for 2030 are: for g-HAT, the number of g-HAT cases reported (global target 0) and the number of countries verified for interruption of transmission (15 countries); and for r-HAT, the number of countries validated for elimination as a public health problem (8 countries) and the areas with more than one r-HAT case per 10 000 inhabitants per year, averaged over the previous 5-year period.

## 5.1 Reported cases

The **number of HAT cases reported** annually reduced by 98% from 26 574 in 2000 to 663 cases in 2020 (Figure 5.1.1). Most cases (97%) were g-HAT (r-HAT 3%); the proportion of r-HAT is increasing. In 2017, for the first time, fewer than 2000 cases were reported, so this target has sufficiently been reached. Fewer than 1000 cases annually have been reported since 2018.

However, the decrease in the number of cases has tended to slow down (Figure 5.1.2). The COVID-19 pandemic led to a decrease in activities and consequently to a decrease in reported cases in 2020. Subsequently, there was an expected increase in cases when the activities picked up. In 2021, there was an increase of cases in Angola, in an area where active screening was resumed. In 2022, case numbers increased in Central African Republic, South Sudan and slightly in DRC. Nevertheless, the number of cases remains below 1000 per year. For r-HAT, a temporary increase of cases occurred due to a peak of cases in Uganda in 2013–2014 and an outbreak in Malawi in 2019–2020.

**Figure 5.1.1.** Progression towards HAT elimination: numbers of cases reported (blue line) in 2000–2020 and benchmark (green line) of the numbers of cases targeted for 2020

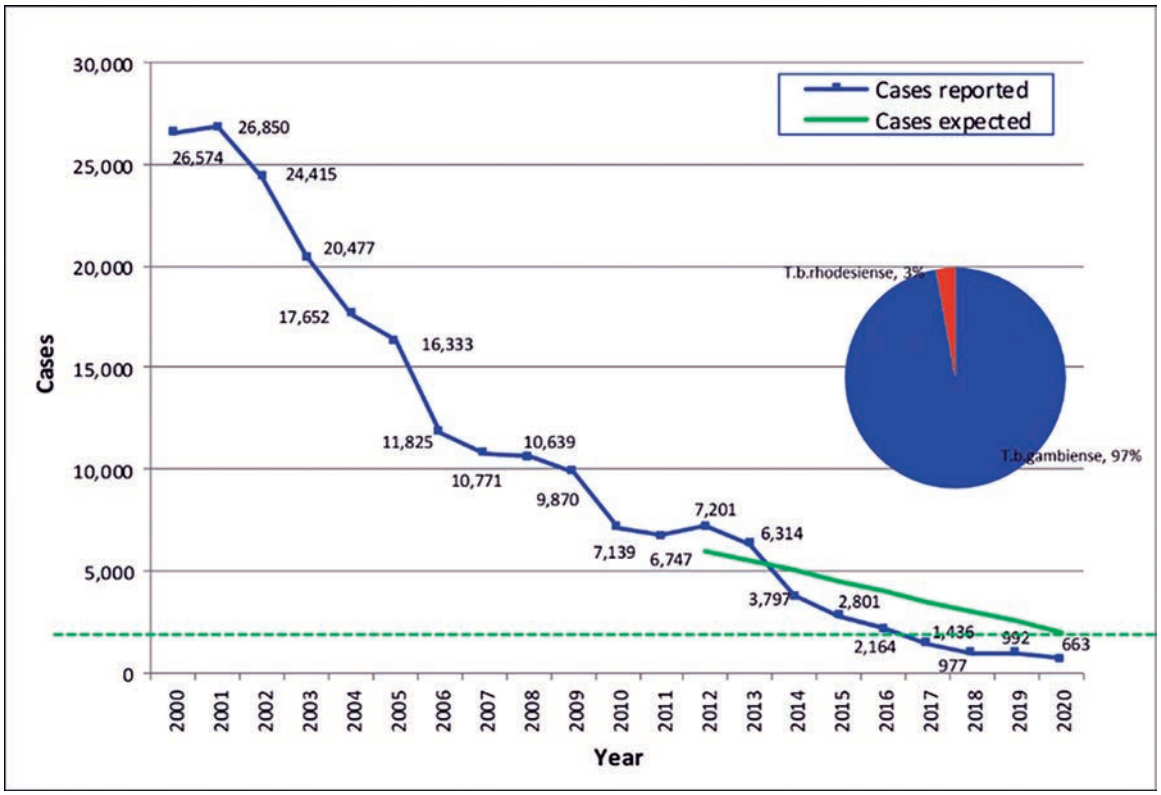
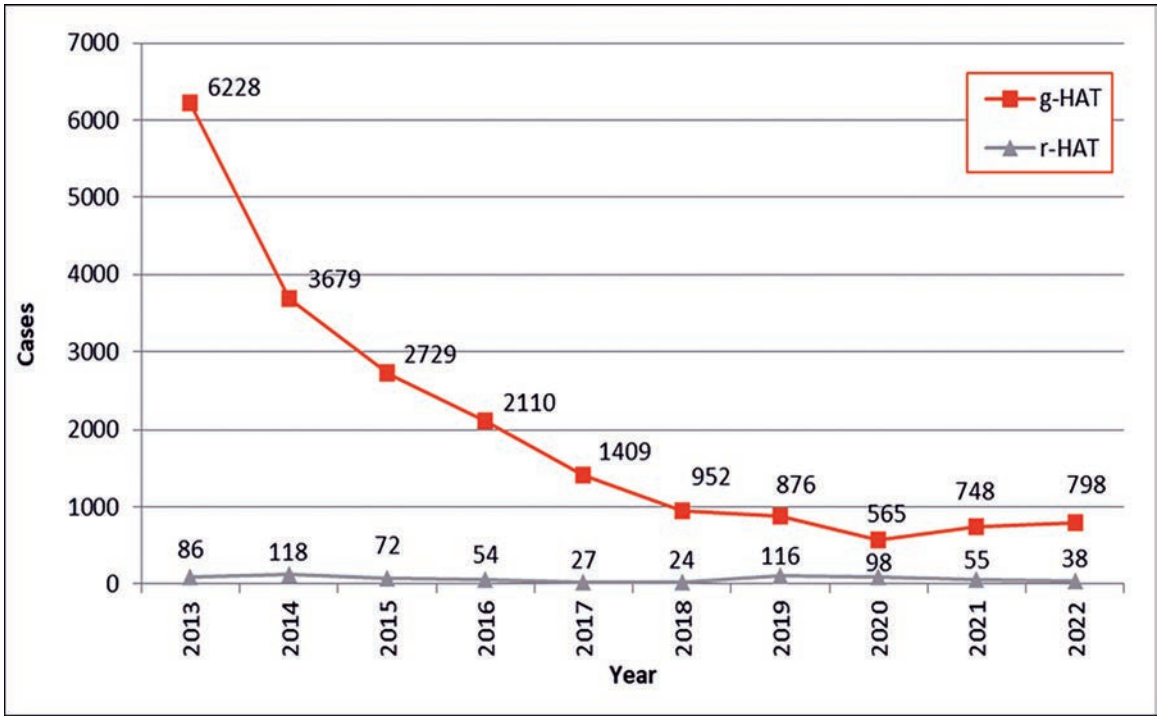



**Figure 5.1.2.** Numbers of g-HAT cases (orange) and r-HAT cases (grey) reported globally, 2013–2022




## 5.2 Geographical distribution of cases

Cases of HAT have been mapped at the village level in the HAT Atlas database since 2000. A comparison of the distribution of cases in the period 2000–2004 (Figure 5.2.1) with the period 2018–2022 (Figure 5.2.2) shows a significant reduction in the area with cases.

Two regions are of particular note. In the north-east of the DRC, cases are no longer reported, but all case-finding activities have ended. Another example is Ethiopia, where cases have reappeared after more than 30 years, highlighting the potential for re-emergence.

**Figure 5.2.1.** Geographical distribution of cumulated HAT cases (g-HAT in red, r-HAT in blue), 2000–2004

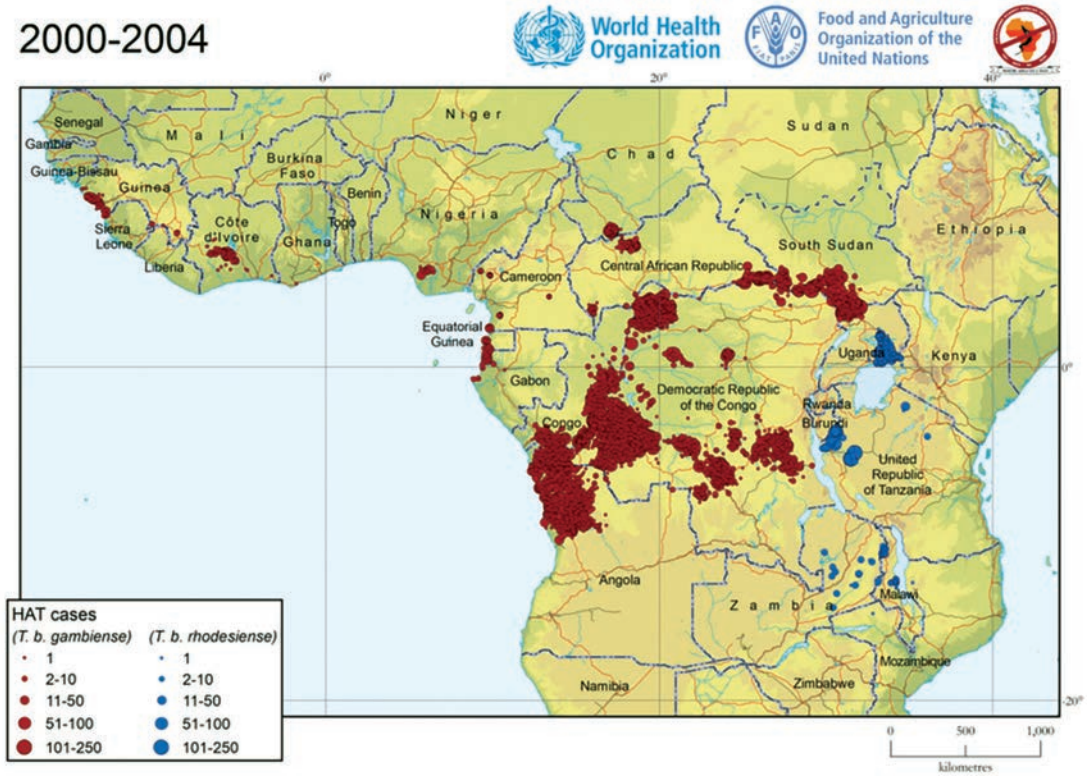
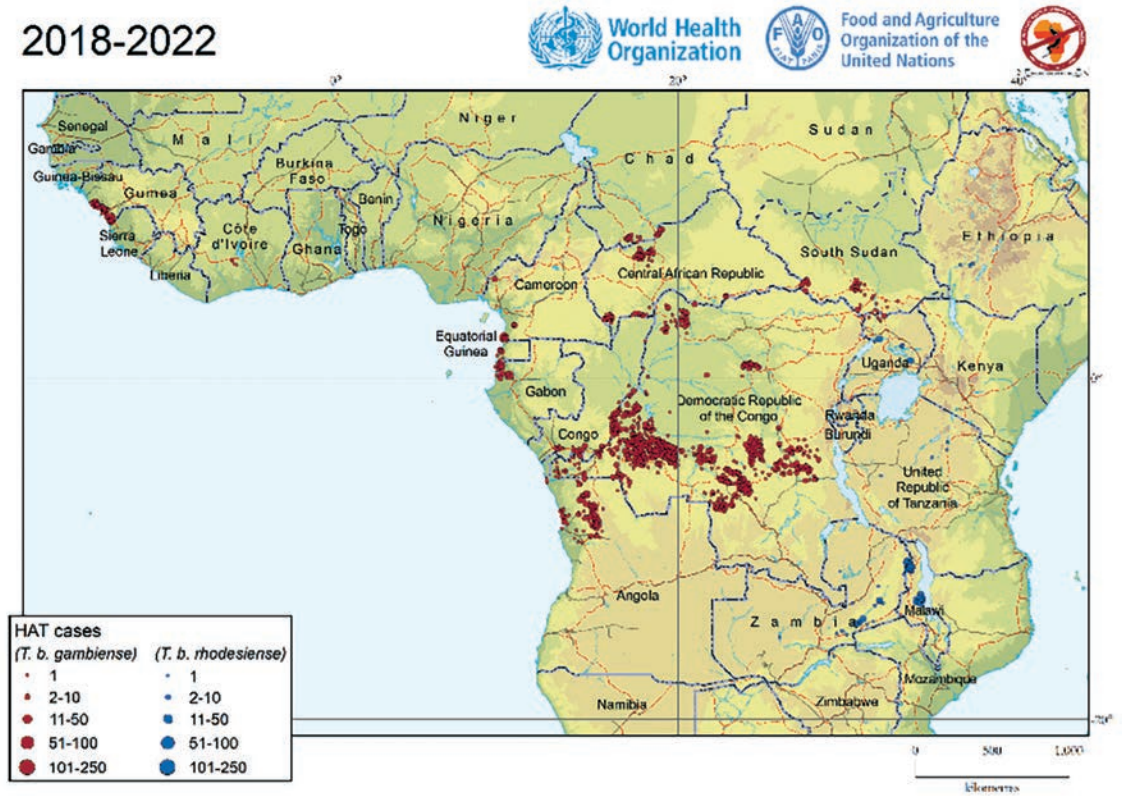



**Figure 5.2.2.** Geographical distribution of cumulated HAT cases (g-HAT in red, r-HAT in blue), 2018–2022



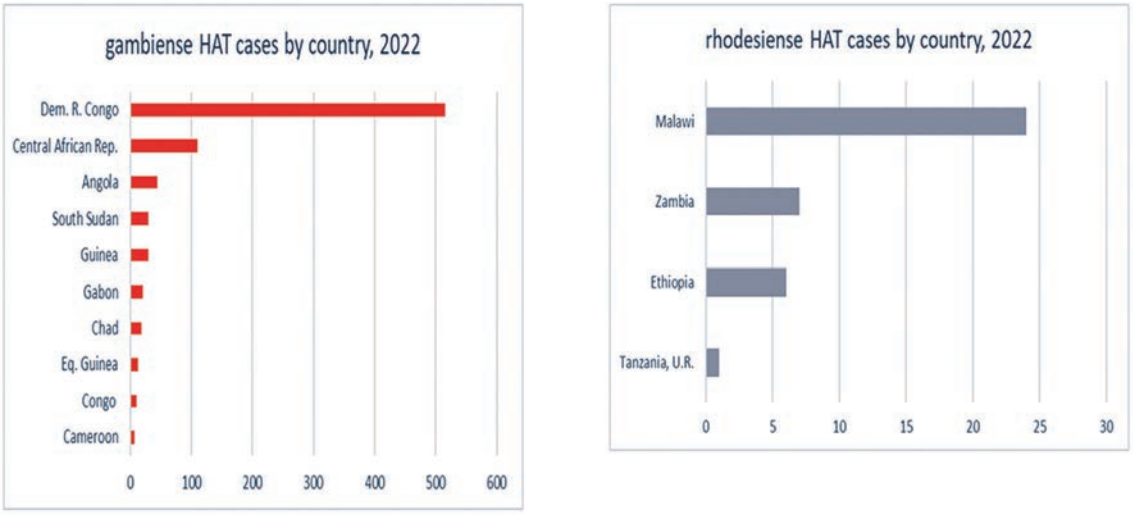
From 2018 to 2022, 4272 cases were reported from 18 endemic countries. In these 5 years, 92% of the cases were g-HAT, of which 87% occurred in DRC, the only country to report an average of over 500 cases per year. Angola, Chad, Central African Republic, Congo, Gabon, Guinea, Malawi and South Sudan reported 10–100 cases on average per year.

In 2022, 837 cases were reported from 14 endemic countries (Figure 5.2.3):

- *Trypanosoma brucei (T. b.) gambiense (799)*: Angola, Cameroon, Central African Republic, Chad, Congo, DRC, Equatorial Guinea, Gabon, Guinea, South Sudan; and
- *Trypanosoma brucei (T. b.) rhodesiense (38)*: Ethiopia, Malawi, United Republic of Tanzania, Zambia.

Some 65% of g-HAT cases were diagnosed in DRC and 81% of r-HAT cases were diagnosed in Malawi.

**Figure 5.2.3.** Numbers of g-HAT (left) and r-HAT cases (right) by country in 2022




Central African Rep.: Central African Republic; Dem. R. Congo: Democratic Republic of the Congo; Eq. Guinea: Equatorial Guinea; Tanzania, U.R.: United Republic of Tanzania.

## 5.3 Areas at risk

The areas at risk for g-HAT or r-HAT are shown by risk category for the period 2000–2004 (Figure 5.3.1) and the most recent period 2018–2022 (Figure 5.3.2). The evolution shows a marked reduction of areas at risk.

Figure 5.3.3 shows the total area at risk reporting ≥ 1 case/10 000 people per year (g-HAT in red, r-HAT in blue) and the associated milestones from 2000 to 2022. The area in all risk categories showed a marked and steady reduction by 83%, taking the mean of the 2016–2020 period. This important reduction (83%) was below the target of a 90% reduction from the 2000–2004 baseline levels. High and very high-risk areas have been extremely reduced (98.8%) with only very few km$^2$ remaining. In the latest data for the period 2018–2022, the global target of 90% reduction was achieved. Importantly, the areas at risk reduced from 708 827 to 73 609 km$^2$ (mean of the 2018–2022 period). The elimination of HAT as a public health problem at the global level has been achieved.

**Figure 5.3.1.** Areas at risk for g-HAT (red) and r-HAT (blue) from 2000 to 2004, by risk category

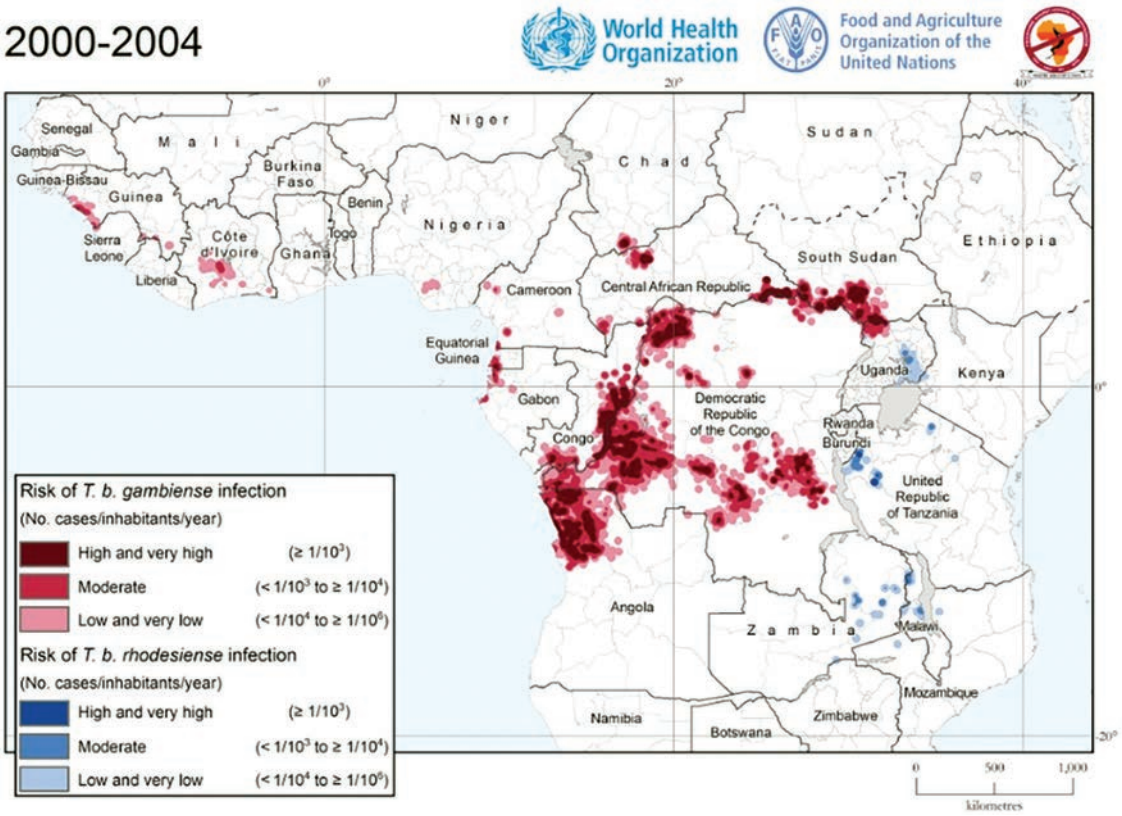



**Figure 5.3.2.** Areas at risk for g-HAT (red) and r-HAT (blue) from 2018 to 2022, by risk category

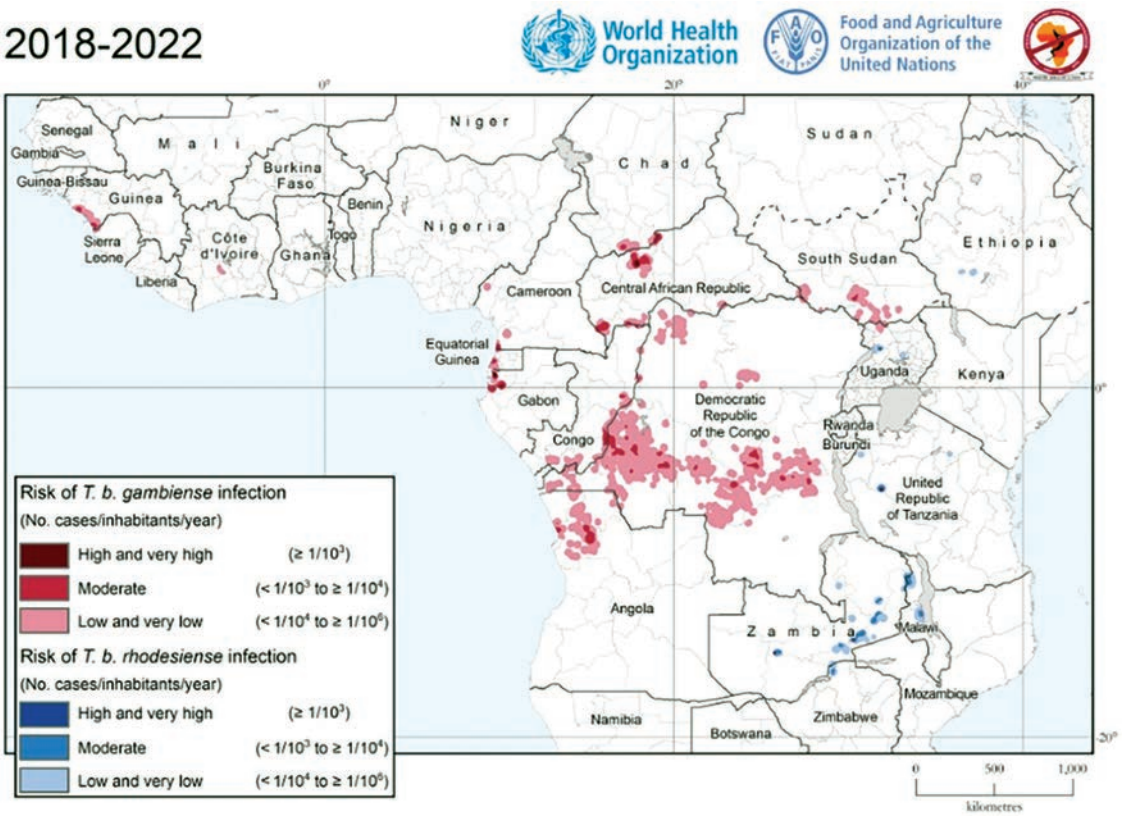
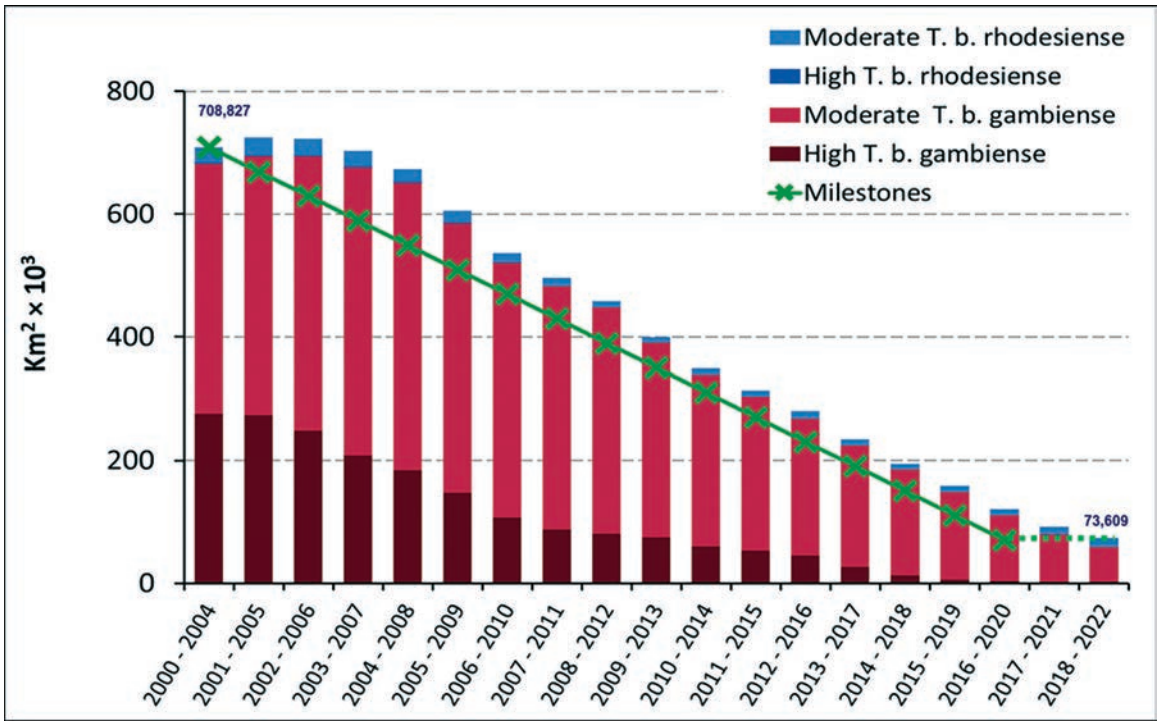


**Figure 5.3.3.** Total area at risk (high and moderate) for g-HAT (red) and r-HAT (blue) reporting ≥ 1 case/10 000 people per year, 2000–2022; the green line is the set milestone




## 5.4 Population at risk

During 2000–2004, 55.9 million people were estimated to be at risk of infection (Figure 5.4.1), of which 5.8 million were at very high and high risk, and 12.2 million at moderate risk. Therefore, 18 million people lived in areas where g-HAT was 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 nowadays. During 2018–2022, still 40.8 million people were estimated to be at risk of infection (Figure 5.4.2). However, a dramatic reduction was achieved in the very high and high-risk categories, which decreased to 0.01 million people; 1.5 million people were at moderate risk in this period; and 39.3 million people were at low or very low risk, which is not considered a public health problem.

## 5.5 Coverage of the population at risk

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 5.5.1). In 2019, nearly 3 million people were actively screened for HAT through concerted efforts by the countries, with DRC as a major contributor. The marked reduction in 2020 is explained by the impact of the COVID-19 pandemic. In 2022, there was again a significant reduction in the number of people screened, mainly due to organizational and funding problems for active screening in DRC.

From 2013 to 2022, some 21 140 931 people have been actively screened, thereof 92% in DRC (Figure 5.5.2); and 4 419 403 people were screened passively, thereof 89% in DRC (Figure 5.5.3). Despite the disruptions caused by the COVID-19 pandemic, the number of people passively screened remained stable, while active screening activities decreased in 2020. Even though the number of diagnostic facilities was increasing, the number of people passively screened dropped slightly in 2022, due to the problems referred before in DRC.

