Report of a WHO meeting on elimination of African trypanosomiasis (Trypanosoma brucei gambiense)

Geneva, 3–5 December 2012

« Le but n'est pas toujours placé pour être atteint mais pour servir de point de mire »

"The goal is not always meant to be reached, but to serve as a mark for our aim."

Joseph Joubert, 1754-1824





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Introduction

Joint efforts by the World Health Organization (WHO) and partners since 2000 have led to a decline in the number of new cases of human African trypanosomiasis (HAT) being reported to WHO annually. This process has been associated with improvements in the epidemiological knowledge of the disease.

In May 2007, representatives of countries in which HAT is endemic gathered in Geneva, Switzerland, to consider elimination of the disease as a public-health problem.³ In 2011, WHO's Strategic and Technical Advisory Group (STAG) for neglected tropical diseases (NTDs) deemed elimination to be technically feasible and included HAT in the WHO Roadmap on NTDs with a target date for elimination of 2020.⁴

In January 2012, a number of partners from the public and private spheres came together in London, United Kingdom, to launch the largest coordinated effort against NTDs. The ensuing London Declaration on Neglected Tropical Diseases⁵ represents a new, coordinated approach for accelerating progress towards eradication, elimination or control of 10 NTDs by 2020. Partners at the meeting pledged to work together to improve the lives of the 1.4 billion people worldwide affected by NTDs – most of whom are among the world's poorest people – and to enhance the supply of existing medicines, stimulate collaborative research for new treatments and increase the funding needed for control or elimination activities. During the meeting, HAT was targeted for elimination alongside five other diseases, and the WHO Roadmap was endorsed by the participants, officially launching the elimination and control processes.

On 3–5 December 2012, WHO convened a meeting of national sleeping sickness control programmes (NSSCPs), experts from WHO collaborating centres and a member of the STAG at its headquarters in Geneva to discuss strategies, tools and criteria for the process of eliminating HAT (*Trypanosoma brucei gambiense*).

There are two forms of HAT: Gambiense trypanosomiasis caused by infection with the parasite *Trypanosoma brucei gambiense* (prevalent in the west and central part of Africa, south of the Sahara); and Rhodesiense trypanosomiasis caused by infection with *Trypanosoma brucei rhodesiense* (found in the eastern part of the continent). Both forms of the disease have distinct epidemiological characteristics that require different approaches for surveillance and control. Today, Gambiense trypanosomiasis accounts for some 98% of all reported cases of HAT; thus immediate attention must be given to this form of the disease.

Rhodesiense trypanosomiasis has been shown to be a zoonotic disease with both domestic and wild hosts, which complicates control activities and the sustainability of zero cases in humans. Approaches to elimination must therefore be adapted to accommodate zoonotic transmission. Vector control will undoubtedly play a substantially more important role in achieving the elimination objective in Rhodesiense trypanosomiasis than in Gambiense HAT.

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¹ Simarro PP et al. The Human African Trypanosomiasis Control and Surveillance Programme of the World Health Organization 2000–2009: the way forward. *PLoS Neglected Tropical Diseases*, 2011, 5:e1007.

² Simarro PP et al. The Atlas of human African trypanosomiasis: a contribution to global mapping of neglected tropical diseases. *International Journal of Health Geographics*, 2010, 9:57.

³ Report of a WHO informal consultation on sustainable control of human African Trypanosomiasis. Geneva, 1–3 May 2007. Geneva, World Health Organization, 2007 (WHO/CDS/NTD/IDM/2007.6; also available at http://whqlibdoc.who.int/hq/2007/WHO_CDS_NTD_IDM_2007.6_eng.pdf; accessed 28 February 2013).

⁴ Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation. Geneva, World Health Organization, 2012 (WHO/HTM/NTD/2012.1; also available at http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf; accessed 28 February 2013).

⁵ The London Declaration on Neglected Tropical Diseases (available at

http://www.unitingtocombatntds.org/downloads/press/london_declaration_on_ntds.pdf; accessed 28 February 2013).

For these reasons, and given the particularities of both forms of the disease, the meeting focused on Gambiense trypanosomiasis. Elimination of Rhodesiense trypanosomiasis will be addressed more precisely at a later stage.

Objectives

The objectives of the meeting were:

- 1. To endorse WHO's elimination objective for Gambiense trypanosomiasis.
- 2. To define the criteria and indicators for elimination.
- 3. To elaborate the strategies and tools for achieving the elimination objective.
- 4. To identify the obstacles to be overcome to achieve elimination.

Opening remarks

Dr Lorenzo Savioli, Director of the WHO Department of Control of Neglected Tropical Diseases, opened the meeting, stressing both the current successes in control and the need for sustainable actions in the field to achieve the recently defined elimination objective.

Dr Jean Jannin, Coordinator of the Innovative and Intensified Disease Management unit in the Department, emphasized the importance of this group of participants, which comprised national control programme directors and coordinators, and of this meeting in defining the approaches and criteria for elimination of Gambiense trypanosomiasis. Success in reducing the number of reported cases is due to national ownership of control programmes and strong partnership between disease-endemic countries, bilateral cooperation agencies, nongovernmental organizations, the private sector and WHO. The forthcoming deliberations would be important in defining the milestones and indicators for reaching elimination by 2020.

Dr Anne C. Moore was elected as Chairperson. Mr Pierre Cattand and Dr Jose Antonio Ruiz Postigo were elected as rapporteurs.

Background of disease elimination

Recommendations of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases on control, elimination and eradication

The WHO STAG for NTDs is the main advisory group to WHO for the control, elimination and eradication of NTDs. It is mandated to advise WHO on overall global policies and strategies, ranging from epidemiology, monitoring, implementation, and developments in research on delivery of interventions and their linkages with other health interventions.

The STAG is composed of 12–20 members who are appointed by the WHO Director-General. Members serve in their personal capacity and represent a broad range of disciplines covering NTD control activities.

During its meeting in Geneva on 24–25 April 2012, the STAG addressed the long debated issue of operational definitions of eradication and elimination, and recommended that the Department of Control of Neglected Tropical Diseases should hereafter use the following definitions:

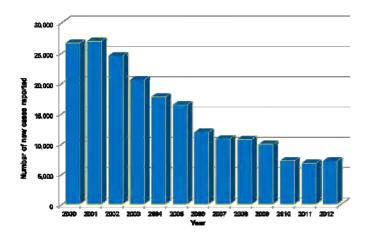
- <u>eradication</u> to mean "permanent reduction to zero of the worldwide incidence of infection caused by a specific pathogen, as a result of deliberate efforts, with no more risk of reintroduction";
- <u>elimination</u> to mean interruption of transmission or "reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, as a result of deliberate efforts; continued actions to prevent re-establishment of transmission may be required";
- To facilitate understanding among different disciplines of certain commonly used words, the STAG defined "control" and "elimination as a public-health problem" as follows:
- <u>control</u> to mean "reduction of disease incidence, prevalence, morbidity, and/or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction".
- <u>elimination as a public-health problem</u> should be used only where necessary for political (rather than scientific) reasons, upon achievement of measurable targets set by Member States in relation to a specific disease.

Why attempt elimination of Gambiense trypanosomiasis?

Elimination of Gambiense trypanosomiasis is deemed feasible since:

- Humans are the main reservoirs of the infection, making the disease epidemiologically vulnerable. However, the role of animal reservoirs, although considered negligible, needs to be elucidated.
- Political will exists, as demonstrated in 2000 by the Pan African Tsetse and Trypanosomiasis Eradication Campaign and promoted by the African Union following the declarations of Head of States and Government of African countries. Resolution WHA56.7 on control of human African trypanosomiasis adopted by the World Health Assembly in 2003 commended Member States "to implement a programme for the elimination of African trypanosomiasis as a public health problem". Elimination was endorsed in 2005 in resolution AFR/RC55/R3 during the 55th WHO Regional Committee for Africa and in the conclusions of the International Scientific Council for Trypanosomiasis Research and Control. WHO included in 2011 the elimination of Gambiense trypanosomiasis in its Roadmap on NTDs. Partners including pharmaceutical companies, donors, endemic countries nongovernmental organizations committed in 2012 to support the Roadmap through the London Declaration and subsequently to sustain, expand and extend programmes to help eliminate, among other NTDs, HAT, by 2020.
- Although better tools are needed to implement more appropriate and sustainable strategies, current control tools and strategies have proven effective in progressively reducing prevalence by 75% since 2000 (Figure 1). The new tools for diagnosis and treatment in the development pipeline have renewed prospects for elimination.
- Current antitrypanosomal medicines are affordable through donations from manufacturers and are available through the WHO distribution system in collaboration with MSF.
- The geographical distribution of the disease is well known and limited.
- There are economic benefits from elimination versus control of a deadly disease.

Figure 1. Number of new cases of Gambiense trypanosomiasis reported to WHO, 2000-2012



Experiences from other WHO elimination programmes

Other active WHO elimination programmes were presented to introduce the adopted approach for managing the elimination process. Two vector-borne disease control programmes were selected: the Global Programme to Eliminate Lymphatic Filariasis and the Onchocerciasis Control Programme.

Global Programme to Eliminate Lymphatic Filariasis

Launched by WHO in 2000, the Global Programme to Eliminate Lymphatic Filariasis aims to eliminate the disease as public-health problem by 2020. The elimination process involves conducting a detailed situation analysis, developing an implementation policy and elaborating a detailed plan followed up by operational actions. This process has culminated in a number of achievements towards the ultimate goal of elimination. Progress is monitored through carefully selected indicators that allow the achievement of various milestones to be assessed. Continuous monitoring and evaluation provides essential information for evaluating achievements, determining new challenges and shaping the next steps for implementation.

Major milestones include:

- the elaboration of guidelines for interrupting transmission and of approaches for postintervention surveillance (after achieving control); and
- the preparation of guidelines and definition of criteria for verifying the absence of transmission.

Monitoring consists of baseline and follow-up surveys in sentinel and spot-check sites; evaluation is based on specific criteria; surveillance consists of active surveys; and verification of the absence of transmission relies on the elaboration of a dossier.

The elimination process involves an initial assessment of the situation (mapping); interventions; surveillance; verification of the absence of transmission; and certification.

Onchocerciasis Control Programme

Onchocerciasis has had a long history of control since the launch of the Onchocerciasis Control Programme in 1974. The disease has been considered for elimination because of the successes achieved through vector control operations and the subsequent mass distribution of ivermectin (since 1988). It is expected that by 2020, 12 out of 17 targeted countries may achieve elimination, thus protecting more than 60 million people.

The main lessons learnt from the Onchocerciasis Control Programme that are applicable to elimination of HAT are the importance of strong partnerships and the elaboration of appropriate surveillance, monitoring and evaluation methods with clear indicators and criteria for elimination.

Epidemiological situation

Historical background

Human African trypanosomiasis has the extraordinary history of having been almost eliminated in the 1960s only some 60 years after the discovery of the infectious agent and its mode of transmission. At that time, the African continent was reorganizing its recently acquired new social status as independent nations. Preoccupied by this new function, focus on the disease lapsed and it subsequently re-appeared in successive epidemics during the next half century. By the end of the 20th century, some 30 000 cases were reported annually. For the past 12 years, WHO has coordinated massive efforts with disease-endemic countries, bilateral cooperation agencies, nongovernmental organizations and the private sector to control this deadly infection, resulting in a sustained decrease in the number of reported cases during the past 10 years. By 2010, the number of infected individuals had reduced to less than 10 000 new cases. In 2012, the African continent accounted for some 7000 new reported cases.

The history and recent success of intensified control operations that led to such an important reduction in the number of cases were reasons to include HAT in WHO's Roadmap on NTDs, together with international commitment and improved epidemiological knowledge.

Disease distribution and population at risk

WHO assembles comprehensive data on surveillance activities undertaken by mobile teams and health-care facilities involved in HAT control in a centralized repository. The data are subsequently harmonized and entered in a database. A Geographic Information System (GIS) combines the epidemiological and geographical data and presents the distribution of the disease on a range of scales, from local to continental. Figure 2 provides an example of mapping the distribution of HAT cases at continental level.

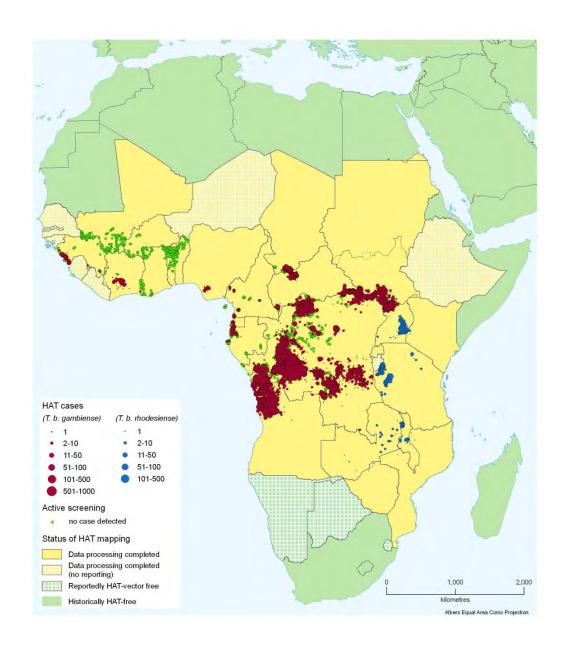
The data repository, the database and the resulting maps constitute the key elements of the "Atlas of HAT.⁶ An initiative of WHO, the HAT Atlas is implemented jointly with the Food and Agriculture Organization of the United Nations (FAO) within the framework of the Programme Against African Trypanosomosis. The Atlas provides substantially improved

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⁶ Cecchi G et al. Towards the Atlas of human African trypanosomiasis. *International Journal of Health Geographics*, 2009, 8:155.

knowledge of the distribution of HAT and serves as a powerful epidemiological tool for planning control activities and monitoring their impact.

Figure 2. Distribution of human African trypanosomiasis (HAT) cases, 2000–2009: Gambiense trypanosomiasis (dots in red), Rhodesiense trypanosomiasis (dots in blue) and formerly endemic areas under active surveillance during 2000–2009 where no cases have been identified (dots in green)



The initial focus of mapping is for the period 2000–2009. At the time of writing, 86.2% of the total number of HAT cases reported during this period (175 381) and 79.3% of the total number of reported locations (30 081) have been mapped. The process is ongoing to refine and complete the database. The next step, currently in progress, is to update the Atlas with data for 2010–2012, and to update it regularly thereafter.

More than ever before, the Atlas has also laid the foundations for accurate estimation and mapping of the population and areas at risk. Continental estimates of people at risk of HAT had last been provided by a WHO Expert Committee held in 1995. At that time, the risk figures were largely based on heterogeneous field data from the different national control programmes, complemented by expert opinion and educated guess. Not only did the Atlas allow updating of these estimates, but also their grounding more firmly in the epidemiological records. By combining the data assembled in the Atlas with spatially-explicit human population layers, up-to-date, evidence-based estimates of population at risk could be generated at a high spatial resolution. Different levels of risk could also be differentiated. Today, it is estimated that in Africa, 69 million people are at risk of contracting HAT, of whom 57 million are at risk of *T. b. gambiense* infection, and 12 million are at risk of *T. b. rhodesiense* infection. Detailed information on the population at risk of Gambiense trypanosomiasis infection is presented in Table 1.

