



DEFINING CRITERIA TO DECLARE ELIMINATION OF LEPROSY

Report of an informal consultation



Mexico City, Mexico, 10-12 February 2020

Contents

Ab	brevia	tions	4
1.	Inau	gural session	5
	1.1.	Introductory messages	5
	1.2.	Statement by partners	5
	1.3.	Introduction of participants	6
	1.4.	Objectives and expected outcomes	6
2.	Ove	rview of leprosy control	7
	2.1.	Current global leprosy situation	7
	2.2.	History of leprosy control	8
3.	Elim	ination of leprosy as a public health problem	8
	3.1.	Generic framework for control, elimination and eradication of NTDs	8
	3.2.	World Health Assembly resolutions, definition of leprosy as a public health problem	
		and global progress	10
	3.3.	From control to elimination as a public health problem: experience from Mexico	11
	3.4.	Validation of elimination as a public health problem: example of other diseases	12
	3.5.	Validation of elimination of leprosy as a public health problem: outcome of a	
		consultation in the Region of the Americas	13
	3.6.	Group work: elimination of leprosy as a public health problem	14
4.	From	n elimination as a public health problem to interruption of transmission	15
4.	Fro r 4.1.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030	<mark>15</mark> 15
4.	From 4.1. 4.2.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy	 15 15 15
4.	From 4.1. 4.2. 4.3.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease	15 15 15 17
4.	From 4.1. 4.2. 4.3. 4.4.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission	15 15 15 17 17
4.	From 4.1. 4.2. 4.3. 4.4. 4.5.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively	15 15 17 17 17 20
4.	Fron 4.1. 4.2. 4.3. 4.4. 4.5. 4.6.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends	15 15 17 17 17 20 21
4.	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases	15 15 17 17 20 21 21
4.	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases – "Elimination dossier"	15 15 17 17 20 21 21 21
4.	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases Verification of elimination for other diseases – "Elimination dossier" Further research needs	15 15 17 17 20 21 21 21 23
4.	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Othe	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases Verification of elimination for other diseases – "Elimination dossier" Further research needs	15 15 17 17 20 21 21 21 23
4 . 5 .	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Other 5.1.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases Verification of elimination for other diseases – "Elimination dossier" Further research needs	15 15 17 20 21 21 21 23 23 24 24
4.	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Othe 5.1. 5.2.	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases. Verification of elimination for other diseases – "Elimination dossier" Further research needs Lucio phenomenon Global Partnership for Zero Leprosy	15 15 17 20 21 21 21 23 24 24
 4. 5. 6. 	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Other 5.1. 5.2. Cone	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030 Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases Verification of elimination for other diseases – "Elimination dossier" Further research needs Lucio phenomenon Global Partnership for Zero Leprosy	15 15 17 20 21 21 21 23 24 24 24 24
 4. 5. 6. 7. 	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Other 5.1. 5.2. Concerner	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030. Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively. Modelling to predict future trends. Elimination criteria for other diseases. Verification of elimination for other diseases – "Elimination dossier" Further research needs Lucio phenomenon. Global Partnership for Zero Leprosy erences	15 15 17 20 21 21 21 23 24 24 24 24 24 24
4. 5. 6. 7. An	From 4.1. 4.2. 4.3. 4.4. 4.5. 4.6. 4.7. 4.8. 4.9. Othe 5.1. 5.2. Conce Refe	n elimination as a public health problem to interruption of transmission NTD Roadmap 2021–2030. Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy Conceptual framework: interruption of transmission and elimination of disease Possible strategies to achieve interruption of transmission Defining interruption of transmission retro-actively Modelling to predict future trends Elimination criteria for other diseases Verification of elimination for other diseases – "Elimination dossier" Further research needs Lucio phenomenon Global Partnership for Zero Leprosy clusions and recommendations rences : List of participants.	15 15 17 20 21 21 21 21 23 24 24 24 24 24 24 24 24 24 24

Abbreviations

BCG	bacille Calmette-Guérin
G2D	grade-2 disability
GPZL	Global Partnership for Zero Leprosy
HAT	human African trypanosomiasis
ILEP	International Federation of Anti-Leprosy Associations
LEM	leprosy elimination monitoring
MB	multi-bacillary
MDA	mass drug administration
MDT	multidrug therapy
MIP	Mycobacterium indicum pranii
NTD	neglected tropical disease
РАНО	Pan-American Health Organization
PEP	post-exposure prophylaxis
SDG	sustainable development goal
SHF	Sasakawa Health Foundation
TAS	transmission assessment survey
Π	trachomatous trichiasis
WHA	World Health Assembly
WHO	World Health Organization

1. Inaugural session

1.1. Introductory messages

Mr Cristian Morales, Pan-American Health Organization (PAHO)/World Health Organization (WHO) Representative to Mexico formally opened the Informal consultation on defining criteria to declare elimination of leprosy.

On behalf of the host country, Dr Ruy López-Ridaura, Director-General of the Disease Control and Prevention Centre, Ministry of Health, welcomed all participants to Mexico. In his opening remarks he highlighted the achievements of Mexico's leprosy control programme. Leprosy was once a very prevalent disease, but new cases have become rather rare and are increasingly confined to fewer geographic areas.

1.2. Statement by partners

Ms Arielle Cavaliero, Global Franchise Lead (Leprosy) of Novartis International AG, reiterated the long-time commitment of Novartis, donating medicines for multidrug therapy (MDT) since 2001. She also mentioned that since 1 May 2019, all activities of the leprosy portfolio (apart from digital health) of the Novartis Foundation are now being coordinated by Novartis. She further summarized that the Leprosy Post-Exposure Prevention programme, funded by the Novartis Foundation, has created a shift in thinking about preventing leprosy beyond treating persons with the disease. As a founding member of the Global Partnership for Zero Leprosy (GPZL), the Novartis Foundation (and now Novartis) emphasizes the need for partners to work in a collective spirit.

Ms Courtenay Dusenbury, Director of the GPZL Secretariat, stated that GPZL is keen to support a joint strategy for zero leprosy, by working together with endemic countries to build national capacity and contributing to broadening the financial resource base for leprosy control. A proposal for US\$ 100 million was thereto submitted to the McArthur Foundation and passed already the first iteration. This event already triggers interest from other financial partners.

Mr Geoff Warne, Chief Executive Officer of the International Federation of Anti-Leprosy Associations (ILEP) summarized the work undertaken by the 14 members of ILEP in 60 countries, both high and low burden countries. ILEP is also a founding member of GPZL, subscribing to its ultimate goal of a world free of leprosy, which includes zero new disease but also zero disability due to leprosy and zero stigma and discrimination.