**Figure 5.4.1.** Population at risk of g-HAT (red) and r-HAT (blue), by level of risk in 2000–2004

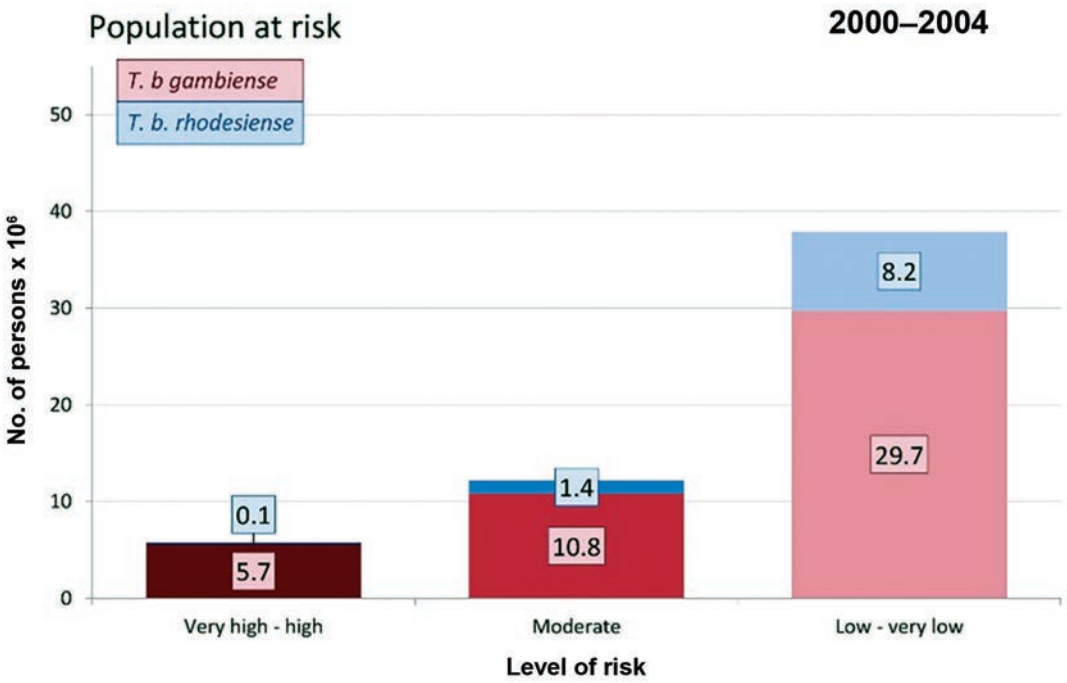



**Figure 5.4.2.** Population at risk of g-HAT (red) and r-HAT (blue), by level of risk in 2018–2022

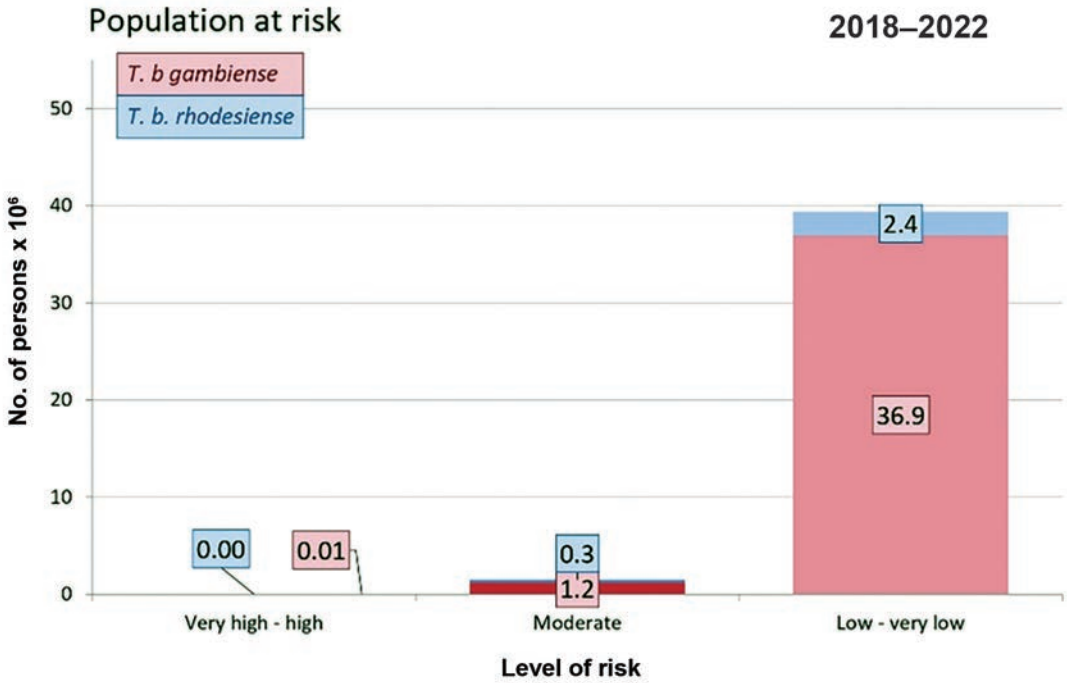


**Figure 5.5.1.** Numbers of people actively screened and numbers of reported cases, globally, 2000–2022

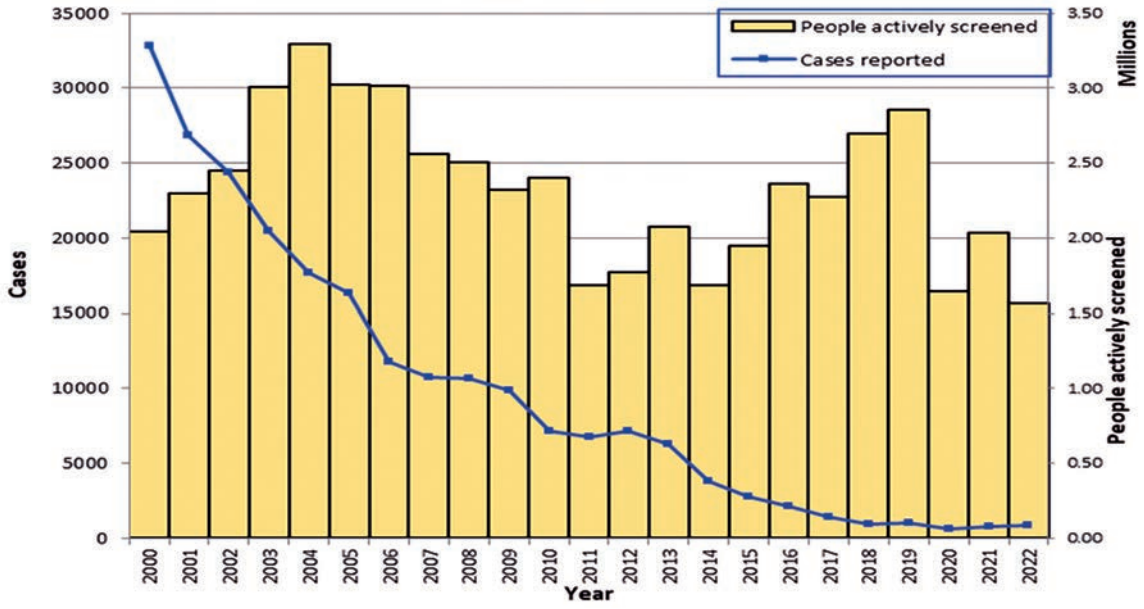



**Figure 5.5.2.** Numbers of people actively screened in DRC (blue) and other countries (orange), 2013–2022

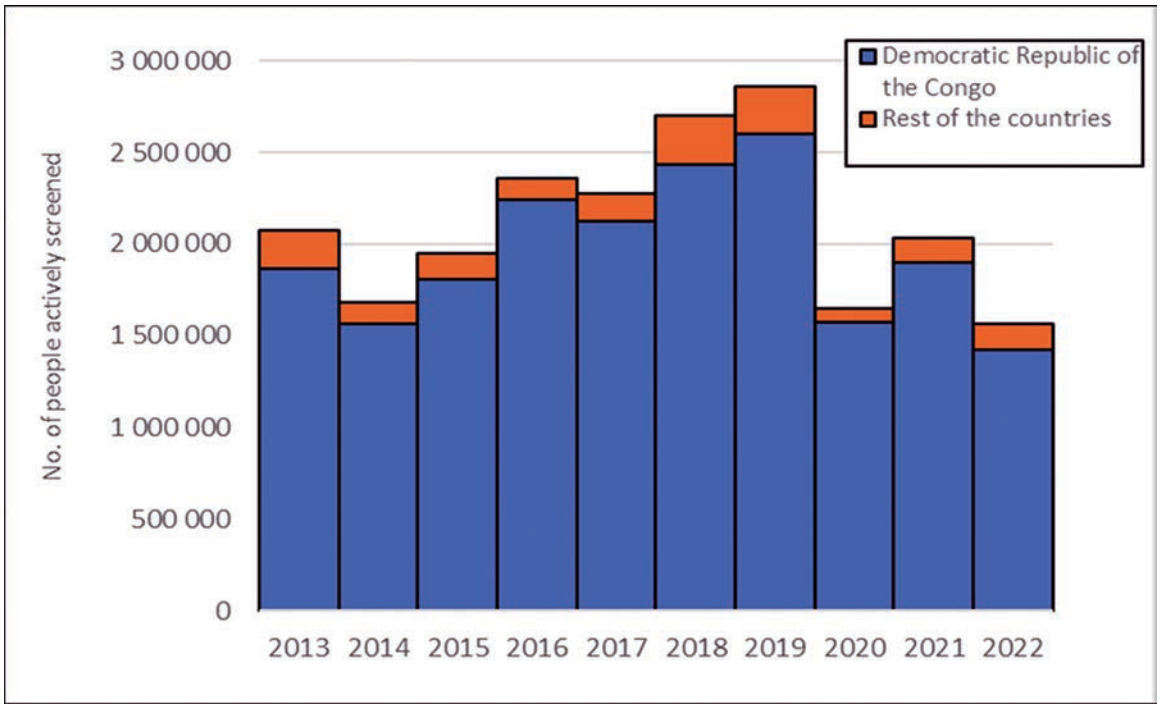



Figure 5.5.4 illustrates the places where active screening was carried out. Most of the areas where cases have been detected are also covered by active screening. However, in South Sudan, there are areas with cases that have not yet been reached by active screening.

**Figure 5.5.3.** Numbers of people passively screened in DRC (blue) and other countries (orange), 2013-2022

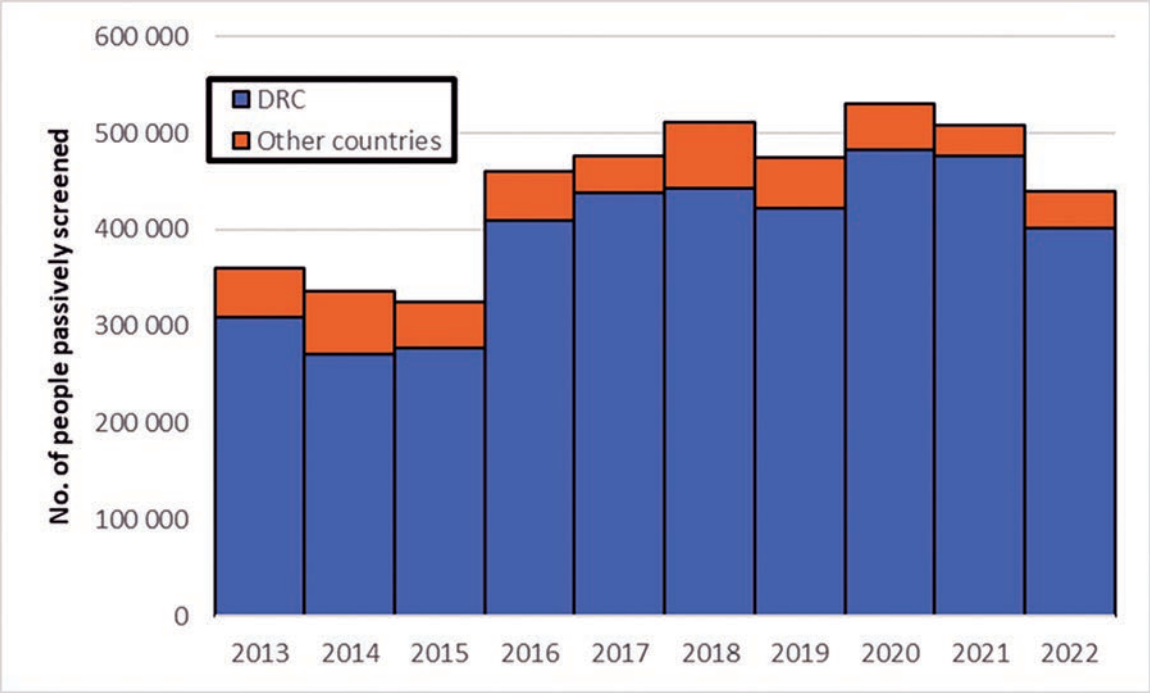
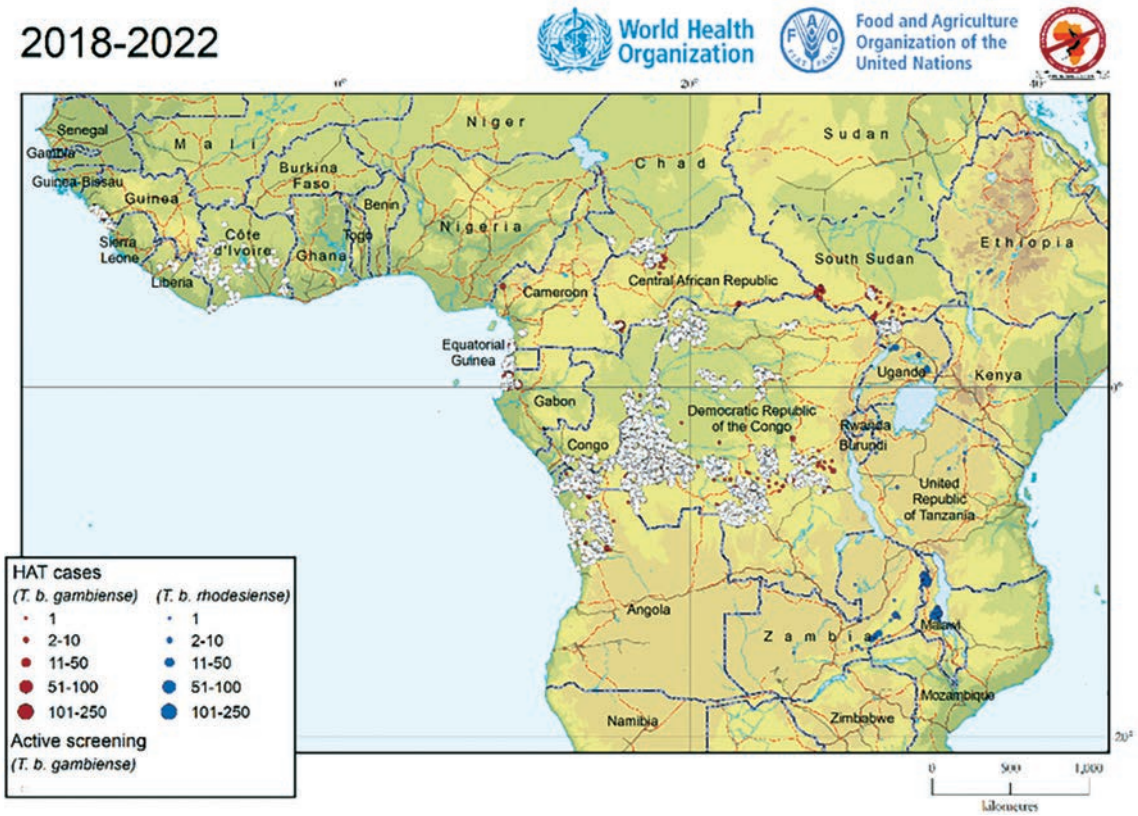
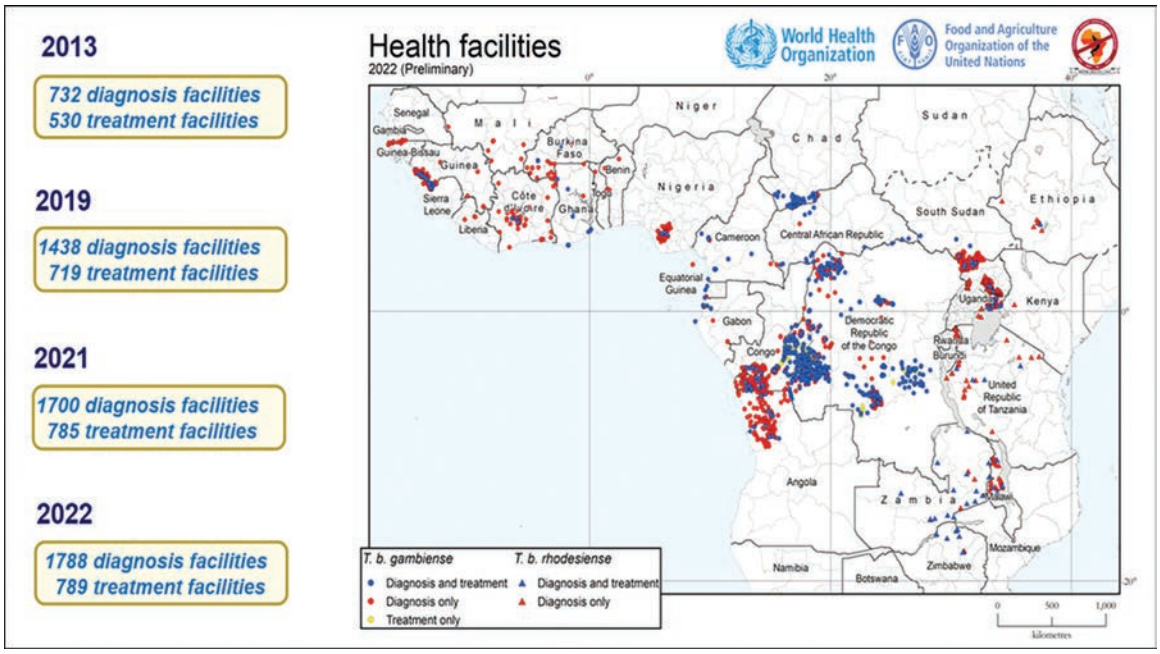



**Figure 5.5.4.** Geographical distribution of cumulated HAT cases (g-HAT in red, r-HAT in blue) and active screening sites (white dots), 2018–2022



The number of health facilities with capacity to screen (passively), diagnose and treat HAT has increased annually, thereby improving access to diagnosis and treatment (Figure 5.5.5). In 2013, 732 fixed health facilities provided diagnosis of HAT and 530 provided any treatment for HAT. In 2022, 1788 fixed health facilities provided diagnosis and 789 provided any treatment for HAT. Surveys are conducted biannually. In 2022, HAT sites were established in Ethiopia and Senegal as new countries. Through the increased diagnostic capacity, the epidemiological knowledge is better than ever before.

**Figure 5.5.5.** Health facilities providing g-HAT (dots) and r-HAT (triangles) diagnosis and treatment in 2022; red indicates only diagnostic capacity, blue diagnostic and treatment capacity




In the current situation, HAT is eliminated as a public health problem. However, several challenges remain. There is little awareness about the disease in communities, resulting in low population participation in active screening. Furthermore, there is an insufficient number of well-trained personnel due to retirement of experienced staff and staff turnover. Politicians and health authorities set other priorities, bearing the risk of re-emergence.

## 5.6 Conclusions

The elimination of HAT as a public health problem has been achieved. All stakeholders can be congratulated for this accomplishment.

Fewer than 1000 cases of HAT annually have been reported over the past 5 years, which is a historic achievement. Importantly, the area at risk has been reduced, reaching the target established for 2020. There are still 41 million people at risk for HAT, but only 1.5 million at moderate risk and the remaining 39.5 are at low or very low risk. The COVID-19 pandemic had a significant negative impact on the process of HAT elimination; adaptive strategies limited its impact (e.g. virtual meetings, adapted active screening, reinforcement of passive screening). With the low number of cases, it is crucial to ensure adequate diagnosis and timely treatment. The risk for r-HAT epidemics is always present.

In this situation it is essential to keep partners' commitment, to promote ownership by national health authorities, and to maintain adequate coordination of partners. The new targets have now to be addressed for 2030.

# 6. Status of validation of elimination as a public health problem at country level

A country could be considered as having eliminated HAT as a public health problem when dedicated medical activities have shown that there are < 1 case per 10 000 people in all the health districts of the country over the previous 5-year period. Countries meeting these criteria can request the validation of elimination as a public health problem. A validation dossier has to be prepared and submitted to WHO documenting this achievement. A reviewing validation team is constituted to evaluate the completeness, accuracy and reliability of the country dossier. The reviewing validation team ascertains the likelihood that HAT is no longer a public health problem in the country and that the criteria established for this purpose are met. The validation team assesses whether the surveillance system is adequate and the data can be considered reliable. The WHO secretariat coordinates that process and produces the final report. The final report is submitted to the WHO Regional Office for Africa and is endorsed by its Regional Director. The Director-General of WHO then 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.

Table 6.1 categorizes the eligibility of the HAT endemic countries according to national indicators and control/surveillance activities – to request the validation of elimination as a public health problem.

**Table 6.1.** Eligibility of HAT-endemic countries for claiming the validation of elimination as a public health problem, according to the epidemiological situation and control and surveillance activities (update May 2023)

| Elimination as a PHP still not reached | Elimination as a PHP reached but surveillance insufficient | Elimination as a PHP reached and country ready to submit dossier for validation | Elimination reached and dossier submitted for validation | Post-validation surveillance ongoing |
|---|---|---|---|---|
| Angola, Central African Republic, Congo, Democratic Republic of the Congo, South Sudan | Gambia, Guinea-Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone | Burkina Faso, Cameroon, Gabon, Guinea | Chad | Benin, Côte d'Ivoire, Equatorial Guinea, Togo, Uganda (T.b.g), Ghana |
| Malawi | Botswana, Burundi, Eswatini, Ethiopia, Mozambique, Namibia, Uganda (T.b.r.), United Republic of Tanzania, Zambia, Zimbabwe | Kenya | | Rwanda |

PHP: public health problem; T.b.g: *Trypanosoma brucei gambiense*; T.b.r: *Trypanosoma brucei rhodesiense*.

The elimination of HAT as a public health problem was validated in Côte d'Ivoire and Togo in 2020; and in 2021 and 2022 in Benin, Equatorial Guinea, Ghana, Uganda (all for g-HAT) and in Rwanda (for r-HAT). Chad has submitted its dossier for validation.

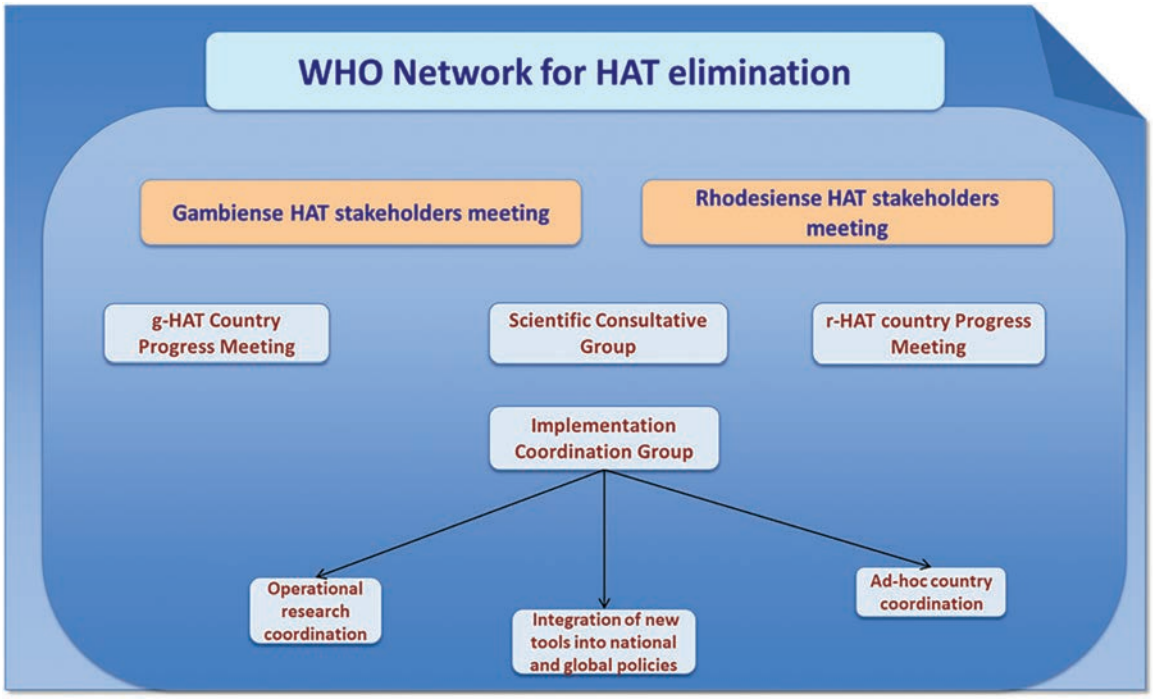
Post-elimination surveillance is ongoing. Some declining surveillance was observed in Togo, but measures were taken in response, and activities were intensified again. An increase of cases post-elimination has been detected in Equatorial Guinea, but the country was able to react accordingly, and the numbers of cases are falling again this year.

Countries are encouraged to advance the validation of elimination, but the limited support for elimination makes it difficult for countries to achieve this objective. WHO will assist the countries in this process.

# 7. WHO network for HAT elimination: report on the past 2 years

In order to coordinate the different stakeholders involved in the HAT elimination process and to strengthen and sustain efforts, WHO launched the network for HAT elimination in 2014 (Figure 7.1).

**Figure 7.1.** Configuration of the WHO Network for HAT elimination




In the past 2 years, the different groups and subgroups of the network have conducted various activities.

- **Stakeholder meetings**
  - 4th stakeholders meeting for g-HAT and r-HAT, for the first time as a joint event and as a virtual event due to the COVID-19 pandemic in June 2021; and
  - 5th stakeholders meeting for g-HAT and r-HAT in Geneva in June 2023.
- **Annual country coordination meetings**
  - for francophone g-HAT endemic countries in February 2022 and February 2023; and
  - for anglophone g-HAT and r-HAT endemic countries in March 2022 and February 2023.
- **Ad-hoc country coordination**
  - Democratic Republic of the Congo: PNLTHA partners meeting (July 2022, January 2023);
  - Guinea (June 2022);
  - Chad (January 2022); and
  - Ethiopia (November 2022 and February 2023), together with many national institutions as a response to the re-emergence of r-HAT.

- **Scientific Consultative Groups**
  - Technical Advisory Group for HAT elimination (HAT-e-TAG): 6th meeting in February 2022, and 7th meeting in January 2023.
  - HAT-DTAG (WHO Diagnostic Technical Advisory Group) subgroup (Development of Diagnostic TTP): 3rd meeting (March 2022) and 4th meeting (June 2022), followed by remote collaboration; and
  - WHO Regional Office for Africa Case management Review Group: 3rd meeting (March 2022).
- **Integration of new treatment tools into national and global policies subgroup**
  - Vector control for g-HAT elimination: 1st meeting, virtual (October 2021), 2nd meeting, Rome (December 2022), the meeting reports are available;
  - Sociocultural dimensions in HAT elimination: 1st meeting, virtual (July 2021), coordinated by the Institute of Hygiene and Tropical Medicine (IHMT), Lisbon; and
  - Sub-group "New oral drugs": 12th meeting (March 2022), 13th meeting (March 2023).

The coordination of the different technical partners and NSSCPs is a high priority for WHO. The HAT elimination network continues actively at different levels as a very useful tool for coordination. NSSCPs play a central role in efforts to eliminate HAT.

# 8. Diagnostics for neglected tropical diseases

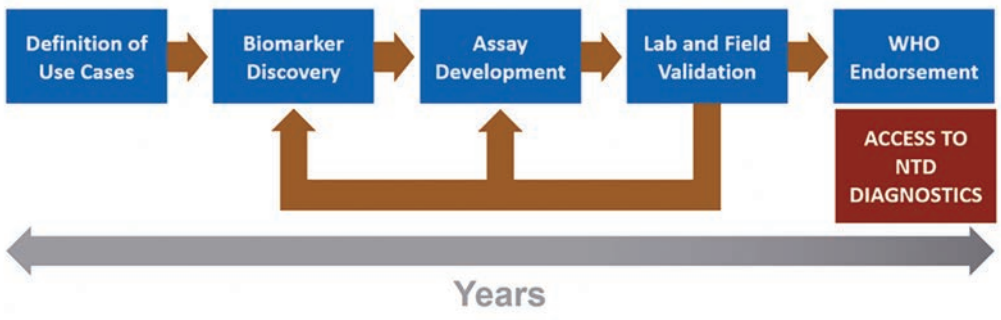
The road map establishes targets across the NTD portfolio. It defines the critical actions needed to achieve these targets and calls for new approaches to accelerate programmatic action, intensify cross-cutting approaches and facilitate country ownership. A gap assessment was performed across the several dimensions of all NTDs. The four critical areas identified were:

- diagnostics and other key innovations;
- monitoring and evaluation;
- access and logistics; and
- advocacy and funding.

The current diagnostic tools are insufficient to meet WHO's ambitious road map targets, in terms of their performance, quality and access (low number of manufacturers, limited manufacturing capacities). In 2019, the WHO Department of Control of Neglected Tropical Diseases created the Diagnostic Technical Advisory Group (DTAG) for NTDs to establish a harmonized approach, and to identify and prioritize diagnostic needs for all NTDs. The goal is to foster end-to-end solutions for NTD diagnostics (Figure 8.1).

The DTAG consists of global experts in various fields (diagnostics, public health, policy-makers, epidemiologists, donors, implementing partners, programme managers, etc.), and is organized in subgroups which are focused on disease-specific and cross-cutting themes through a hub and spokes model.

**Figure 8.1.** The various steps for solutions in NTD diagnostics




The DTAG is working to:

- define the needs and costs of NTD biobanks supporting test development;
- address the challenge of test validation in the absence of a gold standard;
- stress the importance of external quality control; and
- define regulatory pathways for NTD diagnostics.

Some NTD diagnostics for diseases with high individual risk or moderate/high public health risk may enter into the WHO prequalification process for in-vitro diagnostics to ensure that products are quality-assured and appropriate for their intended use. However, it is unrealistic to include all NTD diagnostics within the scope of WHO prequalification. If in-vitro diagnostics do not qualify for WHO prequalification, there will be an **Expert Review Panel for Diagnostics** as an interim mechanism, providing time-limited recommendations following review of risks and benefits associated with their use. It is intended for in-vitro diagnostics that have not undergone prequalification or assessment by a stringent regulatory authority. It is planned to pilot test this Expert Review Panel mechanism in Q4 2023. Manufacturers will be engaged in order to have a clear pathway. A further major area is to strengthen NTD laboratory capacity and networking. A network of laboratories will also facilitate sending samples, external quality control, provision of trainings and capacity building.

# 9. Diagnostics for HAT

## 9.1 WHO Diagnostic Technical Advisory Group subgroup

The DTAG was established to address the need for improved diagnostics in NTD programmes. Established subgroups work it to analyse the diagnostic landscape and diagnostic priorities. Use cases are being developed to describe the context of a diagnostic application, followed by WHO target product profiles (TTPs), outlining the desired characteristics of a target diagnostic for a particular disease and help test developers focus on the tests needed by programmes. The HAT-DTAG is the subgroup working on diagnostic innovation needs for HAT, and it has identified four diagnostic priorities:

### 9.1.1 Test for r-HAT usable in peripheral health facilities

The diagnostic landscape is characterized by the lack of a simple screening test for r-HAT. Because trypanosomes must be microscopically observed in the blood or other tissues, r-HAT is often detected incidentally during the examination of stained thick or thin blood slides for malaria diagnosis. The progressive introduction of malaria RDTs has been accompanied by a decrease in microscopy equipment and capacity. As a result, incidental diagnosis of r-HAT is decreasing. Diagnosis is often missed or delayed.

The following **use case** was defined:

- a simple test to facilitate control and surveillance and allow faster prescription of treatment, applicable in places where people seek malaria diagnosis;
- to capture information on the incidence of r-HAT transmission; and
- restore lost surveillance capacity and potentially strengthen it.

**TPP 1** describes the following **technical scope and highlights**.

- Regarding the analyte: ideally, an antigen-detection RDT but, alternatively, a molecular test that detects DNA or RNA, or a microscopy-free test that detects the presence of trypanosomes.
- Regarding the use of the information obtained: ideally, immediate results to guide therapeutic decisions. In the current situation, it could be a screening test that, if positive, would be followed by confirmatory microscopy (parasitaemia is usually high); but, for the future, a test to identify individuals for treatment.

### 9.1.2 Diagnostic tool to identify individuals with suspected but microscopically unconfirmed g-HAT, to receive treatment

The diagnostic landscape is characterized by the reduction of g-HAT prevalence, as a consequence of repeated serological screening and treatment of confirmed cases. The current methods are laborious, have 85–95% diagnostic sensitivity and require skilled personnel. In this situation, it is known that seropositive but microscopically unconfirmed individuals have a variable probability of harbouring the parasite and of thus maintaining the reservoir and the risk of transmission. At the same time, the current treatment is logistically challenging, not sufficiently safe and not recommended on clinical suspicion alone; a new safe and easy-to-use treatment will allow the treatment of highly suspected individuals in the future (widened treatment).

The following use case was defined:

- a simple diagnostic tool; and
- to identify individuals with suspected but microscopically unconfirmed g-HAT infection who are eligible for treatment with safe and easy-to-use medicines.

**TPP 2** describes the following **technical scope and highlights**.

- Regarding the method: easy to use, applicable at the point of care (including mobile laboratories with no infrastructure); and requiring minimal training.
- Regarding the assay performance: a high sensitivity is required and, ideally, only one test to make a therapeutic decision but alternatively, a tandem of 2 simple sequential tests.
- Regarding the use of the information obtained: it has to identify individuals with a high enough suspicion of infection to warrant treatment with a drug with a good safety profile.