Table 1 Population at risk of Gambiense trypanosomiasis by endemic country, 2000–2009 (no. of people \times 10 3)

Country	Total population* (no. of people × 10 ³)	Population at risk (no. of people × 10 ³)						
	,	High and very high	Moderate	Low and very low	Total at risk	% of total population		
Angola	12 799	740	749	3 278	4 767	37.2		
Cameroon	18 879	-	28	603	631	3.3		
Central African Republic	4 511	69	130	237	435	9.6		
Chad	10 329	109	114	243	465	4.5		
Congo	4 013	113	451	2 002	2 566	63.9		
Côte d'Ivoire	20 617	_	230	2 442	2 672	13.0		
Democratic Republic of the Congo	68 693	3 569	10 767	21 911	36 247	52.8		
Equatorial Guinea	633	2	27	14	43	6.8		
Gabon	1 515	2	21	780	803	53.0		
Guinea	10 058	-	187	2 420	2 606	25.9		
Nigeria	149 229	-	-	2 182	2 183	1.5		
Sierra Leone	5 132	-	1	170	170	3.3		
South Sudan	6 996	416	453	401	1 270	18.2		
Uganda	32 370	142	1 275	707	2 124	6.6		
Other endemic countries**	103 673	_	_	_	_	_		
Total	449 447	5 162	14 431	37 390	56 983	12.7		

^{*} As per Landscan, 2009.

⁷ Simarro PP et al. Risk for human African trypanosomiasis, Central Africa, 2000–2009. *Emerging Infectious Diseases*, 2011, 17:2322–2324.

^{**} Countries at marginal risk: Benin, Burkina Faso, Gambia, Ghana, Guinea-Bissau, Liberia, Mali, Niger, Senegal and Togo.

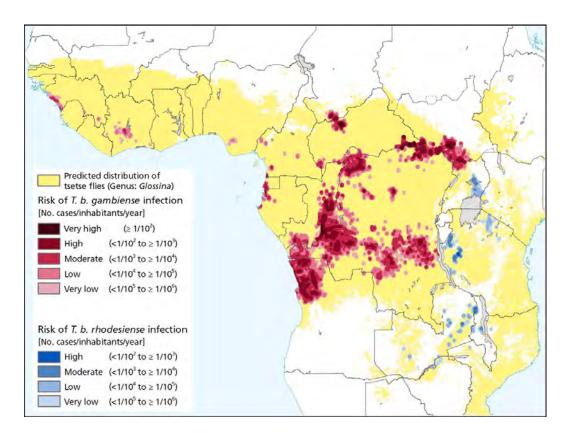
⁸ Simarro PP et al. Estimating and mapping the population at risk of sleeping sickness. *PLoS Neglected Tropical Diseases*, 2012, 6:e1859.

By using data for the period 2000–2009, the level of risk has been categorized according to disease intensity as follows:

- *High and very high risk*. Areas reporting an annual average of at least 1 new case per 10³ people. These areas account for 5 million inhabitants.
- Moderate risk. Areas reporting an annual average of between 1 new case per 10⁴ people and 1 new case per 10³ people. These areas account for 14.5 million inhabitants.
- Low and very low risk. Areas reporting an annual average of between 1 new case per 10⁶ people and 1 new case per 10⁴ people. These areas account for 37.5 million inhabitants.

Figure 3 shows the distribution of the levels of risk for Gambiense trypanosomiasis and Rhodesiense trypanosomiasis.

Figure 3. Distribution of risk levels for human African trypanosomiasis (Gambiense trypanosomiasis shaded red; Rhodesiense trypanosomiasis shaded blue)



Country reports

Representatives of Angola, Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Guinea, Mali, Nigeria, Togo and Uganda presented the disease situation in their countries. The following issues were addressed:

- 1. Epidemiological situation, by providing a map showing foci of Gambiense trypanosomiasis. Foci were drawn in a sketched country outline, indicating the name of each focus and the current epidemiological status.
- 2. Description for each focus of the following epidemiological information for 2007–2011 and partially, when available for 2012:
 - a. focus name.
 - b. number of people screened during active screening,
 - c. number of new cases identified through active surveillance,
 - d. number of new cases identified through passive surveillance, and
 - e. total number of new cases diagnosed.
- 3. Provision of operational information about health structures available in each focus, describing their current role in Gambiense trypanosomiasis control (clinical screening, serological screening, parasitological diagnosis, diagnosis of phase, treatment of first-stage cases, treatment of second-stage cases with melarsoprol, treatment of second-stage cases with eflornithine, and treatment of second-stage cases with nifurtimox–eflornithine combination therapy).
- 4. Description of difficulties encountered by the NSSCP in carrying out surveillance and control activities, including administration, politics (i.e. at ministry level), logistics, finances, human resources, and any disease-associated obstacles and other pertinent information.
- 5. Future plans concerning the NSSCP in relation to its structure, surveillance and control strategies, integration of activities and relations with partners.

Country reports allowed improved knowledge of the operational capacities of health systems for control and surveillance, and of any particular difficulties encountered during implementation. The data provided also permitted updating of the list of foci (Annex 1) and the total number of new cases reported from 2000 to 2012 (Table 2).

Epidemiological settings⁹

The highly focal distribution of Gambiense trypanosomiasis is determined by a complex interplay of ecological and biological factors that are not yet fully understood. The pattern of distribution has been fairly stable over time throughout infested tsetse fly zones.

Foci of Gambiense trypanosomiasis have been defined and classified in three epidemiological scenarios according to the intensity of transmission during the 10-year period 2000–2009:

• Foci with transmission of high and very high intensity. Areas reporting an annual average of at least 1 new case per 1000 inhabitants. These foci are found in Angola, Chad, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Guinea, South Sudan and Uganda. They represent an area of 234 600 km² (Table 3).

⁹ Simarro PP et al. Diversity of human African trypanosomiasis epidemiological settings requires fine-tuning control strategies to facilitate disease elimination. *Research and Reports in Tropical Medicine*, 2013,4:1–6.

Table 2. Total number of new cases of Gambiense trypanosomiasis reported to WHO by endemic country, 2000–2012

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012 [*]
Angola	4 546	4 577	3 621	3 115	2 280	1 727	1 105	648	517	247	218	154	70
Cameroon	27	14	32	33	17	3	15	7	13	24	16	15	7
Central African Republic	988	718	572	539	738	666	460	654	1 194	1 054	395	132	376
Chad	153	138	715	222	483	190	276	97	196	510	232	276	197
Congo	111	894	1005	717	873	398	300	189	182	87	87	61	39
Côte d'Ivoire	188	92	97	68	74	42	29	13	14	8	8	10	9
Democratic Republic of the Congo	16 975	17 322	13 853	11 481	10 369	10 269	8 023	8 162	7 326	7 183	5 629	5 595	5 975
Equatorial Guinea	16	17	32	23	22	17	13	15	11	7	8	1	2
Gabon	45	30	26	26	49	53	31	30	24	14	22	17	9
Ghana	1	0	0	0	0	0	0	0	0	0	0	0	0
Guinea	52	72	132	130	95	94	48	69	90	79	68	57	70
Nigeria	14	14	26	31	10	21	3	0	0	0	2	3	2
South Sudan	1 801	1 919	3 121	3 061	1 742	1 853	789	469	623	373	200	272	317
Uganda (T.b.g. only)	948	310	604	517	378	311	290	120	198	99	100	38	18
TOTAL	25 865	26 117	23 836	19 963	17 130	15 644	11 382	10 473	10 388	9 685	6 985	6 631	7 091
Benin	NO cases	s identifie	ed since 1	1999									
Burkina Faso	NO cases	NO cases identified since 1999											
Mali	NO cases	NO cases identified since 1995											
Togo	NO cases identified since 1995												
Gambia, Guinea- Bissau, Liberia, Niger, Senegal, Sierra Leona	NO cases reported in more than 20 years												

^{*} During the meeting, only provisional figures were presented for 2012; country representatives provided the final figures after the meeting.

- Foci with transmission of moderate intensity. Areas reporting an annual average of at least 1 new case per 10 000 inhabitants but less than 1 new case per 1000 inhabitants. These foci mainly surround the high and very high intensity transmission zones but also include some other foci in Guinea, Côte d'Ivoire and Cameroon. They represent an area of 459 100 km² (Table 3).
- Foci with transmission of low and very low intensity. Areas reporting an annual average of at least 1 new case per 1 000 000 inhabitants but less than 1 new case per 10 000. These areas include foci around moderate intensity transmission zones, plus a few foci in Cameroon, Côte d'Ivoire, Guinea and Nigeria. They represent an area of 687 100 km² (Table 3).

In addition to these three settings, some foci occur where epidemiological knowledge is weak or unknown and action is needed to assess levels of transmission intensity.

• Foci requiring further investigation to assess intensity of transmission (i) Foci with known transmission in which intensity has not been quantified mainly due to difficult topography (in the Democratic Republic of the Congo) or to security

constraints (in some areas of Côte d'Ivoire, Nigeria, the Central African Republic and the Democratic Republic of the Congo).

(ii) Foci where transmission is presumed not to exist due to a lack of reported cases during the past decades in which an assessment of transmission status is needed because there is no effective surveillance (mainly in Gambia, Guinea-Bissau, Liberia, Niger, Senegal and Sierra Leone).

Table 3. Areas at risk of Gambiense trypanosomiasis, by endemic country, 2000–2009 (km² x 10²)

Country	Total land area* (km² × 10²)	Area at risk (km² × 10²)						
		Very high and high	Moderate	Low and very low	Total at risk	% of total country area		
Angola	12 538	568	597	638	1 803	14.4		
Cameroon	4 664	-	22	150	173	3.7		
Central African Republic	6 244	196	204	258	659	10.6		
Chad	12 725	33	34	75	142	1.1		
Congo	3 385	220	388	554	1 162	34.3		
Côte d'Ivoire	3 214	_	23	264	286	8.9		
Democratic Republic of the Congo	23 041	1 023	2 717	4 162	7 902	34.3		
Equatorial Guinea	270	4	37	24	65	24.1		
Gabon	2 660	6	57	104	167	6.3		
Guinea	2 461	1	42	141	184	7.5		
Nigeria	9 089	-	-	71	70	0.8		
Sierra Leone	728	-	-	18	18	2.5		
South Sudan	6 334	281	379	341	1 001	15.8		
Uganda	2 055	13	91	70	175	8.5		
Other endemic countries**	60 316	_	_	_	-			
Total	149 722	2 346	4 591	6 871	13 808	9.2		

^{*} Land area: the area of surface water bodies as depicted in the Shuttle Radar Topography Mission – River-Surface Water Bodies dataset is not included.

The road to eliminating Gambiense trypanosomiasis

Elimination concept

The WHO Roadmap on NTDs targets the elimination of HAT as a public-health problem by 2020. The meeting agreed to observe this goal and therefore to define a threshold for elimination as a public-health problem as the detection of less than 1 new case per 10 000 inhabitants in at least 90% of endemic foci reporting less than 2000 new cases annually at continental level by 2020.

Achieving elimination as a public-health problem by 2020 represents an intermediate objective. Sustainable efforts should be maintained to achieve the interruption of transmission to avoid past experiences where the disease reemerged after intense reduction of transmission without ensuring permanent surveillance to detect recrudescence. The meeting agreed that the

^{**} Countries at marginal risk: Benin, Burkina Faso, Gambia, Ghana, Guinea-Bissau, Liberia, Mali, Niger, Senegal and Togo.

intermediate objective should be followed by the elimination of the disease as defined by STAG: "reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, as a result of deliberate efforts; continued actions to prevent reestablishment of transmission may be required". The newly adjusted objective of HAT elimination will be the absence of transmission resulting in zero cases reported in all foci. Participants estimated that the deadline for this new outcome should be settled for 2030. Partners should consider this new concept and objective.

Indicators and milestones

The meeting discussed and endorsed the indicators and milestones for the elimination of HAT as a public-health problem as specified in WHO's Roadmap on NTDs (Table 4).

Table 4. Milestones for eliminating human African trypanosomiasis as a public-health problem by 2020

Indicator	2012	2013	2014	2015	2016	2017	2018	2019	2020
Endorse elimination criteria	1								
Convene Expert Committee on control and surveillance		_							
Quantitative indicators									
Number of new cases reported annually	6 000	5 500	5 000	4 500	4 000	3 500	3 000	2 500	<2 000
Number of foci validated as eliminated (reporting less than 1 new case per 10 000 inhabitants)				10%	30%	40%	60%	80%	>90%
Qualitative indicators							_		
Provide biennial update of population at risk covered									
Provide biennial update of disease distribution									
Provide biennial update of population at risk									
Joint agenda									
Prepare biennial country progress report meeting									
Convene annual partnership meeting									
Convene consultative group									

Primary indicators (*quantitative*). These indicators provide a raw figure on progress towards elimination of Gambiense trypanosomiasis to be updated on an annual basis:

- number of new cases reported annually
- number of foci validated as eliminated.

Secondary indicators (*qualitative*). These indicators provide useful monitoring information on the quality of elimination activities and will therefore ensure the robustness of progress of the primary indicators. The basis for obtaining these indicators is the annual update of the HAT Atlas database. To be updated on a biennial basis:

• population at risk covered by control and surveillance activities

This indicator measures the intensity of actions taken towards elimination.

geographical extent of the disease and population at different levels of risk

These indicators provide geographical evidence of progress made in reducing the risk of Gambiense trypanosomiasis.

In order to follow and assess the elimination process, WHO will convene a biennial meeting with disease endemic countries to present country report progress.

WHO will organize an annual meeting of partners to review progress, maintain advocacy and awareness among donors, and attract new partners in the elimination process to fill the funding gap.

The meeting proposed establishing a consultative group of experts to advise WHO annually on the process of elimination.

Strategies for intervention*

Since "elimination as a public-health problem" is considered an advanced degree of control and an intermediate stage of eliminating Gambiense trypanosomiasis, the strategies discussed in this section refer to elimination as "reaching zero cases", as defined by the STAG and adopted by the meeting.

It has been undoubtedly stated that the elimination process must concentrate at focus instead of country level. A "focus" was designated by a WHO Expert Committee in 1986 as: "a zone of transmission to which a geographical name is given (locality, region or river)". ¹⁰ The list of current foci is presented in Annex 1 and will be a useful tool for monitoring the elimination process.

The smallest epidemiological unit is the village. Current knowledge of the disease's distribution through the database of the HAT Atlas will allow classification of villages according to cases reported and subsequent planning of targeted control activities at village level, as the unit for intervention.

Since elimination is not eradication and the risk of re-establishing transmission exists, it was also clearly understood that during and after elimination, continued and adapted actions would be required to sustain zero cases within a focus.

The epidemiological settings described above require different types of interventions. These interventions have to combine the three classical control methods (active case-finding through mobile teams, passive case-finding involving available health facilities and vector control).

The "dosage" of each control method relies on:

• the epidemiological setting defined by the intensity of transmission,

^{*}This section should be considered a technical note that includes all the topics discussed during the meeting, those presented in the supporting documents, and those contained in individual and country presentations. Some aspects were developed in more detail after the meeting by the Secretariat according to the recommendation made by participants that: "Following the agreement on Gambiense trypanosomiasis elimination principles, a strategic plan will be elaborated by WHO to pilot countries in planning and implementing national elimination strategies".

¹⁰ Transmission sites: definition of a "focus". In: *Epidemiology and control of African trypanosomiasis. Report of a WHO Expert Committee*. Geneva, World Health Organization, 1986 (Technical Report Series, No. 739:40).