Ms Aya Tobiki, Programme Officer of the Sasakawa Health Foundation (SHF), conveyed a congratulatory message on behalf of both The Nippon Foundation and SHF to WHO and partners for supporting leprosy control and having demonstrated impact in countries. Leprosy is increasingly confined to pockets. Following the achievement of elimination as a public health problem, interruption of transmission is an ambitious new goal. She also conveyed the regards of Mr Yohei Sasakawa, WHO Goodwill Ambassador for Leprosy Elimination, who is showing keen interest in these new developments.

1.3. Introduction of participants

All participants introduced themselves. The list of participants is provided in Annex 1.

1.4. Objectives and expected outcomes

Dr Erwin Cooreman, Team Leader, WHO Global Leprosy Programme, highlighted the objectives of the informal consultation.

The general objectives were:

- To discuss and review the current context, criteria and procedures for validation of elimination of leprosy as a public health problem;
- To discuss, analyze and propose the criteria and procedures for verification of interruption of transmission/elimination of disease.

The specific objectives were:

- Elimination of leprosy as a public health problem:
 - To define the criteria and procedures to validate elimination of leprosy as a public health problem in countries not yet having achieved this goal or in countries eager to properly document it;
- > Determine the intermediate steps:
 - To analyze, define and discuss the steps, benefits and challenges of moving from elimination as a public health problem to interruption of transmission/elimination of disease;
- Interruption of transmission/elimination of disease:
 - To establish the conceptual framework needed to understand the basis for interruption of transmission;
 - To identify the (most likely) main strategies to achieve interruption of transmission;
 - To determine criteria for elimination of leprosy;
 - To propose a mechanism to verify the elimination of transmission in time and territory;
 - To explore surveillance and prevention actions for the post-elimination period;
 - To develop a draft protocol and guidelines for piloting.

The programme of the informal consultation is included in Annex 2.

2. Overview of leprosy control

2.1. Current global leprosy situation

Leprosy is one of the neglected tropical diseases (NTDs) with one of the highest record of cases annually when compared to other case management NTDs (e.g. dracunculiasis, Buruli ulcer, human African trypanosomiasis (HAT), visceral leishmaniasis or yaws; only Chagas' Disease reports a higher incidence).

Worldwide, 208 641 new cases were reported for 2018. Most cases occur in only three countries: India, Brazil and Indonesia while another 12 countries reported each more than 1000 cases. The overall trend is a steady decline in new cases, especially in the WHO South-East Asia Region. The decline is however off set by active case detection and a more complete reporting in other regions.

Detailed information was also provided, by WHO region, on the following indicators: prevalence (rate); proportions of multi-bacillary (MB) cases; female cases; children and patients with visible deformities at the time of diagnosis (grade-2 disability or G2D). The last indicator is showing a steady decline (1.5 per million population in 2018). Zero leprosy in children is another key indicator of the Global Leprosy Strategy. Table 1 highlights the achievements versus this indicator.

Parameter	Number of countries
Countries reporting zero new leprosy case [A]	32
Countries reporting at least one new case [B]	129
Countries reporting leprosy data [C]={A]+[B]	161
Countries reporting zero leprosy in children [D]	40
Countries reporting at least one leprosy child case [E]	81
Countries with leprosy reporting child data [F]=[D]+[E]	121
Countries reporting zero G2D in children (including [A]) [G]	37
Countries reporting at least one child case with G2D [H]	33
Countries reporting on the status of G2D in children $[I]=(g]+[H]$	70

Table 1: Genera	l aspects of leprosy	notification	for 2018
-----------------	----------------------	--------------	----------

Leprosy among foreign-born was a new indicator, collected since the last three years. This indicator provides proxy information on imported disease. An outlier is Nepal which reported 784 foreignborn cases, virtually all of them cross-border patients residing in a neighbouring country. More than 25 such cases were reported by Malaysia, Thailand and Argentina; while small absolute numbers were reported from high income countries (with very high proportions, up to 100%), reflecting likely import cases; as well as from endemic countries (with lower proportions).

He also provided information on the status of discriminatory laws since annulling such laws is also one of the key targets of the Global Leprosy Strategy. Still 21 countries reported having such laws, though they are not necessarily applied. In addition, there are customary (non-codified) laws and practices as well as societal attitudes that continue the discrimination of persons because of having or having had leprosy.

2.2. History of leprosy control

Dr Erwin Cooreman made this presentation on behalf of Dr Vijay Kumar Pannikar, Chair of the WHO Technical and Advisory Group for Leprosy.

The history of leprosy control is linked to many mistakes as well as great advances. Different strategies have been designed for its control, including isolation and various treatments.

In the absence of medical knowledge about the disease and medication to prevent or cure it, ancient communities chose isolation of those affected as the best strategy for control. Many of these practices are now considered as inhumane (e.g. compulsory separation from family, travel ban).

Early treatment – practiced in the middle ages – included drinking blood, snake venom, scorpions, various ointments. In the 19th century chaulmoogra, an oil obtained from *Hydnocarpus wightianus* tree seeds, was used with very limited success. Its application was improved (known as "Ball method") and formed the mainstay of treatment till the advent of antibiotics.

The discovery of the causative agent of leprosy in 1873 gave the basis for a modern treatment. In the 1940s sulphones introduced the antibiotic era, allowing domiciliary treatment (instead of in leprosaria) and in the 1950s it was aspired to gain control of leprosy with dapsone and other interventions, paving the way for leprosy control programmes. However, within less than ten years after introducing dapsone monotherapy, resistance was recognized and increased to more than 50% in the 1970s, rendering control programmes very ineffective.

In the 1980s, MDT became the cornerstone of leprosy treatment and has continued to be so since then. Due to its limitation in time, patients could be declared "cured" and return to normal life. Since its introduction, more than 17 million patients have been cured. Donation of MDT free-of-charge has proven to be a game-changer in leprosy control, prompting the World Health Assembly (WHA) to pass a resolution in 1991 to eliminate leprosy as a public health problem, defined as less than one case per 10 000 population on treatment. The registered leprosy prevalence decreased indeed from over 5 million to less than 200 000.

It is, however, now clear that MDT has reached its maximum potential and that it has now a much lesser impact on further reducing the incidence. The end game in leprosy will necessitate the introduction of prophylactic tools, of which chemoprophylaxis with single-dose rifampin is currently recommended by WHO. With regard to immunoprophylaxis, only vaccination with *bacille Calmette-Guérin* (BCG) has shown some protection against leprosy while two other vaccines (*Mycobacterium indicum pranii* or MIP and LepVax) are currently being tested.