### 9.1.3 Individual test to assess *T. b. gambiense* infection in low prevalence settings

The diagnostic landscape is characterized by the low HAT prevalence, which increases the low predictive positive value of serological tests. Furthermore, the best parasitological tests have limited sensitivity. At the same time, the low number of HAT cases has led to a loss of experience with microscopy, which has in turn become unavailable or potentially less reliable. Data are needed to assess HAT elimination and zero transmission in endemic countries, and the introduction of widened treatment will require monitoring of g-HAT, adjusted control strategies and stop criteria for widened treatment.

The following use case was defined:

- confirm *T. b. gambiense* infection in settings where microscopy is absent or unreliable due to low case numbers and lack of experience; and
- to assess *T. b. gambiense* infection a posteriori in individuals who have received presumptive treatment in the field.

**TPP 3** describes the following **technical scope and highlights**:

- used at the individual level in suspected cases to determine whether they are/were infected with *T. b. gambiense*.
- Ideally, test sites are located in national or subnational reference laboratories, alternatively in regional reference laboratories. Specimens are collected ideally from finger-prick blood, but alternatively venous serum/plasma/blood, in a carrier allowing stability for 4 weeks at 40 °C and 12 months at 4 °C. If shipping is required, the infectivity of the shipped specimen must be reduced to zero or near zero.
- Test performance should be highly specific. Sensitivity is not the primary concern, as a screening test is usually performed first; and the duration of test positivity after treatment needs to be established.

### 9.1.4 High throughput g-HAT test for verification of elimination

The diagnostic landscape is characterized by the current validation (incidence < 1/10 000) and verification (zero autochthonous cases for 5 years) of HAT elimination targets. At the same time, dedicated surveillance must be maintained because of the risk of re-emergence or re-introduction. Large-scale testing of at-risk populations is needed to verify the absence of *T. b. gambiense* transmission; and taking into account that the low/zero prevalence means loss of specialist staff, requiring feasible methods using non-specialist staff.

The following use case was defined:

- high-throughput methods to complement classic passive/active screening with appropriate tools for cross-cutting surveillance for *T. b. gambiense* transmission at population-level; and
- testing of at-risk populations with comprehensive coverage. Populations thought to have become risk-free, where absence of transmission needs to be confirmed.

**TPP 4** describes the following **technical scope and highlights**.

- Test numerous samples collected in remote rural areas.
- Ideally, collection of samples and specimens should be non-invasive and simple, with no cold chain required for transfer to the reference laboratory.
- Ideally, the testing site is in national or sub-national reference laboratories.
- Test performance has high sensitivity and specificity with results available in a relatively short time.
- The test is applicable in animals to assess parasite presence.
- Low total cost per sample when tested in batches of hundreds or thousands.

The WHO TTPs are available on the WHO website *(10–13)*. In addition, the four TPPs on HAT diagnostics (Figure 9.1.1) have been published in the WHO Bulletin *(14)*.

**Figure 9.1.1.** The four WHO TPPs developed by the HAT-DTAG

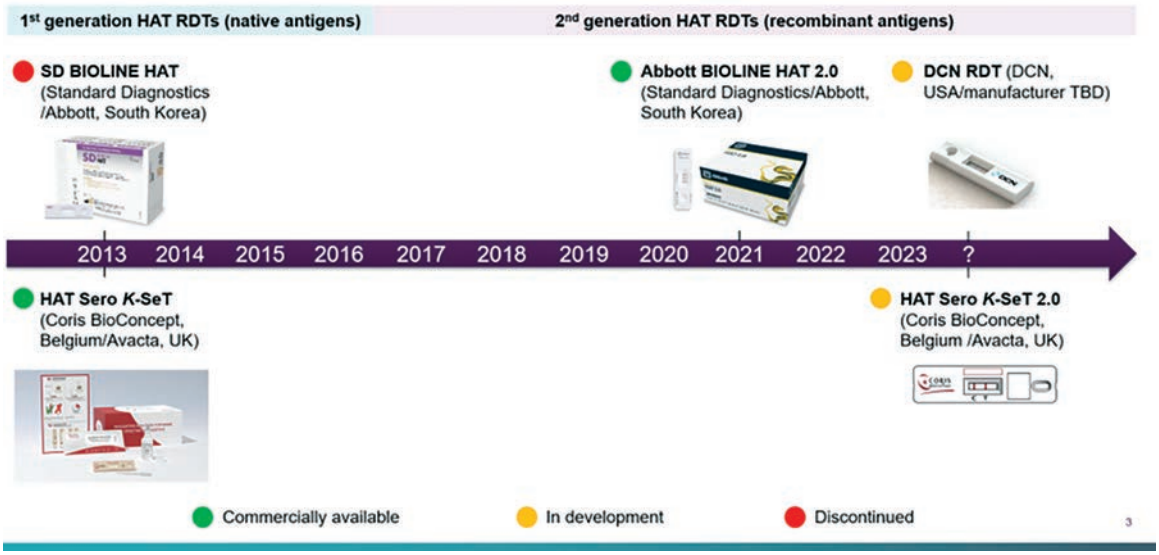

## 9.2 Advances and perspectives

### 9.2.1 Rapid diagnostic tests

The HAT RDTs are used as screening tests followed by confirmatory testing. Nowadays, their commonest use is for passive screening, but they are also used for active screening (e.g. door-to-door screening, by motorcycle teams or large mobile teams). For mass screening, the card agglutination test for trypanosomiasis (CATT) is the better option because of its higher specificity and practicality. It is hoped that there will be a transition to a new test-and-treat strategy, whereby RDT-positive individuals would be treated directly without confirmation. Before such a new strategy can be implemented, treatment strategies need to be established, more drug safety data collected and RDT performance criteria specified, particularly with regard to specificity.

Figure 9.2.1 illustrates the development and commercialization pipeline for HAT RDTs

**Figure 9.2.1.** Development and commercialization pipeline for HAT RDTs




The first generation RDT (**SD BIOLINE HAT**) uses two native antigens supplied by the Institute of Tropical Medicine, Antwerp (ITM), the VSG LiTat 1.3 and the VSG LiTat 1.5, which are manufactured by Standard Diagnostic, Inc. (SD), now part of Abbott. The test features two test lines for the two different antigens. A total of approximately 2.3 million tests have been delivered since 2013 at a price of US$ 0.50/test, thanks to a grant from the BMGF through the Foundation for Innovative New Diagnostics (FIND). Production has stopped multiple times due to issues related to quality control of native antigen. In response, Abbott has recently attempted to change the product design to use antigens in a different format as suggested by ITM. Unfortunately, this has not yielded any improvement and some specificity problems remain. The product is currently unavailable and there are no plans to resume production.

Coris BioConcept, Belgium/Avacta, UK developed the **HAT Sero *K*-SeT** RDT in 2012 based on the same two native antigens (VSG LiTat 1.3 and VSG LiTat 1.5) supplied by ITM. The test shows a single test line with the mixture of the two antigens and is therefore easy to read. The test was commercialized in 2013 by Coris BioConcept (Belgium) and is currently available. The price ranges from € 1.95 to € 3.00 per test depending on the order volume. More than 4 million tests have been supplied to HAT-endemic countries since being commercialized, with no significant interruptions even during the COVID-19 pandemic.

The second-generation RDT (**Abbott BIOLINE HAT 2.0**, SD/Abbott) uses two recombinant antigens (ISG65 and VSG LiTat 1.5) produced in-house by Abbott (using *Escherichia coli* and baculovirus expression systems respectively). The test has two test lines for the two different antigens. The test is commercially available at US$ 0.50/test. This test has also been made available to HAT-endemic countries as part of an Abbott donation through FIND and WHO, for a total of 450 000 tests, of which 85% have already been delivered.

**DCN HAT RDT** was developed by DCN (Diagnostic Consulting Network), Carlsbad, USA. The design is similar to that of the Abbott BIOLINE HAT 2.0, with two test lines using the same two recombinant antigens. The test was developed to mitigate the risks associated with potential production or supply issues with the Abbott Bioline HAT 2.0. The development of the prototype has been completed. The prototype is ready to be transferred to a manufacturer if or when required, but is not currently planned.

The prototype **HAT Sero *K*-SeT 2.0** (Coris BioConcept/Avacta, UK) uses three recombinant antigens (ISG65, VSG LiTat 1.3 and VSG LiTat 1.5) expressed in insect cells. The prototype needs to be optimized based on the results of recent evaluation studies, in particular with regard to specificity.

The performance data on the three commercialized RDTs are summarized in Table 9.2.1. Their performance appears quite similar, albeit with inconsistencies in the different studies, making a solid conclusion difficult.

**Table 9.2.1.** Performance data from retrospective and prospective studies of the three commercially available RDTs

| Test | Country | Reference | Sensitivity | Specificity |
|---|---|---|---|---|
| **HAT Sero-K-SeT**<br>Sensitivity: 98.5–100%<br>Specificity: 79.7–98.6% | DRC | Büscher et al., 2014 *(15)* | 98.5% | 98.6% |
| | Guinea, Côte d'Ivoire (retrospective) | Jamonneau et al., 2015 *(16)* | 99.1% | 88.3% |
| | DRC | Boelaert et al., 2018 *(17)* | 100.0% | 97.0% |
| | Côte d'Ivoire | Koné et al., 2021 *(18)* | 100.0% | 97.8% |
| | Burkina Faso | Compaoré et al., 2022 *(19)* | - | 89.1% |
| | Guinea | Camara et al., 2023 *(20)* | 100.0% | 97.5% |
| | Chad, DRC, Guinea, Uganda (retrospective) | Tablado Alonso et al. [manuscript in preparation] | 99.4% | 79.7% |
| **SD Bioline HAT**<br>Sensitivity: 59.0–100%<br>Specificity: 72.0–98.9% | Guinea, Côte d'Ivoire (retrospective) | Jamonneau et al., 2015 *(16)* | 99.6% | 87.9% |
| | DRC | Lumbala et al, 2017 *(21)* | 92.0% | 97.1% |
| | DRC | Lumbala et al, 2018 *(22)* | 59.0% | 98.9% |
| | Côte d'Ivoire | Koné et al. 2021 *(18)* | 100.0% | 98.9% |
| | Burkina Faso | Compaoré et al. 2022 *(19)* | - | 92.9% |
| | Guinea | Camara et al. 2023 *(20)* | 93.8% | 97.9% |
| | Chad, DRC, Guinea, Uganda (retrospective) | Tablado Alonso et al. [manuscript in preparation] | 98.7% | 72.0% |
| **Abbott Bioline HAT 2.0**<br>Sensitivity: 71.2–96.8%<br>Specificity: 79.0–98.1% | DRC | Lumbala et al, 2018 *(22)* | 71.2% | 98.1% |
| | Chad, DRC, Guinea, Uganda (retrospective) | Tablado Alonso et al. [manuscript in preparation] | 96.8% | 79.0% |

DRC: Democratic Republic of the Congo; HAT: human African trypanosomiasis; SD: Standard Diagnostics.

In general, all RDTs have very good sensitivity. In one study in DRC, the Abbott Bioline HAT 2.0 showed a sensitivity of only 71.2%. However, the HAT Sero K-SeT RDT was not included in this study, so a direct comparison is not possible. This leaves uncertainty regarding sensitivity, at least in DRC.

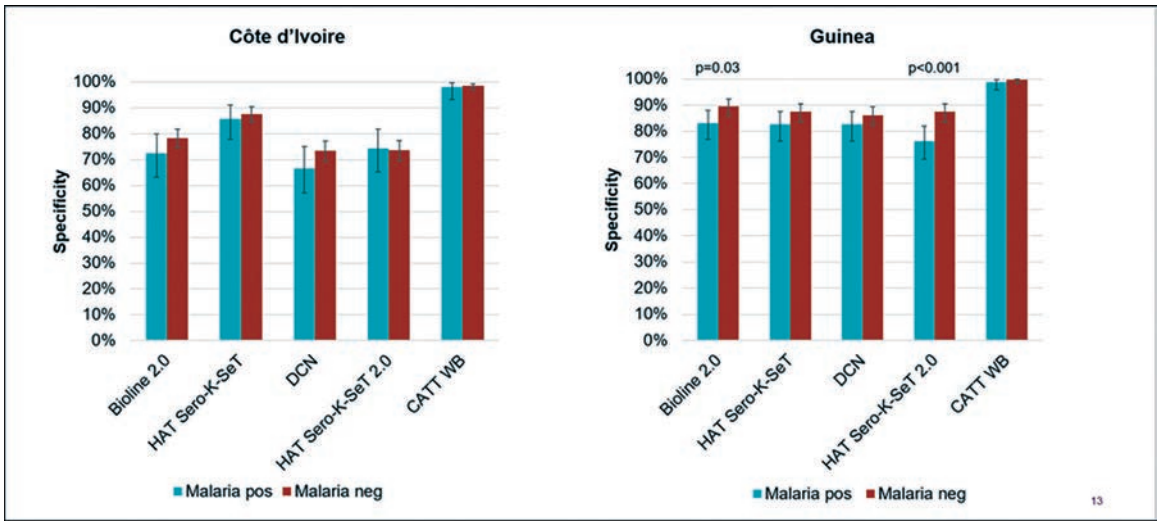
The specificity ranges from 72% to 98.9%. A clear conclusion is rather difficult, but two trends are apparent: first, the specificity of these tests is lower in retrospective studies than in prospective studies; second, their specificity is higher in passive screening than in active screening.

The primary objective of the HAT SpeSerTryp study in Côte d'Ivoire and in Guinea in 2022 was to evaluate the specificity of five serological tests (Abbott Bioline HAT 2.0, HAT Sero *K*-SeT, HAT Sero *K*-SeT 2.0, DCN HAT RDT and CATT). One secondary objective was to evaluate the specificity of serological tests in participants testing positive vs negative with a malaria RDT, based on a hypothesis that malaria could cause a false–positive reaction to the HAT RDTs. Among 1095 participants, one case of HAT was diagnosed in Guinea. CATT on whole blood showed a high specificity of 98.9%, similar to previous studies. Surprisingly, the specificity of the RDTs was rather low, much lower than in previous studies. There is no clear explanation for this at present. One hypothesis is that the specificity may be influenced by the type of sample collection (venous blood on heparin vs capillary blood collected by finger prick), on which a study will be initiated soon.

The problem of low specificity was evident in both countries, with a slightly higher specificity in Guinea. No significant association was found between specificity and gender or age. In general, there was a trend that

the specificity of HAT RDTs was slightly lower in malaria-positive patients (Figure 9.2.2). However, a significant difference was only found in two of the tests in Guinea. Even though malaria status did not show a strong effect, it could be part of the explanation for the low specificity of the RDTs.

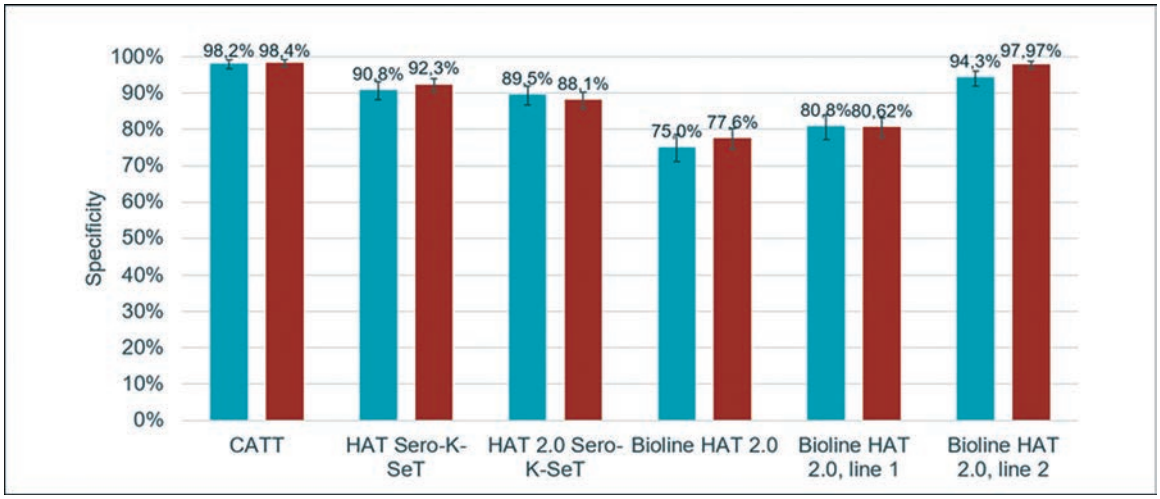
**Figure 9.2.2.** Specificity results of the SpeSerTryp study in Côte d'Ivoire (left) and in Guinea (right) according to malaria status (positive in blue, negative in red)




A similar study was conducted in DRC in 2022, with the primary objective of evaluating the specificity of four serological tests for HAT (Abbott Bioline HAT 2.0, HAT Sero *K*-SeT, HAT Sero *K*-SeT 2.0 and CATT; the DCN HAT RDT was not available for this study).

Among 1506 eligible participants (592 in Kwilu and 914 in Lomami), one case of HAT was diagnosed. The results again showed a high specificity for CATT and a rather low specificity for RDTs, with better results for the Coris tests (Figure 9.2.3). For the Bioline HAT 2.0 with two test bands for the different antigens, an analysis of the individual test bands was carried out. One test band proved to be very specific, which could be valuable information for future test developments.

**Figure 9.2.3.** Specificity results of four serological HAT tests in a study in DRC in 2022 (blue: results in Kwilu; red: results in Lomami)




Performance data from routine use of the Abbott Bioline HAT 2.0 in FIND projects showed a specificity of 97.2–99.4% for passive screening, and of 93.9–98.5% for active screening (Table 9.2.2). The results for the primary use in passive screening in the field are reassuring in that the test does not produce too many false–

positives, increasing the workload of subsequent diagnostics. However, the specificity for active screening varies more. In a large dataset from DRC, routine use of RDTs for passive screening showed also high specificity (Table 9.2.3).

**Table 9.2.2.** Specificity data from routine use of the Abbott Bioline HAT 2.0 in FIND projects

| | Screening strategy | Country | Year | Population tested | False positives* | Specificity |
|---|---|---|---|---|---|---|
| **Passive screening** Specificity: 97.2–99.4% | Passive | Uganda | 2022 | 1393 | 39 | 97.2% |
| | Passive | DRC | 2022 | 16 796 | 210 | 98.7% |
| | Passive | Guinea | 2022 | 13 604 | 96 | 99.3% |
| | Passive | Chad | 2022 | 2114 | 13 | 99.4% |
| **Active screening** Specificity: 93.9–98.5% | Active, large team | Uganda | 2022 | 16 111 | 296 | 98.2% |
| | Active, large team | DRC | 2022 | 13 494 | 497 | 96.3% |
| | Active, door-to-door | Guinea | 2022 | 15 216 | 777 | 94.9% |
| | Active, motorcycle teams | Chad | 2022 | 5991 | 90 | 98.5% |
| | Active, large team | Chad | 2022 | 1969 | 121 | 93.9% |

DRC: Democratic Republic of the Congo; FIND: Foundation for Innovative New Diagnostics.
* Not all the "false positives" were referred and tested by parasitology, so they could have included a few cases.

**Table 9.2.3.** Specificity data from routine use of the RDTs (Coris and SD/Abbott combined data) and CATT in DRC

| RDTs (passive screening) – Coris and SD/Abbott RDTs combined Specificity = 99.1% CATT (active screening) Specificity = 99.7% | Year | Population tested with CATT | CATT pos | Population tested with RDTs | RDT pos | HAT cases |
|---|---|---|---|---|---|---|
| | 2020 | 1 111 518 | 3791 | 924 625 | 8265 | 389 |
| | 2021 | 1 431 078 | 5112 | 909 460 | 6768 | 425 |
| | 2022 | 1 177 541 | 4273 | 456 653 | 5491 | 516 |
| | **Total** | **3 720 137** | **13 176** | **2 290 738** | **20 524** | **1330** |

CATT: card agglutination test for trypanosomiasis; HAT: human African trypanosomiasis; pos: positive; RDT: rapid diagnostic test.

**Several questions remain** about the performance of currently available HAT RDTs, including

- Why is specificity usually lower with active than with passive screening?
- What factors are responsible for false-positive results (other pathogens, host factors, etc.)?
- Does specificity depend on the type of blood sample (e.g. venous vs. finger-prick capillary)?

There is also the question of the most appropriate testing strategies/algorithms with current HAT RDTs. RDTs seem suitable for passive screening (number of false-positives is manageable). CATT may be preferred for active screening by large mobile teams due to its higher specificity, but for smaller mobile teams (e.g. door-to-door screening) where RDTs are more practical, should several RDTs be combined sequentially to improve specificity (e.g. Abbott Bioline HAT 2.0 and HAT Sero-*K*-SeT)? What would be the trade-off in terms of sensitivity? What would be the most cost–effective strategies? Which operational and compliance issues must be considered?

RDTs continue to show limitations, especially for active screening and possibly for future screen-and-treat strategies. Further developments are necessary; for example, removing the ISG65 antigen to improve specificity could be an option.

In the discussion it was suggested that combined RDTs for malaria and HAT in one cassette are an approach that should be developed further.

### 9.2.2 Serological laboratory tests

Referring to the use case documents published by WHO, laboratory diagnostics can be used on an individual basis to raise suspicion or to confirm infection in suspected cases. Also, when presumptive treatment is applied to individuals who are not parasitologically confirmed, it may be of interest to collect a sample before treatment that can be analysed a posteriori to confirm or exclude actual infection. Laboratory tests can also be used for surveillance of transmission.

High-throughput laboratory tests are needed to verify elimination or to explore epidemiological blind-spots. These are applied to larger numbers of samples from the human population. If one is interested in assessing animal exposure to *T. b. gambiense*, current serodiagnostic tests are of limited use because it has now been shown that *Trypanosoma brucei brucei*, which is not infectious to humans but is also transmitted by tsetse flies, sometimes expresses variant surface glycoproteins (VSGs) that were thought to be *T. b. gambiense* specific, such as LiTat 1.3 and LiTat 1.5. It should also be noted that successfully cured HAT patients can remain seropositive for several years and should therefore be excluded from post-elimination testing.

There are several options for antibody detection tests (Table 9.2.4), all based on the native form of the variant surface glycoproteins LiTat 1.3 and LiTat 1.5 expressed by *T. b. gambiense* trypanosomes. Today, researchers are working on replacing the native antigens with recombinant ones.

**Table 9.2.4.** Characteristics (specimen throughput, used antigen, appropriate laboratory level, required technical skills, suitability for dried blood spots) of different antibody detection tests

| | Throughput | Antigen | Laboratory level | Technical skill | DBS |
|---|---|---|---|---|---|
| Trypanolysis | Low | N/R | High | High | Yes |
| Immunofluorescence | Medium | N | Low | Medium | Yes |
| Indirect ELISA | High | N/R | Medium | Medium | Yes |
| Inhibition ELISA | High | N/R | Medium | Medium | Yes |

DBS: dried blood spots; ELISA: enzyme-linked immunosorbent assay; N/R: not reported.

The **immunofluorescence test** has long been forgotten but has, in the past to a greater or lesser extent, been used to control g-HAT in Chad, Equatorial Guinea and Gabon. The availability of low-cost LED (light-emitting diode) fluorescence microscopes, such as those promoted by FIND, opens up the prospect of an updated version of IFAT (immunofluorescence antibody tests) for HAT elimination.

Interestingly, all of these serological tests can be performed on dried blood spots (DBS). This advantage is applied in the "**Kit pour le Prélèvement de Sang**", which is available from the WHO Collaborating Centre at the Institut National de Recherche Biomédicale (INRB) in Kinshasa. The kit is produced by the same team that produces the mini-anion exchange centrifugation technique (mAECT) columns. It contains all the materials needed to collect venous blood, from which DBS are prepared on Whatman filter-paper, while the remainder is stored in DNA/RNA shield, a buffer that preserves RNA and DNA for molecular testing. The kit allows blood to be collected in remote locations and shipped to regional, national or provincial laboratories for testing. In the DRC, an initiative has been launched to establish a provincial laboratory in Mbuji-Mayi, in the province of Kasaï Oriental. This provincial reference laboratory for HAT diagnosis is expected to be operational by the end of 2024.

**Immune trypanolysis** (TL) is an antibody-mediated complement lysis test. It makes use of living cloned trypanosome populations grown in mice that express VSG LiTat 1.3 or LiTat 1.5. The test is considered the reference serological test for g-HAT in humans with high specificity and high sensitivity. It is complex and bears biosafety risks and therefore is applied in only a few laboratories, including the three WHO collaborating centres in Bobo Doulasso (Burkina Faso), Kinshasa (DRC) and Antwerp (Belgium). Recently, the test has been introduced at the Institute Pierre Richet (IPR) in Bouaké (Côte d'Ivoire). The value of this test in the verification of elimination of g-HAT has been studied in Burkina Faso, Côte d'Ivoire and DRC. These studies confirm that in

active g-HAT foci, TL-positive cases are found, in contrast to foci where g-HAT is no longer present. The WHO Collaborating Centre at ITM is developing a recombinant version of TL.

The **ELISA/*T. b. gambiense*** is an indirect ELISA developed more than 20 years ago. The antigen consists of a mixture of two purified VSGs (LiTat 1.3 and LiTat 1.5). The reaction is developed with an anti-human IgG peroxidase conjugate. It can be applied to serum, plasma, cerebrospinal fluid and saliva. The test is inexpensive but is not available as a commercial kit. The replacement of native antigens by recombinant antigens is being investigated. It has shown adequate accuracy when performed in samples taken on DBS, as a "high throughput g-HAT test for verification of elimination" or as an "individual diagnostic test on persons with suspected but microscopically unconfirmed g-HAT". An overview of the results of these studies is given in Table 9.2.5.

**Table 9.2.5.** Results of recent studies on the ELISA/T.b. gambiense

| Country | Guinea [1] | Côte d'Ivoire [2] | Burkina Faso [3] | DRC [4] |
|---|---|---|---|---|
| Use case | Individual diagnostic test on persons with suspected but microscopically unconfirmed g-HAT | | High throughput g-HAT test for verification of elimination | |
| Strategy | Passive screening of clinical suspects with three RDTs | | Active door-to-door screening with three RDTs | Door-to-door collection from all participants |
| Sample | DBS from RDT-positive participants | | | DBS from everybody |
| No. of participants | 2353 | 3433 | 5883 | 11 535 |
| Positivity rate on gHAT cases | 23/34 | 1/1 | NA | NA |
| Sensitivity | **67.6%** | **100%** | NA | NA |
| Negativity rate on non-HAT | 41/43 | 88/89 | 809/817 | 11 438/11 535 |
| Specificity | **95.3%** | **98.9%** | **99.01%** | **99.2%** |

DBS: dried blood spots; DRC: Democratic Republic of the Congo; HAT: human African trypanosomiasis; NA: not applicable; RDT: rapid diagnostic test.
[1] Camara et al., 2023 *(20)* ; [2] Koné et al., 2021 *(18)* ; [3] Compaoré et al., 2022 *(19)*; [4] Inocêncio da Luz et al., 2021 *(23)*

On the one hand in Guinea, the sensitivity of the ELISA appears to be low and certainly not within the TPP limits. On the other hand in Côte d'Ivoire, the sensitivity seems to be 100%. In both countries, the specificities, although probably underestimated by the study design, are within the TPP limits. In Burkina Faso and DRC, sensitivities cannot be calculated because no microscopically confirmed patients were recorded. In both countries, the specificity of the ELISA equals the lower limit given in the TPP for a high throughput test for verification of elimination.

New data on the specificity of TL and ELISA/*T. b. gambiense* are available for Côte d'Ivoire and Guinea from the "SpeSerTryp" study, which compared the diagnostic accuracy of several serological and molecular tests. Of the 399 non-parasitologically confirmed RDT seropositives detected in 1095 participants, 397 were negative by TL on three VSGs and 394 were negative by ELISA/*T. b. gambiense*. In this study, the apparent specificity of the ELISA in Guinea is much higher and exceeds 99%.

A more sophisticated ELISA for g-HAT serodiagnosis is the **inhibition ELISA (iELISA)**. Its principle is based on the inhibition of the binding between a monoclonal antibody and its corresponding epitope on a VSG of *T. b. gambiense*. The iELISA has been developed at ITM and is now commercialized by apDia in Belgium. It uses serum, plasma and dried blood eluate. It is intended to replace immune TL as a highly specific reference test.

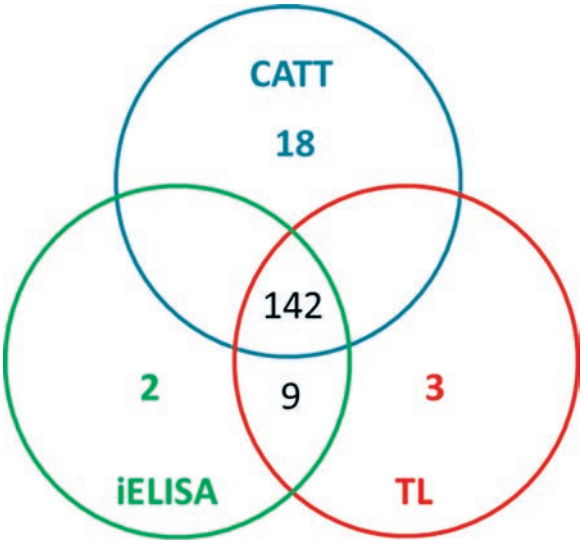
Retrospective evaluation of archived specimens from the WHO HAT Specimen Bank showed a high diagnostic accuracy.

The iELISA was included for phase III evaluation together with TL and several RDTs in two prospective studies: "SpeSerTryp" in Côte d'Ivoire and Guinea and "recombinant RDTs" in DRC. The iELISA appeared to be less robust than expected, with an unacceptably high plate-to-plate variation in the optical densities obtained with the negative and positive controls. The origin of this poor robustness remains unclear and requires further investigation.

With several tests available for serodiagnosis of g-HAT, it is interesting to know whether one test can replace another or whether a combination of several tests, in parallel or in series, can improve overall accuracy of a diagnostic strategy towards elimination of g-HAT. For one test to replace the other, we would like to see a very high agreement between the two.

Figure 9.2.4 shows the agreement (Venn diagram) of CATT, iELISA and immune TL in a study on 150 g-HAT plasmas and 150 endemic controls from the WHO HAT Specimen Bank. Of note, a few iELISA positives are negative in TL and vice versa. In addition, 14 plasma positives in iELISA or TL or both, including one collected from a confirmed patient, are negative in CATT. As CATT is commonly used as a screening test, it would mean that the 14 donors would not have undergone parasitological examination if suspicion for g-HAT had been based on CATT alone. These are retrospective data from archived specimens.

**Figure 9.2.4.** Venn diagram demonstrating the positive agreement of three serological tests for g-HAT in a retrospective study with the WHO HAT Specimen Bank




CATT: card agglutination test for trypanosomiasis; iELISA: inhibition ELISA; TL: trypanolysis.