- the accessibility and capabilities of existing health facilities, and
- vector knowledge including the sites where human–vector contact occurs.

Interventions must be flexible and dynamic enough to be periodically adapted to the epidemiological progress of the disease in the focus as well as to changes in local health services, including their level of preparedness for an involvement in the elimination process.

To ensure appropriate planning of activities for the entire elimination process, it is essential to maintain a register of activities carried out and the results obtained to guarantee correct and regular reporting to national and international levels.

The types of intervention for tackling the different epidemiological settings have been described as follows:

1. Reaching zero cases in foci with transmission of high and very high intensity

Foci reporting an annual average of at least 1 new case per 1000 inhabitants during the past 5 years should implement intensive control by mobile teams with additional support from the health system. The role of mobile teams is crucial.

- Villages reporting at least 1 new case during the past 3 years by active or passive case-finding will be included in the planning of mobile teams for *annual active case-finding surveys* through serological screening until zero cases are reported for 3 consecutive years.
- Villages in formerly known areas of transmission reporting zero cases during the past 3 years but reporting at least 1 new case during the past 5 years will be surveyed by a mobile team once every 3 years. If zero cases are reported during this period, the village will be not be eligible for annual *active case-finding* surveys and will be put under *selective serological surveillance* in sentinel sites as described below.
- Villages in formerly known areas of transmission reporting zero cases during the past 5 years will not be included in the annual planning of mobile teams. Sentinel sites will be called to perform *selective serological surveillance* as described below.

Mobile teams will continue to perform active case-finding surveys in selected villages as per national protocols. In addition, health-care facilities in the focus will be evaluated and selected in terms of population coverage and capacities in order to act as sentinel sites. Sentinel sites, after previous training and equipment, will include in their routine activities selective serological surveillance in patients seeking health care and presenting evocative signs and symptoms of Gambiense trypanosomiasis* through individual serological screening tests (IST). Staff working in primary health-care centres within the focus will be sensitized to the possible presence of the disease. They will be trained to recognize those signs and symptoms suggesting Gambiense trypanosomiasis infection. In the presence of suggestive symptoms and signs, the suspects will be referred to the sentinel site. Those presenting a

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^{*} Evocative signs and symptoms of Gambiense trypanosomiasis are long-standing fever resistant to usual treatment; chronic headaches; enlarged cervical nodes; behavioural disorders (aggressiveness, apathy, mental confusion); motor disorders (convulsions, abnormal movements, tremors, difficulty with walking); severe weight loss and weakness; and sleep disorders (excessive day-time sleep).

positive serological result will be submitted to parasitological diagnosis following national guidelines. If a parasitological diagnosis is established, the patient will be treated according to national rules. If the parasitological tests are negative, support will be provided by a WHO Collaborating Centre through immune trypanolysis test. If immune trypanolysis is positive, follow-up must be implemented by the health-care facility detecting the serological suspect until the serological suspicion disappears or a parasitological diagnosis is established. If immune trypanolysis is negative, no more action is required.

Elimination of Gambiense trypanosomiasis foci emphasizes detecting and treating the human reservoir. However, in some foci, several contributing factors may thwart this objective when targeting the human reservoir only, including:

1. The tools used

Serological and parasitological tools used for screening and diagnosis are not 100% sensitive. Therefore some infected people may not be detected during active or passive screening and remain as reservoirs.

2. The approach to reaching human reservoirs

- The mobile team may not detect infected people due to low coverage or attendance of the population.
- Sentinel centres may not detect infected people due to difficult access.

3. The epidemiology of the disease

- Healthy carriers may never seek medical care and continue to carry the parasite and subsequently to infect vectors.
- An animal reservoir of *T.b.gambiense* could play a role in continuous transmission.

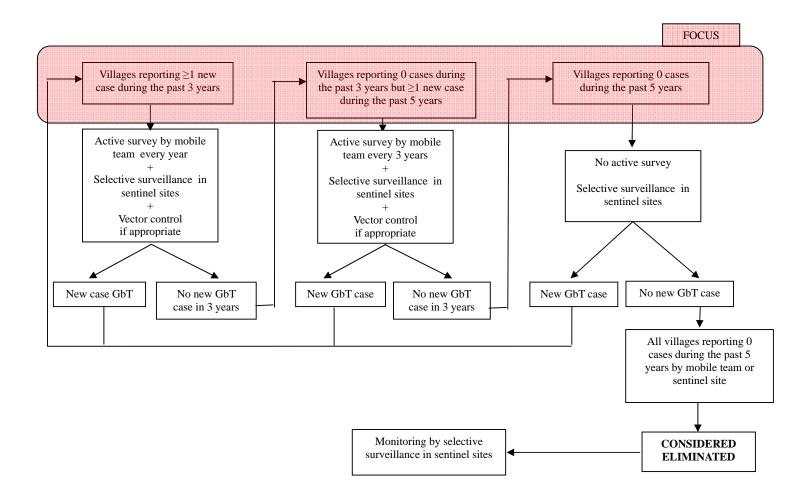
Where one or several of these factors prevents medical teams from achieving the expected result or where NSSCPs wish to accelerate the elimination process, vector control must be able and ready to respond. Implementation of appropriate vector control strategies reinforces elimination activities by reducing human–vector contact. A vector control strategy must be tailored to the specific characteristics of each focus (including the methods to be used, the frequency and intensity of actions and the sites for application).

• Where during the past 5 years zero cases have been reported in the villages listed in the focus either by mobile teams or through sentinel sites, **the focus is considered eliminated** and no more *annual active case-finding surveys* will be planned through mobile teams. Sentinel sites should initiate monitoring and evaluating of elimination by *selective serological surveillance* (see monitoring section and Algorithm 1).

* All people who are positive in the serological tests for Gambiense trypanosomiasis but without evidence of the parasite are eligible for individual management.

[•] Support through immune trypanolysis could also be provided to seropositive cases detected by mobile teams but non-parasitologically confirmed to ascertain serological results and facilitate follow-up if appropriate. This will depend on the national guidelines for active case-finding surveys.

Algorithm 1. Strategy for eliminating Gambiense trypanosomiasis (GbT) in foci with transmission of high and very high intensity (foci reporting on average at least 1 new case per 1000 inhabitants per year during the past 5 years)



2. Reaching zero cases in foci with transmission of moderate intensity

Several foci display an epidemiological transmission status classified as moderate (that is, foci reporting on average at least 1 new case per 10 000 people but less than 1 new case per 1000 per year during the past 5 years). In these foci, the approach is similar to that applied in foci with high and very high transmission intensities (see section above for more details); however, the number of villages to be included in *annual active case-finding surveys* is expected to be less numerous than in previous settings. The role of the health system is anticipated to be more crucial to reaching zero cases.

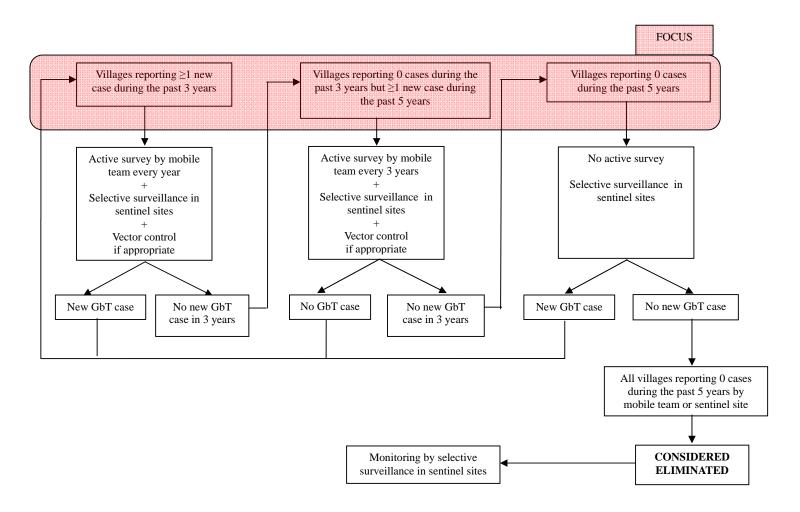
- Villages reporting at least 1 new case during the past 3 years: *annual active case-finding surveys* by mobile teams.
- Villages reporting zero cases during the past 3 years but at least 1 new case during the past 5 years: *active case-finding surveys* by mobile teams once only every 3 years.
- Health-care facilities in the focus are evaluated and selected to act as sentinel sites.
 Routine activities include selective serological surveillance through IST screening in
 patients seeking health care and presenting evocative signs and symptoms of
 Gambiense trypanosomiasis.
- Staff working in primary health-care centres in the focus are sensitized to the possible
 presence of the disease and the need to refer patients with symptoms and signs
 suggestive of Gambiense trypanosomiasis to the sentinel site.
- Support with additional immune trypanolysis tests if parasitological diagnosis is not established during *selective serological surveillance*.*

As stated in the epidemiological section above, the possibility for different reasons of persistent foci must be considered (as the result of, for example, insufficient sensitivity of screening methods, low coverage of active screening, difficult accessibility of sentinel sites, presence of healthy carriers and role of animal reservoir). The use of vector control to reinforce elimination activities has the potential to overcome such factors.

• When in the villages listed in the focus reporting zero cases during the past 5 years through mobile teams or a sentinel site, **the focus is considered eliminated**. No more *active case-finding survey* by mobile teams is planned. Sentinel sites then initiate monitoring and evaluating of elimination by *selective serological surveillance* (see monitoring section and Algorithm 2)

^{*} Support through immune trypanolysis could also be provided to seropositive cases detected by mobile teams but non-parasitologically confirmed to ascertain serological results and facilitate follow-up if appropriate. This will depend on the national guidelines for active case-finding surveys..

Algorithm 2. Strategy for eliminating Gambiense trypanosomiasis (GbT) in foci with transmission of moderate intensity (foci reporting on average at least 1 new case per 10 000 inhabitants but less than 1 new case per 1000 inhabitants per year during the past 5 years)



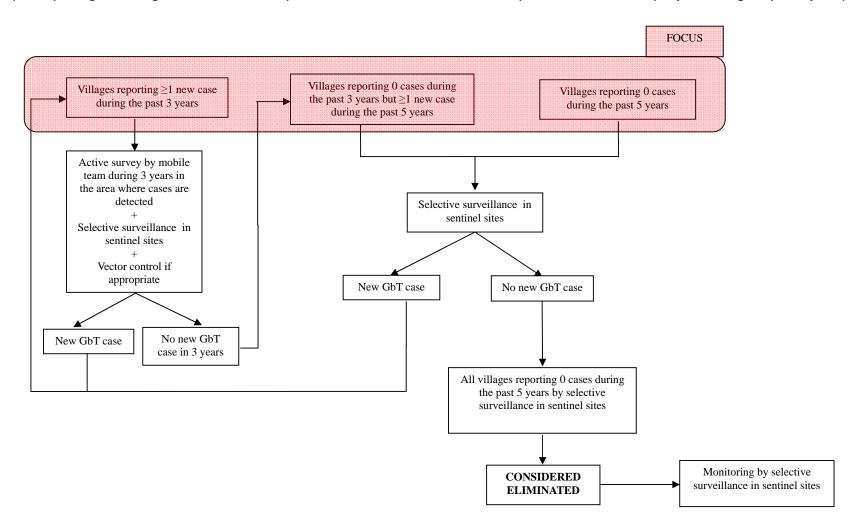
3. Reaching zero cases in foci with transmission of low and very low intensity

Several foci display an epidemiological transmission status classified as low or very low (that is, foci reporting on average at least 1 new case per 1 000 000 inhabitants but less than 1/10 000 inhabitants per year). Efforts should focus on maintaining the health system's awareness of Gambiense trypanosomiasis and its ability to diagnose the disease. *Selective serological surveillance* must be part of the daily activities of global health surveillance in sentinel sites selected from existing health-care facilities. However, if one village has reported at least 1 case during the past 3 years, it will be submitted to *active case-finding surveys* until zero cases are detected during 3 consecutive years, even if the entire foci does not justify the action of mobile teams.

If 1 case is detected in the sentinel site or by the mobile team, a *reactive active case-finding survey* will be implemented in the area where transmission has most likely occurred (such as in the place of residence of the patient or the area in which he or she conducted activities). An epidemiological assessment of each new detected case will help to locate the probable area of transmission. This *reactive active case-finding survey* will be maintained for up to 3 years when zero cases are reported.

When zero cases are reported during 5 years, **the focus is considered eliminated.** Sentinel sites will initiate monitoring and evaluating of the focus through *selective serological surveillance* (see monitoring section and Algorithm 3).

Algorithm 3. Strategy for eliminating Gambiense trypanosomiasis (GbT) in foci with transmission of low and very low intensity (foci reporting on average at least 1 new case per 1 000 000 but less than 1 new case per 10 000 inhabitants per year during the past 5 years)



4. Assessing transmission status in foci reporting zero cases for at least 5 years

A former transmission area (focus) could have been reporting zero cases following either active case-finding surveys (usually with low coverage and subsequent weak reliability of results obtained) or a lack of control activities. Both situations justify additional assessment.

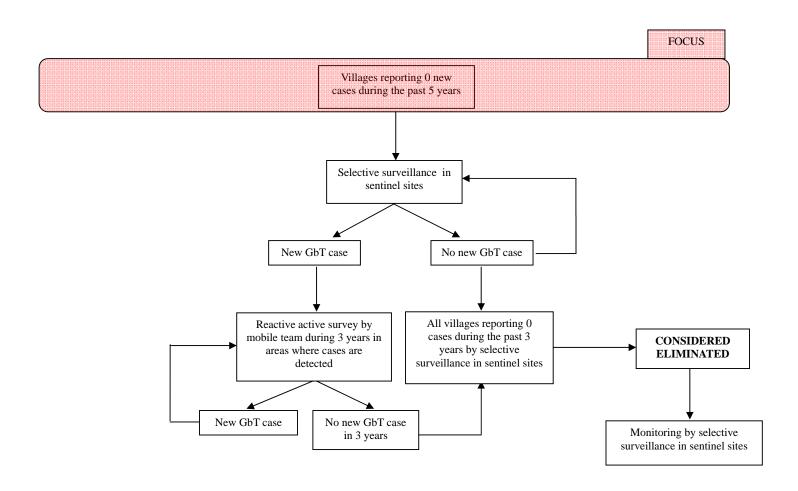
- Selective serological surveillance through the use of IST should be implemented in sentinel sites and applied to all patients with clinically suspected Gambiense trypanosomiasis (that is, patients presenting evocative signs and symptoms of the infection) seeking health assistance in selected health-care facilities located in the focus under assessment. Staff working in primary health-care centres in the focus will be sensitized to the possible presence of the disease. They will be trained to recognize those signs and symptoms suggestive of the infections and, where they are present, to refer suspects to the sentinel site. In those presenting a positive IST, a dried blood sample on filter paper will be sent to a WHO Collaborating Centre for further serological testing through immune trypanolysis. Those with a positive immune trypanolysis result will undergo parasitological examinations to confirm or discard serological suspicion by parasite detection. If the serological suspicion is confirmed by parasitological examinations, a reactive active case-finding survey will be carried out for 3 consecutive years in the area of activity of the new case to check whether other inhabitants are infected. Vector studies and control measures could be included to decrease human-vector contact. The results obtained during this period will determine the actions to be implemented to avoid re-establishing disease transmission. As a general rule, mobile team actions must continue to observe 3 consecutive years with zero cases reported. If the parasitological examinations of immune trypanolysis positive are negative, a follow-up will be established until the serological suspicion disappears or the diagnosis is established.* In this last circumstance, case reactive active case-finding survey will be implemented as described above. If the country considers that its staff have lost their expertise on parasitological diagnosis of Gambiense trypanosomiasis and in organizing active case-finding surveys, external support will be provided from a sub-regional pool of control experts.
- If zero cases are reported during 3 consecutive years of selective serological surveillance, **the focus is considered eliminated**. Selective serological surveillance must be maintained in sentinel sites for monitoring and evaluating elimination (see monitoring section and Algorithm 4).