3. Elimination of leprosy as a public health problem

3.1. Generic framework for control, elimination and eradication of NTDs

The concepts of "control", "elimination as a public health problem", "elimination", "eradication" and "extinction" were introduced by Dr Albis Gabrielli, Medical Officer, Department of Control of NTDs, WHO HQ. Definitions refer to WHO's publication entitled "Generic framework for control,

elimination and eradication of NTDs", published in 2016, and following adaptations included in disease-specific normative guidance (Table 2).

Concept	Acknowledgement process	Public health implications	Targeted NTDs (by 2030)	Risks
Control	None	Reduction of morbidity	Buruli ulcer chikungunya cutaneous leishmaniasis dengue echinococcosis food-borne trematodiases mycetoma, chromoblastomycosis and other deep mycoses scabies and other ectoparasitoses snakebite envenoming taeniasis/cysticercosis	Increased morbidity and/or mortality
Elimination as a public health problem	Validation	Elimination of morbidity and/or reduction of transmission	Chagas disease HAT-rhodesiense lymphatic filariasis rabies schistosomiasis soil-transmitted helminthiases trachoma visceral leishmaniasis	Reintroduction, recrudescence
Elimination	Verification	Interruption of transmission at the national level	HAT-gambiense leprosy onchocerciasis	Reintroduction
Eradication	Certification	Global transmission disruption	dracunculiasis yaws	Reintroduction
Extinction		Complete eradication of a pathogen in nature and in the laboratory		Possibly none

Table 2: Summary of definitions of control, elimination and eradication

The NTD Road map 2012–2020 listed diseases targeted for eradication, elimination, elimination as a public health problem and control. The list has been updated in the draft NTD Road map 2021–2030. Targets envisaged in this new Road map are listed in Table 2.

WHO has set up acknowledgment processes to validate, verify or certify the achievement of set targets by an applicant country. Global processes currently established include those for certification of eradication of dracunculiasis and yaws, verification of elimination of onchocerciasis, validation of elimination of lymphatic filariasis, trachoma, visceral leishmaniasis and rabies as a public health problem; while others are being developed.

It is general practice that only endemic countries that have implemented disease control interventions and successfully achieved a set target can request WHO to acknowledge such achievement; only in case of diseases targeted for eradication, non-endemic countries are also

subject to the certification process. The processes of certification and verification are typically coordinated at HQ level, while validation is done at Regional level. Three key steps are required for a country to go through the acknowledgment process: (i) the development of a dossier (including all evidence supporting the country's claim); (ii) the establishment of a reviewing authority (usually a group of expert), tasked with confirming or rejecting the country's claim; and (iii) the official acknowledgment of the achievement by WHO's Director-General, based on the reviewing authority's advice.

Post-acknowledgment surveillance is required to mitigate the risks inherent in the targets, including the risk of reintroduction of transmission in certified and verified countries; and risk of recrudescence in validated countries. Although it is generally understood that the monitoring & evaluation system in place during the transmission phase should continue after acknowledgment, disease-specific protocols have not yet been developed.

The participants emphasized during the discussion the specificities linked to leprosy epidemiology; notably the fact that because of the long incubation period, interruption of transmission may be achieved years before occurrence of the last incident case.

3.2. World Health Assembly resolutions, definition of leprosy as a public health problem and global progress

Through Resolution WHA44.9 of the Forty-fourth WHA session in May 1991, it was indicated that, with less than one case per 10 000 inhabitants on treatment, the goal of eliminating leprosy as a public health problem would be achieved. This indicator is based on the registered prevalence (typically at the end of the calendar year) and is not applicable to jurisdictions with a population of less than 1 million. It is much influenced by operational factors such as programme coverage, duration of treatment and data quality; and to a lesser extent by disease incidence. As the indicator is defined, no formal validation mechanism has been instituted as it is a simple mathematical exercise to confirm.

Table 3 provides an overview of the different WHA resolutions related to leprosy and their key provisions.

Resolution	Year	Key provision	
WHA2.43	1949	Establishment of a committee of experts	
		Provision for the supply of sulphones and other drugs for control trials	
WHA5.28	1952	Encourage active control programmes	
WHA6.19	1953	Specifications for biopsy sample collection	
WHA9.45	1956	Study the feasibility of holding a conference on leprosy control in 1958	
WHA5.27.58	1954	Strengthen leprosy control measures by using all available sources of cooperation	
WHA28.56	1975	Intensive case detection	
		Supervised treatment for infectious cases	
		Integrate leprosy in health services	

Table 3: WHA resolutions on leprosy

Resolution	Year	Key provision
WHA29.70	1976	Support to the countries most affected for the development of leprosy programmes Provide assistance in drug supply and rehabilitation Stress importance of psycho-social factors
WHA5.32.39	1979	Progressive integration of patients from isolation into the society Contribute to "Health for All"
WHA40.35	1987	Calls for adequate resources for control of leprosy as part of primary health care Strengthen health education to overcome stigma Promote partnerships
WHA44.9	1991	Elimination of leprosy as a public health problem by the year 2000.
WHA51.15	1998	Intensify efforts to reach all cases through national elimination campaigns and making MDT available at all peripheral health centres

Elimination as a public health problem, as defined above, has been claimed by all countries except Brazil. While it was earlier achieved in Nepal, the country jumped above the threshold at the end of 2018, likely as a result of active case detection campaign rather than a true increase in incidence.

3.3. From control to elimination as a public health problem: experience from Mexico

Dr Fátima Leticia Luna López, Director Mycobacterial Diseases, Ministry of Health, Mexico presented the experience of Mexico in controlling leprosy.

As a result of introducing MDT, the registered prevalence was reduced by over 97%. Leprosy is now mainly confined to some municipalities in nine states along the Pacific Ocean and Gulf of Mexico.

Mexico recorded 352 cases on treatment at the end of 2019. This corresponds to a national prevalence rate of 0.03 per 10 000 population which is much below the benchmark for elimination as a public health problem. During the same year 163 new cases were notified. Of them 74% were classified as MB, 14 (8.6%) cases presented with G2D, which corresponds to a G2D rate of 0.1 per million population (thus much below the global target for G2D defined as less than one per million population). Children constituted 4.9% of all new cases. This is consistent with the progressive decrease in childhood leprosy cases notified in recent years.