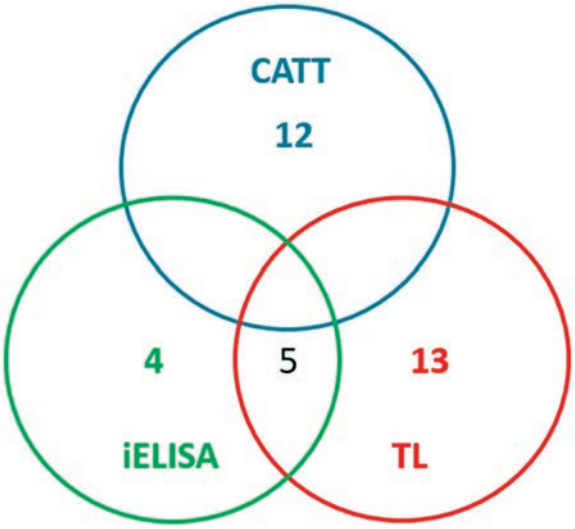
Study on 150 controls and 150 g-HAT plasma from the WHO HAT Specimen Bank

Specificities: CATT 90.00%, TL 92.67%, iELISA 93.33%

Sensitivities: CATT 98.67%, TL 97.33%, iELiSA 97.33%

Data collected from prospective studies are quite different (Figure 9.2.5). In an ongoing prospective study in DRC, several versions of RDTs and CATT were used to screen the population at risk. Among the 600 participants, no one was confirmed with g-HAT. For an unknown reason, the specificity of the CATT was rather low while that of the iELISA and TL were similar to the specificities seen in the retrospective study. The agreement between iELISA and TL was lower than in the retrospective study, which may be due to the problem of iELISA plate-to-plate variation. It is concerning that none of the 22 positives in iELISA or TL or both was positive in CATT. The 12 CATT-positives were not confirmed, neither in the field with mAECT nor in the laboratory with iELISA and TL. The pending results of the molecular tests on all these samples should provide clarification.

**Figure 9.2.5.** Venn diagram demonstrating the positive agreement of three serological tests for g-HAT in a prospective study in DRC




CATT: card agglutination test for trypanosomiasis; iELISA: inhibition ELISA; TL: trypanolysis.

Study on 150 controls and 150 g-HAT plasma from the WHO HAT Specimen Bank

Specificities: CATT 90.00%, TL 92.67%, iELISA 93.33%

Sensitivities: CATT 98.67%, TL 97.33%, iELiSA 97.33%

### 9.2.3 Molecular laboratory tests

Molecular tests aim to detect trypanozoon nucleic acid in patient samples. The main difference with serology is that the success of detection is linked to the number of circulating parasites and is therefore more similar to parasitological detection. Molecular testing often involves a multi-step workflow, with each step contributing to the final sensitivity and specificity of the test. In principle, molecular tests accept all sample types, but success is determined by how such samples are handled (transport and storage) before extraction. While some formats can be performed directly on the samples (whole blood), sensitivity is often increased by lysing and concentrating the samples using extraction techniques. Extracts need to be amplified using either isothermal amplification or the more common polymerase chain reaction. Many targets are identified, of which the most sensitive are multi-copy genes or transcripts, whereas subspecies-specific genes are mostly single-copy. Finally, once amplified, there are various methods of detecting the nucleic acids, such as colourimetric or, more commonly, fluorescence (ultraviolet or quantitative polymerase chain reaction (qPCR)), with the possibility of using lateral flow or laboratory-on-chip devices. While some could be performed at the point of care, most are not. None are commercialized.

**Advances in sampling** have been made in recent years. One interesting finding was that serum from infected cattle contains some micro RNA nucleic acids (7SL-cRNA) from trypanosomes that cause animal African trypanosomiasis (AAT), which can be amplified with very high sensitivity. It is still unknonw if the 7SL-cRNA PCR has value for the detection of HAT. The presence of trypanosomes in the skin of seropositive individuals has been demonstrated, but assessing this requires skin biopsies. The question remains whether these skin trypanosomes contribute to transmission. Molecular diagnostics can be applied to identify the trypanosomes in the dermis.

Regarding **advances in transport media and extraction**, a study used DBS taken on mass screening. The comparative analytical sensitivity on DBS was low for both loop-mediated isothermal amplification (LAMP) and qPCR. High-throughput molecular tools are still needed to process these samples.

High sensitivity can be reached when **nucleic acid preservation** is used. In clincial studyies, such as DiTECT (diagnostic tools for HAT elimination and clinical trials), it was shown that venous blood and cerebrospinal fluid (CSF) collected from patients in PAXGene tubes increased senstivity of trypanosome detection, outperforming mAECT and lymph node parasite detection using SL-RNA (spliced leader RNA). Larger volumes of blood allow detection of relapse without lumbar puncture.

Regarding progress in **targets (Trypanozoon)**, the *Trypanosoma brucie* repeat (TBR), a sequence that has been targeted for years, contains single nucleotide polymorphisms (SNPs) and copynumber variations in Trypanzooon strains. The TBR is not the same within the Trypanozoon, and *T. b. gambiense I* has microheterogeneity.

**RNA detection** is becoming increasingly important. 18S DNA is found in the CSF of cured patients and SL-RNA is a better marker of cure. At ITM, an 18S PCR kit has been improved that detects 18S RNA better than SL-RNA at low parasite concentrations.

Also for *T. b. gambiense I*, **next-generation sequencing** has led to the discovery of specific minicircles in the kDNA. These can be targeted in qPCR using a specific set called mini3 and has higher sensitivity than TgsGP. At the Institut de Recherche pour le Développement (IRD), a combination of transcriptomics and variant analysis has led to the identification of the DT8 and DT9 probes that can be targeted by qPCR. In addition, absolute quantificiation of these markers via ddPCR is under development.

Advances in **amplification and detection** have been made by the Institut Pasteur with the Sherlock method, a Crispr-cas9 based detection of RT-RPA amplified RNA. Several targets are in the portfolio (such as 7SL, TgsGP, SRA), and high-throughput fluorescence or lateral flow readout are used. Other targets (18SZoon and 18STids) are forthcoming.

**Perspectives** for molecular laboratory testing include prospective studies to improve the molecular diagnostic workflow and comparative molecular diagnostic studies. The goal of molecular diagnostics should be to replace on-site parasitological diagnosis. The question remains whether these tests should be performed at the point of care or a posteriori for confirmation in a reference laboratory, and whether there is room for a commercial molecular diagnostic test.

# 10. Treatment of HAT

## 10.1 Report of the working group on integration of new tools into national and global policies

The working group on integration of new tools into national and global policies is part of the WHO Network for HAT elimination. The group aims to facilitate the integration of newly developed tools (new drugs, diagnostic tests and algorithms, as well as vector control tools and methodologies) into national and global policies as they become available. It facilitates regulatory processes at national and international levels for the introduction of new tools and coordinates actions in this regard. The group works with countries to develop policies, guidelines and strategies in order to harmonize and standardize the procedures used. The group has celebrated 13 meetings – 10 on new drugs and 3 on diagnostics – since December 2014.

The subgroup on new drugs is coordinated by the WHO/NTD HAT team and includes various participants: NSSCPs, DND*i*, FIND, BMGF, Sanofi and Bayer, and several other WHO groups (Prequalification of Medical Products; Regulatory Systems Strengthening; WHO Essential Medicines List; Safety and Vigilance; Innovation, Access and Use; and the Special Programme for Research and Training in Tropical Diseases (TDR). Collaborations are established with the European Medicines Agency (EMA), the United States Food and Drug Administration and the HAT-e-TAG.

At the last meeting on 30 March 2023, the implementation of fexinidazole in g-HAT, the development and approval process for acoziborole and the prospects for improving r-HAT treatment were discussed.

One focus of the subgroup was on **fexinidazole for the treatment of g-HAT**, with discussions on clinical trials, access and deployment plans, regulatory procedures, and roles and responsibilities. The meeting on 24 January 2019 addressed access to this medicine, taking into account the positive scientific opinion of the EMA. This led to the development of the WHO interim treatment guidelines for g-HAT including treatment with fexinidazole *(24)*.

So far, 12 countries have officially adopted fexinidazole for g-HAT treatment. In 2022, about half of g-HAT patients were treated with it. WHO has collected pharmacovigilance data from 104 treatment sites in 10 countries, as of May 2023. Adverse events are frequent but minor, with 3 patients dying during treatment (fatality rate below 1%).

The clinical trial of **fexinidazole for the treatment of r-HAT** was first discussed and approved in December 2016. In 2018, the European and Developing Countries Clinical Trials Partnership (EDCTP) approved and funded this trial in Malawi and Uganda. The study was successfully completed (last visit, last patient October 2022). Some 45 patients were enrolled, 34 of them in phase II. No deaths related to fexinidazole for r-HAT were observed. A rapid clearance of the trypanosomes was observed. One relapse occurred. Three serious adverse events were considered unrelated to fexinidazole, which can be considered a milestone achievement as the treatment of r-HAT is a particularly neglected aspect of a neglected disease.

Discussions on the **use of acoziborole** started in June 2015. The pivotal clinical trial started in October 2016. The DNDi-OXA-02 trial (open-label, multi-centre, assessing efficacy and safety in adults with late and first stage) enrolled 208 adults with g-HAT, with 18 months of follow-up. Treatment success was 100% (41/41) in early and intermediate stage, and 95.2% (159/167) in stage 2. No serious adverse events or drug-related serious adverse events were observed.

Discussions on the **extended use of acoziborole** for g-HAT elimination started in December 2019. The DNDi-OXA-04-HAT study on the use of acoziborole in unconfirmed serosuspects (extended use) completed recruitment in March 2023 (sample size 1200 patients, random 3:1). Follow-up is expected to be completed in July 2023. To date, no safety signals have emerged from the study. The final clinical study report is expected in Q3 2024.

The DNDi-OXA-05-HAT trial on the **paediatric use of acoziborole** (ACOZI-KIDS project, funded by EDCTP) has been ongoing since 2022 in DRC. Step 1 (children ≥ 40 kg body weight (30–40 kg) and up to aged 14 years with a dose regimen of 640 mg (2 adult tablets)) has been completed. Pharmacokinetics results confirmed that the dose adjustment, based on body weight, is appropriate. Step 2 (children ≥ 10 kg body weight (10–40 kg) and aged 1–14 years) is expected to be launched in the near future.

The primary objective of the **STROGHAT** (Stop Transmission of g-HAT) study is to evaluate a "screen and treat" strategy. Secondary objectives are to provide further evidence on the safety of acoziborole in seropositive g-HAT suspects and to estimate the costs of a "screen and treat" strategy. Enrolment is planned to start in Q1 2024. Approximately 2500 serosuspects are expected to be treated over 3 consecutive years. The data generated should complement the safety data from the DNDi-OXA-04-HAT trial.

Discussions have started with partners on the best way forward for the **use of acoziborole in r-HAT**.

In terms of the **development timeline for acoziborole** (as of March 2023), an Article 58 submission to the EMA is planned for Q2 2025. The EMA scientific opinion is expected in early 2026 and first country registration in the DRC in Q2 2026 (best-case scenario).

Overall, the development and introduction of new treatments is largely on track, despite unexpected difficulties with the formulation of acoziborole. The new medicines are expected to make a significant contribution towards achieving the HAT elimination targets.

## 10.2 Current situation

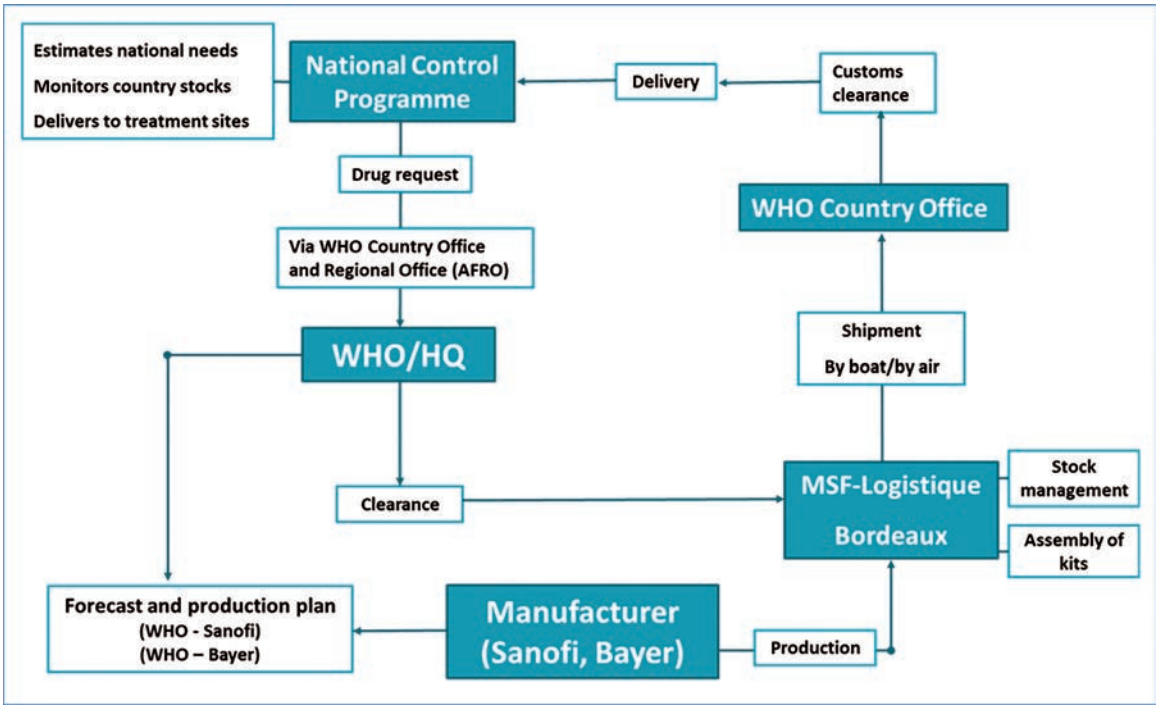
Once new treatments are developed and available, WHO facilitates their implementation in countries and their regular supply. All HAT medicines are donated by the manufactures (Sanofi and Bayer) and distributed by WHO to endemic countries. Small stockpiles of medicines are maintained in strategic centres in non-endemic countries, including Geneva (Switzerland), so that they can be shipped quickly should any exported cases be diagnosed. For implementation, WHO provides guidelines, training of medical staff (e.g. cascade training/training of trainers) and technical support.

The supply system for HAT medicines is detailed in Figure 10.2.1.

At present there is a new, more complex situation. The number of cases is decreasing while at the same time more treatment sites are being established to improve access. There are now six different HAT medicines available. Only a small amount of medicines is needed, but availability must be guaranteed. Their production is greater than the demand (the size of the batch is not compressible). Medicines that have not been used must be destroyed. Medicines must be accessible, even though many facilities treat few or no patients.

Certain adaptions are ongoing. The presentation of eflornithine has changed from 100 mL to 50 mL vials. A new manufacturing plant allows smaller batch sizes. This also allows more flexibility with regard to the 3-year expiry date for eflornithine and its distribution in kits. Fexinidazole allows treatment in peripheral, rural sites. Stocks are strategically positioned at different levels within the country to enable fast dispatch and avoid wastage. In view of the complex drug supply system, short shelf-lives are often problematic. The shelf-life of fexinidazole has been extended from 3 to 5 years, thanks to major efforts by Sanofi. However, the discontinuation in the production of melarsoprol has been announced, and this could be an important problem.

**Figure 10.2.1.** Supply system for HAT medicines




For example, in DRC, a populous country with widely dispersed endemic areas, stocks are needed at different levels. In other countries the situation is less complex, but in general a two-level stock is also maintained.

There are critical components in the supply chain.

- Requests for medicines require accurate information (about the medicine, the stock, the expiry dates and the recipient).
- Country import requirements/customs clearance can be complicated and time-consuming.
- Logistics are complicated and costly.
- In some cases, there is weak stock management in the national programme and last-minute requests occur, leading to delays in treatment.

For example, there was an unexpected shortage of medicines in DRC in 2022. Staff conflicts due to ending of allowances led to stock management problems. Stock monitoring failed at central, provincial and peripheral levels, leading to requests made too late, resulting in a temporary shortage of all medicines.

With the introduction of fexinidazole in 2019, six different HAT drugs are available for **first-line treatment** (Figure 10.2.2).

To implement fexinidazole, countries must comply with certain requirements:

- official indication of the adoption of fexinidazole through inclusion in national protocols, or in the National Medicines List, or through a letter from the Ministry (high level);
- list of sites chosen to use fexinidazole;
- staff trained in use of fexinidazole, and in pharmacovigilance; and
- commitment to monitoring pharmacovigilance and data transmission.

**Figure 10.2.2.** First-line treatment of HAT since 2019

<table>
<tr><th></th><th>Adults and children aged<br>≥ 6 years</th><th>Children aged<br>< 6 years</th></tr>
<tr><td colspan="3">Gambiense HAT</td></tr>
<tr><td>1st stage</td><td rowspan="2">Fexinidazole</td><td>Pentamidine</td></tr>
<tr><td>2nd stage<br>< 100 WBC/µL CSF</td><td>NECT</td></tr>
<tr><td>2nd stage<br>≥ 100 WBC/µL CSF</td><td colspan="2">NECT</td></tr>
<tr><td colspan="3">Rhodesiense HAT</td></tr>
<tr><td>1st stage</td><td colspan="2">Suramin</td></tr>
<tr><td>2nd stage</td><td colspan="2">Melarsoprol</td></tr>
</table>

CSF: cerebrospinal fluid; HAT: human African trypanosomiasis; NECT: nifurtimox–eflornithine combination therapy; WBC: white blood cells.
*Source*: WHO interim guidelines for the treatment of gambiense human African trypanosomiasis *(24)*.

As of June 2023, 12 countries have officially adopted fexinidazole (Table 10.2.1). It has not yet been adopted in Côte d'Ivoire (very little case numbers, administrative process for adoption not yet done) and in Nigeria (not declaring any cases for a long period). So far, 270 treatment sites have been trained in the use of fexinidazole (cascade training).

**Table 10.2.1.** Fexinidazole implementation by country (June 2023)

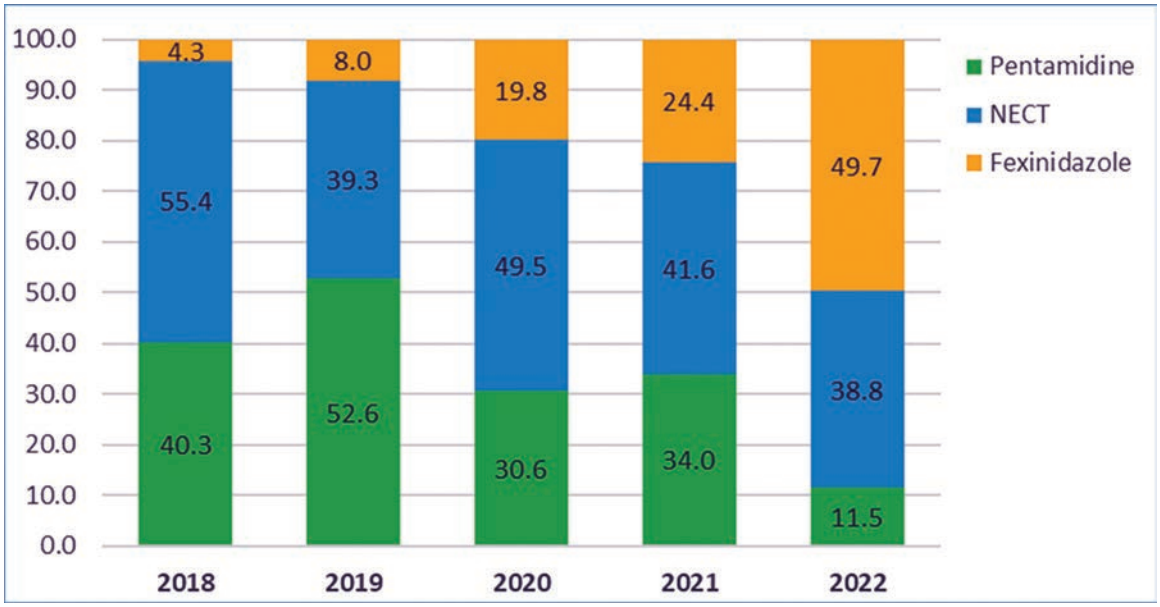
| Country | Official adoption | List of sites | Trained staff | Medicine requested | Shipped | Pharmaco-vigilance |
|---|---|---|---|---|---|---|
| Angola | + | 7 | + | + | + | + |
| Burkina Faso | + | - | - | - | - | no case |
| Cameroon | + | 9 | + | + | + | + |
| CAR | + | 13 | + | + | + | + |
| Chad | + | 9 | + | + | + | + |
| Congo | + | 7 | + | + | + | + |
| Côte d'Ivoire | - | - | - | - | | |
| DRC | + | 179 | + | + | + | + |
| Gabon | + | 8 | + | + | + | + |
| Guinea | + | 23 | + | + | + | + |
| Guinea Eq. | + | 2 | + | + | + | + |
| Nigeria | - | - | - | - | | |
| South Sudan | + | 9 | + | + | + | + |
| Uganda | + | 4 | + | + | + | no case |
| **Total** | **12** | **270** | **11** | **11** | **11** | **10** |

CAR: Central African Republic; DRC: Democratic Republic of the Congo; Eq.: Equatorial.

Figure 10.2.3 shows the increasing proportional use of fexinidazole for treatment of g-HAT during a 5-year period (2018–2022). Initially, this was an in-clinical-trial use, since 2020 also in "real life" use, starting in DRC, followed by Guinea and other countries. In 2022, about half of the patients were treated with fexinidazole, with a decline mainly in the use of pentamidine.

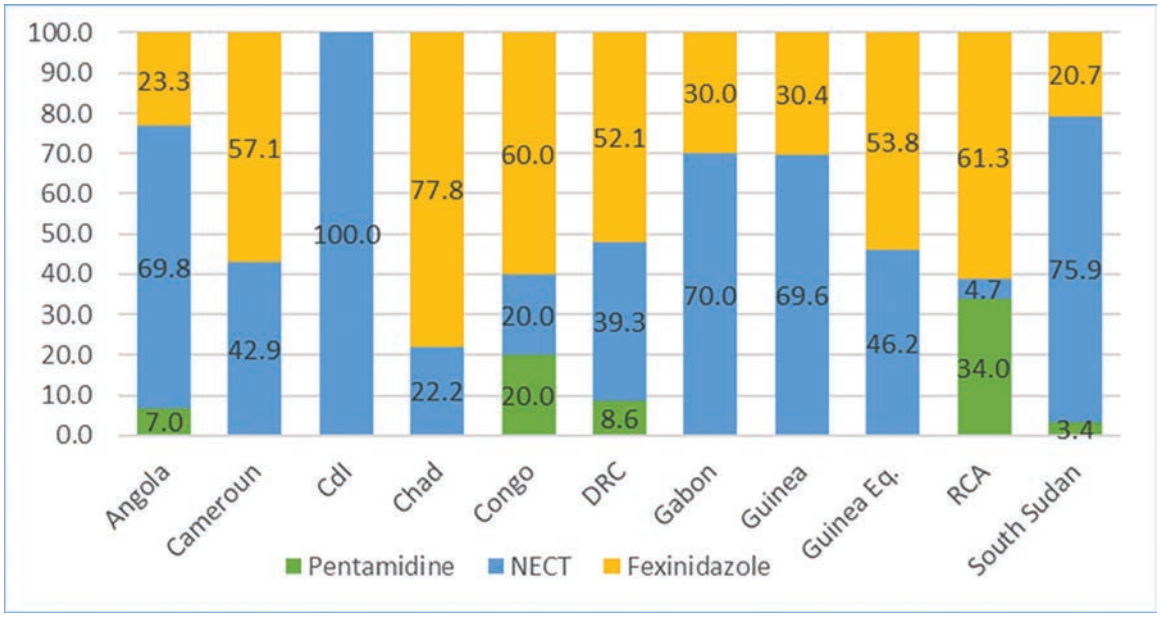
There is considerable variability in the use of fexinidazole among countries (Figure 10.2.4). This is due to a delay in implementation, different epidemiological situations (e.g. more advanced disease) and different treatment policies (as in some countries serosuspects without parasitological confirmation are treated). In some countries, fexinidazole was only implemented in 2022, so fewer cases were treated with this medicine. Currently, about half of the cases are treated with fexinidazole and this proportion may increase further. In the future, the use of fexinidazole is likely to become more uniform among countries.

**Figure 10.2.3.** Percentual change of g-HAT treatment per year, 2018–2022




NECT: nifurtimox–eflornithine combination therapy.

**Figure 10.2.4.** Treatment given for g-HAT (%) per country in 2022




Cameroun: Cameroon; CAR: Central African Republic; Cdl: Côte d'Ivoire; DRC: Democratic Republic of the Congo; Eq.: Equatorial; NECT: nifurtimox–eflornithine combination therapy; RCA: Central African Republic.

As of 31 May 2023, WHO has collected pharmacovigilance data from 104 treatment sites in 10 countries (Table 10.2.2), representing 452 (78%) of the 579 patients treated with fexinidazole. Delays in data transfer, especially from distant treatment centres, must be taken into account. Queries for incomplete data are ongoing and more pharmacovigilance data will follow. A fairly good follow-up rate was achieved with pharmacovigilance data of 367 follow-up visits available (6 months: 226; 12 months: 164; 18 months: 107; 24 months: 52; unscheduled: 9).

Table 10.2.3 shows the main characteristics of 420 patients treated with fexinidazole. About half of the patients were men and half were women. The mean age was 26 years. Of these, 4 (1%) were pregnant women (with special follow-up of pregnant women and children after birth), 96% were parasitologically confirmed cases, with an adult/paediatric treatment ratio of 3.3. The full dosage was given to 97% of the patients, whereas this was not possible for 3% mainly because of adverse events. The majority (65%) of patients experienced at least one adverse event. Three patients experienced serious adverse events during treatment. Another three serious adverse events occurred during the follow-up. In most cases, the causes do not appear to be treatment-related, but the analysis is ongoing. So far, no relapses were recorded.

**Tables 10.2.2 and 10.2.3**. Summary results of fexinidazole pharmacovigilance data transmitted to WHO, as of 31 May 2023

| | N° sites | N° patients |
|---|---|---|
| Angola | 3 | 8 |
| Cameroon | 1 | 2 |
| CAR | 2 | 45 |
| Chad | 5 | 14 |
| Congo | 1 | 4 |
| DRC | 61 | 334 |
| Eq. Guinea | 1 | 9 |
| Gabon | 4 | 5 |
| Guinea | 17 | 26 |
| South Sudan | 1 | 5 |
| **Total** | **104** | **452** |
| | | |

| Main features (*n*= 420) | | Missing info |
|---|---|---|
| Sex ratio (M:F) | 0.89 (213/239) | |
| Age in years (median, range) | 26 (6–85) | |
| Pregnant women | 4 | 18 |
| Trypanosomes seen (T+) | 96% | 16 |
| Dosage prescribed (adult:paediatric) | 3.3 (332/100) | 20 |
| Full dosage given | 97% | |
| Any AE during treatment | 65% | |
| SAE during treatment | 3 | |
| SAE during follow up | 3 | |
| Relapses | 0 | |
| Pregnancy outcome reports | 0 | |
| AE during the first 2 years of life | 0 | |

AE: adverse event; CAR: Central African Republic; DRC: Democratic Republic of the Congo; Eq.: Equatorial; NECT: nifurtimox–eflornithine combination therapy; SAE; serious adverse event.

In summary, the preliminary results indicate a safety profile of fexinidazole in line with the clinical trials. The efficacy data appear so far very good. The absence of relapses could be associated with the WHO and EMA recommendations to treat severe cases with nifurtimox–eflornithine combination therapy (NECT), according to the evidence from the clinical trials. The current cohort size of 452 patients is smaller than expected by the EMA. This can be explained by the fact that past projections did not assume such a rapid decline in the number of HAT cases, and that implementation has been delayed and gradual (fexinidazole only started in the DRC in March 2020; other countries took longer, up to 2022). It is proposed to the EMA to continue recruitment for one more year, which could reach about 1000 patients.

## 10.3 New developments

The treatment of r-HAT is still limited to two drugs: suramin in first stage and melarsoprol in second stage. Melarsoprol is very unsafe but, because most cases are detected in second stage, it is their only option, and melarsoprol is the most used treatment.

The current g-HAT control strategy is based on large-scale screening, laboratory confirmation and treatment of confirmed cases, which requires a massive logistical investment. We are moving towards a paradigm shift with the availability of acoziborole, an effective single-dose drug that, if shown to be safe enough in clinical trials, could offer the potential to expand the treatment indication to individuals at high risk of HAT (e.g. serosuspects or household members of infected patients).

### 10.3.1 Fexinidazole in treatment of r-HAT

The **DNDi-Fex-07-HAT** trial is assessing the efficacy and safety of fexinidazole in patients with r-HAT. The aim of this phase II/III study is to evaluate if fexinidazole offers an alternative over melarsoprol in stage 2 and over suramin in stage 1 r-HAT patients. Some 45 patients have been included at two clinical sites in Malawi and in Uganda. Out of the 45 patients included, 35 were in second stage (34 evaluable). The targeted sample size of evaluable patients in stage 2 was reached. The recruitment period was 26 months, with a 12-month follow-up period (first patient first visit: 29 September 2019; last patient last visit: 12 October 2022).

There were no deaths related to fexinidazole or r-HAT at the end of the hospitalization period (0 (0.00%), [90% KI] [0.00–8.43]). The primary objective of the study was reached, as the fatality rate of r-HAT or treatment-related death at the end of hospitalization in stage 2 patients treated with fexinidazole was smaller than a threshold defined as an unacceptable rate of 8.5%.

One relapse was detected at week 9 (1 (2.86%) [90% KI] for stage 2, [0.15–12.85]). The secondary objective was not achieved, as the confidence interval of the failure rate slightly exceeded the defined unacceptable rate of 12% in stage 2. There were no new aspects in the study regarding safety or pharmacokinetics.