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[•] Evocative signs and symptoms of Gambiense trypanosomiasis are long-standing fever resistant to usual treatment; chronic headaches; enlarged cervical nodes; behavioural disorders (aggressiveness, apathy, mental confusion); motor disorders (convulsions, abnormal movements, tremors, difficulty with walking); severe weight loss and weakness; and sleep disorders (excessive day-time sleep).

^{*} All people who are positive in the serological tests for Gambiense trypanosomiasis but without evidence of the parasite are eligible for individual management.

Algorithm 4. Strategy for eliminating Gambiense trypanosomiasis (GbT) in foci reporting zero cases during the past 5 years



Monitoring and evaluating*

Continuous monitoring and evaluating is needed not only to ensure the sustainability of zero case reporting and to prevent the re-establishment of transmission but also to ascertain the accessibility, coverage and adequate quality of *selective serological surveillance* activities.

When a focus is declared eliminated either due to control measures or as a result of the assessment of an historical focus reporting zero cases, selective serological surveillance will continue in previously identified sentinel sites through serological screening by IST in patients seeking health care and presenting evocative signs and symptoms of Gambiense trypanosomiasis. Staff working in primary health-care centres in the focus will be requested to continue to check for the possible presence of the disease. Staff in sentinel sites and health centres will receive refresher training to recognize the signs and symptoms suggestive of the infections. In the presence of suggestive symptoms and signs, the suspects will be referred to the sentinel site. Those presenting positive results will be submitted to national rules for HAT diagnosis. If the serological suspicion is confirmed by parasitological examinations, a reactive active case-finding survey will be carried out for 3 consecutive years in the area of activity of the newly detected case to check whether other inhabitants are infected. Vector studies and vector control measures will be included to decrease human-vector contact. The results obtained during this 3-year period will determine the actions to be implemented to avoid re-establishing disease transmission. As a general rule, mobile team actions must continue to observe 3 consecutive years with zero cases reported. If the parasitological examinations of the serological-positive individual detected during selective serological surveillance are negative, a dried blood sample will be sent to a WHO Collaborating Centre for an immune trypanolysis test. If the result of this test is positive, follow-up must be implemented until the serological suspicion disappears or the diagnosis is established.* In this case, reactive active case-finding survey will be implemented as described above. If the immune trypanolysis result is negative, no further action is required (Algorithm 5).

The duration of monitoring for *selective serological surveillance* is not yet agreed but must continue while the risk of re-establishment of disease transmission exists. It will depend on the results obtained during its implementation and the epidemiological setting of neighbouring foci (see validation in the elimination section above).

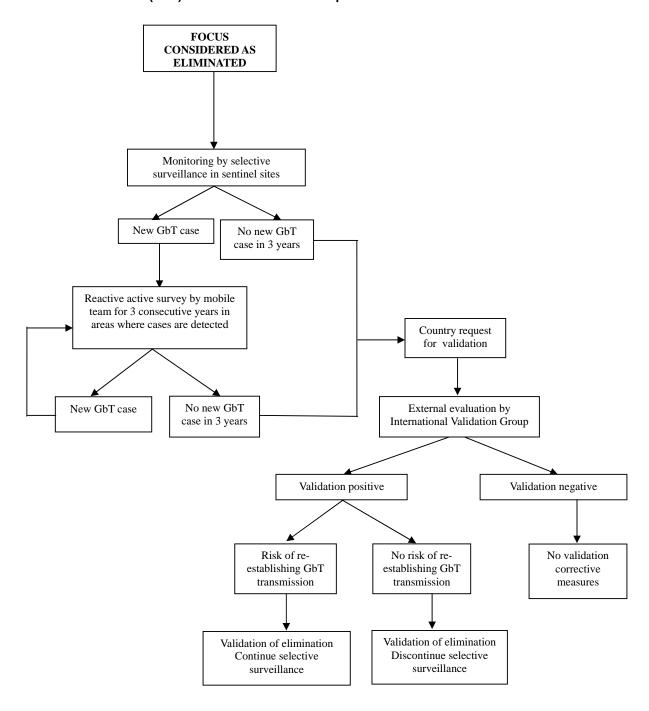
Standard survey and sampling methods are not useful for monitoring and evaluating of Gambiense trypanosomiasis elimination due to the low prevalence of the disease: no sampling methods have sufficient statistical power for decision-making. Therefore, monitoring of elimination will rely on strong overall health systems, mainly in rural areas, while maintaining expertise and reaction capacity at central level.

^{*} This section should be considered a technical note that includes all the topics discussed during the meeting, those presented in the supporting documents, and those contained in individual and country presentations. Some aspects were developed in more detail after the meeting by the Secretariat according to the recommendation by participants that: "Following the agreement on HAT elimination principles, a strategic plan will be elaborated by WHO to pilot countries in planning and implementing national elimination strategies".

[•] Evocative signs and symptoms of Gambiense trypanosomiasis are long-standing fever resistant to usual treatment; chronic headaches; enlarged cervical nodes, behavioural disorders (aggressiveness, apathy, mental confusion); motor disorders (convulsions, abnormal movements, tremors, difficulty with walking); severe weight loss and weakness; and sleep disorders (excessive day-time sleep).

^{*} All people who are positive in the serological tests for Gambiense trypanosomiasis but without evidence of the parasite are eligible for individual management.

Algorithm 5. Strategy for monitoring and evaluating a focus of Gambiense trypanosomiasis (GbT) declared eliminated and process of validation



Xenomonitoring strategies could also contribute to monitoring the elimination of sleeping sickness by ascertaining the absence of infective parasites circulating in the vector, but this would require catching of important amount of flies to get reliable results. Unfortunately, a validated protocol for pooling tsetse flies does not exist. In addition, robust, sensitive and specific primers to detect midgut infections of *T. b. gambiense*, although ongoing, are not yet available. Currently, therefore, no role for entomological indicators or assessment of elimination is envisaged.

Validation of elimination*

Although declaration of elimination of a Gambiense trypanosomiasis focus is the responsibility of national authorities, validation of elimination requires external evaluation by an International Validation Group (IVG) convened by WHO, with rules and guidelines to be developed. Countries should submit a request to WHO to verify the absence of transmission in a defined focus and present a technical report indicating the activities performed and the results obtained.

Assessment by the IVG will be based on the documentation provided, demonstrating clearly that appropriate surveillance was effectively implemented and that the result is "no case identified". The IVG will then make appropriate recommendations to WHO regarding validation of elimination of the assessed focus if the validation is positive. However, if validation is negative, the IVG will not endorse elimination in the focus, and will recommend corrective measures and the way forward.

The IVG has to estimate the risk of re-establishment of transmission of the disease and therefore recommend or not the continuation of *selective serological surveillance* after validating elimination. How and for how long such *selective serological surveillance* should continue has not yet been defined (Algorithm 5).

Research

The control tools currently available are not the most appropriate to design fine-tuned strategies for each epidemiological setting identified. Continuous research is needed to improve these weaknesses, mainly to allow the involvement of health services in eliminating Gambiense trypanosomiasis.

Screening and diagnostic tools

Diagnosis of Gambiense trypanosomiasis is a complex, multi-procedural process that involves serological screening, parasitological confirmation of infection and determination of the stage of the disease.

Despite the availability of a mass serological screening tool (the card agglutination test for trypanosomiasis, or CATT), it is not adaptable to the prevalent epidemiological situation as elimination advances and the health system is required to play a crucial role in sustainable control and surveillance. Basic and operational research must therefore be sustained to provide simple individual serological screening tests that allow integrated control and

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surveillance of Gambiense trypanosomiasis in health-care facilities.

New, lateral flow tests for individual screening are now available. These tests are rapid (results are obtained after 15 minutes), thermostable (not requiring a cold chain), simple to perform (requiring minimal training), affordable and do not require power supply or equipment. Their use is therefore highly advantageous for basic health personnel in peripheral health-care facilities. Unfortunately, because they are serological tests for detecting antibodies, the results indicate only suspicion of the disease. Diagnostic and parasitological confirmation of Gambiense trypanosomiasis is always needed.

The first step is to confirm the serological suspicion. Immune trypanolysis is considered the most specific test for detection of antibodies for Gambiense trypanosomiasis. Immune trypanolysis is an expensive and complex test that requires animal facilities to maintain live human infective trypanosomes and highly trained personnel; therefore, only specialized reference laboratories are able to perform the test. Nevertheless, a new approach to execute immune trypanolysis test on dried blood samples in filter paper has been developed to facilitate transport of samples from the field to reference laboratories. Given its very high sensitivity (97–100%) and very high specificity (~100%), the immune trypanolysis test is currently used as a remote reference test to refine serological procedures of surveillance.

The final step for the diagnosis of Gambiense trypanosomiasis is to conduct parasitological confirmation tests, which are complex and tedious and have limited sensitivity. The parasitological techniques currently applied are the classical lymph node aspirate to examine the lymph; the thick drop; the micro-hematocrit centrifugation; the mini-anion exchange centrifugation technique to examine blood; and the modified simple centrifugation to examine cerebrospinal fluid. The availability of simple LED fluorescence microscopes has revitalized parasite detection techniques based on DNA intercalating fluorescent dyes or on trypanosome-specific conjugates that can be combined with prior concentration techniques. Techniques for detecting DNA could be considered a new contribution to molecular diagnosis of Gambiense trypanosomiasis (PCR, NASBA, real-time PCR and LAMP) but they all require highly skilled personnel, sophisticated equipment and proper validation. In addition, most of the molecular tests are *Trypanozoon*-specific and thus cannot exclude a transient infection with non-pathogenic trypanosomes such as *T.b. brucei*.

Once the diagnosis of Gambiense trypanosomiasis has been achieved, determination of the stage of the disease is needed for appropriate treatment. Despite the availability of new markers such as neopterin, the invasive lumbar puncture is still required, although there are in the pipelines studies of specific markers also detectable in the blood of sleeping sickness patients.

Treatment tools

Two new treatment tools are in the development pipeline but will not be available before 2017–2018 even in the most optimistic scenario. The profile of these drugs has to facilitate management of cases by peripheral health staff in an out-patient context, making integrated activities in the health system possible. An ideal scenario is that of drug administration without safety and efficacy concerns, avoiding both laborious parasitological confirmation of clinical or serological suspects and invasive staging procedures.

Fexinidazole entered phase II/III clinical trials in October 2012 to determine its efficacy against both stages of the disease. Administration is per os and the duration of the treatment is 10 days.

Oxaborole has been in phase I trials since September 2012 to determine its efficacy against both stages of the disease. Administration is per os in one single dose.

Vector control

At present, major research efforts for vector control are concentrated on optimizing insecticide-treated targets. It is known that different tsetse species respond differently to targets. Traditionally, target-based control of the Palpalis fly group relied on complex and larger 3-dimensional traps. Recent work in Kenya and Uganda on *Glossina fuscipes*, and in Burkina Faso and Guinea on *G. palpalis*, has shown that these species respond effectively to simple targets of smaller sizes. In riverine savannah and lakeshore habitats, tiny targets (total size 25 x 50 cm) are highly effective even when deployed at densities of <10 per km² because they are placed along rivers only. In mangrove foci, targets of 75 x 50 cm show promising results but require higher densities. These smaller targets will reduce the costs of vector control because they are not only easier and cheaper to manufacture but also cheaper to deploy, more portable to deployment sites and require less maintenance. Tiny targets could therefore facilitate appropriate community involvement in sustainable vector control after the required initial 'professional' phase of target deployment carried out by trained personnel.

Methods to detect *Trypanosoma brucei gambiense* in tsetse fly are under development and could be useful for monitoring the presence of the parasite in a focus.

Epidemiological tools

The HAT Atlas is a useful tool that will play an important role in developing epidemiological maps for planning, monitoring and evaluating progress towards the elimination objective. It is also a safe digital repository for data and information on HAT.

Capacity-building at country level is planned for optimal use and future regular updates of the Atlas. It consists of providing hardware (desktop computers), open source software, harmonized national-level HAT databases, training courses and material to endemic countries.

A new approach (identification of villages at risk, or IVR) has been developed in West Africa to identify villages in active or historical foci that are most likely at risk for the disease and most likely to require surveillance. Geographical and medical field data are used to create comprehensive datasets and facilitate planning of projected interventions. A geo-referenced village database (name and location) is merged with six information layers (history of HAT distribution; population growth; landscape evolution; hydrological network; tsetse fly distribution; and distribution of health facilities). The combined information provides a risk scale from which to prioritize surveillance decisions. While the technique may be useful, the amount of information required is not systematically available for all endemic areas of the continent. Furthermore, if all the information needed became available, the technique would need to be evaluated in different epidemiological and environmental settings to demonstrate its usefulness.

Issues and challenges

Elimination of Gambiense trypanosomiasis is sustainable based on three pillars in a turmoil-free environment provided there is:

Ownership by endemic countries of the objectives and process of elimination. International commitment to elimination must be followed by political support at national level. Policy-makers should prioritize elimination of Gambiense trypanosomiasis as a health objective when competing with other national priorities.

Appropriate funding support from partners to implement elimination strategies. The current funding gap should be resolved through effective commitment from partners coupled with strong advocacy at national and international levels.

Capacity of the health system in rural areas to implement control and surveillance activities. The overall performance of the health system in rural areas where Gambiense trypanosomiasis is prevalent must be reinforced to perform the activities included in the elimination strategies.

Additional technical issues that need to be resolved:

- Improving knowledge of current gaps in geographical distribution. No data are available in several foci of Gambiense trypanosomiasis, mainly due to difficult access in some areas (Democratic Republic of the Congo) or security constraints (Central African Republic, Côte d'Ivoire the Democratic Republic of the Congo and Nigeria). There is also a lack of knowledge in foci reporting zero cases for decades and an absence of effective surveillance questioning zero case reporting (Gambia, Guinea Bissau, Liberia, Niger, Senegal and Sierra Leone).
- Elucidating the role of seropositive/aparasitaemic human cases and healthy carriers in maintaining transmission of the disease. These human parasite reservoirs probably act as subsequent sources of infection for flies, which could maintain transmission and cause reemergence of the disease. The immune trypanolysis test seems to be a promising tool for use as a marker of Gambiense trypanosomiasis infection in these individuals. An individual case management approach has to be elaborated.
- Understanding fully the epidemiological role of animal reservoir on Gambiense trypanosomiasis transmission. Only a few studies have been performed of T.b. gambiense infections in domestic and wild animals, and very little is known of the probability of the parasite being transmitted from animals to humans in the field. The persistence of an animal reservoir could play a role in maintaining a focus of transmission.
- Availability of new diagnostic and treatment tools to improve the ease and accuracy of case management. These tools are expected to enhance the integration of control and surveillance activities into the health system.
- Sustainability of the elimination process as essential to detecting the epidemiological risk of disease reintroduction. Elimination could be sustained by (i) developing and implementing appropriate surveillance strategies adapted to each epidemiological scenario involving the health system and (ii) ensuring the availability of required institutional and financial support to sustain effective

surveillance in the field. In that context, the permanent motivation of staff will require an imaginative approach, and regular training and sensitization for the full health system.