With regard to Leprosy Elimination Monitoring (LEM), Mexico has carried out this activity in 13 states with the use of a guide adapted by the country. The country has observed benefits after having carried out the different LEMs in some of the country's entities by finding opportunities to improve the care of patients with leprosy and generating greater political and strategic commitment from the different states.

A minimum level of capacity is retained, including involvement of designated dermatologists, basic training of frontline health workers, surveillance, contact tracing, MDT management,

chemoprophylaxis and supervision. Time-place analysis is undertaken showing the shifts towards hot spots, with increasingly larger areas of the country becoming leprosy free.

3.4. Validation of elimination as a public health problem: example of other diseases

This topic was introduced by Dr Santiago Nicholls, highlighting the processes followed for lymphatic filariasis and trachoma.

Lymphatic filariasis

The country requesting such validation must meet criteria such as: (i) stopping the transmission of the parasite through mass drug administration (MDA) with all endemic areas passing a final Transmission Assessment Survey (TAS) completed at least four years after the last MDA round; and (ii) alleviation of suffering through managing morbidity and preventing disability; this implies having a minimum package of care in all areas with known patients.

A dossier is prepared by the country and submitted to WHO, following which a regional ad-hoc dossier review group will be established to validate the claim (or postpone till more evidence is provided). If validated, a letter from the WHO Director-General officially acknowledging the achievement is sent to the Minister for Health of the requesting country.

The minimum information in the dossier encompasses: (i) how endemic and non-endemic areas were classified; (ii) implemented interventions with supporting process and monitoring data; (iii) results from TASs (TAS 1 to 3) from endemic areas; (iv) reported number of patients with lymphoedema and (in case of *Wuchereria bancrofti*) hydrocele; and (v) data indicating availability and provision of basic package of care to manage patients with chronic morbidity (including lymphoedema or hydrocele).

Trachoma

Elimination of trachoma as a public health problem is defined as: (i) a prevalence of trachomatous trichiasis (TT) "unknown to the health system" of <1 case per 1000 (total) population; and (ii) a prevalence of trachomatous inflammation-follicular in children (aged 1–9 years) of <5%, in each formerly endemic district. There must also be evidence that the health system is able to identify and manage incident TT cases, using defined strategies, with evidence of appropriate financial resources to implement those strategies.

Once the country considers it has met the criteria for the validation, it must submit a formal request through the WHO Regional Office, accompanied by a dossier with all the necessary evidence. Member States may request assistance from WHO to support the preparation of the dossier. A Regional Ad-hoc Dossier Review Group will be established. The Group's task is to evaluate the evidence of elimination as a public health problem and recommend to WHO to validate the claim or to postpone the validation until more evidence is provided. If the achievement is validated, a letter from the WHO Director-General officially acknowledging this is sent to the Minister for Health of the requesting country.

Validation is a reversible state, and all stakeholders should bear this in mind in their communication at all stages. Countries should continue to conduct post-validation surveillance. A commitment to continue surveillance should be stated in the dossier. Surveillance data should be reported to WHO.

3.5. Validation of elimination of leprosy as a public health problem: outcome of a consultation in the Region of the Americas

In addition to the criteria established in the WHA Resolution on elimination of leprosy as a public health problem, a consultation held in the Americas Region on this subject recommended to include reaching the goals established in the Global Leprosy Strategy 2016–2020: Accelerating towards a leprosy free world: (i) zero children diagnosed with leprosy and visible deformities; (ii) rate of newly diagnosed leprosy patients with visible deformities of less than 1 per million; and (iii) absence of legislation allowing discrimination on the basis of leprosy.

Countries must guarantee access to services to manage chronic morbidity and disability in persons affected by leprosy. This includes high quality chronic morbidity and disability prevention and management services to address complications and ensure rehabilitation, including reconstructive surgery. Countries would also have to ensure access for affected persons and their families to psychological support systems, social protection and inclusion measures.

Public health surveillance of leprosy should be strengthened, and strategies implemented to move forward towards the interruption transmission. This includes the documented active search in high-risk groups (contacts) and historically endemic conglomerates, and an intensified post-elimination surveillance and adequate response in case of detecting new cases.

Countries and territories must document their request for validation as a public health problem through a dossier containing the following components:

- ✓ The technical description of the measures that led the country to achieve the goal;
- ✓ The evidence to confirm that the established indicators have been reached;
- A description of how care for chronic morbidity and services for disability management and prevention, rehabilitation and social inclusion will be included within the existing health services and be made available to all the patients who require them;
- ✓ A description of how public health surveillance will be intensified in the post-validation phase.

The process for validation of elimination as a public health problem should be similar to those described above for lymphatic filariasis and trachoma.

3.6. Group work: elimination of leprosy as a public health problem

Two groups discussed the merits of defining criteria for validating elimination as a public health problem, possible documentation processes, and level of application.

From the onset it was clear that there is no mandate to modify WHA resolutions. As the resolution on elimination of leprosy as a public health problem defines this benchmark as a registered prevalence – as reported by countries – of less than 1 per 10 000, there is no real further need to validate this apart from checking completeness and correctness of reports. The indicator was never intended to be used by countries with a population of less than one million. In the same spirit, it may be applied to endemic sub-national jurisdictions that have a population of more than one million.

The groups recommended to formulate criteria that 'pre-elimination' has been reached, acknowledging achievement, but also pointing to the work that lies ahead to achieve interruption of transmission. This may involve inclusion of other, more stringent impact indicators (e.g. new case detection, G2D rate, child rate). Such indicators still qualify for elimination as a public health problem, though it was agreed to avoid using "validation" in order not to make countries confused or undo their status of having achieved elimination as a public health problem often many years ago. This process would entail ascertaining the work-in-progress towards elimination and would apply to countries, regardless of their stage in the elimination process, that are yet to achieve these benchmarks.

The groups opined the importance of communication. Leprosy elimination activities need to be sustained as a marathon, rather than a sprint. The different stages should be linked to set time frames during which a set of activities need to be followed (e.g. surveillance). The focus should be on where the problem is; national statistics may mask considerable burden at sub-national levels.

Useful additional indicators may include:

- New case detection;
- Children: number of children with G2D, age-specific child rate; leprosy in young children (under 5). Absolute numbers may be more workable than percentages or rates in view of the small numbers.
- Availability and coverage of essential care packages;
- Social integration.
- Qualitative indicators, showing that the programme is performing well:
 - o Surveillance practices (both active and passive screening)
 - Laboratory-verified cases and quality of laboratory (skins smears, pathology);
 - Treatment outcomes (MDT completion rates);
 - Diagnostic and treatment delays;
 - Proportion of new cases in whom disability has been assessed (especially G1D);
 - Mode of detection (active vs passive);
 - Information about secondary cases;
 - o Antimicrobial resistance

The teams expressed caution over the potential dangers of target setting, especially at a subnational level as it may lead to perverse actions, e.g. stopping to look after cases in order to achieve a reduction in new cases.