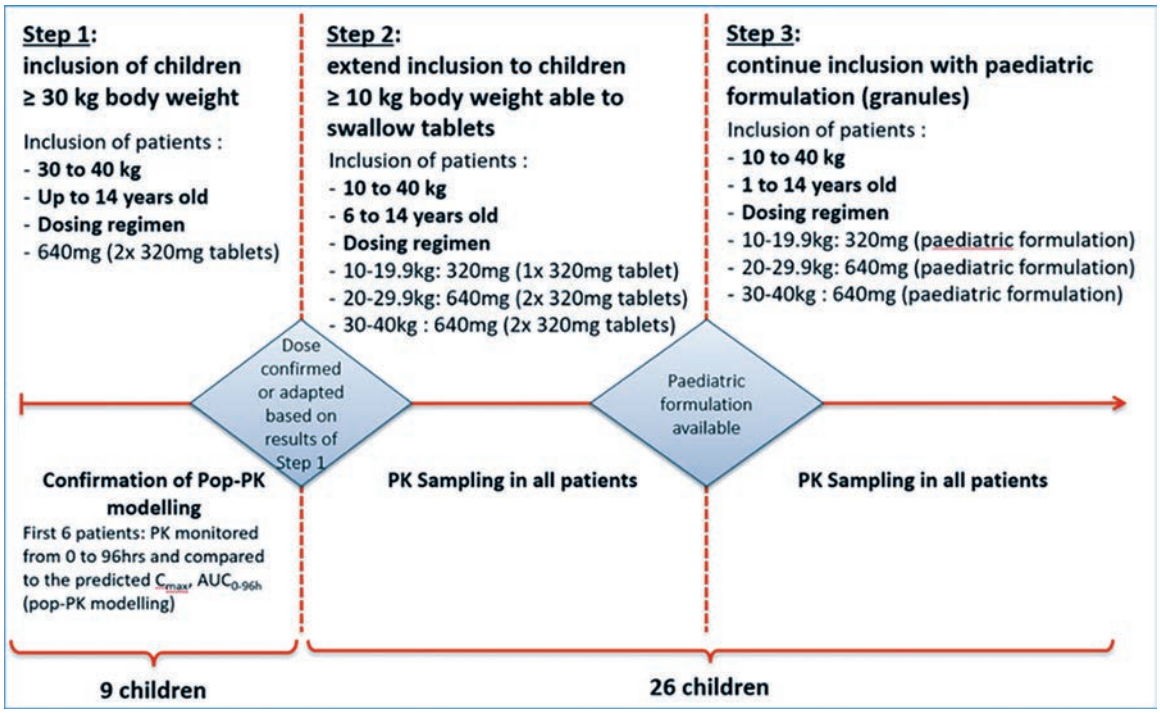
The regulatory strategy aims for early access of fexinidazole for treatment of r-HAT in the endemic countries. The initial clinical study report was submitted very recently to the EMA. The opinion of the EMA Committee for Medicinal Products for Human Use (CHMP) is expected in December 2023 (best-case scenario). The local approval in DRC is targeted 3 months after the EMA CHMP scientific opinion in Q1 2024. The review of the WHO guidelines by the Guideline Development Group is envisaged for Q1/Q2 2024. The inclusion in the WHO Essential Medicines List could be realized in Q2 2025.

### 10.3.2 Paediatric use of acoziborole (DNDi-OXA-05-HAT)

The aim of the study is to develop a paediatric formulation of acoziborole for children aged 1–14 years as a safe, effective, all-oral single-dose treatment for first- and second-stage g-HAT. The primary objective is to validate weight-based exposure based on population-pharmacokinetics modelling. The secondary objectives are to assess: (i) the efficacy (12-month follow-up); (ii) the time course of the efficacy response; (iii) the safety profile; (iv) the potential relationship between concentration and corrected QT interval (QTc); and (v) the palatability and acceptability of the paediatric formulation in paediatric patients.

The study is planned in **three steps** (Figure 10.3.1).

**Figure 10.3.1.** New three-step study design of the DNDi-OXA-05-HAT trial in children




PK: pharmacokinetics.

Step 1 with the adult formulation is completed and has confirmed that the dose adjustment, based on body weight, is adequate. The study coul d continue with the planned dose regimen. There were no safety issues, and all subjects were cured. The study is ready for step 2 (start planned for Q3 2023). After the completion of the paediatric formulation development, it is planned as a step 3 to use the formulation (granules) for children aged 1–14 years and weighing 10–40 kg.

### 10.3.4 Widened use of acoziborole (DNDi-OXA-04-HAT)

The **primary objective** of the DNDi-OXA-04-HAT trial is to assess the security profile of acoziborole in g-HAT seropositive individuals not confirmed parasitologically. The **secondary objectives** are to assess the security of acoziborole by haemato-biochemistry and electrocardiogram, to assess the blood pharmacokinetics, and to correlate the QTc changes with drug blood concentrations at day 5.

The study design is randomized, multi-centre, double-blind, placebo-controlled (N=1200, random 3:1, hence 900 receiving acoziborole). Recruitment for the study has just been completed. The OXA-04-HAT is coupled with the Trypskin sub-study (N=725), with the exploratory objective of estimating the prevalence of extravascular dermal *T. b. gambiense* in g-HAT seropositive individuals and to assess the efficacy of new diagnostic tools.

Some 6.2% of the participants in the OXA-04-HAT trial experienced at least one treatment emergent adverse event related to the study drug, including nervous system disorders (3.1% of subjects), mainly headaches; gastrointestinal disorders (2.7%), mainly abdominal pain; general disorders (1.3%), mainly asthenia and metabolic disorders (0.6%), mainly decrease in appetite. As observed in the pivotal study, all treatment emergent adverse events were mild and moderate.

Out of 1208 participants, 11 serious adverse events occurred in nine participants (0.7%), all of which were considered non-related to acoziborole; 12 women were exposed during pregnancy (4 abortions, 1 delivery). Electrocardiogram analysis showed that acoziborole had no effect on electrocardiogram parameters.

Data cleaning is ongoing but up to date, no safety signal has been raised, reinforcing, so far, the safety profile of acoziborole observed in the pivotal trial.

### 10.3.4 Impact of the STROGHAT study on acoziborole development

The sponsor of the STROGHAT study (Stop Transmission of g-HAT) is ITM, in charge of the epidemiological part of the study. DNDi is as an associate in charge of the clinical safety part. The inclusion of the first patient is planned for Q1 2024.

The primary objective is to evaluate a screen-and-treat strategy. The secondary objectives are to provide further evidence for the safety of acoziborole in seropositive g-HAT suspects and to provide an accurate cost estimate for a screen-and-treat strategy. The study design is a cohort study and a nested clinical study. The study will be conducted in Nord Equateur (DRC) with a population of about 170 000 people. For 3 consecutive years, a screening will take place and seropositives will be treated with acoziborole. In the fourth year, another screening in the study area and the surrounding area will be conducted to evaluate how this strategy can help to interrupt the transmission of g-HAT. The main measures are the incidence after the intervention (< 1/50 000 per year) and a comparison of the incidence before and after, as well as the safety profile.

The assumption for treatment needs a 99% specificity of the screening test, with about 1500 individuals treated with acoziborole in year 1 and approximately 1000 more in years 2 and 3. With the DNDi-OXA-04 trial and the STROGHAT study, a total of around 3500 serosuspects may be treated by 2027, providing more evidence on the safety profile for future guidelines recommendations.

### 10.3.5 Other studies

A drug–drug interaction study (DNDi-OXA-07) has just completed enrolment and data analysis is ongoing. A protocol for a breastfeeding study has been finalized and recruitment is planned for early 2024. The aim is to measure the concentration of acoziborole in breast milk to estimate the exposure of breast-fed infants.

### 10.3.6 Exploration of the use of acoziborole

The current treatment recommendation for r-HAT in adults and children is suramin (intravenously) for stage 1 and melarsoprol (intravenously) for stage 2. Fexinidazole could be approved for treatment of r-HAT as early as Q1 2024. Melarsoprol production is expected to be discontinued in 2027. However, this would leave only one medicine (fexinidazole) for treatment of stage 2 r-HAT and none for stage 2 disease in children aged under 6 years and those who cannot swallow. So another treatment option is needed. As r-HAT is a very rare disease, the question is what type of investment should be made to expand the indication of acoziborole for treatment of r-HAT.

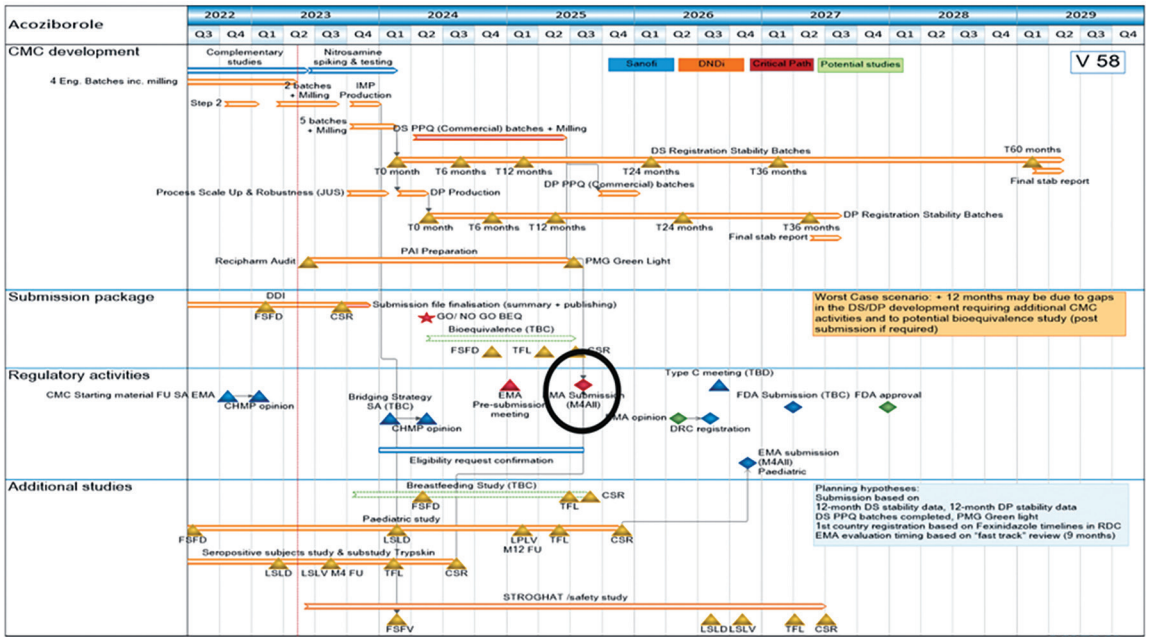
The very limited preclinical data on one parasite strain suggest that acoziborole is as effective against *T. b. rhodesiense* as against *T. b. gambiense* (same CPSF3 factor as *T. b. gambiense*: target of acoziborole, same minimum inhibitory concentration (MIC) as *T. b. gambiense*, same half maximal inhibitory concentration ($IC_{50}$) time to kill). This may allow a lighter clinical trial with a similar study design to the fexinidazole trial for r-HAT (open label II/III non-randomized, compared to unacceptable mortality of 8.5%, minimum 34 stage 2 patients). With approximately 50–60 r-HAT reported cases per year, recruitment would take a long time. The fexinidazole trial in r-HAT took more than 2 years to recruit, with 1 year follow-up, and cost approximately US$ 3 million.

The next steps are to determine the drug susceptibility of *T. b. rhodesiense* strains in vitro (in collaboration with the Swiss Tropical and Public Health Institute (STPH)) and efficacy in the *T. b. rhodesiense* mouse model.

### 10.3.7 Acoziborole development plan

The development plan for acoziborole envisages an Article 58 submission to the EMA in Q2 2025 (Figure 10.3.2).

**Figure 10.3.2.** Acoziborole development plan, best-case scenario




## 10.4 Paediatric gaps in treatment

The Global Accelerator for Paediatric Formulations (GAP-f) is a WHO network hosted within the Research for Health Department in the Science Division and was created to respond to the paediatric treatment gap. There are several challenges to developing medicines for children, which over the years have led to a general lack of paediatric medicines. These include natural history, co-morbidities and drug metabolism, lack of data for development and use of new drugs, delay in completion of clinical studies, lack of child-friendly formulations, challenges with taste and administration, complexity and cost of the projects, internal prioritization within companies, lack of market incentives and small markets, and difficult and slow market uptake.

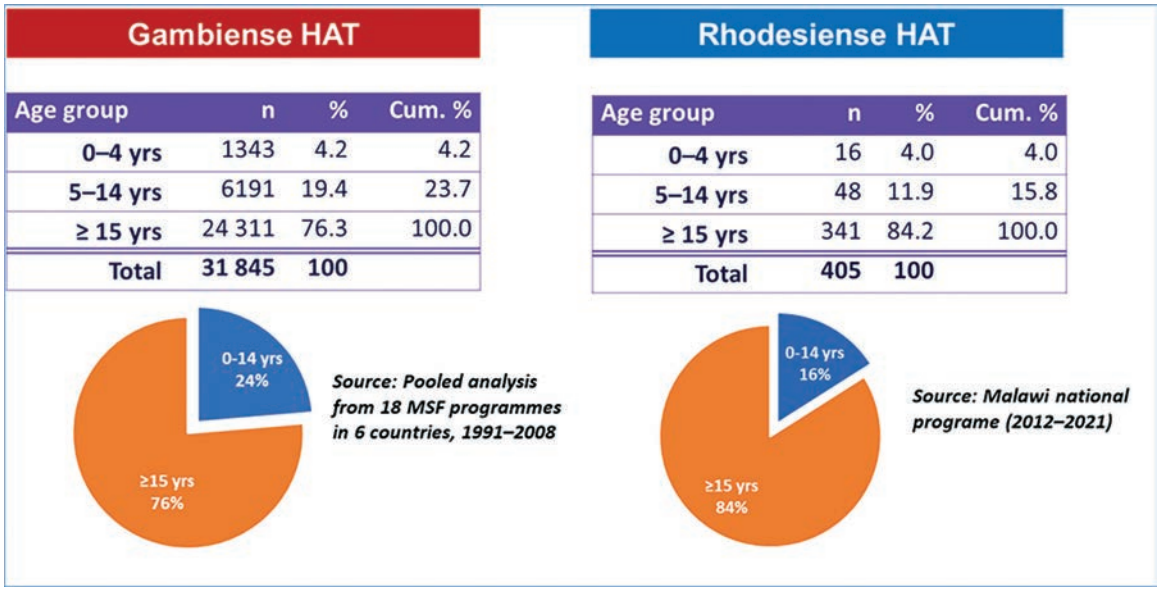
GAP-f was launched in 2020 to address these issues, with the vision that all children will have equitable access to the medicines they need. Its mission is to remove barriers and foster collaboration to identify gaps, set priorities and achieve acceleration across the product life cycle. GAP-f is a network hosted by WHO that provides an umbrella function for partners across the spectrum of innovation and access to better paediatric medicines, spanning multilateral, public, private and non-profit sectors.

GAP-f covers the entire product life cycle (end-to-end), starting with the prioritization and evaluation of new products, through their development into appropriate formulations, and their launch, with support, roll-out and safe use.

An initial phase from 2020 to 2021 has focused on HIV, tuberculosis and hepatitis C. From 2022 to 2024, expansion will include hepatitis B, COVID-19, antibiotics, childhood cancer and NTDs. The aim is to expand to the full range of essential medicines (including diabetes, epilepsy and others) from 2025 onwards.

Data on the HAT burden in children are summarized in Figure 10.4.1. The burden in children varies by location, depending on exposure during routine activities. Vertical transmission of g-HAT can infect newborns. In general, children are less affected than adults.

**Figure 10.4.1.** Human African trypanosomiasis burden in children




Very few trials have focused on treatment for paediatric HAT. Typically, young children are excluded from trials, so new drug labels exclude them. Dosages are often extrapolated from adult dosages, and specific paediatric formulations are lacking. The specific gaps in and challenges for treatment of g-HAT and r-HAT are:

For g-HAT:

- Paediatric dosage is empirical.
- The intravenous route is problematic in children (NECT requires intravenous cannulation for 7 days and eflornithine monotherapy for 14 days).
- Pentamidine is administered intramuscularly for 7 days.
- Fexinidazole (oral and since 2019) excludes children aged under 6 years or below 20 kg body weight and the tablets, which must be swallowed whole (not broken or crushed), provoke frequent nausea and vomiting (69%).

For r-HAT:

- Melarsoprol is given through intravenous injections daily for 10 days and suramin in 6 intravenous injections.
- The intravenous route is problematic in children.
- Both treatments are highly toxic.
- Paediatric dosage is empirical, as for adults.

Progress is expected with the use of fexinidazole for r-HAT and a future single-dose oral treatment with acoziborole for g-HAT. A specific paediatric formulation of acoziborole is under development and a study in children aged 1–14 years is planned. Evaluation of the use of acoziborole in r-HAT may also bring progress in the future.

PAediatric Drug Optimization (PADO) for treatment of HAT is planned with the following background. Fexinidazole is available as 600 mg tablets and is indicated for g-HAT patients aged ≥ 6 years and ≥ 20 kg body weight. An extension of the indication to include r-HAT in the same age group is currently in progress. Fexinidazole tablets cannot be crushed and administered, as their bioavailability is unknown. Children aged under 6 years may soon have no treatment options for r-HAT.

The PADO group agrees that acoziborole will meet most needs, but recognizes the need to accelerate the paediatric development of acoziborole for both indications. With regard to the research agenda, the following priorities were identified:

- acceleration of acoziborole development for both indications;
- crush studies of fexinidazole (600 mg) tablets for interim use; and
- experience with off-label use of fexinidazole in r-HAT (given the discontinuation of melarsoprol).

The results of PADO HAT have been shared with GAP-f partners to trigger appropriate actions and ensure acceleration through the product life cycle. Most work will be led by DNDi. In parallel, a short technical brief will be developed to allow wide and rapid dissemination, and a short peer review paper will be drafted. A meeting report on PADO for NTDs is expected in Q3 2023.

# 11. Vector control

## 11.1 Report of the working group on vector control in HAT elimination, WHO Network for HAT elimination

The working group 'Vector control in HAT elimination' has been established within the WHO network for HAT elimination and supported by FAO within the Programme Against African Trypanosomosis (PAAT). PAAT is an inter-agency collaboration, combining the efforts of FAO, WHO, the International Atomic Energy Agency (IAEA) and the African Union-Interafrican bureau for animal resources (AU-IBAR).

Two meetings have been held so far. The first expert meeting (virtual) was held in October 2021 on vector control and g-HAT elimination. There were 65 participants, including health officials from endemic countries (Angola, Cameroon, Côte d'Ivoire, Chad, DRC, Guinea and Uganda), research and academic institutions, the private sector and international organizations. The following topics were discussed: recent and ongoing field activities in g-HAT endemic countries (country reports); tools and approaches; costs and feasibility; reporting metrics and impact assessment; the process of verification of g-HAT elimination and the possible role of entomological indicators; molecular biology and tsetse control.

The following conclusions were drawn.

- Vector control contributes to reducing the transmission of g-HAT and is therefore a valuable addition to medical interventions.
- Progress in bait technologies, particularly "tiny targets", has provided novel, more affordable tools with which to implement vector control. A wider range of tools exists, which can be used individually or in an integrated manner.
- Metrics for estimating vector control coverage must be improved and harmonized to improve reporting and monitoring.
- Efforts to improve tsetse mapping should be continued and synergies with the WHO Atlas of HAT explored.
- Better criteria and approaches should be developed to prioritize areas for vector control.
- Interventions against g-HAT and AAT need to be better integrated within a One Health framework.
- The challenges of sustainable vector control and sustained community engagement need to be addressed in the context of declining g-HAT cases. Innovative approaches to vector control should be explored.
- Existing vector control tools and approaches should be improved (e.g. through use of less polluting devices, promotion of safe disposal after use).
- Coordination of vector control activities implemented in g-HAT endemic areas needs to be strengthened. This working group and PAAT provide an appropriate platform for information exchange and coordination.
- Country ownership of vector control activities should be increased and reliance on external partners progressively reduced.
- Tools for detecting *T. b. gambiense* in tsetse flies and other blood-feeding insects need to be improved.
- Vector control expert meetings in the framework of the WHO HAT Elimination Network should be convened regularly (e.g. annually).

The meeting report is available in English *(25)* and French *(26)*.

The second meeting on indicators of vector control coverage in g-HAT elimination was hosted by FAO in Rome, Italy, in December 2022. There were 23 people attending, as it was a more technical meeting, including health officials/researchers from endemic countries (Angola, Burkina Faso, Cameroon, Côte d'Ivoire, Chad, DRC, Guinea and Uganda), other research and academic institutions, and international organizations. It was decided to focus the meetings initially on vector control and g-HAT. r-HAT would merit a separate meeting as the challenges are different and many activities are ongoing. FAO is undertaking major work on mapping vector control activities and AAT distribution. The following topics were discussed: management of vector control coverage data for g-HAT elimination at country level (country reports); reporting and monitoring of vector control activities at continental/global level; estimation of vector control coverage using tools other than tiny targets; dossiers on g-HAT elimination at national level: options for vector control indicators; vector control indicators at project level; estimation of probability/detection of tsetse elimination.

WHO/FAO proposed a methodology for global coverage of vector control similar to the HAT risk methodology (i.e. spatial smoothing of vector control by kernel density (30 km radius)). This approach greatly facilitates the comparison of estimated vector control coverage with (i) estimated areas at risk and (ii) estimated populations at risk. Preliminary tests were conducted for two countries (Chad and Côte d'Ivoire), with a one-year period of data analysis and four separate years (2018, 2019, 2020, 2021). Figures 11.1.1–11.1.3 and Tables 11.1.1–11.1.2 show, as an example, the existing targets in a region of Côte d'Ivoire in 2018 and the area covered by vector control (intensity of targets, targets/km$^2$ per year). The effect of the targets extends to a radius of 30 km. This does not mean that all tsetse flies within this radius will be caught, but that people within this radius will benefit from the effect of the targets (i.e. reduced risk of HAT transmission). By comparison of the area at risk of HAT (risk categories by cases/people per year), the area at risk of HAT covered by vector control can be calculated.

The following conclusions were drawn.

- From 2022, WHO will require countries to provide detailed information on vector control in their annual reports.
- Options or proposals for vector control indicators need to be further discussed and refined.
- Key discussion points and conclusions from this meeting to be presented include:
- 7th meeting of the HAT-e-TAG, 17-18 January 2023;
- 5th WHO HAT stakeholders meeting, 7-9 June 2023;
- Methods need to be tested or developed to demonstrate the absence of tsetse flies.
- The activities of the vector control group of the WHO HAT Elimination Network should be continued (i.e. further meetings, joint activities, e.g. development of indicators).

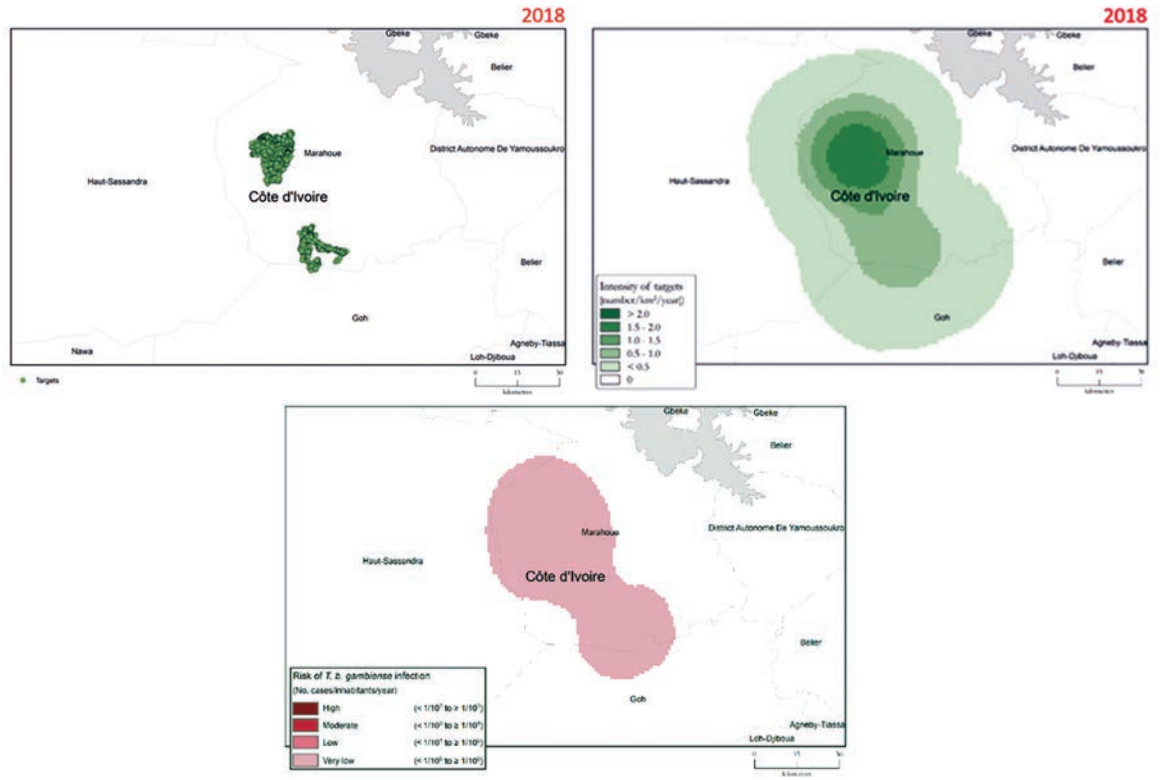
The discussion highlighted the difficulties of measuring impact at a global level. Therefore, first, the measure of vector control coverage is established as a realistic measure.

## 11.2 Current vector control interventions in HAT

There is a long tradition of joint vector control projects between IRD and the Liverpool School of Tropical Medicine (LSTM), in collaboration with other local and international partners, contributing to the HAT elimination targets.

The "riverine" tsetse/*Glossina palpalis* group includes the important vectors of g-HAT in West and Central Africa. The riverine tsetse vector relies on the humidity found in dense riverine habitats. The "savannah" tsetse/*Glossina morsitans* group includes the major vectors of r-HAT and AAT in eastern and southern Africa, which thrive in drier and more open areas of woodland and savannah.

**Figures 11.1.1–11.1.3** and Tables 11.1.1– 11.1.2. Existing targets in a region of Côte d'Ivoire in 2018, the area covered by vector control (intensity of targets) and area at risk of HAT (risk categories), as well as the area covered by and the area at risk of HAT covered by vector control




| | Intensity of targets [targets/km²/year] | Area covered [km²] | | | |
|---|---|---|---|---|---|
| | | 2018 | 2019 | 2020 | 2021 |
| | > 0 and < 0.5 | 4907 | 4877 | 6723 | 6723 |
| | 0.5 - 1.0 | 1369 | 1369 | 464 | 464 |
| | 1.0 - 1.5 | 541 | 536 | 0 | 0 |
| | 1.5 - 2.0 | 401 | 411 | 0 | 0 |
| | 2.0 - 2.5 | 0 | 25 | 0 | 0 |
| | Total | 7217 | 7217 | 7187 | 7187 |

| | HAT risk categories [cases/people/year] | Area at risk covered by VC [km²] | | | |
|---|---|---|---|---|---|
| | | 2018 | 2019 | 2020 | 2021 |
| | Very low | 3336 | 3356 | 2264 | 2914 |
| | Low | 167 | - | - | - |
| | Moderate | - | - | - | - |
| | High | - | - | - | - |
| | Very high | - | - | - | - |
| | Total | 3503 | 3356 | 2264 | 2914 |

Tsetse control strategies have been used to control r-HAT vectors and were not considered cost–effective for g-HAT vectors. Vector control tools with the following characteristics were identified: cost–effective; easy to use with limited external support (ownership); acceptable to communities; and suitable for large- and small-scale interventions (by professional teams or communities).

Between 2007 and 2010, behavioural field experiments were conducted on five main g-HAT vectors in four countries in Central and West Africa and the first tiny target prototype was developed. Between 2011 and 2013, field trials in Kenya and Uganda showed that the tiny targets are cost–effective and require little training for inexperienced technicians, and that community acceptance is essential to the technology's success. Implementation started in 2014 in Uganda, followed by DRC. Capacity strengthening (staff, institutions, equipment), community involvement (sensitization and community-based interventions), and data management and analyses (e.g. database, Apps, dashboard) were essential for implementation.

The two main vector control projects for g-HAT were the "Trypa-No!" partnership project and the "Tryp-Elim" project. Key activities in these project are: pre-selection of sites using GIS based on number of cases; pre-intervention entomological surveys and baseline catch data; deployment of targets along rivers (~20 targets/km); entomological evaluations at selected sentinel sites; and operational research.

In **Uganda**, operations were led by district entomologists under the supervision and coordination of COCTU (Coordinating Office for Control of Trypanosomiasis in Uganda). After 3 years of tsetse control with no new cases (elimination of g-HAT as a public health problem validated in 2022), vector control activities have been scaled down. There has been a strong capacity strengthening programme to enable the transfer of responsibilities and to maintain capacity in the post-elimination phase. District entomologists continue to carry out biannual entomological surveillance (over ~ 4000 $km^2$) and sensitization about the scale down of vector control activities. The importance of maintaining capacity in the districts to respond to any future new cases is recognized ("reactive vector control").

In the **DRC**, vector control is organized at central level (by the Programme National de lutte contre la trypanosomiase humaine africaine (PNLTHA) headquarters), provincial level (through provincial coordination) and peripheral level (via health zones). A strong capacity strengthening programme has enabled the transfer of responsibilities. Vector control activities have been scaled up from sporadic interventions before 2015 to a coverage of 12 500 $km^2$ in 2022. A further increase is planned to cover 360 km of river length by 2025. The community is involved in sensitization and community-based vector control in selected areas (increase from 101 to 213 villages). Vector control activities are currently only carried out in the former Bandundu province. Challenges are expected to arise after the project ends in 2025. The size of the DRC, with about 2 344 858 $km^2$, and Bandundu with about 295 658 $km^2$, is a challenge.

In **South Sudan**, vector control is being implemented by the Ministry of Health and FIND with technical support from LSTM. The intervention in Mundri West covers about 170 $km^2$ with about 30 km of river to be controlled. A baseline survey has been completed and the first small targets are being deployed, but the security situation is challenging.

In **Angola**, some vector control activities are already taking place as part of the Instituto de Combate e Controlo das Tripanossomíases strategy. The addition of a new intervention with an innovative strategy is planned for 2023.

Table 11.2.1 illustrates the vector control activities in **Chad, Côte d'Ivoire and Guinea** and the different contexts in which the activities take place.

**Table 11.2.1.** Overview of vector control activities in Chad, Côte d'Ivoire and Guinea

| | | | Start of intervention | Area ($km^2$) | Tiny targets | Population |
|---|---|---|---|---|---|---|
| **Chad** | | | | | | |
| *G. fuscipes fuscipes* | Mandoul | Savanah swamp | 2014 | 960 $km^2$ | 4600 | 80 000 |
| | Maro | Riverine habitat | 2018 | | | |
| **Côte d'Ivoire** | | | | | | |
| *G. palpalis palpalis* | Bonon | Degraded forest | 2016 | 250 $km^2$ | 3000 | 170 000 |
| | Sinfra | | 2017 | | | |
| **Guinea** | | | | | | |
| *G. palpalis gambiensis* | Boffa | Mangrove forest | 2012 | 1 900 $km^2$ | 20 000 | 200 000 |
| | Dubreka | | 2016 | | | |
| | Forecariah | | 2018 | | | |

In the Mandoul focus in **Chad**, tiny targets have been shown to reduce tsetse numbers, potentially interrupting transmission since 2015, and the combination of tsetse control with medical intervention has played a major role in reducing HAT incidence.