• Elucidating the convenience and feasibility of xenomonitoring for monitoring and evaluating elimination.

Furthermore, NSSCPs encounter the following additional difficulties in the daily management of control and surveillance activities that demand responses and solutions:

- Low participation rates of the population at risk during active screening by mobile teams and low attendance rates at health-care facilities in charge of passive surveillance.
- Lack of preparedness of staff in health-care facilities to incorporate Gambiense trypanosomiasis in their routine activities, either because control and surveillance of the disease historically has been considered a matter for specialized teams with external support or they are already overwhelmed.
- Progressive retirement of experienced staff, and lack of perspective, interest or motivation of the new generation to assume the roles and responsibilities of control and surveillance.

Conclusions

The participants in the WHO meeting on elimination of human African trypanosomiasis (*Trypanosoma brucei gambiense*) concluded that:

1. Commitment to eliminating the disease as a public-health problem, as agreed at a meeting of countries in which the disease is endemic in Geneva in 2007, should be maintained in response to resolution WHA56.7 of the World Health Assembly of 2003, resolution AFR/RC55/R3 of the 55th WHO Regional Committee for Africa of 2005, and the target of WHO's Roadmap on neglected tropical diseases, which includes elimination of human African trypanosomiasis as a public-health problem by 2020.

Nevertheless, elimination of Gambiense trypanosomiasis as a public-health problem by 2020 represents an intermediate objective, which should be followed by the elimination of the disease as defined by the Strategic and Technical Advisory Group for neglected tropical diseases. Thus, the newly adjusted objective for HAT elimination is the absence of transmission resulting in zero cases reported in all foci. Participants estimated the deadline for this new outcome by 2030. Partners should consider this new concept and objective.

- 2. The geographical unit for elimination is the focus, as defined by a WHO Expert Committee in 1986, whereas the village is the unit for intervention.
- 3. The parameters for global indicators of elimination are:
 - a. Number of new cases reported annually
 - b. Number of foci eliminated.

A threshold of less than 1 new case per 10 000 population in at least 90% of HAT foci reporting annually less than 2000 new cases at continental level was established as the objective of elimination of HAT as a public-health problem by 2020.

The milestones for the two indicators for eliminating HAT as a public-health problem have been considered and accepted as follows.

Indicator/milestone	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of new cases reported annually	6 000	5 500	5 000	4 500	4 000	3 500	3 000	2 500	<2 000
Number of foci validated as eliminated (reporting less than 1 new case per 10 000 inhabitants)	-	-	-	10%	30%	40%	60%	80%	>90%

4. The elimination agenda involved:

- i. Endorsing in December 2012 the concept of elimination and the milestones agreed by disease endemic countries during a WHO meeting on elimination of Gambiense trypanosomiasis.
- ii. Convening a WHO Expert Committee on HAT control and surveillance in 2013.
- iii. Creating in 2013 a consultative group of experts to advise WHO annually on the process of eliminating Gambiense trypanosomiasis.
- iv. As of 2013, convening annual meetings with current partners to advocate new potential partners.
- v. As of 2014, convening biennial meetings with endemic countries to report countries' progress.
- vi. As of 2014, preparing biennial updates on the disease's distribution, the populations at risk and the coverage of people at risk as secondary indicators.
- 5. Strategies for control and surveillance to achieve the elimination objective combine three elements:
 - i. active case-finding through mobile teams;
 - ii. passive case-finding involving available health facilities; and
 - iii. vector control.

The selection and "dosage" of each element must be flexible and dynamic, adapted to the epidemiological situation, and defined according to the intensity of transmission and the characteristics of existing local health services in each focus. Active case-finding using mobile teams is more important when the intensity of transmission is high, while passive case-finding integrated in health-care facilities should be present in all epidemiological situations, but is more prominent in the low transmission settings. Vector control should be applied according to medical needs.

- 6. Since elimination is not eradication and the risk of re-establishing transmission exists, continued and adapted actions will be required to sustain zero cases within a focus during and after elimination.
- 7. Gaps in knowledge have been identified. Operational research is needed to fill these gaps, including among others:
 - a. improved knowledge of current gaps in geographical distribution,
 - b. better knowledge of the epidemiological role of animal reservoirs, aparasitemic seropositive individuals and 'healthy carriers' in transmitting the disease.
 - c. Current control tools are not the most appropriate for elimination. Continuous research is needed to improve control tools in order to facilitate the engagement of health services in HAT elimination. This research has to include mainly (i) development of improved diagnostic tools and (ii) development of new drugs.
- 8. Following the meeting's agreement of HAT elimination principles, WHO will elaborate a strategic plan for pilot countries in planning and implementing national elimination strategies.

Annex 1: List of Gambiense trypanosomiasis foci by country and administrative division

Country	Administrative division	N°	Focus
Angola	Zaire	1	Soyo
		2	Noqui
		3	Mbanza Kongo
		4	Cuimba
		5	Tomboco
		6	Nzeto
	Uige	7	Maquela
		8	Quimbele
		9	Buengas
		10	Damba
		11	Sanza Pombo
		12	Bungo
		13	Mucaba
		14	Songo
		15	Bembe
		16	Ambuila
		17	Quitexe
		18	Negage
		19	Uige
		20	Puri
	Bengo	21	Ambriz
		22	Nambuangongo
		23	Dande
		24	Quibaxe
		25	Bula Atumba
		26	Pango Aluquem
		27	Icolo e Bengo
		28	Quissama
	Luanda	29	Viana
		30	Cacuaco
	Kwanza norte	31	Camabatela
		32	Quiculungo
		33	Bolongongo
		34	Samba Caju
		35	Banga
		36	Gonguembo
		37	Lucala
		38	Golungo Alto
		39	Cazengo
		40	Cambambe
	L		

	Kwanza sud	41	Libolo
		42	Mussende
		43	Quibala
	Malange	44	Cacuso
	Kuando Kuwango	45	Mavinga
		46	Rivungo
Benin	Atacora	47	Atacora
	Alibori	48	Alibori
	Donga	49	Donga
Burkina Faso	Comoé	50	Diarabakoko
	Houé	51	Sangulema
		52	Dourula
	Poni	53	Loropeni
	1	54	Koudougou
Cameroon	Océan	55	Campo
	Cocan	56	Bipindi
	Haut Nyong	57	Doumé
	Lebialem	58	Menyi
	Lobialom	59	Mbeta
		60	Fotabong
	Manyu	61	Manfé
	Mbam et Inoubou	62	Bafia
	Wibaiii et illoaboa	63	Bokito
		64	Ombessa
	Kadei	65	Yokadouma
	Menua	66	Santchou
Central African	Obo	67	Obo
Republic	Mboki	68	Mboki
	Zemio	69	Zemio
	Djema	70	Djema
	Matikoulou	71	Matikoulou
		71	
	Batangafo		Batangafo
	Nola	73	Nola
Chad	Lobaye	74	Lobaye
Chad	Moissala	75	Moissala
	Mandoul	76	Mandoul
	Gore	77	Gore
0	Tapol	78	Tapol
Congo	Cuvette	79	Mossaka
		80	Loukolela
	Cuvette Ouest	81	Ewo
		82	Mbomo
		83	Kellé
	Plateaux	84	Mpouya

		127	Mangebo
		126	Kongo Songololo
		125	Boma
		124	Luima Palabala
		123	Kiniati
		122	Matadi
		121	Kwilu Ngongo
		120	Boma Bungu
		119	Luwala
		118	Luhombo-Luala
		117	Kibunzi
		116	Inga
		114	Lukula
Republic of the Congo	-	114	Wombo
Democratic	Bas-Congo	113	Kimpese
	Duekoué	112	Duekoué
	Guiglo	111	Guiglo
	Danane	110	Danane
	San Pedro	109	Gabiagui
	Soubre	108	Grand Zatry
	Sassandra	107	Sassandra
	Vavoua	106	Vavoua
	Aboisso	105	Ayamé
		104	Gboguhué
		103	Gonaté
	Daloa	102	Zoukougbeu
	Gagnoa	101	Bayota
	Oumé	100	Oumé
	Sinfra	99	Sinfra
Côte d'Ivoire	Bouaflé	98	Bonon
	Niari	97	Komono
		96	Yamba
		95	Mfouati
		94	Madingou
		93	Nkayes
		92	Nkayi
		91	Boko-Songho
	Bouenza	90	Loudima
		89	Mindouli
		88	Ignie
	Pool	87	Ngabe
		86	Mokotimpoko
		85	Gamboma

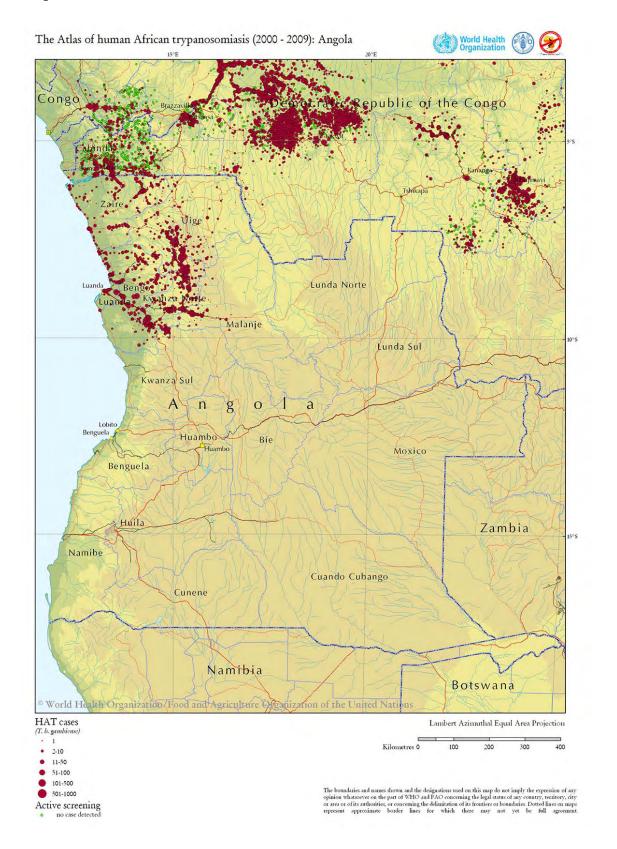
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	129	Kimvula
	130	Kakongo
	131	Bundi
Kinshasa	132	Route Bandundu
Milonasa	133	Chenal Fleuve Congo
	134	Dingi Dingi
	135	Ndjili Kilambo
	136	Ndjili Lukaya
	137	Muwana
	_	
	138	Muanamputu
	139	Buma
	140	Boye
	141	Ndjili Brasserie
	142	Buma Rivière Tshuenge
Bandundu Nord	143	Kwilu
	144	Inzia
	145	Kasai
	146	Bandundu
	147	Fankana Kalakitini
	148	Fleuve/Mbee
	149	Djuma Mikwi
	150	Fleuve/Mbwema
	151	Fleuve/Batende
	152	Fleuve/Banunu
	153	Ngampoko/Bwema
	154	Molokai/Bat
	155	Molokai/Mbelo
	156	Mfimi Lukeni
	157	Kwa-Fleuve
	158	Mfimi Fleuve
	159	Etrack
	160	Lac Mai Ndombe
Bandundu Sud	161	Lubue
	162	Piopio
	163	Loano
	164	Kamouts
	165	Loandji
	166	Wamba Kwango
	167	Wamba Bakali
	168	Bakali Konzi
	169	Konzi Insia
	170	Kafi Gobari
	171	Kwilu Kwenge
	'''	Tivila Twenge

	172	Kwenge
	173	Kwenge Vushie
	174	Kwily Kabanga
	175	Kwily Kikwit
	176	Kwilu Lutshima
	177	Luie
	178	Lukula
	179	Lukula Sud
	180	Lukula Sabari
	181	Lukula Inzia
	182	Inzua Luie
	183	Kasai Kamoutsha
	184	Kwango
	185	Kwilu
	186	Wawa Lubisi
	187	Kwango Luie
	188	Kwango 1
Kasai-Oriental	189	Mbuji Mayi Kalelo
	190	Lubilanji
	191	Lubilanji Sankuru
	192	Lubi
	193	Katanga
Kasai-Occidental	194	Lulua
	195	Rail
	196	Dimbelenge
Equateur Sud	197	Chenal Fleuve
	198	Lac Ntumba
	199	Maringa
	200	Ngiri
Equateur Nord	201	Riviere Ubangil
	202	Rliviere Ngiri
	203	Fleuve Congo
Province Oriental	204	Riviere Lua-Mongala
Trovinso chomai	205	Isangi
	206	Yahuma
	207	Tshopo
	208	Doruma
	209	Ango
	210	Dingila
	210	Bili
Maniema	212	Fleuve Congo
Ivianiena	212	Riviere Lomami
	213	Foyer Rail
	214	Riviere Lulindi
	213	IXIVIELE LUIIIIUI

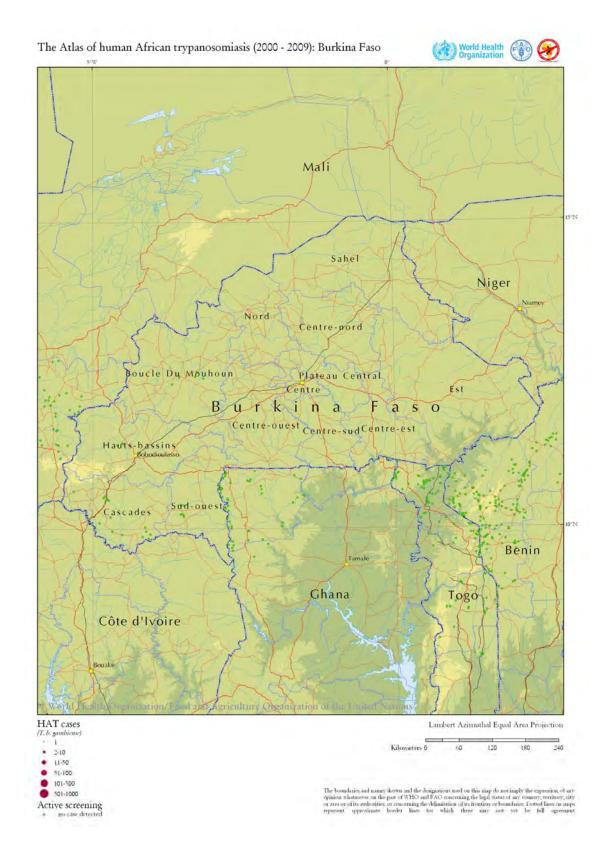
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		217	Riviere Kama Kama 1
		218	Riviere Kama II
		219	Riviere Kama III
	Katanga	220	Riviere Ndanda
		221	Fleuve Congo
		222	Lukuga
		223	Foyer Rail
		224	Nyemba
		225	Nyemba II
	Sankuru	226	Nyemba III
		227	Riviere Lomami
		228	Fleuve Congo
		229	Riviere Sankuru
		230	Riviere Lokenye
Equatorial Guinea	Litoral	231	Mbini
		232	Kogo
		233	Campo
	Bioko Norte	234	Luba
Gabon	Estuaire	235	Noya
		236	Komo Kango
		237	Komo Mondah
		238	Komo Ocean
	Ougoué maritim	239	Bendje
		240	Omboué
	Moyen Ougoué	241	Ougoué et lacs
	Ngounié	242	Tsamba Magotsi
Gambia	Gambia	243	Gambia
Ghana	Western Region	244	Sekondi-Takoradi
Guinea-Bissau	Cacheu	245	Cacheu
	Biombo	246	Biombo
	Bijagos	247	Bijagos
Guinea	Boke	248	Boffa
	Kindja	249	Dubreka
		250	Forécariah
		251	Coyah
	Boke	252	Boké
	N'zérekoré	253	N'zérekoré
		254	Guéckedou
	Kankan	255	Siguiri
		256	Mandiana
		257	Kankan
	Mamou	258	Pita
		259	Mamou