4. From elimination as a public health problem to interruption of transmission

4.1. NTD Roadmap 2021–2030

The current NTD Roadmap (2012–2020) will be concluded at the end of 2020. WHO has therefore started working towards the development of a new Roadmap covering the period 2021 to 2030. This Roadmap is a high-level strategic document, an aid to policy and advocacy efforts and a tool that aims at aligning efforts across all stakeholders. It is being developed through a wide consultative approach, includes specific and measurable targets, and has a focus on cross-cutting approaches.

The Roadmap encourages and accompanies three key shifts: (i) from process to impact (i.e. from action taken to measurable improvements in health status); (ii) from vertical, disease-specific programmes to holistic, cross-cutting approaches; and (iii) from agendas shaped by partners and donors to a stronger country ownership and financing.

The life of the Roadmap will come to an end in 2030, together with the Sustainable Development Goals (SDGs). In fact, its entire content is shaped by the SDGs: this is clearly visible from the targets and indicators that constitute its monitoring and evaluation framework. Three sets of targets have been envisaged: overarching targets, reflecting SDG3 – Ensure healthy lives and promote well-being for all at all ages – and its high-level guidance; cross-cutting targets, reflecting the Roadmap's drive for integration and inter-sectoral approaches; and disease-specific targets, reflecting the technical expertise of the different constituencies that form the NTD galaxy. All targets will be assessed in 2023, 2025 and finally in 2030, against 2020 baselines values.

The Roadmap classifies each NTD as targeted for eradication, elimination (interruption of transmission), elimination as a public health problem or control. Leprosy is included in the diseases targeted for elimination, and it is envisaged that by 2030, 120 countries will have achieved this goal, i.e. they will no longer be reporting autochthonous cases.

4.2. Leprosy profile in NTD Roadmap 2021–2030 and post-2020 Global Leprosy Strategy

Dr Erwin Cooreman elaborated the leprosy profile annexed in the NTD Roadmap 2021–2030. The leprosy burden is determined mainly by three factors: (i) annual number of new cases; (iii) estimated number of persons living with (lifelong) disabilities due to leprosy: (iii) estimated population-at-risk that can be targeted with chemoprophylaxis.

Though leprosy is classified as a case management NTD, several of its interventions fit under other strategies, including preventive chemotherapy, water and sanitation or even other (such as the interventions to address stigma and discrimination or need for counseling and health education).

Table 4 shows the proposed 2030 targets and earlier milestones.

Indicator		Target		
Indicator	2020	2023	2025	2030
Annual number of new leprosy cases detected	184,000	148,000	123,500	62,500
Rate (per million pop.) of new cases with G2D	1.3	0.92	0.68	0.12
Rate (per million children) of new leprosy cases in children	7.81	5.66	4.24	0.77

Table 4: Global milestones and targets, leprosy, NTD Roadmap 2021–2030

Critical actions to be taken include:

- ✓ Update country guidelines to include post-exposure prophylaxis (PEP) for contacts and actively implement; advance research on new preventative approaches;
- ✓ Continue investments into research for diagnostics for disease and infection;
- ✓ Develop surveillance strategies, systems and guidelines to enable case finding and treatment; ensure resources for validation;
- Ensure drug supply including access to MDT, prophylactic drugs, second-line drugs and drugs to treat reactions; monitor adverse events (pharmacovigilance) and resistance;
- Ensure capacity for case finding (screening, diagnosis), treatment, surveillance and case finding; integrate with primary care, skin and other NTDs, tuberculosis and other programmes where appropriate;
- ✓ Combat stigma and discrimination to ensure access to services and inclusion in society; ensure human rights of leprosy affected persons are respected.

While leprosy is well covered in the NTD Roadmap 2021–2030, members of the leprosy community still felt the need to develop a stand-alone Global Leprosy Strategy, to provide increased visibility to leprosy. The work-in-progress on this strategy was presented.

- Long-term vision: zero leprosy
- The primary targets and milestones are identical to those formulated in the NTD Roadmap (Table 4).
- > Four strategic pillars are identified:
 - 1. Country-owned zero leprosy roadmaps in all endemic countries;
 - 2. Scale-up of preventive chemotherapy programmes alongside selected active case detection
 - 3. Prompt treatment with MDT, management of complications and prevention of new disability

4. Combat stigma and discrimination.

4.3. Conceptual framework: interruption of transmission and elimination of disease

Interruption of transmission [of the causative organism] and elimination of disease is not the same. For most other NTDs, interruption of transmission falls under "elimination" and elimination of disease under "elimination as a public health problem"; this is because the term "disease" is usually understood as "morbidity associated with infection" rather than "new incident case of disease". In such model, interruption of transmission is not a prerequisite for eliminating the disease, as transmission may continue at low levels, resulting in infections that may not be associated with morbidity.

The above model is, however, challenged by the peculiar epidemiology of leprosy. This happens because, in view of the very long incubation time of leprosy, new cases will continue to occur for many years (decades) after interruption of transmission has taken place

In the case of leprosy, it is generally said that ~95% of persons presumed to be infected apparently do not develop the disease while preventive interventions, such as PEP can prevent disease in already infected persons (though with an efficacy of less than 100%). A preventive vaccine (BCG or any novel future vaccine) may prevent infection after inhaling the bacilli.

Indicators and criteria to measure what has been termed "interruption of transmission" have been proposed for other NTDs. Such indicators range from incidence reported through surveillance to specific tests carried out during active surveys. In dracunculiasis, it is agreed that this is reached after three consecutive years with zero new cases of emerging worms in humans and animals. In yaws, at least three consecutive years with zero serologically confirmed cases (assessed through serological surveys in children under 5 years). In onchocerciasis, interruption of transmission is assessed following active surveillance for three to five years after treatment has been stopped. Absence of infection in vector as well as in children (under 10 years) is to be documented through surveys. Postelimination surveillance should, however, continue.

4.4. Possible strategies to achieve interruption of transmission

4.4.1. Chemoprophylaxis: experience from Cuba

Dr Raisa Rumbaut Castillo, NLP Manager, presented data from Cuba. Cuba records about 200 new cases a year in a population of more than 11 million. The prophylactic approach to leprosy in Cuba has had different approaches for several years starting in 1962. At the start (in 1962) lepromin and BCG were used while currently chemoprophylaxis with rifampicin is given to all contacts. Despite these interventions, it has not been possible to confirm interruption of transmission. It remains, however, necessary to continue to assess the impact of this strategy at national and subnational levels.