Also in **Guinea**, the combination of medical and vector control was shown to be decisive in reducing g-HAT transmission and accelerating progress towards elimination. During the Ebola outbreak in Guinea, active HAT

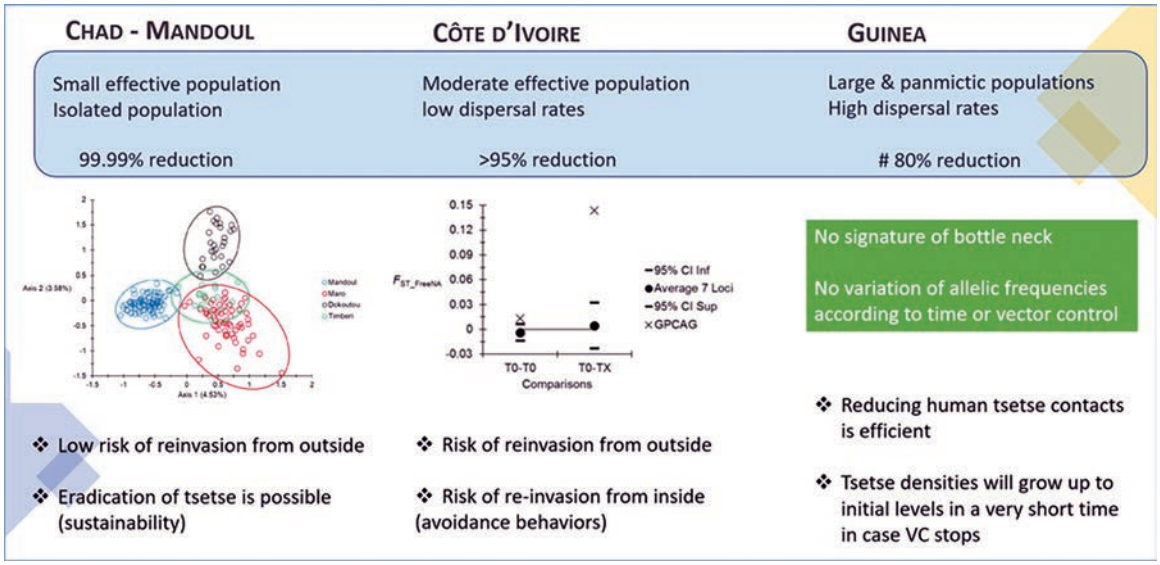
screening activities were postponed or compromised. However, tiny target tsetse control was maintained in the Boffa focus, where a pilot project had been launched in 2012. While the interruption of screening activities led to an increase in HAT prevalence over 2 years, HAT remained under control in areas with tsetse targets.

There is a transition from focus-wide control to more targeted and reactive use of tiny targets through spatial follow up of newly diagnosed HAT patients. Community involvement is key to the success and sustainability of vector control. Community-based monitoring can increase the number of sentinel traps. With xenomonitoring and modelling, entomological indicators for end of transmission are being developed.

Operational research is under way for the phase after 2025. The aim is to develop new monitoring and reactive vector control strategies in the post-elimination phase by addressing the following issues: optimal target density and deployment frequency; minimum operational scale; community-based vs top-down interventions for reactive vector control; trials of insecticide-treated cattle (for acceptability and sustainability); and post-elimination monitoring with xenomonitoring and risk-based monitoring.

The IRD in Montpellier is working on the genetic characterization of tsetse flies. A panel of microsatellites has been developed to study the genetic structuration of tsetse fly populations, providing information on population size, dispersal parameters and quantification of tsetse invasion/re-invasion (Figure 11.2.1).

**Figure 11.2.1.** Analysis of genetic characteristics of tsetse flies in Chad, Côte d'Ivoire and Guinea foci




VC: vector control.

An analysis of tsetse fly and r-HAT dynamics in the interface areas of Serengeti, Simanjiro and Pangani districts in the United Republic of Tanzania and the Rumphi district in Malawi was undertaken. Traps were deployed in each of these areas to quantify tsetse fly abundance across the wildlife–farming interface; the results of this work are contributing to predictive maps of tsetse fly distribution. Tsetse flies were absent in some places where they were predicted to be abundant. Flies were abundant in protected areas, where people and livestock living close to these areas are at risk. In the United Republic of Tanzania, most livestock keepers spray cattle with pyrethroids at the correct dosage, and the high use of pyrethroids is likely to reduce the tsetse fly population in farming areas.

The situation is different in northern Malawi, in the Vwaza wildlife reserve, where an outbreak of r-HAT occurred in 2019. The risk is inside the reserve and there are not enough cattle for control. The intervention will use targets inside the reserve and insecticide-treated baits with monitoring of tsetse populations. In the Nkhotakota wildlife reserve, new activities have started with the collection of baseline entomological data and training in entomology and GIS. Possibly the best form of control intervention there will be a combination of the methods used in both the United Republic Tanzania and northern Malawi.

# 12. Sociocultural dimensions and community perspectives on HAT elimination

A first virtual meeting (webinar) on sociocultural dimensions and community perspectives on HAT elimination was held in July 2021, coordinated by IHMT Lisbon.

With the re-emergence of HAT in the 1990s, there have been syndemics, parallel outbreaks and epidemics of, for example, Ebola or HIV. The focus on community health in the context of these epidemics was a big change in the 1980s and 1990s. There was also a paradigm shift from thinking about NTDs to thinking about poverty diseases and the disease burden in vulnerable communities. At the same time, we have a rapid evolution of sociology and anthropology moving into the questions of health, public health, and social and cultural epidemiology. This is particularly the case for anthropology. This has led to increased focus on the issue of community engagement and participation.

Household and community involvement and participation in screening, diagnosis, treatment and follow-up of patients with HAT has been a major concern. Two illustrative quotes from the webinar were: "Follow the rhythm of the communities" and "This disease is for poor people".

The programme focused on nine scientific studies:

## Community-centred programmes

- Severine Thys (University of Antwerp). Perception, feasibility and acceptability of community-based activities against HAT implemented in the active area of Boffa, Republic of Guinea.
- Catiane Vander Kelen (ITM). Where are all the dead flies! Perceptions of local communities towards the deployment of Tiny Targets to control tsetse in DRC.
- Alain Mpanya (University of Kinshasa). Home screening vs mass screening for HAT elimination: community perspectives.

## Socioeconomic and cultural dimensions

- Stella Neema (Makerere University). Socio-cultural factors and experiences of sleeping sickness (r-HAT) patients in Kaberamaido, Eastern Uganda: implications for treatment-seeking.
- Salome Bukachi (University of Nairobi). Socio-economic and gender considerations in human African trypanosomiasis control/elimination.
- Jeremi Rouamba (IRD). The role of human mobility in the persistence of HAT: an essential aspect to reach the elimination/eradication objectives.

## Pluralist care and knowledge systems

- Jennifer Palmer (London School of Hygiene and Tropical Medicine). From certainty to surprise: understanding 'passive' systems of HAT case detection and the role of local embodied diagnostic knowledge.

- Charlie Kabanga Hughes (Independent Consultant). Les perceptions et les pratiques des communautés locales en rapport avec la maladie du sommeil dans 14 zones de santé endémiques en République Démocratique du Congo.
- Alister Munthali. Barriers to accessing treatment among patients with R-HAT around Vwaza Marsh Wildlife Reserve in Northern Malawi.

These studies focused on tiny targets, home screening versus mass screening, health-seeking behaviour, gender, human mobility and migration, clinical diagnosis, community perceptions of HAT and barriers to treatment. The studies were conducted in Chad, Côte d'Ivoire, DRC, Guinea, Kenya, Malawi, South Sudan, Sudan and Uganda. The venues included village clusters, health zones, district levels, a hospital setting and a wildlife reserve. The methods used were mainly qualitative, such as focus group discussions, in-depth interviews, semi-structured interviews, informal interviews/discussions, life histories, meetings, workshops with community members, (participatory) observation, field work, thematic content analysis, literature review and training. There were also some publications using mixed methods, focusing on demographic data, public health data, clinical data, epidemiological data, archives and literature review.

Several barriers have been identified, such as fear of lumbar puncture or pluralistic health-seeking behaviours, including traditional healers (Table 12.1). Work rhythms, work time, costs of transport or hospitalization and gendered health-seeking behaviour are further examples of barriers. Barriers for guardians and carers are also important to consider and these are often ignored. Stigma was considered an important aspect, especially in the context of active screening. Therefore, home screening was generally preferred. However, there were also people who preferred to go to the hospital for diagnosis, as more expertise was assumed there. The lack of knowledge about the disease, especially among young people, was pointed out. Witchcraft and the extraction of body fluids were identified as other aspects to be considered. Fear of getting infected with a test, fear of HIV testing, decreasing fear of the disease with low incidence, mistrust in the diagnosis and in authorities were other influencing factors, as well as staff shortages with lack of expertise, lack of cultural affinity with patients and carers, lack of food provision and interference with social life.

**Table 12.1.** Different dimensions of barriers to HAT screening, diagnosis, treatment and follow-up

| | Active screening barriers | Passive screening barriers | Diagnostic barriers | Treatment barriers | Follow-up barriers |
|---|---|---|---|---|---|
| **Clinical** | Lumbar puncture | Pluralistic health-seeking behaviours (healers); self-medication | Lumbar puncture | Side-effects | Side-effects; lumbar puncture |
| **Seasonal** | Work rhythms, mobility | Work rhythms, mobility | | Work time | Work time |
| **Financial** | Transport, hospital care | | Transport, hospital care | Transport, hospital care | Transport, hospital care |
| **Income** | Lost revenue | | | Lost revenue | Lost revenue |
| **Family** | Guardian | | Carer | Carer | Carer |
| **Distance** | | | Waiting times | Distance | Distance |
| **Attendance** | Waiting times | | Waiting times | | |
| **Absence** | Absence | | Absence | Hospitalization | Absences |

| | Active screening barriers | Passive screening barriers | Diagnostic barriers | Treatment barriers | Follow-up barriers |
|---|---|---|---|---|---|
| **Gender** | Gendered health-seeking behaviour; gender HCWs) | Gender (HCWs); gendered knowledge | Gender (male reticence) | Gendered division of labour | Gendered division of labour |
| **Stigma** | Stigma; extraction liquids | (Lack of) Knowledge/age | Witchcraft; loss of (male) virility/ loss of genitalia | Abstinence required if positive | Stigma; extraction liquids |
| **Contagion** | Fear of contagion: exams, bush meat; mother–child | Fear of contagion | Fear of contagion; fear of HIV test | | Fear of contagion; fear of HIV test |
| **Disease/ Illness** | Low incidence: decreasing fear of disease | | Low incidence: decreasing fear of disease | | |
| **Trust** | Mistrust of authorities (e.g. Ebola); attitude of HCWs | Mistrust of authorities | Misdiagnosis; overdiagnosis malaria; asymptomatic early disease stage | (Mis)trust of authorities; Attitude of HCWs; treatment failures | (Mis)trust of authorities; attitude of HCWs |
| **HCWs** | Staff shortages; lack of expertise | Staff shortages; cultural affinity | Staff shortages; lack of expertise | Staff shortages | Staff shortages |
| **Food** | Lack of food | | Lack of food | | Lack of food |
| **Social** | Social life | | | Social life | Social life |

HCW: health care worker.

Even though facilitators were not a major aspect of the publications, nine facilitators for community engagement were identified and should be focused on, including proximity, seasonality, expediency, relatability, knowledge/familiarity, sociocultural affinity, syndemic perspective/care, integrated care and patient carer focus.

Recommendations regarding the communities are highlighted in Table 10.2. The Ebola crisis also showed that knowing what community is cannot be taken for granted. Local power relations and social relations are rather complex and need to be understood. For community engagement, the aspects of reciprocity, relatability, relationships and respect were emphasized, as well as the co-development of activities from the beginning, an open, reflexive and adaptative interaction, and synchronization of activities with the rhythm of the communities. Community participation should be based on local knowledge (of ex-patients, informal carers, people familiar with HAT control). A local collective decision-making process should be used and endorsement of local authorities obtained. Local narratives need to be listened to and cultural acceptance needs ensured. Social differentiation and stratification should be recognized, and vulnerable groups and sources of local resilience identified. Bonds of trust with traditional authorities need to be re-established and the positive effects of the measures needs to be emphasized. To motivate the community, local resources should be used with involvement of ex-patients and carers. A clear communication chain should be established and essential logistics including food be provided.

**Table 12.2.** Recommendations regarding the communities

| Aims | Vectors | Priorities | Interactions | Practice |
|---|---|---|---|---|
| **Define the community** | Local meanings: heterogeneous. Malleable, dynamic | Learn from Ebola experience | Complex social relations and power structures | Manageability community-based approach |
| **Engage the community** | Reciprocity, relatability, relationships, respect | Co-develop activities from start | Open, reflexive and adaptive | Synchronization: "Follow the rhythm of the communities" |
| **Community participation** | Build upon local knowledge (ex-patients, informal carers, persons familiar with HAT control and jointly assess them) | Use local collective decision-making processes; consult village chiefs and elders; obtain their endorsement | Listen to local narratives; awareness and dialogue avoid misleading interpretations | Implement projects within sphere of community norms; ensure cultural acceptability |
| **Relate to communities** | Recognize social differentiation and stratification (individuals, households and groups) | Identify vulnerable groups and sources of local resilience; coping strategies | (Re)establish bonds of trust with traditional authorities and HCWs and programme | Highlight visible and positive effects of measures |
| **Motivate communities** | Mobilize local resources for treatable disease; involve ex-patients and carers | Local legitimacy of intervention | (Community) liaison; clear communication chain; provide training; awareness campaigns; | Provide food, remuneration, (other) treatment and transport |

The **knowledge gaps** that were identified by the webinar participants are shown in Figure 12.1. A second meeting is planned to develop intervention strategies. It is important that evidence emerges from the field, because that is where the expertise lies. As the communities are different, there will be no uniform answer, which makes approaches more difficult.

**Figure 12.1.** Gaps in knowledge of sociocultural dimensions and community perspectives on HAT elimination

# 13. Statements from HAT stakeholders

Statements were provided by donors, public and private partners, WHO collaborating centres, international organizations and nongovernmental organizations.

## 13.1 Donors, public and private partners

### Sanofi

Philippe Neau thanked WHO and stressed the importance of the meeting. Sanofi has been involved in the fight against HAT for a long time. A year ago, Foundation S – the Sanofi Collective – was created with a renewed purpose, driven by the desire to stimulate, innovate and orchestrate a new approach to corporate philanthropy.

There are three areas of focus: (i) childhood cancer, supporting the global goal of achieving at least 60% child survival by 2030; (ii) climate change and health resilience, helping vulnerable communities adapt and build resilience to the impacts of climate change; and (iii) NTDs, with a commitment to eliminating sleeping sickness by 2030.

Sanofi has a 22-year long-term partnership with WHO, renewed for 5 years in December 2020, which includes donations of HAT medicines, financial support to WHO for screening, and information and education in countries. There has been tremendous success with a 98% reduction in sleeping sickness cases between 2001 and 2021. A partnership with DNDi has been in place since 2009, leading to the approval of fexinidazole in 2018 and the development of acoziborole. Very encouraging data for acoziborole were published and support is being given to regulatory approval and future access to this drug. HAT medicines are donated by Sanofi and Bayer and distributed by WHO to national HAT control programmes. Regular meetings are held with WHO to update long-term forecast needs, manage short-term requests and distribution, and anticipate potential risks of shortages due to manufacturing and supply.

The important role of all stakeholders was stressed. For the first time, a deadly human disease can be eliminated without the use of a vaccine, but the last mile is the most difficult and only by working together will we succeed in eliminating sleeping sickness.

### Bayer

Ulrich-Dietmar Madeja recalled that the partnership with WHO began in 2002, at a time when the number of patients infected with HAT was high. Bayer's commitment dates back to the 1920s, when suramin was invented as the first effective treatment for HAT and remains an essential drug today. The introduction of NECT was a major breakthrough, and Bayer extended its support with the donation of nifurtimox. Together with Sanofi's donation of eflornithine, it was possible to provide treatment kits to reach the most remote and poorest areas. In addition to donating drugs, Bayer is taking an integrated approach and has been supporting mobile intervention teams in the DRC since 2013. Although demand for suramin and NECT is low, Bayer is committed to continue production and donations for as long as needed. Bayer is very proud to be part of the success story and grateful for the trusting relationship.

## Bill & Melinda Gates Foundation (BMGF)

Rachel Bronzan indicated that the BMGF vision is a world where everyone has the opportunity to lead a healthy and productive life. The Foundation works with partner organizations around the world to reduce inequity. In 2021, it provided US$ 6.7 billion in total charitable support through more than 2000 grants, working in 144 countries with 41 programme strategies (disease or topic-driven, such as the NTD programme strategy). The BMGF is headquartered in Seattle (USA), with offices in eight other cities around the world. The Global Health Division (covering NTDs) of the BMGF spent US$ 1.6 billion in 2021, of which more than 50% directly funded research and development efforts. Approximately 40% of the Global Health Division's research and development support went to drug development and a further 35% to vaccine development. Strategies are guided by burden of disease and cost–effectiveness.

Interventions to combat NTDs are particularly cost–effective. The elimination of Guinea worm and HAT is considered to be of inherent value, where cost–effectiveness becomes in the endgame less a factor. The goal of the BMGF NTD team is to eradicate, eliminate or control eight diseases included in the London Declaration, each of which is at a different point on the pathway to elimination.

The three aims of the HAT portfolio are: (i) to eliminate HAT in all the BMGF-supported regions except DRC by 2030; (ii) to ensure that tools are available to accelerate and sustain HAT elimination by 2030; and (iii) to ensure that HAT endgame strategies are informed by research, modelling and data. The BMGF supports the full range of HAT projects from development to programme implementation.

- Programme implementation: Guinea, Sierra Leone, Côte d'Ivoire, Chad, Central African Republic, South Sudan, Uganda, Angola (FIND) and DRC (ITM)
- Diagnostics: native and recombinant RDTs (FIND), iELISA and molecular diagnostics (ITM)
- Vector control: tiny targets (LSTM)
- Modelling (University of Warwick)
- Therapeutics: fexinidazole and acoziborole (DNDi)
- Advocacy: DRC (CNRSC [National Coordination for Strengthening Community System])

Progress towards elimination is the best way to advocate for continued support, and for the BMGF it is a privilege to support the elimination efforts.

## Belgium Government

Pieter Vermaerke emphasized the importance of the meeting where WHO brings together all stakeholders. It shows the progress made but also the challenges ahead with possible solutions. Belgium has a strong commitment to combating NTDs, with a long tradition in the support of HAT control, especially in DRC. In 2017, the Government of Belgium announced that it would take the lead in supporting HAT control together with the BMGF. The commitment will continue until 2030, with confirmed strong financial support for the period 2022–2026 and beyond. Cooperation with the Congolese institutions is very important, and it has received political support for a joint programme. Hopefully, this collaboration will be useful to other affected countries and lessons learnt will be transferable. Belgium is also committed to the development of HAT diagnostics and availability in endemic countries, together with the Belgian partners ITM and Coris.

## Coris BioConcept

Pascal Mertens thanked WHO for inviting Coris BioConcept to take part in this coordination meeting. It is considered as recognition of Coris work over the past 20 years and the commitment to helping build the tools needed for this elimination. Coris BioConcept has been active in the development of HAT diagnostic tools for more than 20 years, starting with a PCR and oligochromatographic detection test in collaboration with ITM. Since then, other tests have been developed, including of course the HAT Sero K-Set (native VSG

antigens) and the HAT Sero K-SeT 2.0 (recombinant VSG and ISG antigens). These tests were then produced and validated thanks to the help of partners such as the ITM and the INRB Kinshasa.

Coris is a private partner and, foremost, a small business whose aim is to contribute to people's well-being by offering tools that can be used where they are needed most, with particular attention to ease of use outside the laboratory. To date, we have produced and distributed more than 4 million Sero K-SeT HAT RDTs, even during the difficult phase of the COVID-19 pandemic, and we will soon be exceeding 5 million tests. It is recognized that there is a need to continue developing serological and molecular diagnostics and optimizing the HAT sero K-SET 2.0 test, which will be needed to accompany the new HAT treatments.

Our commitment applies not only to HAT but also to other tropical diseases such as the leishmaniases, for which we have developed a rapid cure test, Chagas disease and viral haemorrhagic fever; we are also developing RDTs for the detection of antibiotic resistance.

The issue of test registration was highlighted. Europe has drawn up very ambitious regulations for in vitro diagnostics, but without the resources to make them work, not only are registration costs very high, but above all the number and availability of in vitro organisms are highly inadequate, and registration times are very long. Tests specifically intended for Africa, such as RDTs for HAT, would benefit from a specific status to be defined by the Expert Review Panel for Diagnostics. A clarification of the conditions for registering tests for NTDs could be included in the TPPs.

## 13.2 WHO collaborating centres

### Institute of Tropical Medicine (ITM), Antwerp

Nick van Reet, on behalf of Jan van den Abbeele, reported on the WHO Collaborating Centre for Research and Training on HAT Diagnostics. The ITM has a large collection of trypanosome strains, with more than 300 strains available, some of which have been genetically manipulated. The strains are used to provide extracts with purified pellets for protein analysis and DNA/RNA/miRNA aliquots that can be shared. There is also a large collection of trypanozoon genome sequences, with > 200 Illumina sequenced strains, which are used for population genetics and discovery of new markers for TbgI. The ultimate goal is to provide molecular diagnostics to the HAT community. Prospective studies are being conducted (e.g. Trypskin DNDi-OXA-04, CHARHAT for the animal reservoir, TrypELIM diagnostic grant, HAT+ passive screening).

In collaboration with the WHO Collaborating Centre for Reference and Training on Diagnosis of HAT in Kinshasa, assistance is provided in terms of training and equipment. Molecular diagnostics are being improved in terms of sample transport (DBS, DNA/RNA shield, PAXGene RNA/DNA, filter plates, biopsies), extraction methods (MTP Maxwell RSC, HTP KingFisher APEX) and targets for qPCR (Trypanozoon RT-qPCR, Subspecies RT-qPCR and Gambiense-qPCR). The TL test, which requires biosafety level A2 and has limited throughput, is performed at ITM, INRB and the Centre International de recherche-développement sur l'élevage en zone subhumide (CIRDES). ITM provides training and external quality control for this technique. Recent work has involved recombinant TL using native recombinant Tbb LiTat 1.3, native recombinant Tbb LiTat 1.5 modified for fixed VSG expression and for fluorescence expression. This technique has improved workflow (no biosafety issues, in vitro culture), read-out (equifluorescence, nuclear staining) and throughput (multiplexed), but still requires endpoint analysis.

### Institut de Recherche pour le Développement (IRD)

Jean Mathieu Bart reported on the WHO Collaborating Center for research on host–vector–parasite interactions to sustain surveillance, control and elimination of HAT, based in the Unit IRD/CIRAD 177 INTERTRYP "Host - Vector – Parasite – environment interactions in NTDs due to Trypanosomatids". INTERTRYP is a joint research department of IRD and CIRAD (Centre de coopération internationale en recherche agronomique

pour le développement) based in Montpellier, dedicated to the control of human and animal diseases caused by Trypanosomatids. The Unit IRD/CIRAD 177 was created in April 2019 and its terms of reference include technical assistance, scientific expertise and specialized training at the request of WHO or in the context of collaborative projects.

The activities are conducted by INTERTRYP and its main African partners: the International Livestock Research and Development Centre in the Subhumid Zone of Bobo Dioulasso, (Burkina Faso), IPR in Bouaké (Côte d'Ivoire) and the PNLTHA in Conakry (Guinea). The work plan includes five activities: (i) support for passive and active HAT case detection and vector control; (ii) reference testing with the TL test (CIRDES, IPR); (iii) training and education; (iv) provision of expertise to WHO; and (v) supporting the WHO HAT elimination strategy by improving diagnostic tools. Research is also being conducted on the animal reservoir of *T. b. gambiense*. A major question to be answered is whether the animal reservoir threatens the elimination of g-HAT transmission, depending on different eco-epidemiological settings of HAT foci and biological (genetic and phenotypic) characteristics of *T. b. gambiense* strains. Another key question is whether we can anticipate an animal-to-human spillover. Funding has decreased in recent years, and it is essential to preserve the unique expertise of the collaborating centres and find the appropriate means. The additional involvement in HAT research includes:

- Clinical trials:
  - On treatment: Acoziborole in kids, Fexinidazole on g-HAT (DRC, Guinea), Acoziborole in r-HAT (Malawi, Uganda), Pivotal clinical trial of acoziborole in g-HAT (DRC, Guinea), Acoziborole in seropositives
  - Diagnostics: SpeSerTryp study
- COMBAT: EU H2020, coordinated by Cirad, including a One Health component on impact of vector control for g-HAT on AAT and the development of innovative antigen detection tests for HAT and AAT
- ANR Trypaderm, coordinated by Institut Pasteur (Côte d'Ivoire, Guinea)
- WT Trypanogen, coordinated by Makerere University (Cameroon, Côte d'Ivoire, DRC, Guinea, Malawi, Uganda)
- ANR SherPa, coordinated by Institut Pasteur and including research on animal reservoirs of T. b. gambiense (Cameroon, Côte d'Ivoire, Guinea), on tsetse microbiota (Cameroon) and on tsetse population genetics (Chad, Guinea)
- IRD involvement ion JEAI RECIT (Guinea), GDRI TROUVE (Burkina Faso, Cameroon, Côte d'Ivoire, Guinea) and PhD Fellowship ARTS
- AFRICAM: from Prezode initiative to prevent emergence/re-emergence of zoonotic diseases (Cameroon and Guinea)
- STROGHAT, coordinated by ITM and funded by UE-Horizon Europe (DRC).

## Clinical Investigation and Access to Research Bio-resources (ICAReB) Platform – Institut Pasteur

Blanca-Liliana Perlaza from the ICAReB platform (Clinical Investigation and Access to Research Bio-resources) of the Center for Translational Science, Institut Pasteur, reported on the WHO HAT specimen bank, developed in a cooperative framework between WHO and the ICAReB Platform-Institut Pasteur and with the financial support of FIND and Sanofi. This biobank hosts samples from donors of sub-Saharan Africa and was constituted to develop and validate new tests for the diagnosis of HAT. Fourteen centres from six endemic countries were implicated: 1877 subjects (975 patients, 875 controls and 117 suspects) were enrolled according to the parasite presence, diversity and load using different parasitological and serological tests.

The ICAReB team supports WHO in the management of the HAT biobank through operational coordination, partnership/collection integration, and coordination of ethical and regulatory requirements. The biobanking

of HAT samples includes aliquoting, storage and labelling, and distribution of material. Other activities include the establishment of adapted databases (samples and bioclinical), compliance with data protection regulations, and the distribution of bioresource and patient-related information. In terms of HAT bank governance, participation in the Exit Committee, technical support and quality control of specimens will be provided. The results are promoted and disseminated through public communication and information (website) and the results of research are returned to the partners.

Almost 10 000 (9680) samples (almost 25%) have been distributed to 26 research teams so far. The biobank is becoming increasingly important in the context of declining numbers of cases. The consolidated collaboration between the Institut Pasteur and WHO opens up new partnership perspectives. A new collaboration is under way between WHO and DNDi: to integrate the TrypSkin collection resulting from the DNDi OXA-04 clinical trial (740 subjects with demographic and bio-clinical data; 1480 whole blood samples in RNA/DNA SHIELD buffer (300 positive samples) and DBS on FTA® card/subject.

### Institut National de Recherche Biomédicale (INRB), Kinshasa

Dieudonné Mumba reported on behalf of INRB in Kinshasa (DRC), which is a WHO Collaborating Centre since 2018 and the national reference centre for HAT. New diagnostic tests are being implemented and evaluated, molecular tests (Sherlock with IP, qPCR with ITM, RT-qPCR multiplex with IRD) and serological tests (iELISA). The TL test is performed at the INRB. There is a need to use a single protocol to compare results and collaboration among the three different WHO collaborating centres.

HAT diagnostic services also include the production and distribution of the mAECT. The gel has been donated by the Swedish company Cytiva (already for 9 years), which reduces the cost of the mAECT, and is supplied through WHO. Its production (400 tests per week) can be doubled according to need. Blood samples (KPS) from serological suspects are sent to the INRB as a reference laboratory, where reference tests (TL, molecular tests, iELISA) are performed. Achieving a turnaround time of 7 days is challenging and requires continuous availability of qualified personnel. In the TrypanoGen project for HAT transcriptomics, 52 individuals were phenotyped as HAT cases, seropositives or controls based on three diagnostic tests (CATT, TL and mAECTs). Another focus is the training of laboratory technicians of NSSCPs from DRC and other countries.

## 13.3 Other research institutions

### Institute of Tropical Medicine (ITM), Antwerp

Paul Verlé spoke on behalf of ITM, indicating that ITM has a long tradition of collaborating closely with Congolese institutions and various stakeholders, supported by long-term donors. Numerous people were trained in HAT. HAT diagnostics are being further optimised, already with a view to the post-elimination phase. Elimination is an objective which requires a long-term commitment, for which we are thankful to the donors.

In addition to research, a main focus of ITM is also on control measures, active/passive screening and vector control, with different partners. Continuous improvement of data quality should be aimed for. ITM has invested heavily in digitalisation over the last ten years (e.g., digital recording of test results for quality control). Further investment is required to enhance the reliability and quality of data. ITM in investing in collection kits for reference testing at centralised laboratories. Participants were encouraged to take advantage of this opportunity to meet again in person.

### Institute of Hygiene and Tropical Medicine (IHMT), Lisbon

Jorge Seixas reminded of the challenges that arise as a result of successful elimination efforts. The question is how to maintain the specialized knowledge of HAT diagnostics and management. The interest of the International course for HAT capacity building was reminded and was proposed to reinvent a new format

with African and non-African participants. The importance of sociocultural dimensions and community perspectives on HAT elimination were emphasized with a need to retain community knowledge of the disease and engagement in the programme, also at the political level. IHMT offered to host a new meeting on the subject.

## Centre International de Recherche-Développement sur l'Elevage en zone Subhumide (CIRDES)

Jacques Kabore spoke on behalf of CIRDES, an institution dedicated to serving the livestock sector in West and Central Africa on a sub-regional level and based in Bobo-Dioulasso (Burkina Faso). Its areas of activity are improving animal health and production; conservation of animal genetic resources; preservation of the environment; sustainable integrated management of agro-sylvo-pastoral resources; and training, exchanges and technology transfer. CIRDES has been designated as: reference laboratory for African trypanosomes of the World Organisation for Animal Health (OIE); Regional Centre of Excellence for Animal Biotechnology; IAEA Collaborating Centre for the Sterile Insect Technique (SIT); and Reference centre for the diagnosis of HAT since 2010, receiving hundreds of specimens annually for TL testing. Since 2020, 3673 sample analyses were conducted using TL. The operations of the 5 laboratories of CIRDES include the production of glossines, parasitological serology, immunoparasitology, acarology, production of laboratory animals, molecular biology, and the genotyping platform.