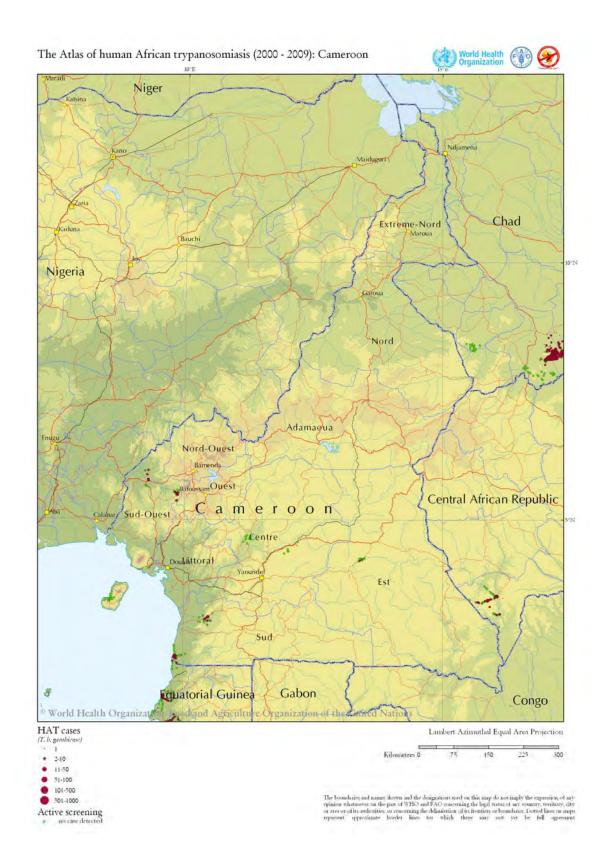
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Liberia	Lofa County	261	Lofa County
	Bong county	262	Bong county
	Nimba county	263	Nimba county
	Monrovia	264	Monrovia
Mali	Kénieba	265	Kenieba
	Dioila	266	Dioila
	Bla	267	Bla
	Koutiala	268	Koutiala
	Bougouni	269	Bougouni
	Sikasso	270	Sikasso
Niger	Say	271	Say
Nigeria	Delta	272	Delta
	Edo	273	Edo
	Ekiti	274	Ekiti
	Ondo	275	Ondo
Senegal	Haute Casamance	276	Kolda
	Moyenne	277	Sédiou
	Casamance Basse Casamance	278	Zinginchor
	Saloum	279	Fatik
	Kédougou	280	Kédougou
Sierra Leone	Tonkolili	281	Tonkolili
Sierra Leone	Bombali	282	Bombali
	Kailahun	283	Kailahun
	Bonthe	284	Bonthe
	Kambia	285	Kambia
South Sudan	Easter Equatoria	286	Nimule
	1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1	287	Kajo-keji
	Central Equatoria	288	Juba
	'	289	Yei
		290	Mundri
	Western Equatoria	291	Maridi
	•	292	Yambio
		293	Ezo
		294	Tambura
Togo	Savane	295	Mango
_	Kara	296	Tchamba
Uganda	West Nile	297	Koboko
		298	Yumbe
		299	Moyo
		300	Adjumani
		301	Amuru
		302	Maracha
		303	Arua