The WHO Guidelines for the diagnosis, treatment and prevention of leprosy recommend that a single dose of rifampin can be used as a preventive treatment of leprosy for contacts of leprosy patients (adults and children more than 2 years old), after excluding leprosy and tuberculosis disease, and in the absence of other contraindications, in countries with adequate contact management and consent of the index case to reveal their disease.

4.4.2. Role of mapping

The topic was introduced by Dr Wim van Brakel, Medical Director of Until No Leprosy Remains. Mapping helps detecting leprosy hot spots (clusters), based on cases and thus assuming underlying transmission. Mapping can be undertaken at global level (identifying high and low burden countries), but more interestingly at intermediate, district or even village level. Analysis can be undertaken purely geographically or by combining time and space factors. By detecting these clusters, specific strategies (e.g. chemoprophylaxis) can be targeted. Mapping can help many more programme actions: visualize the distribution and grouping to better direct the actions, analyze the relationships between the disease and other factors, facilitates the identification of the population at risk. It also favors the analysis of the relationship of health services with patients (including barriers to services). Adding data on age, family associations or socio-economic status can also further enhance the value of spatial analysis.

4.4.3. Role of vaccines

Several vaccine options have been investigated in the last four decades (BCG, BCG + *M. leprae*, the Indian Cancer Research Centre vaccine, *M. w* or MIP). However, only BCG has shown significant protection against leprosy. Two vaccines are currently being tested: MIP and LepVax.

WHO's position with regard to BCG is that this vaccine should be given at birth in areas endemic for TB and/or leprosy. Its protective effect for leprosy was first acknowledged in a position paper published in the WHO Weekly epidemiological record¹.

MIP is a mycobacterium with an immunological cross reaction that causes an immune response against leprosy. It is cultivable in vivo and in vitro.

LepVax consists of a recombinant antigen (LEP-F1), produced by tandem linkage of *M. leprae* encoding ML2531, ML2380, ML2055 and ML2028 linked to an adjuvant (GLA-SE). Immunization delays and reduces the percentage of armadillos with *M. leprae*-induced motor nerve function. It also protected the nerve histomorphology and showed some potential to restore early sensory axonal function. It is thus both a therapeutic as well a preventive vaccine. With regard to human trials, Phase 1a (healthy volunteers in non-endemic area) has been completed. The vaccine was safe and well tolerated. LEP-F1 specific antibody and Th1 cytokine secretion (IFNy, IL2, TNF) were

¹ BCG vaccines: WHO position paper – February 2018. Wkly Epidem. Rec. No. 8, 2018, 93, 73-96

induced. The next steps in the development will include Phase 1b (TT and BT leprosy cases) and later phases.

4.4.4. "Finding the needle in the haystack": experience from Shandong Province, China

On behalf of Professor Furen Zhang from the Shandong Provincial Institute of Dermatology and Venereology, Jinan, China, Dr Erwin Cooreman presented how the rare leprosy cases are being detected in a very large population.

Shandong was one of the most leprosy endemic provinces of China, with more than 54 000 cases registered since 1950s. Most cases were detected prior to roll-out of MDT through active case detection (population surveys, contact examination, etc.). In 1994, Shandong became the first Chinese province to announce elimination of leprosy under the threshold of the Chinese Ministry of Health (registered prevalence of less than 1 per 100 000). Since then, the new case detection reduced to about 20 cases per year with very high G2D proportions.

The key strategies to find the remaining cases include: (i) public education and awareness raising; (ii) screening of close contacts; (iii) continue training of doctors (500 per year); (iv) introduction of molecular diagnostic tests; (v) symptom surveillance and referral; (vi) multi-disciplinary team in referral centre (dermatologists, public health experts, pathologists and researchers); and (vii) patient management.

The programme has achieved significant success in terms of a decline of newly detected cases (from 42 cases in 2008 to 7 cases in 2019) and in the G2D proportion (from 50% to 14%).

4.4.5. Maldives Framework for Zero Leprosy

Dr Md. Jamsheed Ahmed, Regional Adviser (NTDs), WHO Regional Office for South-East Asia, presented the Maldives Framework for Zero Leprosy on behalf of Dr Fathimath Nazla Rafeeq, Programme Manager, Health Protection Agency, Ministry of Health, Maldives.

The country achieved elimination of leprosy as a public health problem in 1997 and since then, both the prevalence and detection of new cases have shown a steady decline. Maldives counts 186 inhabited islands, grouped in 20 atolls. Each island has a health center within an organized hospital infrastructure. The Framework for Zero Leprosy was presented with milestones identified for 2019, 2022, 2025 and 2027 and target of zero autochthonous cases in 2030.

The plan defines interruption of transmission as absence of new autochthonous cases for a period of ten years (twice the average incubation time) while a strong surveillance system is to be maintained. This plan seeks to strengthen detection and cure for leprosy. It also seeks to provide single dose rifampicin as chemoprophylaxis to all contacts which may equate to entire island populations in some small islands.

During the consultation, the plan was discussed. There was much reservation for adopting a blanket approach in a context of very low or nil transmission. It was also flagged that a sporadic case may still occur – during or even after the ten-year period. This should not necessarily invalidate the country's (future) claim for interruption of transmission. In view of the long incubation time and high proportion of foreign work force (many from leprosy endemic countries), strong surveillance will be required for many years.

4.5. Defining interruption of transmission retro-actively

The topic was introduced by Professor Paul Fine from the London School for Hygiene and Tropical Medicine through a presentation titled "Inferring cessation of transmission of *M. leprae*".

Under this concept it is important to glimpse the implications of an autochthonous case. Autochthonous cases can be distinguished as (i) continuous autochthonous case (which implies continuous transmission in a population); and (ii) secondary autochthonous case (i.e. locally acquired through contact with an imported case). An area may be considered as endemic only if there is evidence of continuous autochthones cases. Over the years, continuous autochthonous cases tend to have moved towards the tropics while secondary cases remain very rare in moderate climates for reasons poorly understood.

In theory, the case-free interval, after the last recognized case, to infer that transmission has stopped, is determined by:

- the frequency distribution of time between successive clinical cases (serial interval), which depends on incubation period, infectiousness prior to showing symptoms; and duration of infectiousness; and
- the sensitivity of surveillance (i.e. proportion of infected individuals that are recognized as such), which depends on case definition, proportion of infections with clinical manifestation; and proportion of diagnosed and reported infections.