## Institut Pierre Richet (IPR), Bouaké

Dramane Kaba spoke on behalf of the IPR, recalling the situation in the 1960s when the disease was almost eliminated, the subsequent loss of disease-specific knowledge and the emergence of a new epidemic. The IPR is a reference institute for research into vector-borne diseases, with various groups working on malaria, onchocerciasis, the leishmaniases and other diseases, as well as a large working group on HAT. The IPR supports NSSCPs. IPR has a technical platform composed of several experimental platforms, such as parasitology, serology and molecular biology, with a cartography unit and a geographical information system. Furthermore, a cryobank of trypanosomes and an animal facility are maintained, facilitating the execution of trypanoslysis, as well as the cultivation and identification of human and animal trypanosomes. A large mobile team is deployed for targeted, reactive activities in response to identified cases. Additionally, an entomology team applies vector control solutions suited to various epidemiological contexts. The IPR is a collaboration centre of WHO with Intertryp/IRD. The IPR has forged numerous partnerships with major national, subregional and international research institutions to provide its expertise; it is currently building a research network to combat trypanosomiasis.

## Drugs for Neglected Diseases initiative (DNDi)

Stephane Hugonnet reminded the meeting of the 20th anniversary of DNDi in 2023. When MSF was awarded the Nobel Peace Prize in 1999, they allocated part of the award to address this problem with a new, alternative, not-for-profit model for developing drugs for neglected patients. In the last 20 years, DNDi has developed 20 drugs that are available, including NECT and fexinidazole for HAT. The team comprises approximately 270 committed individuals, including consultants and partners, collaborating across nine offices worldwide (three in Africa, three in Asia, two in the Americas and one at the headquarters in Geneva). The Global Antibiotic Research and Development Partnership developed out of DNDi is a not-for-profit organization that develops new treatments to fight drug-resistant infections. A COVID-19 project will soon develop as an independent entity out of DNDi. DNDi has supported the creation and maintenance of collaborative platforms, such as the HAT platform, which builds and strengthens treatment methods and clinical trial capacity in countries endemic for sleeping sickness. DNDi's portfolio has been enlarged and includes besides HAT the following diseases: Chagas disease, cutaneous and visceral leishmaniasis, Dengue, filariasis, hepatitis C, malaria, mycetoma,

paediatric HIV, cryptococcal meningitis and COVID-19. The feasibility of a project on schistosomiasis and snakebites is currently being evaluated. DNDi remains fully committed to eliminating HAT.

## Foundation for Innovative New Diagnostics (FIND)

Sylvain Biéler reported on behalf of FIND, reminding the meeting that over the past 17 years, FIND has been facilitating the development and implementation of new diagnostic solutions to support the control and elimination of HAT. FIND is committed to pursuing and intensifying this work, collaborating with various stakeholders, including academic and research institutions, commercial companies, international public health organizations, health ministries and NSSCPs, funders and of course WHO.

Two weeks ago, at the 76th World Health Assembly, Member States adopted a resolution on strengthening diagnostics capacity. This historic milestone formally recognized the vital role of diagnostics in delivering Health for All, also highlighting the need for national diagnostics strategies to be put in place and acknowledging that diagnostics data were critical to inform health-care decision-making at every level. FIND is committed to accelerating equitable access to reliable diagnosis around the world, including for NTDs, and in particular for HAT.

FIND efforts will remain focused on ensuring that appropriate diagnostic tools are available to HAT-endemic countries, including in particular RDTs, considering their central importance in current and future HAT elimination strategies. While the RDTs that are currently available have already proven their utility and have already significantly contributed to HAT elimination, FIND will continue to explore options to further improve the performance of RDTs, to ensure that they can play a role in future test-and-treat strategies, which will probably require more specific RDTs.

FIND will try to facilitate regional manufacturing of diagnostic tests, so that they could be manufactured in Sub-Saharan Africa, close to where they are needed. In addition, recognizing the importance of developing new laboratory-based reference tests to accompany future elimination strategies, FIND is planning to support an independent study to evaluate the performance of the various molecular tests that have been developed by several institutions, in order to facilitate the identification of one or several tests that could be further developed and eventually commercialized, so that they could be made widely accessible to all HAT endemic countries.

FIND work will also include providing HAT endemic countries with the necessary support for laboratory strengthening, vector control, training, coordination, logistics and data management, as well as facilitating collaborations between neighbouring countries where HAT foci extend across national borders. More specifically, FIND and partners will continue to support efforts to eliminate HAT and sustain its elimination in Angola, Chad, Côte d'Ivoire, DRC, Guinea, Kenya, South Sudan Uganda, and. Recently, this work was also extended to Sierra Leone and initiation of similar activities is planned in Central African Republic later this year. The elimination work is currently done mostly in partnership with IRD and LSTM, and is funded mainly by the BMGF, the Canton of Geneva and the Swiss Agency for Development and Cooperation.

The immense progress made towards the elimination of HAT was acknowledged. FIND is proud to be part of the HAT community and looks forward to reaching the targets set by WHO.

## Liverpool School of Tropical Medicine (LSTM)

Andrew Hope spoke on behalf of the LSTM to thank WHO and partners for this meeting. He recapped that LSTM has a long history of working on sleeping sickness, particularly in the field of vector control. Over the past 10 years we have seen huge progress in vector control against g-HAT with the introduction of tiny targets which were developed by LSTM, IRD and partners across Africa. To have gone from a research study to large-scale implementation in such a short period of time is remarkable.

LSTM has built strong partnerships with the NSSCPs in Uganda and DRC and with global partners including WHO, ITM and FIND. One of our key strategies is building capacity for vector control in NSSCPs so that they are able to take ownership for implementation. Thanks to this capacity, which was in place at the province and districts levels, vector control operations were able to continue uninterrupted during the COVID-19 pandemic.

The work in DRC on TrypElim with the PNLTHA and ITM has seen vector control expand at an impressive pace, starting from a small-scale pilot project in 2015. When LSTM started in DRC there were only two vector control staff; now it has expanded and there are staff at province levels and focal points in health zones. This structure is enabling the successful national ownership of implementation and is a credit to the commitment of the PNLTHA to vector control. The need to expand and start vector control activities beyond the Bandundu North and Bandundu South is recognized. Support to vector control activities in Angola and South Sudan has been set up last year, but there will also be a need for vector control in other countries to help accelerate the elimination and interruption of transmission. Building on our strong institutional links with health researchers, practitioners and policy-makers in Malawi, and in partnership with global institutions such as WHO and DNDi, Malawi is strengthening its capacity to control tsetse as part of their national strategy to eliminate r-HAT. All this work has been possible, thanks also to all the partners including the SSNCP DRC, COCTU, FIND, ITM, IRD, WHO, HAT MEPP and the University of Glasgow, among many others, to Vestergaard who donates the tiny targets and to the funders, BMGF and MRC. LSTM remains committed and looks forward to working with our partners in the coming years in order to achieve the 2030 targets for g-HAT and r-HAT.

## Institut Pasteur Paris

Brice Rotureau spoke on behalf of the Institut Pasteur in Guinea and in Paris. The HAT elimination programme is a collaborative effort involving four units at the Institut Pasteur in Paris, with several partners. The projects are mainly funded by Agence National de la Recherche (ANR), FIND, BMGF, Institut Pasteur and DNDi.

The research activities range from fundamental research to practical application, addressing biology, epidemiology, diagnosis and treatment. As recently demonstrated, the skin is an important but overlooked anatomical reservoir for trypanosomes. The TrypaDerm projects seeks to (i) unravel the development of skin-dwelling parasites (differentiation, proliferation, migration), (ii) study host–parasite interactions (sequestration, skin remodelling) and (iii) translate these results into applications (prevalence, treatment efficacy and new detection methods). The prevalence of dermal trypanosomes is under investigation in humans, domestic and wild animals at study sites in Burkina Faso, Cameroon, Côte d'Ivoire and Guinea. Different detection techniques are compared on skin and blood samples from symptomatic and latent infected patients.

The partners at Institut Pasteur propose that adapting the recently developed Specific High-sensitivity Enzymatic Reporter unLOCKing (Sherlock) technology, which combines a CRISPR-Cas system and a lateral flow test, to trypanosomes will provide the sensitivity and specificity required for a diagnostic test in the elimination and post-elimination phases. The Trypskin sub-study is part of the DNDi-OXA-04-HAT trial and blood and skin samples of 730 serosuspects are collected in Guinea and DRC. The exploratory objectives are (i) to estimate the prevalence of extravascular dermal *T. b. gambiense* in seropositive individuals; (ii) to evaluate new molecular tests for the detection of blood and skin trypanosomes (multiplex qPCR (ITM), multiplex RT-qPCR (IRD) and Sherlock (IP)); and (iii) to assess an additional benefit of acoziborole on skin trypanosomes.

The Institut Pasteur is dedicated to continuing its collaboration and contributing to the joint efforts towards the elimination of HAT.

## National Institute for Communicable Diseases Johannesburg

Lucille Blumberg reported for the National Institute for Communicable Diseases including the reference centre for parasitic diseases, based in Johannesburg, South Africa. The Institute is supporting case management and diagnosis of HAT and has built significant expertise for over 20 years. Mainly travellers, expatriates and soldiers affected by r-HAT have been treated, either returning from endemic areas or referred from other countries without experience in HAT management. A strategic stock of HAT drugs is maintained. There is also a focus on training, as misdiagnosis and delayed diagnosis are problematic. Patients missed at stage 1 often develop complications and require intensive care

## Swiss Tropical and Public Health Institute (STPH)

Marina Antillon presented the STPH work in the field of HAT and AAT. HAT has been a core mission of STPH's work since its beginning and has shaped the history of the institute. The Unit for Parasite Chemotherapy has a broad panel of strains (*T. b. brucei, T. b. rhodesiense, T. b. gambiense*) and assays for drug efficacy testing in vitro and in vivo for several partners. *T. b. brucei* is used as a model for the deconvolution of drug mode of action and drug targets for compounds that are active against *T. cruzi*. The target is conserved, but molecular genetics are much easier to carry out with *T. b. brucei* than with T. *cruzi.*

The unit for Medicines and Implementation has historically worked on various treatment developments. Currently, the activities focus on chairing the Project Advisory Committee for the AcoziKids study (DNDi). The conceptualization of the DNDi trial on efficacy and safety of fexinidazole in patients with r-HAT was supported.

The unit for Health Systems Research is focusing on economic evaluations of elimination campaigns (costings of active and passive screening, vector control, out-of-pocket payments and follow-up of g-HAT suspects), in close cooperation with the HAT MEPP, TrypElim and Trypa-No! projects. The cost–effectiveness of elimination campaigns is being evaluated in Chad, DRCand Uganda in collaboration with the HAT MEPP programme at the University of Warwick.

A previous project of the Swiss Centre for International Health focused on strategic development. Together with the organization Biovision, community-led interventions for the control of vector-borne diseases in humans, animals and plant diseases were investigated, specifically targeting malaria and AAT control in Ethiopia and Kenya. The interventions were assessed for One Health methodologies that are environmentally sustainable and can be applied to the livestock production sector.

The HAT community was acknowledged for its commitment and engagement with Swiss TPH.

## HAT modelling and economic predictions for policy (HAT MEPP) project – University of Warwick

Katherine Rock, on behalf of the University of Warwick, gave an update of the HAT MEPP project. The project is in its second phase and primarily aims to: (i) support NSSCPs (intervention strategies and cost efficiency), (ii) model efficient use of emergency tools; and (iii) provide forecasting of drugs, diagnostics and target requirements in different settings. The University of Warwick started modelling sleeping sickness in 2014–2015. An important part of this is the modelling cycle, where the model is first calibrated to data from different sites, from different g-HAT foci. Output is generated and the results are evaluated with partners. With new information and new data, the model is adapted and refined, and the cycle continues. For example, in a study with the PNLTHA in the DRC, based on data from 2000 to 2016 at the level of some 170 health zones, regions were identified in need of intensified interventions in order to reach the elimination targets by 2030 with current strategies. A refined model based on updated data from 2000 to 2020 showed more optimistic results, especially in Bandundu. However, regions were still identified that will need intensified interventions to have high confidence of achieving the 2030 targets. Furthermore, the expected impact of modified strategies with the same tools, also factoring in costs, were analysed. A major challenge is to communicate the large number

of results in a straightforward way. A tailor-made graphical user interface (GUI) enables this and can be continuously updated (https://hatmepp.warwick.ac.uk/DRCCEA/v4/; Login: WHOSHM2023; Password: HAT23!). The graphical user interface has been extended to include predictions of expected tool use (and uncertainty) under different strategies, and to allow aggregation to larger spatial scales (e.g. coordinations or the whole DRC), showing the predicted number of treatments. Based on feedback from many stakeholders, modelling was started at smaller spatial scales. The health zone (~150 000 people) was the primary modelling unit in the DRC. Health area modelling (~10 000 people) allows for smaller scale strategy assessment, but this is challenging work: smaller populations and more noisy data require a stochastic modelling approach, and model fitting to data becomes more complex with more than 10 times more locations (more simulation time required). At present, health area modelling has been undertaken for Mosango as an example region, which will be extended first to Bandundu Nord and Sud, and then to all DRC. Work is continuing with the NSSCPs of Chad, Côte d'Ivoire, Guinea and Uganda to assess transmission reduction and expected progress under future strategies. Of particular interest is the modelling of the potential impact of screen-and-treat strategies with acoziborole.

### University of Glasgow

Michael Barrett presented the activities of the University of Glasgow, which are mainly based on laboratory work with molecular studies of trypanosomes and the mechanism of drug action. In collaboration with Novartis, very promising new drug compounds are being investigated and results will be published soon. There is a focus on the development of HAT drug resistance, its mechanism and spread in the field. The University of Glasgow is mainly involved in the molecular biology and basic understanding of trypanosomes, helping to understand what the parasites are causing in the field, using the latest molecular and sequencing technologies to identify the genes that vary between parasite species and participating in the description of skin trypanosomes.

### University of Makerere College of Veterinary Medicine

Enock Matovu spoke on behalf of Makerere University, Uganda's leading public university, which recently celebrated its 100th anniversary. The University is involved in several HAT projects and has its own strategic position, ranging from laboratory to field activities. For example, regular field surveys are conducted and facilities are available for trypanosome propagation in vitro and in laboratory animals (mice), cryopreservation, molecular diagnostics, DNA and downstream molecular analysis including genomics and bioinformatics. Several HAT projects are being undertaken. For example, the collaboration with FIND on bringing diagnostics to the field is appreciated. Other project highlights include participation in the fexinidazole trial for treatment of r-HAT, where field staff were retrained and molecular approaches to monitoring cure were investigated. The TrypanoGEN project looks at genetic markers of trypano tolerance and has been running for 10 years. It has been a very nice collaboration between Anglophone and Francophone Africa. Young scientists have been trained (5 postdocs, 17 PhDs, 3 MScs) in seven countries. Technicians were trained in seven countries. Validation studies of HAT tolerance genes in mouse models are ongoing in collaboration with the University of Glasgow. Makerere University will continue to play a role in HAT research, including AAT, by tracking the animal reservoir, training field staff, particularly in diagnostics in Uganda and beyond, optimizing and rolling out new techniques, working with the national NSSCP and international partners, and investigating post-elimination surveillance.

## 13.4 International organizations

### Food and Agriculture Organization of the United Nations (FAO)

Weining Zhao reported on behalf of FAO. FAO shares with WHO and the other stakeholders attending this meeting the vision of an African continent free from the burden of trypanosomosis, and where the disease no

longer constrains the attainment of the Sustainable Development Goals. FAO is determined to continuously collaborate with WHO, in realization of this vision and to achieve our common final goal. Since 1997, FAO and WHO have collaborated closely within the framework of the PAAT. In particular, in 2008 the continental atlas of sleeping sickness was launched. Since then, the atlas has become a key tool for monitoring the elimination of HAT, and it is also increasingly used for planning field control activities and for scientific research. FAO and WHO also collaborate closely to promote One Health within the framework of the FAO–WHO–OIE tripartite and UNEP. Indeed, the control of AAT has a role to play in the elimination of sleeping sickness, especially for the zoonotic form caused by *T. b. rhodesiense* in eastern and southern Africa. FAO and PAAT welcome the new road map and confirm their commitment to supporting WHO and endemic countries in their efforts to achieve the goal of HAT elimination.

### International Atomic Energy Agency (IAEA)

Chantal de Beer spoke on behalf of the joint FAO/IAEA centre and the Department of Technical Cooperation of IAEA, thanking WHO for the invitation to this meaningful meeting. The General Conference of IAEA requested the IAEA and other partners to strengthen capacity-building in Member States for informed decision-making on the choice of tsetse and trypanosomiasis control strategies and the cost–effective integration of SIT operations in area-wide integrated pest management (AW-IPM) campaigns. The General Conference also requested the Secretary to coordinate with Member States and other partners to allocate resources through the regular budget and the Technical Cooperation Fund for consistent support to the operational field projects of the SIT Programme, and to strengthen support for research and development and technology transfer in African Member States to complement their efforts to establish and expand tsetse-free zones.

The IAEA, through the Department of Technical Cooperation and the FAO/IAEA Joint Centre, has played a central role in developing the successful implementation of SIT for fruit flies and other key insect pests, and has played a similar role in programmes targeting tsetse. The IAEA assists Member States through country programme frameworks to identify the need for the development and implementation of SIT programmes by assisting in the acquisition of the technical baseline data required for the implementation of the field programme, including assistance in the collection of ecological, seasonal and distribution data, and the suitability of pest population levels for the application of SIT as part of an integrated area-wide approach. The IAEA assist in determining whether SIT programmes are justified on economic and environmental grounds, identify and provide research and development support required for the implementation of SIT, assist in the development of the necessary infrastructure and training not limited to SIT but including GIS distribution modelling, population genetics, mass rearing, insect sterilization and more. IAEA also assist in the development of capacity for mass rearing, production of sterile insects and promote the commercialization of products and other activities related to the application of SIT. Finally, IAEA is helping to design the implementation of national, area-wide, integrated management strategies with a SIT component. SIT can play a role in the elimination of riverine species in certain areas where eradication is warranted, feasible and environmentally justified.

## 13.5 Nongovernmental organizations

### Médecins Sans Frontières (MSF)

Doris Arlt Hilares and Arnault Cheval (Supply Chain Director) reported on the activities of MSF Logistique, the supply centre of MSF, raising that MSF Logistique is proud to contribute to the WHO programmes on HAT, a longstanding collaboration. MSF offers its expertise in logistics, procurement and transport to contribute to the WHO elimination targets.

# 14. The road map for neglected tropical diseases 2021–2030

In 2012, WHO published its first road map for NTDs, setting targets for 2020. Their pursual led to substantial reductions in the overall burden of NTDs. In January 2021, WHO launched a new road map – *Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030 (9)* – which builds on the progress of the previous one and places countries at the centre. It was developed through a global consultative process involving different partners, including many of the stakeholders present at this meeting. The road map is aligned with the United Nations Sustainable Development Goals and WHO's Thirteenth General Programme of Work. It was endorsed by the 73rd World Health Assembly in 2020 for implementation by all Member States, with technical assistance of WHO. Progress will be monitored biannually by the World Health Assembly, in accordance with decision WHA73(33) *(27)*.

The overarching 2030 global targets are:

- 90% reduction in people requiring interventions against NTDs;
- 75% reduction in disability-adjusted life years related to NTDs;
- 100 countries having eliminated at least one NTD; and
- 2 NTDs to be eradicated.

The individual diseases are grouped in four categories:

- **Diseases targeted for eradication**: Dracunculiasis and yaws.
- **Diseases targeted for elimination** (interruption of transmission): Human African trypanosomiasis (gambiense), leprosy and onchocerciasis.
- **Diseases targeted for elimination as a public health problem**: Chagas disease, human African trypanosomiasis (rhodesiense), leishmaniasis (visceral), lymphatic filariasis, rabies, schistosomiasis, soil-transmitted helminthiases, trachoma.
- **Diseases targeted for control**: Buruli ulcer, dengue, echinococcosis, foodborne trematodiases, leishmaniasis (cutaneous), mycetoma, chromoblastomycosis and other deep mycosis, scabies and other ectoparasitoses, snakebite envenoming, and taeniasis and cysticercosis.

In the first road map, the defined goal for g-HAT and r-HAT was identical: the elimination of HAT as a public health problem by 2020. In the new road map, the goals for g-HAT and r-HAT differ:

- gambiense HAT: to interrupt transmission of g-HAT (sustainable elimination) by 2030 (zero cases)
- rhodesiense HAT: to keep r-HAT eliminated as a public health problem by 2030.

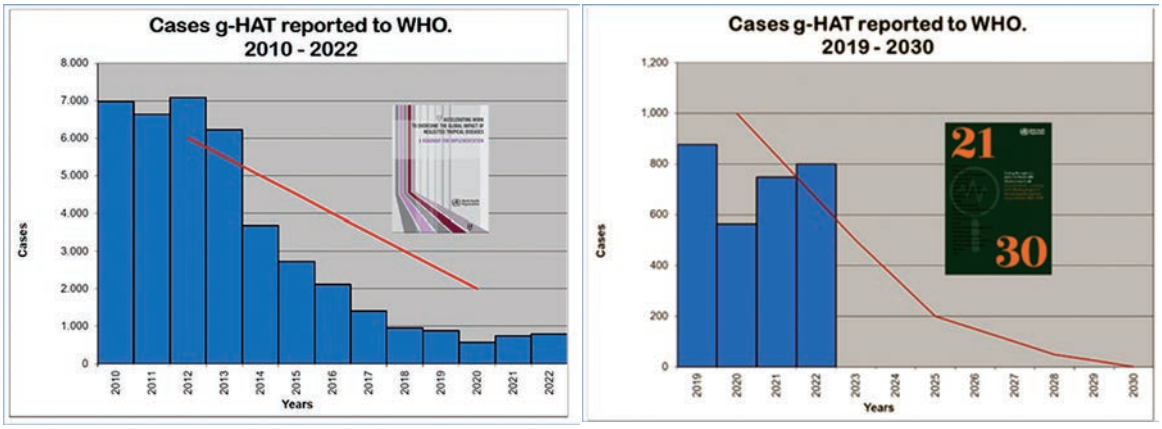
The indicators and the global targets set by 2030 are specified in Table 14.1.

Figure 14.1 illustrates the declining number of HAT cases since 2000, together with the benchmark that was set for elimination as a public health problem and for elimination as interruption of transmission. The case numbers of 2022 were slightly higher than the set benchmark. Even if the future number of cases is low, it must be considered that it will take huge efforts to find the last cases.

**Table 14.1.** WHO indicators and 2030 global targets for g-HAT and r-HAT

| Indicator | Global target |
|---|---|
| **Gambiense human African trypanosomiasis (g-HAT)** | |
| Number of g-HAT cases reported | 0 |
| Number of countries verified for interruption of transmission | 15 (62%) |
| **Rhodesiense human African trypanosomiasis (r-HAT)** | |
| Number of countries validated for elimination as a public health problem (defined as < 1 case/10 000 people/ year, in each health district of the country averaged over the previous 5-year period) | 8 (61%) |
| Areas with ≥ 1 case/10 000 people per year, average of 5 years | 0 |

**Figure 14.1.** Numbers of cases reported in 2000–2020 (blue bars) and benchmark (red line) set for elimination of HAT as a public health problem (2012–2020, left) and for elimination of HAT as interruption of transmission (2021–2030, right)




The national indicators for claiming verification of g-HAT elimination of transmission are:

- zero human cases infected with *T. b. gambiense* for at least 5 years in all health districts of the country; and
- adequate surveillance.

Table 14.2 categorizes the eligibility of the g-HAT endemic countries – according to the national indicator (zero g-HAT cases for at least 5 years) and control/surveillance activities – to request the verification of the interruption of transmission. By 2023, four countries are eligible to request verification (in white). A template for a national verification dossier for g-HAT is being developed and countries will be supported to prepare the dossier.

The main actors of the g-HAT elimination strategies are the NSSCPs, in cooperation with WHO, research institutions, public and private donors, and implementing partners. The elimination strategies include four pillars: active case detection, passive case detection, case management and vector control (Figure 14.2).

**Table 14.2.** Situation of the g-HAT endemic countries according to the criteria for claiming the verification of elimination of transmission, 2022

| | Epidemiological status (national indicator for elimination of transmission) |
|---|---|
| **Two criteria** | Zero incidence of human cases infected by *T. b. gambiense* for a period of at least 5 years |

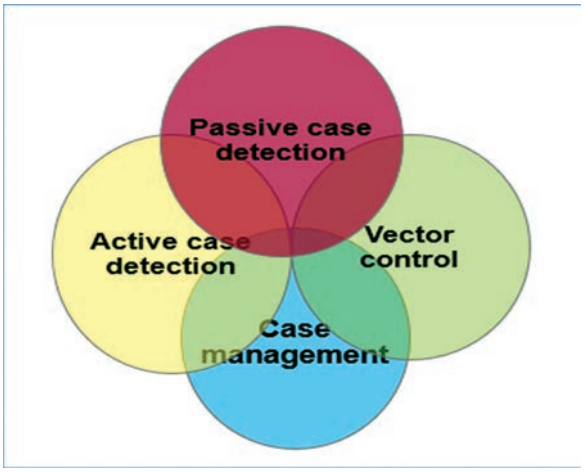
| Control and surveillance activities | Yes | No |
|---|---|---|
| **Appropriate** | Benin, Burkina Faso, Ghana, Togo | Angola, Cameroon, Chad, Côte d'Ivoire, Equatorial Guinea, Guinea, Uganda |
| **Insufficient** | Liberia, Mali, Niger, Nigeria, Senegal, | Central African Republic, Congo, Democratic Republic of the Congo, Gabon, South Sudan |
| **Absent** | Gambia, Guinea Bissau, Sierra Leone | |

Eligible to request verification

Need reinforcement of surveillance before requesting verification

Non-eligible to request verification

**Figure 14.2.** Elimination strategies for HAT




In each pillar, there are some requirements to facilitate them:

- In case detection
  - Simple screening test
  - Sensitive and specific diagnostic tests:
    - If a very safe and simple-use medicine is available, simpler and more sensitive but less specific tests could be used for therapeutic decision (treating serosuspects)
    - Reliable remote tests to identify cases including the capacities for performing the tests
    - Simple methods to refer the samples at low cost (DBS?, microplates?, kits?), without cold chain
    - Reference laboratories able to perform the remote tests
  - High-throughput tests for analysing important amounts of samples
  - Ensure quality of diagnosis

- In passive case detection
  - Integrated in primary health care (PHC), hence requiring a reinforced PHC system with better access
  - Well selected sentinel sites
  - Complemented by reactive screening/reactive vector control?
- In active case detection
  - Well targeted/reactive screening
  - Adapted to situation: lighter teams (e.g. mini mobile teams), door-to-door
  - Screening in historical grey areas
  - Population surveys to assess the situation (elimination): high throughput tests
  - Improve community participation
- In case management
  - Simpler and integrated in PHC
  - If safe and simple medicine, progressively expanding treatment beyond confirmed cases, targeting other possible reservoirs (treating serosuspects)
- In vector control and interventions on animal reservoirs
  - vector control targeted in the transmission sites
  - vector control adapted to the different local conditions
  - affordable methods
  - pool of trained staff
  - community involvement
  - association of vector control with other tools
  - One Health approach, treating animals or protecting them (e.g. net impregnated fences)

A successful elimination strategy requires a combination of factors:

- current interventions progressively **integrated into the health system** to ensure sustainability;
- HAT control and surveillance activities integrated into general health services, while maintaining a vertical approach for planning, monitoring and technical advice (and possibly centralized mobile teams) to strengthen:
  - peripheral health systems (training staff, providing resources and improving access); and
  - reference laboratories;
- research that provides appropriate means for integration, namely:
  - simple diagnostic, treatment and vector control tools that can be used by non-specialized health workers and be adapted to low prevalence and elimination settings;
  - reliable remote testing for case confirmation to monitor elimination and post-elimination surveillance (e.g. high-throughput test, remote test with simple specimen transportation); and
  - expanded use of treatment integrated into PHC and based on lower specificity diagnostics once safer and simpler treatments (e.g. acoziborole) become available;
- access to treatment guaranteed by donors, with access to screening and diagnostic tools ensured for the population at risk;
- interventions adapted to local specificities and different epidemiological settings (low and very low prevalence);
- resilience and adaptation built for unexpected events (e.g. social instability, unrest or epidemics);

- support for research to clarify the epidemiological role of human carriers and animal reservoirs in sustaining transmission and re-emergence of g-HAT;
- interventions against zoonotic and anthroponotic trypanosomiasis integrated (One Health approach);
- ownership and commitment to elimination by national authorities strengthened in endemic countries through advocacy among health authorities, decision-makers and heads of state in a context of declining case numbers, when HAT is no longer a public health problem, with the aim of:
  - demonstrating political will to achieve elimination;
  - providing national resources and funding;
  - involving national authorities in HAT elimination;
- communities involved in the elimination of g-HAT;
- long-term commitment secured from donors; and
- coordination maintained between stakeholders with different agendas to avoid duplication and disruption and synergize efforts towards sustainable elimination.

Table 14.2 categorizes the eligibility of the r-HAT endemic countries to request the **validation** of elimination as a public health problem. By 2022, three countries are eligible to request the validation of elimination, are in the process of doing so or have been already validated. There are endemic countries that are certified for the elimination of the tsetse fly by the African Union. For these countries, a different approach to validation could be taken.

**Table 14.3.** Situation of r-HAT endemic countries according to the criteria for claiming the validation of elimination as a public health problem, 2022

| **Two criteria** | **Epidemiological status (national indicator for elimination as a public health problem)** < 1 case/10 000 people per year, per health district, averaged over the previous 5-year period | |
|---|---|---|
| **Control and surveillance activities** | **True in all districts** | **One or more non-compliant districts** |
| **Adequate** | Kenya, Rwanda, Uganda | Malawi |
| **Insufficient** | Ethiopia, United Republic of Tanzania, Zambia, Zimbabwe | |
| **Absent** | Botswana, Burundi, Eswatini, Namibia, Mozambique | |

Eligible to request validation

Need reinforcement of surveillance before requesting validation

Non-eligible to request validation

The specific **needs for r-HAT** are:

- better tools for diagnosis and treatment;
- integration of interventions against zoonotic and anthroponotic trypanosomiasis (One Health approach), coordination with livestock, wildlife and tourism sectors;
- capacity for rapid response to outbreaks;
- ownership and commitment by national authorities; and
- donor commitment.

# 15. Verification of gambiense HAT elimination

The HAT-e-TAG is the main technical consultative body for WHO concerning HAT elimination. The HAT-e-TAG reviews the indicators to assess HAT elimination and defines the requirements to evidence low or zero transmission and a functioning surveillance system. The group establishes templates for national dossiers of validation/verification and establishes the procedures to review the national dossiers. Furthermore, it follows the post-validation/verification status and defines the revision of the national status. The process is periodically reviewed, according to scientific advances and tools.

The 2020 target (i.e. elimination as a public health problem) needs validation per country. The 2030 target (i.e. zero transmission of g-HAT) needs country verification. For that, the country status is assessed against objective criteria and the achievement is formally recorded. The validation process refers to both g-HAT and r-HAT. The verification process refers only to g-HAT.

For **validation**, a template for **national dossiers** was developed documenting the elimination of HAT as a public health problem. The dossier for g-HAT and r-HAT comprises eight chapters.