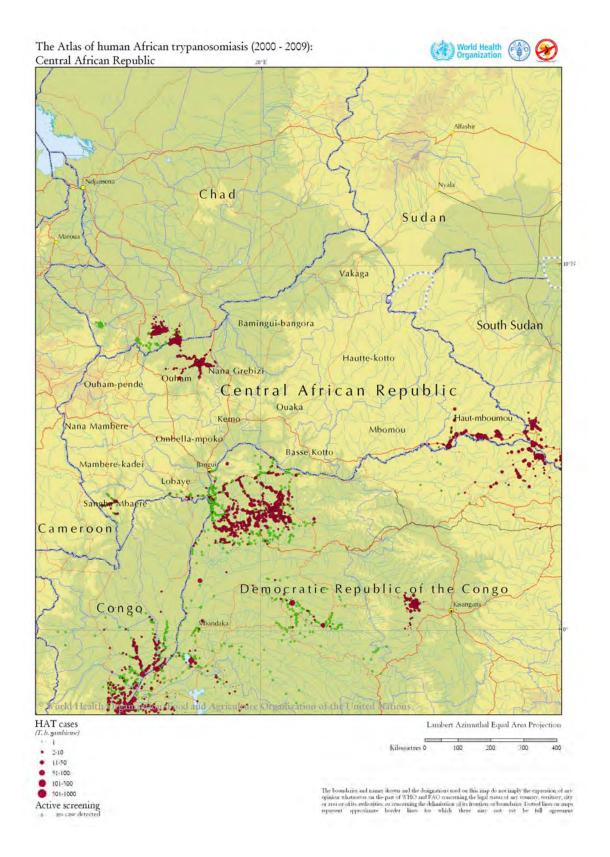
Annex 2: Maps of disease distribution



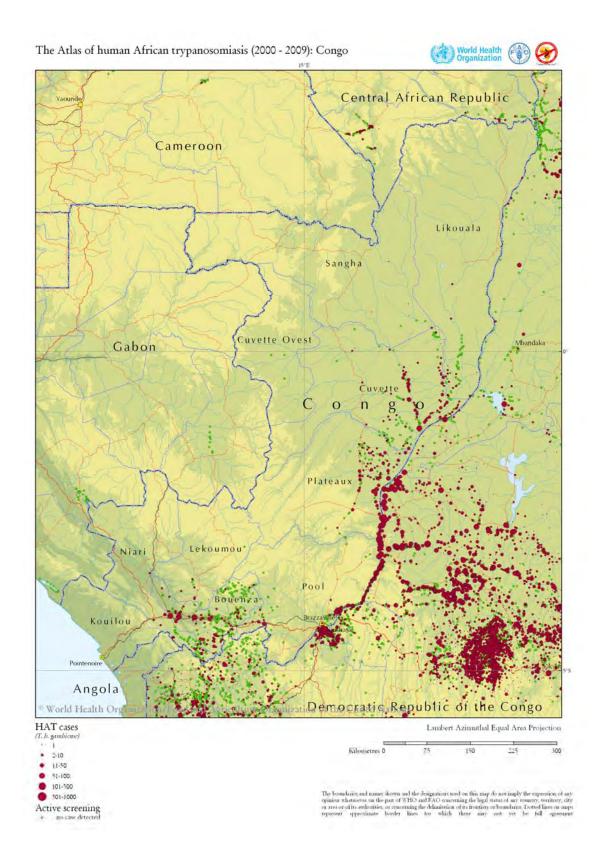




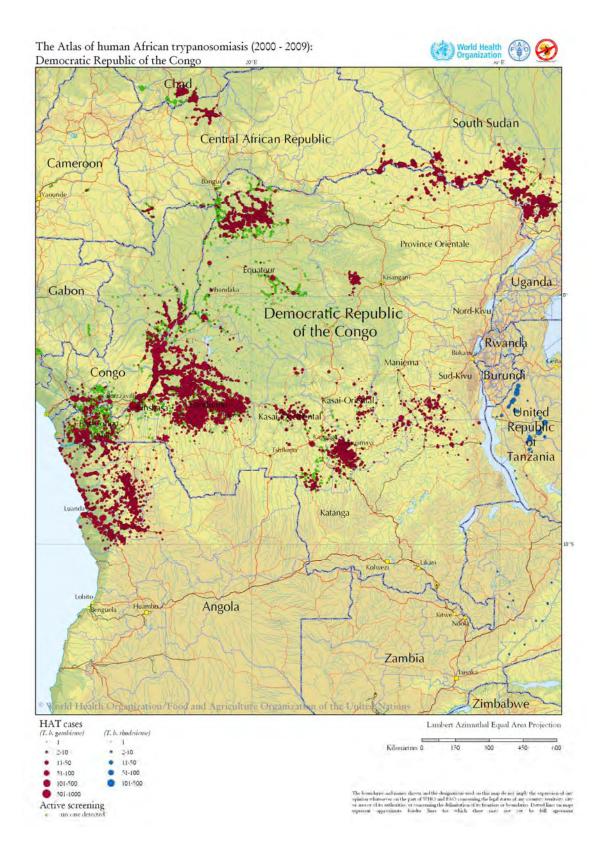




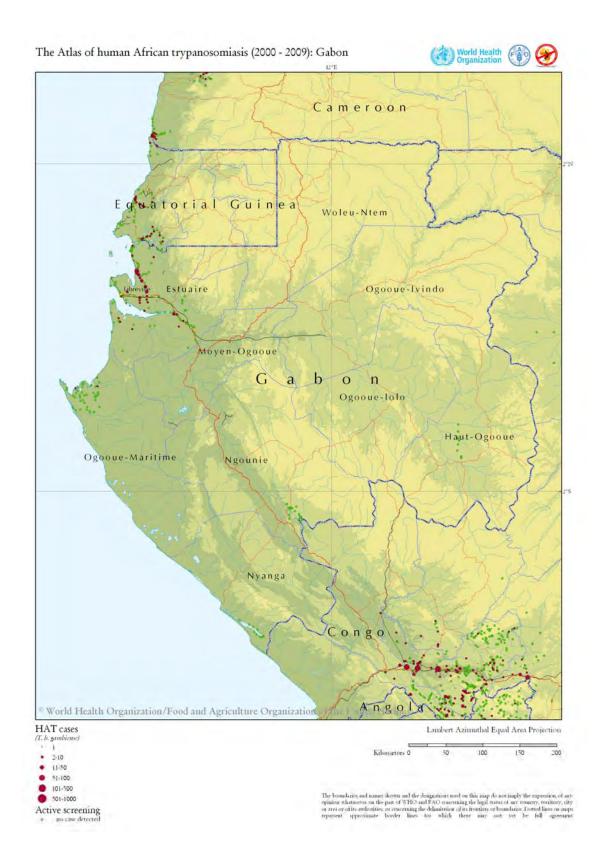


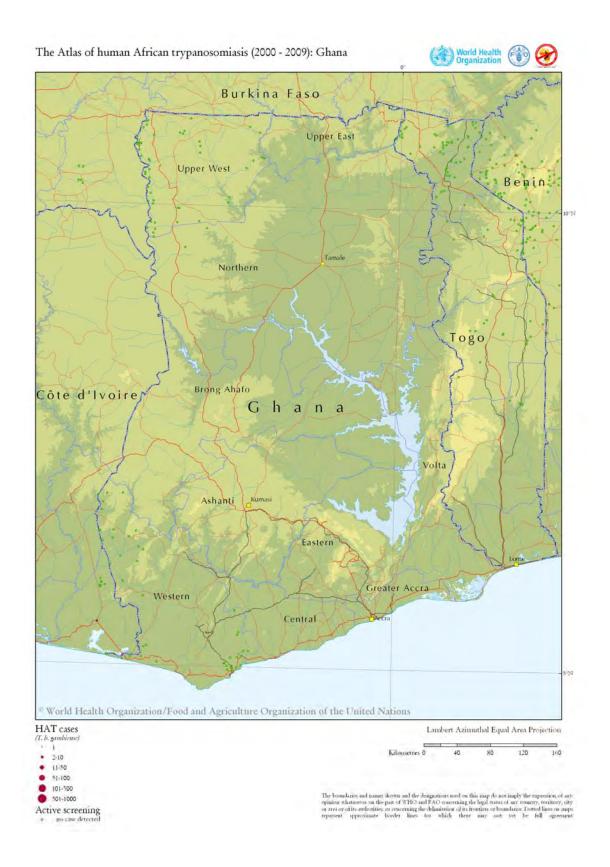






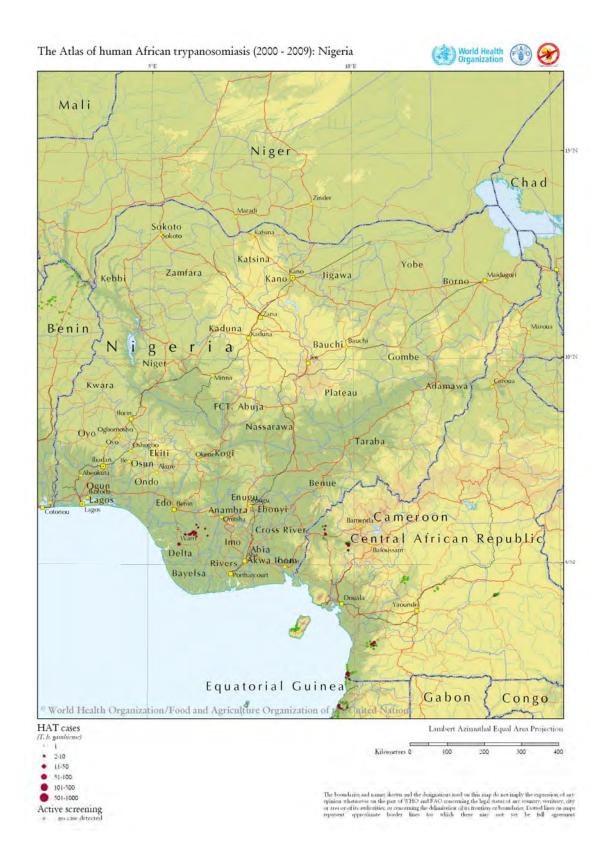


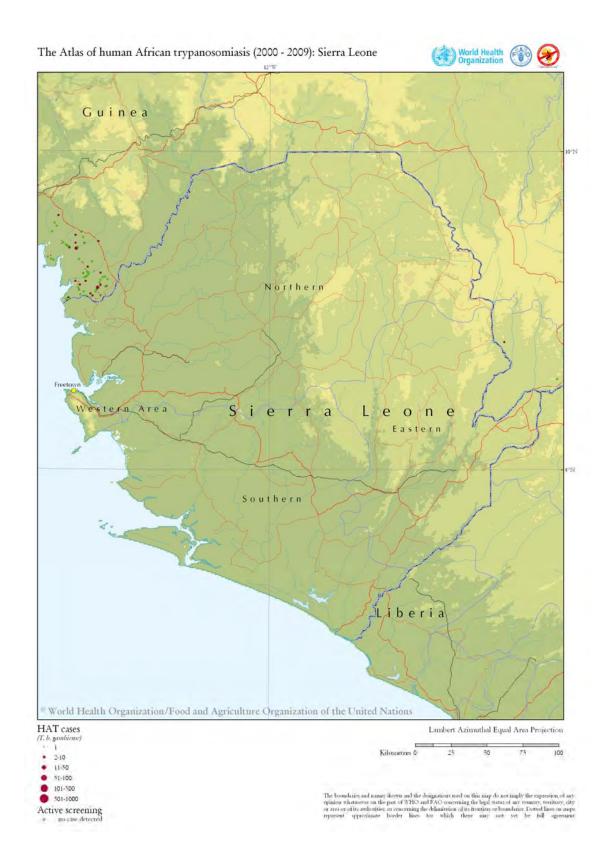


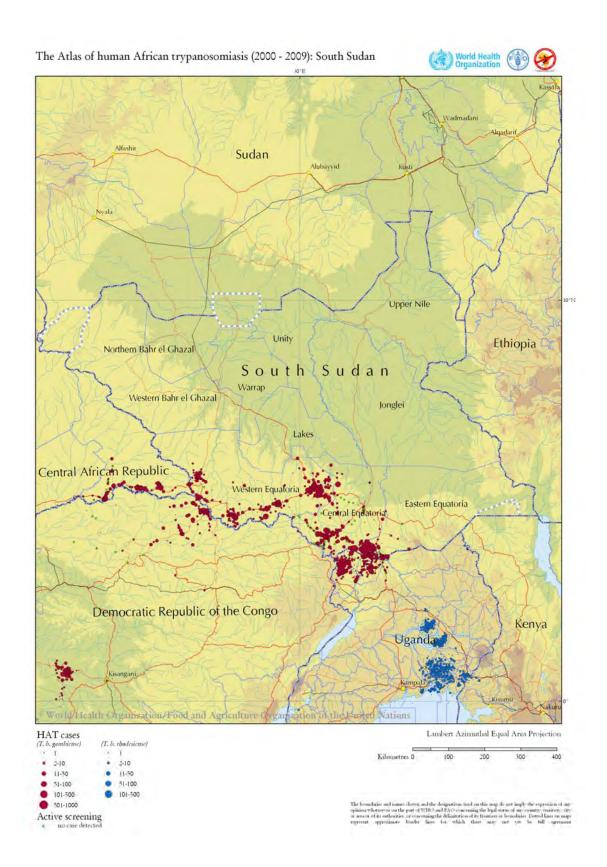


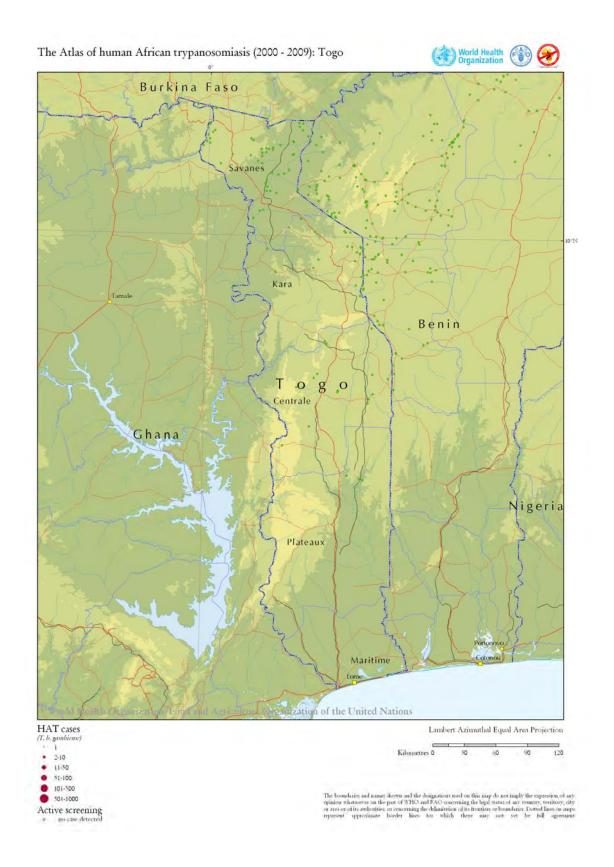


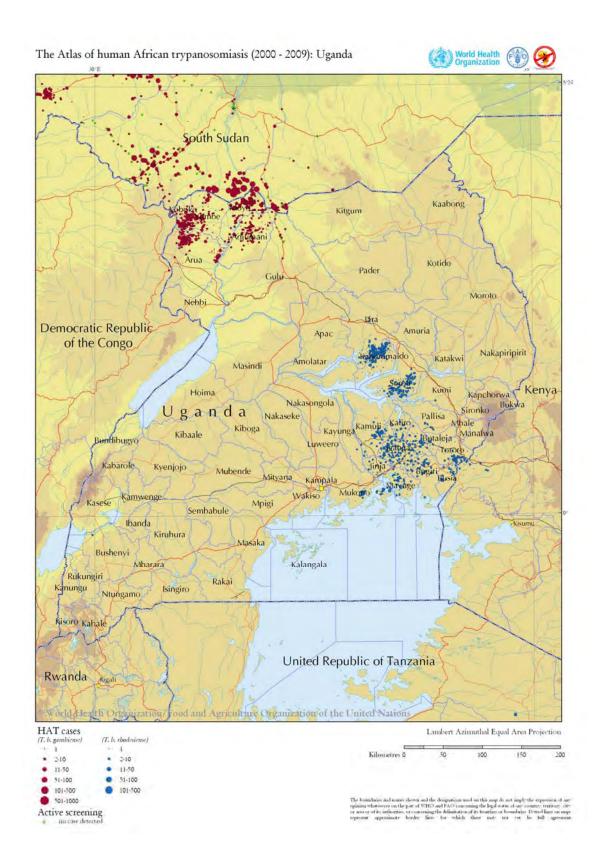




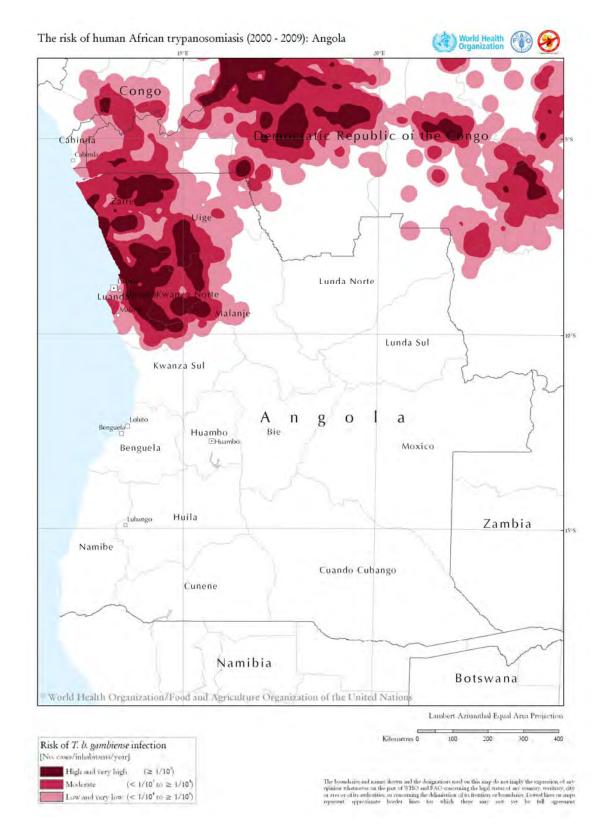


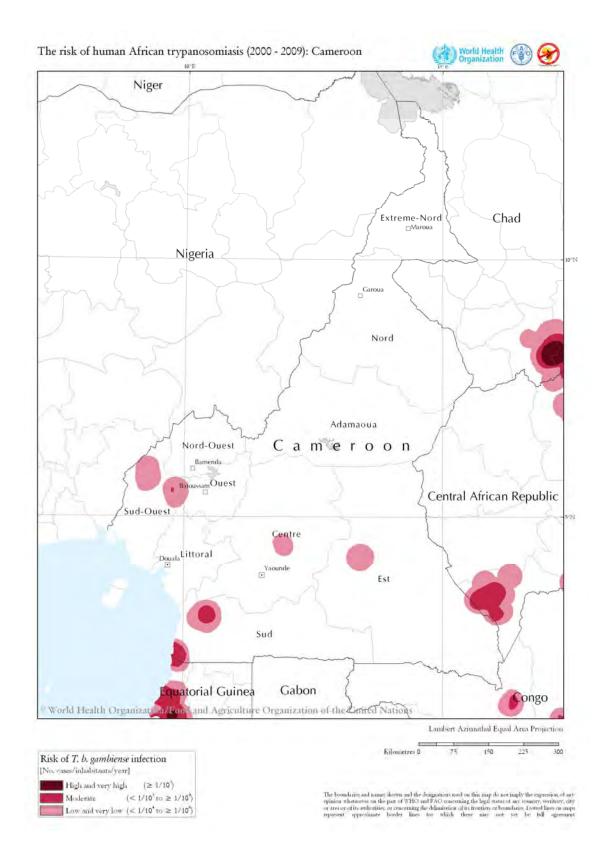


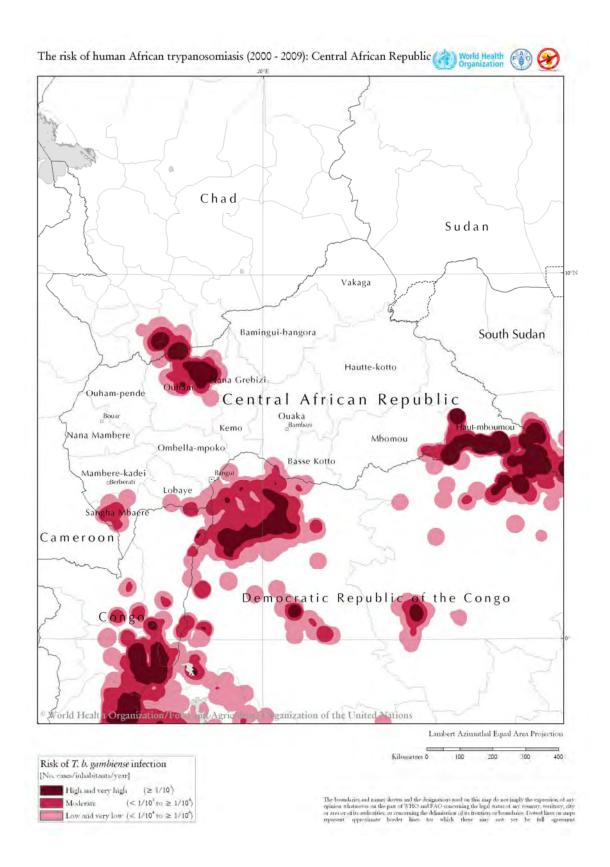




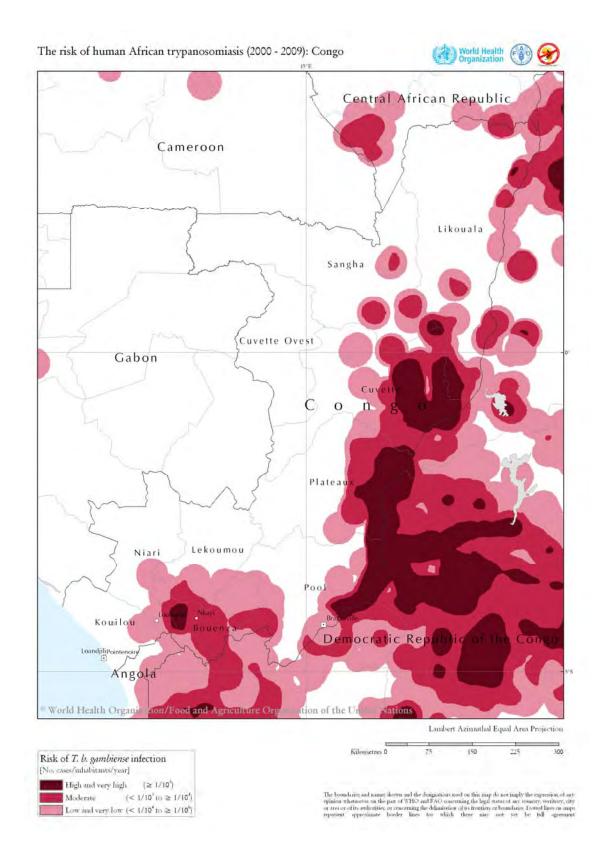
Annex 3: Maps of distribution of populations at risk