Leprosy poses challenges to apply this theory for the following reasons: no test for infection; inference is therefore based upon disease; crucial importance of surveillance efficiency. As transmission declines, the average age increases (cases with longer incubation more predominant); proportion of MB cases increases (since MB leprosy has a longer incubation time, but changes in definition of MB disease aggravates this interpretation); increased proportion of cases among family contacts (typically at higher risk); and geographic patterns. Epidemiological studies undertaken in Japan, the Republic of Korea, Valencia Region (Spain) and Mexico are consistent with these patterns.

Cessation of continuous transmission of *M. leprae* may be based on some simple criteria (time since last case, time since last child case) but should also consider other factors such as: geographic pattern and trend; age distribution; MB proportion and family contacts.

He also pointed out about the poorly understood role of an animal reservoir, for which there is as there is indisputable evidence for armadillo attributable leprosy cases in the United States of America, and suggestive evidence in several Latin American countries. The established reservoir

species, the nine-banded armadillo, has a range which extends from northern Argentina all the way to the southeast quadrant of the United States.

4.6. Modelling to predict future trends

The topic was introduced by Dr David Blok from the Erasmus Medical College, Rotterdam, The Netherlands.

Since leprosy behaves in a non-linear manner, modeling can help investigate the dynamics of the disease in patients and populations as well as in making public health decisions. Through modeling strategies, it can be observed that there is a downward trend in most areas. Interruption of transmission, however, may take many more decades, even beyond 2050, which can be inferred in that some leprosy strategies need changes to accelerate case reduction.

Based on modeling studies in relation to the impact of new strategies or tools, it has been observed that chemoprophylaxis could accelerate the reduction of cases. This result, however, also depends on the detection of cases and other factors.

4.7. Elimination criteria for other diseases

The only disease for which a verification of elimination of transmission procedure has been established is onchocerciasis. The goal established by WHO for onchocerciasis is elimination of transmission and therefore the ascertainment is called "verification". Once an endemic country has met the criteria established by WHO (entomological and or serological) at the end of the post-treatment surveillance (PTS) period, it can submit a request to WHO, through the Regional Office, to verify elimination of transmission in the entire country. This will be accompanied by a dossier that contains all the necessary evidence to support such claim.

WHO then constitutes a team of experts, called an "International Verification Team" which carefully reviews the dossier and visits the country in order to hold interviews with health authorities, health care workers who participated in the distribution of ivermectin and in the entomological and serological evaluations, as well as leaders and people in the affected communities. The purpose of these interviews is to have a thorough first-hand knowledge on how the programme was conducted and perceived by the affected communities.

The team produces a report with a recommendation to the WHO Director-General. After reviewing the report, the WHO Director-General takes a decision on whether or not to confirm the verification of the elimination of the disease and includes recommendations on post-elimination surveillance.

4.8. Verification of elimination for other diseases – "Elimination dossier"

In case of onchocerciasis elimination of transmission, the dossier is the official document compiled by the country that includes all the necessary evidence to support the claim that onchocerciasis has been eliminated. It must include a history of onchocerciasis and of the elimination programme, the interventions and strategies to achieve elimination, the process indicators (i.e. coverage of ivermectin in all treatment rounds) and the results of the impact indicators (epidemiological, parasitological, ophthalmological, entomological and serological) used to monitor the progress of the programme and to assess the interruption of transmission at the end of the 3- to 5-year post-treatment surveillance period. The publications in peer reviewed journals of these results is desirable and the papers can be included as annexes in the dossier.

Group work on interruption of transmission/elimination of disease (with reference to leprosy)

The following three topics were discussed in two groups (Topics 1 and 2 by Group 1 and Topics 1 and 3 by Group 2):

- > Topic 1: Define criteria to declare elimination of disease/interruption of transmission;
- > Topic 2: Define mechanisms to verify elimination;
- > Topic 3: Post-elimination surveillance.

Both groups agreed an autochthonous case can be defined as a person with leprosy presumed to have acquired the infection following local transmission in the reporting area. Currently, WHO is collecting data on "foreign-born" cases which is at best a proxy for "imported" (non-autochthonous) case. The groups agreed that the simplicity of this indicator is preferable to alternatives for routine data collection.

Both groups agreed that an area (country, territory) can be declared free of new autochthonous leprosy cases when there is no evidence of autochthonous cases, i.e. any incident cases can be labelled as imported.

Both groups further agreed that the absence of autochthonous leprosy in children for significant time should be a criterium to claim interruption of transmission. One group proposed zero case in children (below the age of 15) for 15 years while the other group proposed zero new cases in children (below the age of 10) for five years.

The dossier should include process indicators such as a robust surveillance system as well as quality of health services to deal with unexpected (sporadic) cases. The latter one may include: adequate referral system for leprosy suspects with quick and complete investigation (by an adequately trained and experienced national or subnational response team), universal initial screening and rescreening (e.g. after three years) of contacts of all new index cases (with minimal refusals by the index case or contact), involvement of affected persons and general community through awareness raising activities (with the intent to use all available approaches for case detection).

A reward system (as positive incentive) for reporting child cases may be considered especially in countries where target setting, stigma, etc. may discourage reporting. This should only be applied when there are thought to be very few or zero cases. Political commitment would also include

removing counter-incentives that encourage hiding new cases. A reward system facilitating case reporting is currently in place in the context of eradication of dracunculiasis.

When reliable tests become available to detect infection, such tests should show declining trends in infection over time, starting with children.

Confirmation that an area does not have new autochthonous leprosy cases will depend on maintaining the ability to detect, diagnose and treat leprosy correctly for at least ten years; mapping can help in identify areas requiring stronger surveillance; Continuous training should be undertaken in such risk areas about "suspect and refer"; proper documentation and case-by-case search. An external review should also be considered to ascertain that required mechanisms are functional.

As the time frames are fairly long, exceptions should be considered for the sporadic case that may appear after several years of nil cases without need for a country (area, territory) to start all over again.

4.9. Further research needs

The discussion was moderated by Professor Paul Fine.

The multiplicity of possible definitions and concepts ("zero leprosy", zero transmission, elimination of transmission, interruption of transmission, transmission block, elimination of leprosy as a public health problem, etc.) may trigger many questions but at the same time many research opportunities.