1. Description of country and its capabilities
    a. Country health system
    b. General info
2. Historical data and delimitation of endemic areas
    a. Historical foci description
    b. Actual foci description and delineation
3. Description of control and surveillance activities and strategies
    a. Structure, capabilities, resources to combat HAT
    b. Active screening strategy
    c. Passive screening strategy description
    d. Reactive screening
    e. SWOT
4. HAT epidemiological data
    a. National post-2000 data
    b. Health district data for the past 5 years. Calculation of national indicator
    c. Neighbouring countries (transboundary) situation
    d. HAT control
5. Vector control
    a. Control strategy
    b. Results
6. Animal trypanosomosis
    a. AAT data
    b. Structure, capabilities, resources to combat AAT

7. Post-validation surveillance plan

   This chapter is a key chapter that requires a 5-year plan explaining activities to maintain elimination and to advance towards zero transmission (sentinel sites, vector control, other strategies, resources, partners).

8. References & annexes

Benin, Côte d'Ivoire, Equatorial Guinea, Ghana, Togo and Uganda (all for g-HAT) and Rwanda (for r-HAT) went through this process and were validated for the elimination of HAT as a public health problem. Chad has already submitted its dossier for validation.

The new road map sets the 2030 **global targets** of zero reported cases and **verification** of interruption of transmission in 15 countries. The global targets were adapted to **national-level targets**, defined as:

- zero incidence of human cases infected by *T. b. gambiense* for a period of at least 5 years; and
- evidence of appropriate surveillance.

Regarding zero incidence, a **case of g-HAT** was **defined** as any human individual with **epidemiological link** to *T. b. gambiense* infection, in whom **trypanosomes** are detected by **microscopy** in any body fluid or tissue. Despite microscopic observation of trypanosomes in an individual, the zero cases definition can still be fulfilled in **particular conditions** (to be well documented):

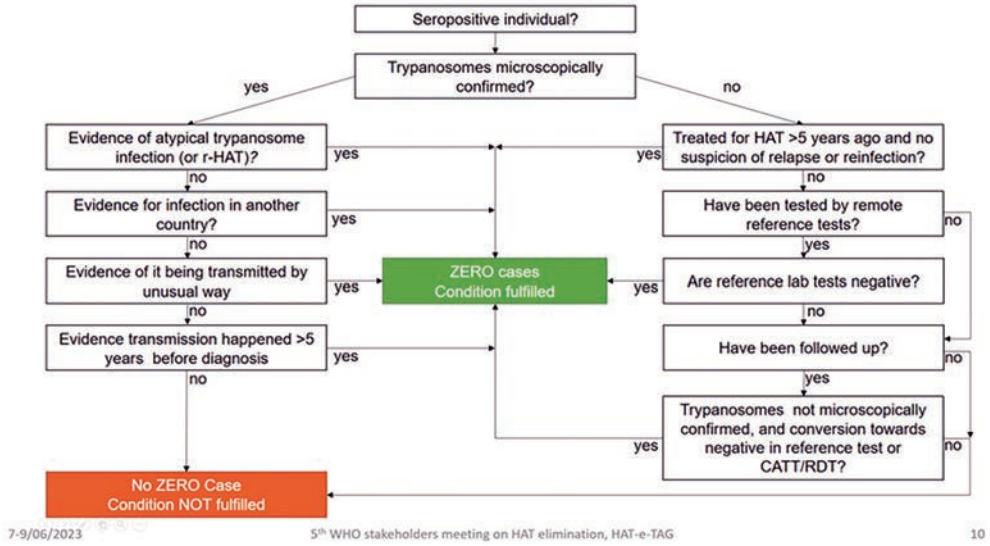
- infection by a species or subspecies other than *T. b. gambiense* (molecular characterization);
- *T. b. gambiense* infection acquired in a different country;
- *T. b. gambiense* transmitted by routes other than vectorial, such as laboratory accident; and
- *T. b. gambiense* infection acquired > 5 years before diagnosis in the period covered by the dossier.

The situation of serological suspects that remain unconfirmed parasitologically has to be considered. In low prevalence settings, the predictive positive value of diagnostic tests is low and further laboratory investigations are required. If these tests are negative, the suspicion of HAT can be dismissed and the zero-case condition is met. If the tests are positive or not performed, the suspicion of HAT is maintained and follow-up is needed. If follow-up tests are negative, suspicion can be dropped and the zero-case condition is met. If follow-up tests are not performed or remain positive or confirm the case microscopically, the zero-case condition is not met.

The possible application of widened treatment in the near future will require sampling - preferably before treatment - for the same tests, so that potential cases can be confirmed or excluded. Serological tests, such as TL, also remain positive after treatment.

The algorithm for fulfilling the zero case definition is shown in Figure 15.2. Additional laboratory testing and reference laboratories will become increasingly important.

**Figure 15.2.** Algorithm for fulfilling the zero case definition




The "appropriate surveillance" indicator refers to the demonstration that surveillance capacity and implementation are adequate. In terms of passive surveillance, this means having fixed health facilities that adequately cover the population at risk of g-HAT and that are regularly monitored to assess and support their performance. In terms of active surveillance, it means that the teams are sufficient to cover the target villages and population, and that the teams are regularly monitored to assess and support their performance.

In addition, serological or strong clinical suspects must be investigated to confirm or discard g-HAT. Specimens from non-parasitologically confirmed cases must be collected and sent to a reference laboratory. All parasitologically unconfirmed suspects should be followed up appropriately. The diagnosis of a g-HAT case must lead to reactive screening of the relevant population.

Additional, non-mandatory indicators of the dossier relate to the presence of tsetse flies, vector control and non-human reservoir testing.

Indicators of tsetse presence and vector control include:

- tsetse presence/absence and geographical distribution;
- geographical and temporal coverage of vector control activities;
- intensity of vector control activities;
- tsetse densities following vector control; and
- number of animals treated for AAT in a g-HAT transmission area.

Indicators of *T. b. gambiense* in tsetse and non-human vertebrates include:

- number of tsetse flies/animals (by species) tested for *T. b. gambiense* infection, proportion positive, geographical origin, methods used; and
- geographical and temporal coverage of potential *T. b. gambiense* transmission area.

Based on these criteria, the template for the **national verification dossier for g-HAT h**as been established. The verification dossier consists of 2 parts:

- Part 1: Data required for validation of the elimination of g-HAT as a public health problem;
- Part 2: Data required for verification of the elimination of transmission.

There are 2 categories of countries, for which the requirements for part 1 and 2 differ: countries that have already been validated, and countries that have not yet been validated but can go straight to verification. Post-verification surveillance is of particular importance.

- In countries claiming for verification with previous validation:
  - Part 1: Replace by validation dossier accompanied by the report of the assessment team
  - Part 2: Activities implemented after validation, and for at least 5 years
    - absence of parasitologically confirmed g-HAT in past 5 years
    - functional epidemiological surveillance system
    - vector control and animal reservoir surveillance
    - post-verification surveillance
- In countries claiming directly for verification, without previous validation
  - Part 1: Present full part 1, with detailed data for the past 5 years in chapters 3–6, replace certain chapters of part 2 (guidelines part 2)
  - Part 2: Present the reasons behind claiming the elimination of transmission
    - chapters on surveillance (active, passive, exceptions), vector control and animal reservoir surveillance to be included in part 1, chapters 3–6.
    - post-verification surveillance

Part 1 of the national verification dossier largely corresponds to the validation dossier. Countries that have been validated previously can replace Part 1 with the previous validation dossier together with the report of the assessment team.

The official document with detailed descriptions and criteria is currently being published by WHO. The dossier should be prepared at the level of the Ministry of Health, in collaboration with HAT control staff and other national stakeholders. The dossier should be submitted to the WHO country office. Requests for clarification should be answered and visits by the review team should be accepted. Procedures are similar to those for validation. Endemic countries are advised to request technical assistance from the WHO secretariat before preparing their national verification/validation dossier.

# 16. Conclusions

1. NSSCPs have continued to make great progress towards the elimination of the disease. Stakeholders expressed their commitment to continue supporting and working towards this goal. Over the past 5 years, fewer than 1000 cases of HAT per year have been reported, which is a historic achievement. The area at risk has been substantially reduced (10-fold since 2004). The elimination of HAT as a public health problem at the global level has been achieved. Some 41 million people remain at risk of HAT but only 1.5 million of these are at a moderate or high risk, the others being at lower risk.
2. By 2022, g-HAT elimination as a public health problem has been validated for Benin, Côte d'Ivoire, Equatorial Guinea, Ghana, Togo and Uganda, and for Rwanda for r-HAT. Chad has submitted its dossier for review, and Burkina Faso, Cameroon, Guinea and Kenya are in the process of preparing their dossier. Countries are encouraged to advance in the validation of elimination; WHO with other partners can support countries in this process, including the development of the dossiers.
3. With the low number of cases, it is crucial to maintain partners' commitment to HAT elimination, to promote ownership of this goal by national health authorities and to maintain coordination among partners. The COVID-19 pandemic has had an impact on the process of HAT elimination, but strategies were adapted to limit this impact. Increasing numbers of cases in some countries and a decrease in the number of people who were actively screened illustrate the need for intensified control efforts.
4. The number of reported r-HAT cases remains low. Nevertheless, under-detection is a concern and surveillance must be strengthened. In 2019–2020, there was an outbreak in Malawi and nearby Zambia. In 2022, r-HAT (6 cases) re-emerged in Ethiopia after 31 years without any reported case. These outbreaks seem to be influenced by climate change and other factors to be elucidated. In Ethiopia, specific knowledge of the disease has been lost. The re-emergence of r-HAT is a constant threat as it is a zoonotic disease with epidemic potential. The decline in the use of microscopy in many diagnostic settings (e.g. malaria testing) in endemic countries presents a particular problem, especially in the case of r-HAT for which no serological test exists.
5. The DTAG subgroup for HAT has identified four priorities for improved diagnosis and developed use cases and four TPPs: (i) a test for r-HAT usable in peripheral health facilities; (ii) a diagnostic tool to identify individuals with suspected but microscopically unconfirmed g-HAT infection, to receive widened treatment; (iii) an individual test to assess g-HAT in low prevalence settings; and (iv) a high throughput g-HAT test for verification of elimination.
6. At present, one first-generation (native antigen) and one second-generation (recombinant antigen) serological RDT is commercially available. In addition, two prototype second-generation HAT RDTs are under development with improvements in diagnostic performance being desirable. Following several evaluation studies, questions remain about the performance of the currently available HAT RDTs, particularly with respect to specificity, which tends to be lower in active screening than in passive screening. Given its higher specificity, CATT might be preferred for active screening by large mobile teams. RDTs are more suited for passive screening, although they might be applied in active screening situations requiring minimal equipment.
7. Studies are ongoing to further develop an iELISA as a highly specific alternative for trypanolysis. Molecular diagnostic tests as alternatives for microscopy are also in the design and evaluation phase. The diagnostic performance of these new laboratory tests requires further evaluation.
8. A total of 12 countries have officially adopted fexinidazole for g-HAT treatment. Some 270 treatment sites have been identified to administer fexinidazole and their staff trained. From 2018 to 2022, 579 patients were treated with fexinidazole in non-trial settings. The progressive adoption and use of fexinidazole over other therapies are progressing well; in 2022, about half of all patients were treated with fexinidazole.

According to pharmacovigilance data collected by WHO, safety appears in line with that observed in clinical trials. No relapses have been recorded so far.

9. The DNDi-Fex-07-HAT trial is showing impressive results against r-HAT and its future availability will substantially improve the treatment of r-HAT. Some 45 patients (35 in stage 2, of whom 34 were evaluable) were treated with fexinidazole at two clinical sites in Malawi and in Uganda, with a follow-up of 12 months. One relapse was detected and there were no treatment-related deaths at the end of the hospitalization period. Study patients already showed a relevant clinical improvement at day 5 after treatment, which contrasts with the experience with melarsoprol. The dossier, including the initial clinical study report, was submitted to the EMA on 30 May 2023. The CHMP opinion is expected in December 2023 (best-case scenario). Local approval in DRC, which has already approved the treatment for g-HAT, is targeted for Q1 2024. WHO plans a review of the therapeutic guidelines in (Q1/Q2 2024).
10. The development of new treatments for g-HAT is proceeding according to schedule, in spite of unanticipated difficulties with acoziborole formulation. The results of the pivotal trial with single-dose acoziborole (DNDi-OXA-02-HAT) showed a high efficacy and no major safety concern. The latest timeline of acoziborole development foresees the EMA submission under article 58 in Q3 2025 and the first country registration in DRC in Q3 2026 (best-case scenario). Other than significantly improving the treatment of patients, the wider use of acoziborole in g-HAT seropositive individuals who have not been confirmed parasitologically is currently under investigation (DNDi-OXA-04-HAT). The related STROGHAT study (Stop Transmission of g-HAT) will evaluate the possibility of an acoziborole-based screen-and-treat strategy to achieve elimination of transmission.
11. Gaps in paediatric HAT treatment need to be addressed. The ACOZI-KIDS Project (DNDi-OXA-05-HAT) started in 2022 to develop a paediatric formulation of acoziborole for children aged 1–14 years. The GAP-f, a network hosted by WHO, provides an umbrella for all partners to tackle those gaps.
12. Sociocultural dimensions and community perspectives on HAT elimination are becoming increasingly important, with a need to retain community knowledge of the disease and engagement in the programme. A working group dedicated to these issues has been established as part of the programme.
13. Vector control, in combination with medical and other interventions, contributes to HAT elimination. Modifications in vector control approaches will be needed in the post-elimination phase. Work is ongoing to develop harmonized metrics to estimate its coverage in g-HAT areas for improved monitoring and reporting at the continental level. Efforts are needed to enhance synergies in the control of the human and animal forms of the disease in a One Health framework, including technical tools (e.g. vector control, trypanocides) and at the level of strategic planning and stakeholder collaboration.
14. Substantial work is needed to sustain the current momentum against the disease(s) and advance towards the 2030 targets of verified interruption of transmission of g-HAT and elimination of r-HAT as a public health problem. Current interventions need to be progressively integrated into the national universal health care package and health systems and be adapted to the different epidemiological situations to ensure sustainability, with research required to define these approaches.
15. The WHO Technical Advisory Group on HAT elimination has defined the criteria for verification at the national level as (i) zero incidence of human cases infected by *T. b. gambiense* for a period of at least 5 years and (ii) evidence from appropriate surveillance. Based on these two indicators, a template for the national verification dossier for g-HAT has been developed, which will be published soon by WHO. Countries meeting these criteria can request verification directly or after having been validated previously. Countries interested in requesting validation or verification are invited to contact the WHO secretariat for guidance in developing the dossiers. The process for validation as a public health problem remains unchanged.
16. With the decreasing prevalence of HAT, and in view of supporting the validation and verification of HAT elimination, reliable laboratory tests and reference laboratories become increasingly important. Sufficient support should be guaranteed to maintain the functioning of reference laboratories and avoid the loss of expertise.

Dr Daniel Argaw Dagne closed the meeting by summarizing its essential aspects. He mentioned and thanked each of the meeting organizers. He also thanked the NSSCPs and all stakeholders for their joint efforts.

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# Annex 1. Agenda

| Day 1: 7 June 2023 | | |
|---|---|---|
| 09:00–09:30 | **Registration. Organizational issues. Welcome café.** | |
| 09:30–10:00 | **Introduction and welcome. Opening**<br>Presentation of the meeting and participants. Addresses from WHO officials. | J. Salomon, ADG UCN (WHO)<br>A. Kadima Ebeja, CDS AFRO (WHO)<br>D. Dagne, Coordinator PCT NTD (WHO) |
| **1st Block: HAT epidemiological status 2022** | | |
| 10:00–11:00 | **Situation report of gambiense HAT (g-HAT)**<br>Update on the epidemiological situation of g-HAT per subregion and country and remarks from the perspective of national programmes in endemic countries<br>⊙ West Africa (Benin, Burkina Faso, Côte d'Ivoire, Guinea, Ghana, Liberia, Mali, Nigeria, Senegal, Togo)<br>⊙ Central Africa (Angola, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, South Sudan, Uganda).<br>⊙ Democratic Republic of the Congo | National Sleeping Sickness Control Programmes (NSSCP) focal points |
| 11:00–11:30 | **Situation report of rhodesiense HAT (r-HAT)**<br>Update on the epidemiological situation of r-HAT per country and remarks from the perspective of national programs in endemic countries<br>⊙ Ethiopia, Kenya, Malawi, Rwanda, Uganda, United Republic of Tanzania, Zambia, Zimbabwe | National Sleeping Sickness Control Programs (NSSCP) focal points |
| 11:30–12:00 | **Report on global situation of HAT**<br>Update on HAT transmission and status of HAT elimination 2023<br>**Status of validation of elimination at country level** | J.R. Franco / A. Kadima Ebeja (WHO) |
| 12:00–12:30 | Q & A. Discussion | |
| 12:30–14:00 | Break | |
| 14:00–14:20 | **WHO network for HAT elimination**<br>Structure and value as tool for HAT elimination coordination: general report of activities | G. Priotto (WHO) |
| **2nd Block: Diagnosis, state of the art** | | |
| 14:20–14:35 | **NTD-DTAG (Diagnostic Technical Advisory Group (DTAG) for Neglected Tropical Diseases)**<br>Description of general structure, objectives and rationale. | D. Dagne (WHO) |
| 14:35–15:10 | **Report from WHO HAT-DTAG (Diagnostic Technical Advisory subGroup for HAT): current diagnostic tools and TPPs** | V. Lejon (IRD) & E. Matovu (U. Makerere), chairs HAT-DTAG |
| 15:10–15:30 | **Advances and perspectives: rapid diagnostic tests** | S. Bieler (FIND) |
| 15:30–15:50 | **Advances and perspectives: ELISA, iELISA, molecular tests** | P. Büscher (ITM) |
| 15:50–16:15 | Q & A. Discussion | |

| | | |
|---|---|---|
| **3rd Block: Sociocultural dimensions of HAT elimination** | | |
| 16:15–16:35 | **Report of the WHO network for HAT elimination working group "Sociocultural dimensions and community perspectives on HAT elimination"** | P. Havik (IHMT) (chair of the group) |
| 16:35–16:50 | Q & A. Discussion | |
| 16:50–17:00 | Conclusions day 1 | |
| **Day 2: 8 June 2023** | | |
| **4th Block: Treatment, state of the art** | | |
| 09:30–09:50 | **Report of the WHO network for HAT elimination working group: "Integration of new treatment tools into national and global policies"** | J. Seixas (IHMT), chair of the group |
| 09:50–10:10 | **Current situation of HAT treatment**<br>**Implementation and pharmacovigilance of fexinidazole** | G. Priotto (WHO) |
| 10:10–10:30 | **New developments in treatment**<br>⊙ Fexinidazole in r-HAT<br>⊙ Acoziborole for r-HAT<br>⊙ Status of development of acoziborole | S. Hugonnet (DNDi) |
| 10:30–10:50 | **Paediatric gaps in HAT treatment** | M. Penazzato, Global Accelerator for Paediatric Formulations, SCI/ RFH (WHO) |
| 10:50–11:10 | Q & A. Discussion | |
| **5th Block: Vector control** | | |
| 11:10–11:30 | **Report of the WHO network for HAT elimination working group "Vector control in HAT elimination"** | G. Cecchi (FAO) |
| 11:30–12:00 | **Current vector control interventions in HAT** | B. Bucheton (IRD) / I. Tirados (LSTMH) |
| 12:00–12:30 | Q & A. Discussion | |
| 12:30–14:00 | Break | |
| **6th Block: Open floor to partners:** | | |
| 14:00–15:00 | **Open floor for statements: donors, public and private partners**<br>⊙ Sanofi<br>⊙ Bayer<br>⊙ BMGF<br>⊙ Belgium Government<br>⊙ SD/Abbott<br>⊙ Coris<br>⊙ Others | |

| | | |
|---|---|---|
| 15:00–17:00 | **Open floor for statements: WHO Collaborating centres**<br>⊙ ITM<br>⊙ IRD<br>⊙ Institut Pasteur/Biobank<br>⊙ INRB<br>**Institutions and academia**<br>⊙ ITM<br>⊙ IHMT<br>⊙ CIRDES<br>⊙ IPR<br>⊙ DNDi<br>⊙ FIND<br>⊙ LSTM<br>⊙ Institut Pasteur<br>⊙ National Institute for Communicable Diseases<br>⊙ Swiss Tropical & Public Health Institute<br>⊙ University of Warwick<br>⊙ University of Glasgow<br>⊙ University of Makerere<br>**International organizations**<br>⊙ PAAT / FAO<br>⊙ IAEA<br>**Nongovernmental organizations**<br>⊙ MSF | |
| **Day 3: 9 June 2023** | | |
| **7th Block: Targeting elimination as interruption of transmission in 2030** | | |
| 09:30–10:00 | **2030 road map**<br>Interruption of g-HAT transmission: indicators and targets/ strategies | J.R. Franco (WHO) |
| 10:00–10:30 | **HAT-e-TAG**<br>Verification of elimination | V. Lejon (IRD), chair HAT-e-TAG |
| 10:30–11:00 | Q & A. Discussion | |
| 11:00–12:00 | **Conclusions and outcomes**<br>Consensus on the main conclusions of the meeting and points to be followed up. Way forward | |
| 12:00–12:30 | **Closing** | |

# Annex 2. List of participants

| Institution | Name |
|---|---|
| **National Sleeping Sickness Control Programmes** | |
| Ministério da Saúde, Angola | Constantina Pereira Furtado Machado |
| | Luis Baião Peliganga |
| Ministère de la Santé, Benin | Ndeye Marie Bassabi |
| Ministère de la Santé et de l'Hygiène Publique, Burkina Faso | Clarisse Bougouma |
| Ministry of Health, Cameroon | Alphonse Acho |
| Ministère de la Santé et de la Population, Central African Republic | Pierre-Marie Douzima |
| Ministère de la Santé Publique et de la Solidarité Nationale, Chad | Mahamat Saleh Oumar Adoum |
| | Justin Darnas |
| Ministère de la Santé et de la Population, Congo | Bienvenue Rolland Ossibi Ibara |
| Ministère de la Santé Publique, Democratic Republic of the Congo | Eric Mwamba Miaka |
| Ministère de la Santé, de l'Hygiène Publique et de la Couverture Maladie Universelle, Côte d'Ivoire | Lingué Kouakou |
| | Hugues Kouadio Aboh* |
| Ministerio de Sanidad y Bienestar Social, Equatorial Guinea | Pedro Ndongo Asumu |
| | Eustaquio Nguema Ndong* |
| Ministry of Health, Ethiopia | Tesfahun Bishaw* |
| Ministère de la Santé et des Affaires sociales, Gabon | Julienne Atsame |
| Ghana Health Service, Disease Control and Prevention Department, Ghana | Thomas Abugbilla Azurago |
| Ministère de la Santé, Guinea | Mamadou Camara |
| | Moise Kagbadouno |
| Ministry of Public Health, Kenya | Roselyne Kasati |
| Ministry of Health and Social Welfare, Liberia | Alexlyn Monluo |
| Ministry of Health, Malawi | Marshal Lemerani |
| Ministère de la Santé, Mali | Mahamadou Doumbia |
| Federal Ministry of Health, Nigeria | Gedeon Uduak Ntuen |
| Rwanda Biomedical Centre, Ministry of Health, Rwanda | Ladislas Nshimiyimana |
| | Jean Bosco Mbonigaba* |
| Ministère de la Santé et de l'Action sociale, Senegal | Ndeye Mbacke Kane |
| Ministry of Health, South Sudan | Lexson Mabrouk Manibe |
| | Edward Losio |
| Ministry of Health, Community Development, Gender, Elderly and Children, United Republic of Tanzania | Jubilate Minia |
| National Institute for Medical Research, United Republic of Tanzania | Lucas Matemba |
| Ministère de la Santé, de l'Hygiène Publique et de l'Accès Universel aux Soins, Togo | Piham Gnossike |
| Ministry of Health, Uganda | Alfred Mubangizi |
| | Charles Wamboga |
| Ministry of Health, Zambia | Victor Mwanakasale* |
| Ministry of Health and Child Care, Zimbabwe | Isaac Phiri* |

| Institution | Name |
|---|---|
| **WHO collaborating centres** | |
| Institut de Recherche pour le Développement, Guinea | Jean Mathieu Bart |
| Institut de Recherche pour le Développement, France | Bruno Bucheton* |
| | Fabrice Courtin* |
| | Vincent Jamonneau* |
| | Veerle Lejon |
| | Philippe Solano* |
| Institut National de Recherche Biomedicale, Democratic Republic of the Congo | Dieudonné Mumba Ngoyi |
| Institut Pasteur-Paris, France | Fay Betsou* |
| Institut Pasteur-Paris/ICAReB Platform, France | Blanca-Liliana Perlaza |
| | Marie-Noelle Ungeheuer* |
| Institute of Tropical Medicine Antwerp, Belgium | Jan Van Den Abbeele* |
| | Nick van Reet* |
| **Academia** | |
| Coordinating Office for Control of Trypanosomiasis in Uganda, Uganda | Albert Mugenyi* |
| | Charles Waiswa* |
| | RobertWangoola* |
| Institut Pasteur-Paris, France | Brice Rotureau |
| Institut Pierre Richet, Côte d'Ivoire | Dramane Kaba* |
| Instituto de Higiene e Medicina Tropical, Portugal | Philip Havik* |
| | Jorge Seixas |
| Institute of Tropical Medicine Antwerp, Belgium | Philippe Büscher |
| | Epco Hasker |
| | Raquel Inocencio da Luz |
| | Nelena Nicco* |
| | Paul Verlé |
| Liverpool School of Tropical Medicine, United Kingdom of Great Britain and Northern Ireland | Sophie Dunkley |
| | Andrew Hope* |
| | Inaki Tirados |
| | Steve Torr |
| Liverpool School of Tropical Medicine-STRESS, United Kingdom of Great Britain and Northern Ireland | Chris Jones |
| | Karina Mondragon-Shem |
| Makerere University, College of Veterinary Medicine, Uganda | Enock Matovu |
| National Institute for Communicable Diseases, South Africa | Lucille Hellen Blumberg |
| Centre de Recherche Agronomique et de Coopération Internationale pour le Développement, Côte d'Ivoire | Alain Boulange* |
| Centre for Research in Infectious Diseases, Cameroon | Tito Trésor Melachio Tanekou* |
| Centre International de Recherche Développement sur l'Elevage en zone Subhumide, Burkina Faso | Jacques Kabore* |
| Swiss Tropical and Public Health Institute, Switzerland | Marina Antillon |
| | Christian Burri |
| | Nakul Chitnis* |
| | Fabrizio Tediosi* |
| Charité - University Berlin, Germany | Ndreas Lindner |

| Institution | Name |
|---|---|
| University of Geneva, Switzerland | Francois Chappuis* |
| University of Glasgow, United Kingdom of Great Britain and Northern Ireland | Michael Barrett (Chair) |
| | Annette Macleod* |
| University of Kinshasa, Democratic Republic of the Congo | Alain Mpanya* |
| University of Liverpool, United Kingdom of Great Britain and Northern Ireland | Eric Fevre* |
| University of Warwick, United Kingdom of Great Britain and Northern Ireland | Emily Crowley |
| | Ron Crump |
| | Ching-I Huang |
| | Katherine Rock |
| | Samuel Sutherland |
| University of Zambia, Zambia | Boniface Namangala* |
| **Nongovernmental organizations** | |
| Médecins Sans Frontières, Switzerland | Gabriel Alcoba* |
| Médecins Sans Frontières, Spain | Francisco Bartolome* |
| | Laurence Flevaud |
| | Liliana Palacios* |
| Médecins Sans Frontières, France | Julien Potet* |
| Médecins Sans Frontières, Netherlands (Kingdom of the) | Koert Ritmeijer* |
| Médecins Sans Frontières-Logistique, France | Doris Arlt Hilares |
| | Arnault Cheval |
| PATH, Democratic Republic of the Congo | Trad Hatton* |
| **United Nations and multilateral institutions** | |
| Food and Agriculture Organization of the United Nations (FAO) | Giuliano Cecchi |
| | Weining Zhao |
| International Atomic Energy Agency (IAEA) | Chantal Janet de Beer |
| Organisation de Coordination pour la lutte contre les Endémies en Afrique centrale (OCEAC) | Aline Okoko* |
| **Research foundations** | |
| Drugs for Neglected Diseases initiative (DNDi), Democratic Republic of the Congo | Florent Mbo |
| Drugs for Neglected Diseases initiative (DNDi), Switzerland | Laurence Fraisse* |
| | Stephane Hugonnet |
| | Sandra Rembry* |
| | Antoine Tarral |
| | Olaf Valverde Mordt |
| Foundation for Innovative New Diagnostics (FIND), Switzerland | Sylvain Biéler |
| Foundation for Innovative New Diagnostics (FIND), United Kingdom of Great Britain and Northern Ireland | Paul Bessell |
| Foundation for Innovative New Diagnostics (FIND), Kenya | Joseph Ndungu* |
| **Donors and manufacturers** | |
| Abbot/Standard Diagnostics, Republic of Korea | Ji Mijung* |
| Bayer AG, Germany | Ulrich-Dietmar Madeja* |
| Bill & Melinda Gates Foundation, United States of America | Rachel Bronzan |
| | Jordan Tappero* |
| Coris BioConcept, Belgium | Pascal Mertens |

| Institution | Name |
|---|---|
| Cytiva, Sweden | Sophie Stille* |
| Permanent Mission of Belgium, Belgium | Pieter Vermaerke |
| Sanofi, France | Michael Macalush* |
| | Catherine Castin Vuillerme |
| Sanofi/Foundation S, France | Celina Beauchard |
| | Philippe Neau |
| Vestergaard, Switzerland | Allan Mortensen* |
| **World Health Organization (WHO)** | |
| WHO Regional Office for Africa, Democratic Republic of the Congo | Dorothy Achu* |
| | Augustin Kadima Ebeja |
| WHO Country Office Benin | Raoul Saizonou |
| WHO Country Office Cameroon | Ettiene Nnomzo'o |
| WHO Country Office Democratic Republic of the Congo | Renéee Nsamba Ntumbannji |
| WHO Country Office Ethiopia | Nigus Manaye |
| WHO Country Office Gabon | Ghislaine Nkone Asseko |
| WHO Country Office Ghana | Felicia Owusu-Antwi |
| WHO Country Office Mali | Tako Ballo |
| WHO Country Office South Sudan | Jane Pita Hillary Ajo |
| WHO Country Office Togo | Kokou Mawule Davi |
| WHO Country Office United Republic of Tanzania | Alphoncina Nanai |
| WHO Country Office Zimbabwe | Anderson Chimusoro |
| WHO headquarters | Jérôme Salomon |
| WHO headquarters | Daniel Argaw Dagne |
| | José Ramón Franco Minguell |
| | Tiziana Masini* |
| | Martina Penazzato |
| | Rosa Maria Perea Ibáñez |
| | Gerardo Priotto |
| | Dieudonné Sankara |
| WHO consultants | Kossi Badziklou |
| | Pere Pérez Simarro |

* Online participant

World Health Organization