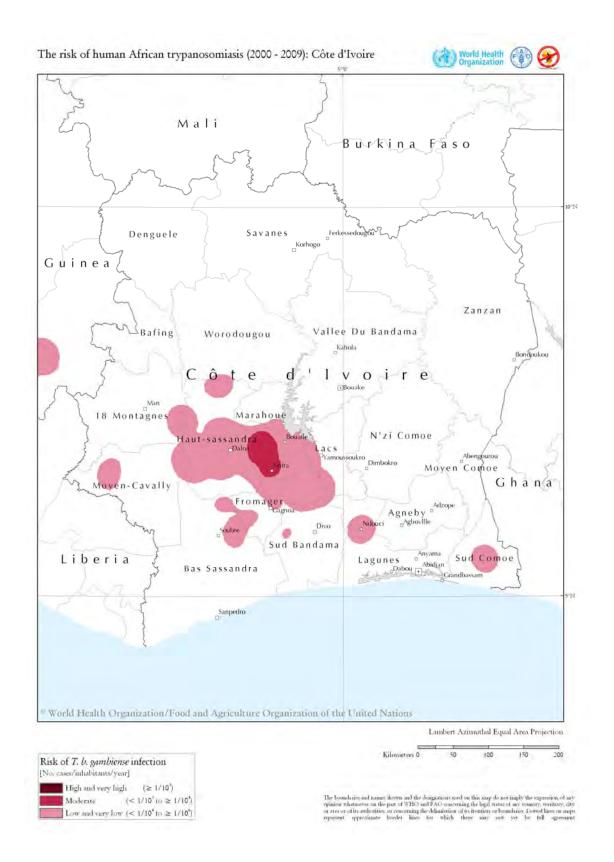


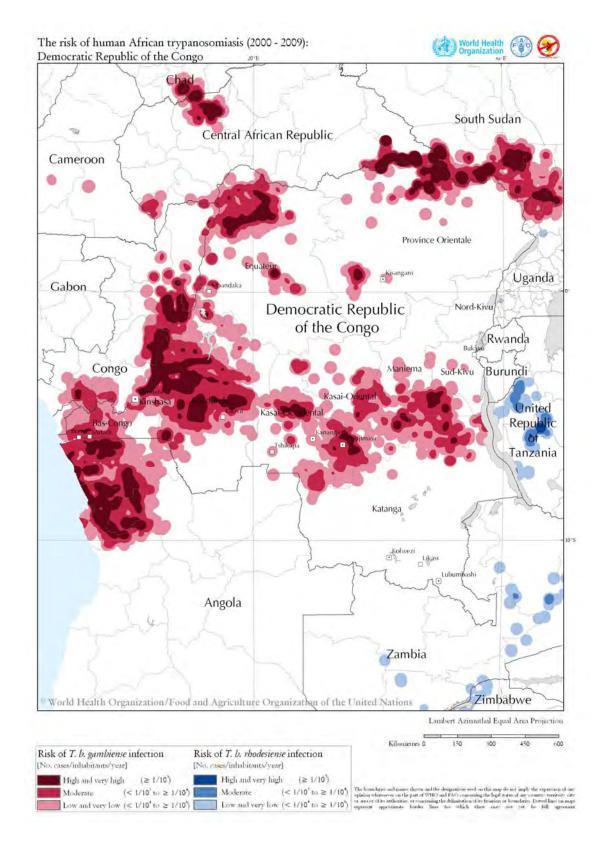


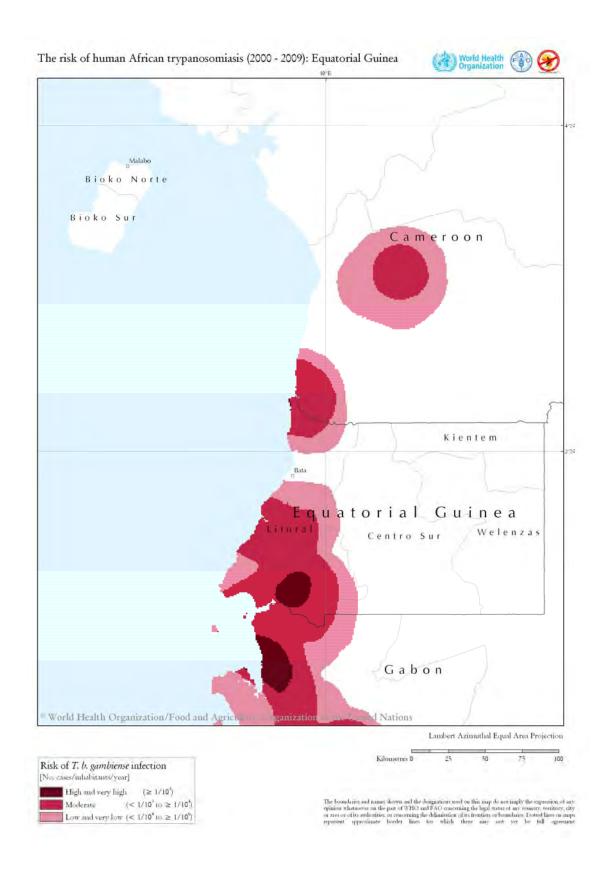


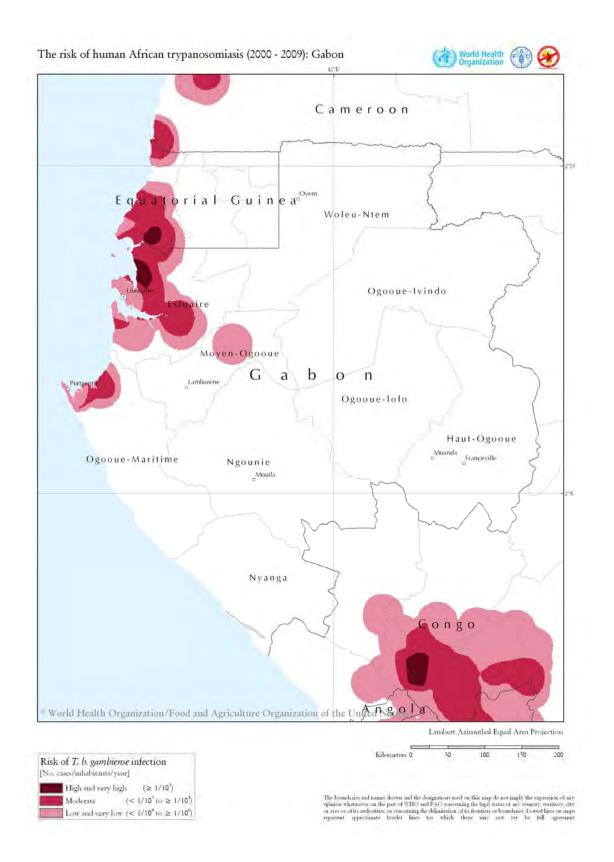


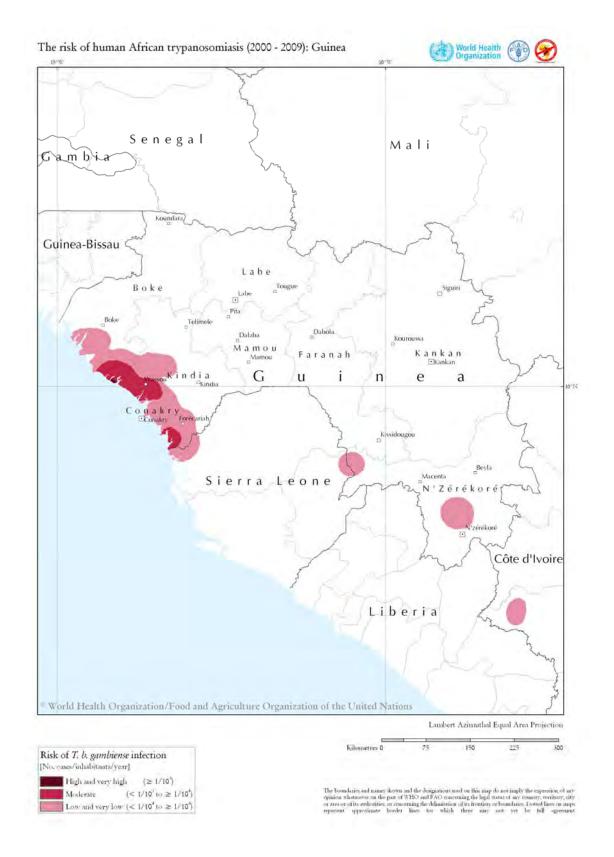


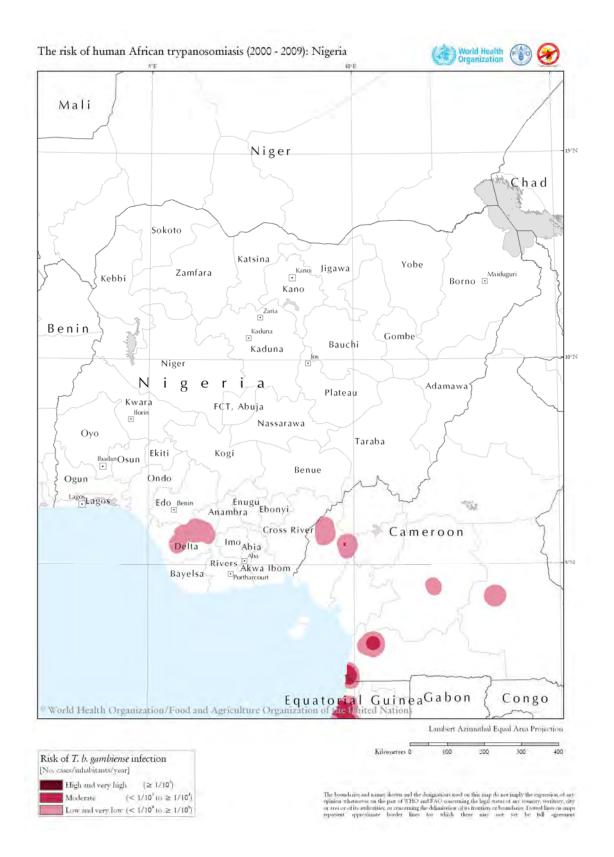


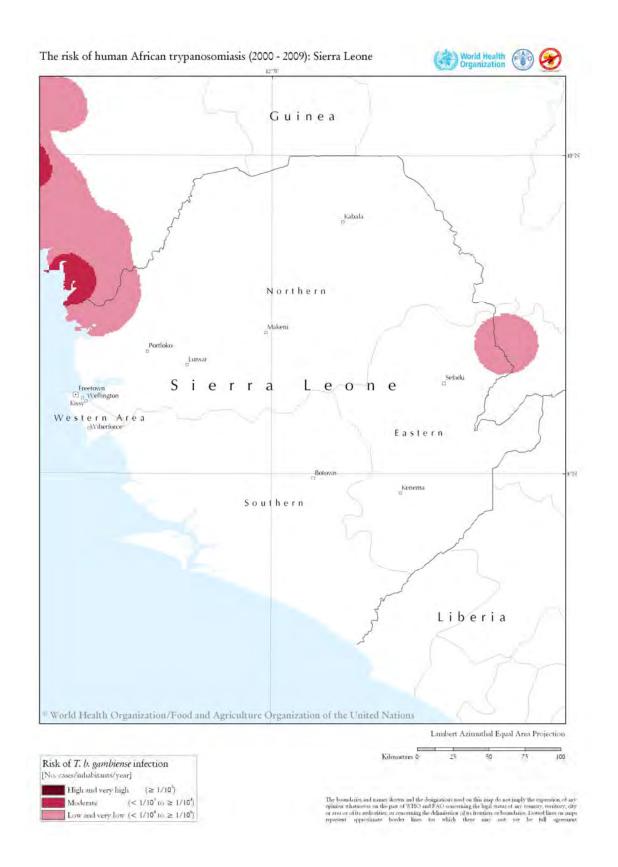


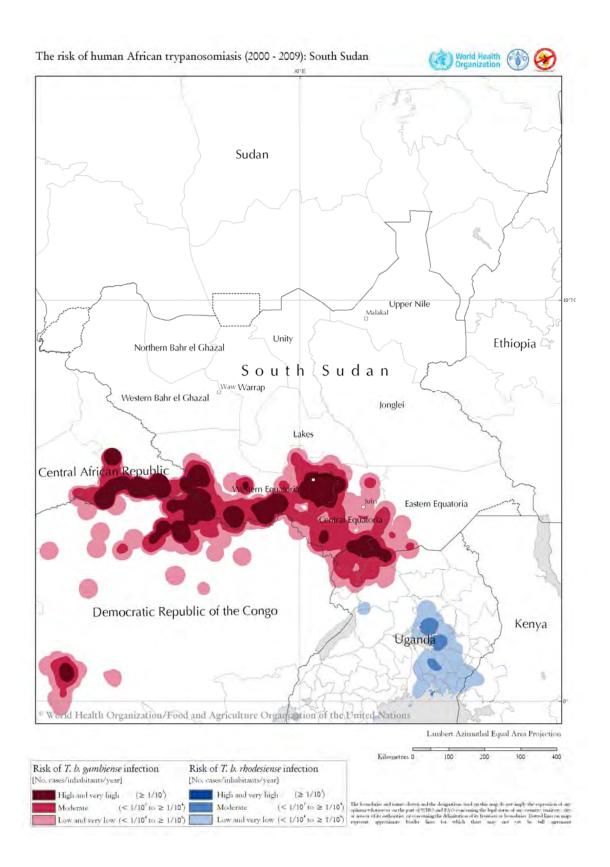


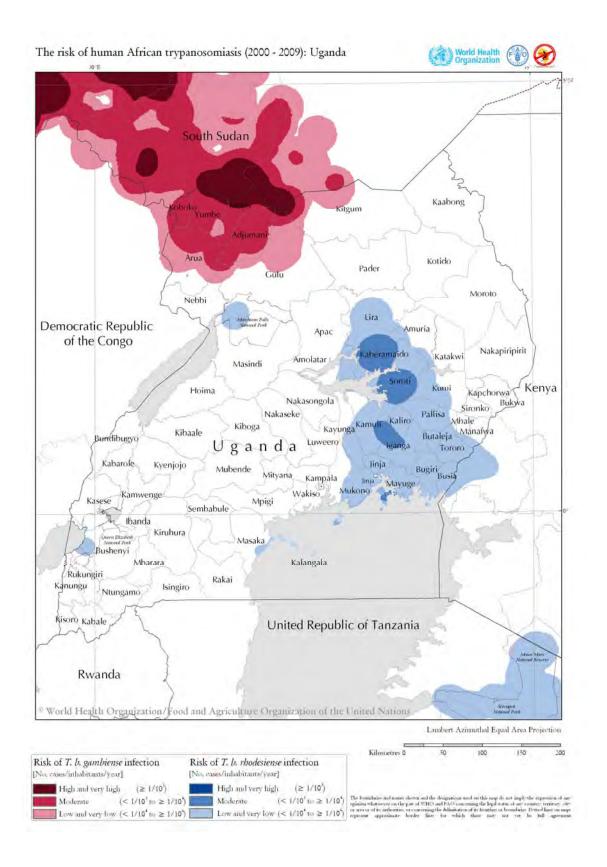












AGENDA

Time	Subject	Presenter
Monday 03 December 2012		
08:30-08:45	Arrival and registration	
08:45-09:30	Welcome and introduction	Dr Savioli (WHO)
	Presentation of the meeting	Dr Jannin (WHO)
09:30–10:30	Current epidemiological status of HAT: disease distribution and population at risk	Dr Franco (WHO)
10:30-11:00	Coffee break	
11:00–12:30	Country reports	Focal point of each country
	Burkina Faso Mali Côte d'Ivoire Guinea Nigeria	
12:30–14:00	Lunch	
14:00–16:00	Country reports (continued) Chad Central African Republic Cameroon Equatorial Guinea Gabon Congo Angola	Focal point of each country
16 :00–16:30	Coffee break	
16:30–17:30	Country reports (continued) South Sudan Uganda Democratic Republic of the Congo	Focal point of each country

Tuesday 4 December 2012			
08:30-09:15	Disease elimination Recommendations on NTD elimination of the WHO Strategic and Technical Advisory Group for NTDs (STAG)	Professor Holmes (STAG)	
	HAT elimination concept and key issues	Dr Moore (CDC)	
09:15–10:15	Ongoing experiences on disease elimination - Lymphatic filariasis: lessons learnt - Onchocerciasis: lessons learnt	Dr Ichimori (WHO) Dr Ukety (WHO)	
10:15–10:45	Coffee break		
10:45–11:15	Strategies for elimination Control and elimination strategies according to epidemiological settings	Dr Simarro (WHO)	
11:15–12:00	Surveillance in areas of "0" prevalence: experiences in Benin and Togo	Dr Batcho (Benin) Dr Badziklou (Togo)	
12:00–12:30	Assessment of zones at risk (IVR approach): experience in Guinea and Côte d'Ivoire	Dr Jamonneau (IRD)	
12:30–14:00	Lunch		
14:00–14:45	Tools for elimination: screening and diagnosis		
	New diagnostic tools useful at the field level: individual serological+ tests, molecular tests	Professor Buscher (ITM)	
	Referral of samples to specialized laboratory; role of reference centres for further tests; trypanolysis	Dr Jamonneau (IRD)	
14:45–15:15	Tools for elimination: treatment		
	New tools for treatment	Dr Diarra (WHO)	
15:15– 15:45	Tools for elimination: epidemiology Atlas of HAT/estimating population at risk	Dr Cecchi (FAO)	
15:45–16:15	Coffee break		
16:15-16 :45	Tools for elimination: vector control		
	Improved targets in HAT control: role of vector monitoring as indicator in the elimination process	Professor Torr (University of Greenwich)	
16:45–17:30	Question marks in elimination		
	Human reservoir: healthy carriers/aparasitemic seropositives	Dr Jamonneau (IRD)	
	Animal reservoir: role of animal infection in the absence of human infection in disease transmission		

Wednesday 5 December 2012			
08:30-09:45	Summary of previous day	Dr Ruiz-Postigo (WHO)	
09:45–10:15	Coffee break		
10:15–12:30	Definition/indicators and milestones for HAT elimination and validation; monitoring and evaluation	Chairperson/WHO	
12:30–13:30	Lunch		
13:30–15:30	Conclusions	General discussion	
15:30–16:00	Coffee break		
16:00–17:00	Meeting closure and next steps		

Annex 5: List of participants

LIST OF PARTICIPANTS

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