These include:

- Tests to diagnose infection that are highly sensitive and specific, yet simple and inexpensive (all these conditions are required to be helpful in assessing interruption of transmission);
- natural history of the disease since there are still unclear aspects (e.g. duration and degree of infectiousness, proportion of self-cure, the importance of asymptomatic nasal carriers, serial interval, etc.); systematic reviews can help but ideally this should be investigated through (expensive) longitudinal epidemiological studies;
- epidemiology of leprosy (to show interruption of transmission);
- importance of studies of the prevalence and distribution of *M. leprae* infections in armadillos and their role in leprosy transmission in the different settings in the Americas;
- role of *M. lepromatosus*;
- practical effectiveness of interventions (e.g. impact of chemoprophylaxis, vaccine);
- operational research (e.g. on surveillance and data quality).

5. Other business

5.1. Lucio phenomenon

Lucio's phenomenon is an unusual reaction seen almost exclusively in patients from the Caribbean and Mexico with diffuse, lepromatous leprosy. It is characterized by recurrent crops of large, sharply demarcated, ulcerative lesions, affecting mainly the lower extremities, but may generalize and become fatal as a result of secondary bacterial infection and sepsis.

The mechanism of pathogenesis is thought to be mediated by immune-complex deposition. Histologically, the lesions are characterized by ischemic necrosis of the epidermis and superficial dermis, heavy infestation of endothelial cells with acid-fast bacilli, and endothelial proliferation and thrombosis in the larger vessels of the deeper dermis. Lucio's phenomenon is treated by anti-leprosy therapy (dapsone, rifampin and clofazimine), optimal wound care, and treatment for bacteremia, including antibiotics. In severe cases, exchange transfusion is helpful.

Lucio's phenomenon is seen mainly in the Caribbean and Mexico, and rarely in other parts of the world. Genetic and regional factors and factors specific to *M. leprae* have been shown to alter the manifestation of Lucio's phenomenon.

5.2. Global Partnership for Zero Leprosy

Dr Courtenay Dusenbury informed the meeting participants about GPZL and shared its Action Framework for Zero Leprosy as currently defined.

The Partnership was set up in a context of few donors interested to fund leprosy. It aims to lead a new movement towards zero leprosy with new and reinvigorated stakeholders.

The Partnership is organized along three main areas: (i) strengthening country programmes; (ii) research and innovation; and (iii) leadership and advocacy. Under each area, activities and milestones have been identified to be reached in 2020, 2025 and 2030.

Overarching themes for each year include:

- By 2020: GPZL program, research, governance, and advocacy priorities aligned with a vision of achieving the WHO 2030 global leprosy targets leading to zero leprosy;
- By 2025: Priority research and country plans supported; strong national leprosy programmes are integrated into country clinical and public health systems;
- By 2030: Countries meet global targets, i.e. reduction in (i) overall new cases; (ii) rate in new cases with G2D; (iii) rate of new child cases; and (iv) no discriminatory laws.

Details were presented for each area under each theme.

Achievements till date include a generic "Country Model" which was put together by more than 140 participants including many representatives from endemic countries. It encompasses a country review and development of country roadmap for zero leprosy. A toolkit which includes best

practices from across the globe has been developed and is available on the Partnership's website. A research agenda, covering eight thematic areas has also been developed and is published in a peer-reviewed journal.

6. Conclusions and recommendations

Elimination of leprosy as a public health problem has been achieved in almost all countries, often many years ago. An acknowledgement of such achievement can be given to countries, requesting this.

The meeting agreed that past achievements should be built on and directly linked to the preparations needed to work towards interruption of transmission, as specified in the NTD Roadmap 2021–2030. To move forward certain conditions should be met. This would include (but is not limited to) a country roadmap towards zero leprosy, a case-based management information system (including additional indicators such as G2D, child cases, duration of symptoms), a good surveillance system, sustained capacity on detection and management of cases.

To prepare for working towards interruption of transmission and ultimately zero new leprosy cases, the participants of the informal consultation recommend that:

- Countries should conduct a detailed analysis of available data, especially looking at data trends and indicators that capture interruption of transmission (which may already have occurred or is near), e.g. age at the time of diagnosis, number of child cases, MB proportion among new cases, proportion of cases with known cases in the family, etc.);
- Countries should conduct mapping of all cases detected during at least the past five years to visualize the distribution and level of clustering;
- > Contact tracing and PEP should be universally applied;
- Research should be undertaken to better understand the role of armadillos in the natural history of leprosy;
- Criteria for interruption of transmission and zero incidence of disease should be consolidated and further developed. A Taskforce should be set up to do this.
- Until a valid laboratory test to diagnose infection is available, criteria for interrupting transmission will rely on proxy measures;
- Verification of interruption of transmission can be based on the absence of new child cases during a given minimum period of time. The exact cut-off point for these criteria will be recommended by the Taskforce after further analysis of available data;
- Acknowledgement of zero incidence of disease can be based on the absence of autochthonous cases with other stringent conditions in place (such as strong surveillance system and case management system). Autochthonous cases can be defined as cases of leprosy who are presumed to have been infected in the country.

Surveillance will continue to be required even after a country has officially been ascertained of having interrupted transmission or eliminated the disease, and this in view of the possibility for rare cases due to the possible very long incubation time.

7. References

Global Leprosy Strategy 2016–2020 "Accelerating towards a leprosy-free world". WHO. SEA/GLP/2016

Global Leprosy Strategy 2016–2020 "Accelerating towards a leprosy-free world"; Operational Manual. WHO. SEA/GLP/2017

Global Leprosy Strategy 2016–2020 "Accelerating towards a leprosy-free world"; Monitoring and Evaluation Guide. WHO. SEA/GLP/2018

Guidelines for the Diagnosis, Treatment and Prevention of Leprosy. WHO. SEA/GLP/2018

Global leprosy update, 2018: moving towards a leprosy-free world. WHO. Wkly Epidem Rec Nos. 35/36, 2019, 94, 389-412;

Generic framework for control, elimination and eradication of neglected tropical diseases. WHO/HTM/NTD/2016.6

Validation of elimination of lymphatic filariasis as a public health problem. WHO/HTM/NTD/PCT/2017.01

Validation of elimination of trachoma as a public health problem. WHO/HTM/NTD/2016.8

Informe Reunión Regional Bienal de Directores de Programas de Control de Lepra de los países de América Latina y el Caribe. Organización Panamericana de la Salud (OPS/OMS). Buenos Aires, Argentina. 2018

Validación de la eliminación de la lepra como problema de salud pública -propuesta borrador-Actualización de los conceptos y procedimientos para la documentación. Organización Panamericana de la Salud (OPS/OMS). Washington, DC. 2019.

Working together to control and eliminate neglected tropical diseases – a Roadmap for 2030; sustaining the gains and accelerating progress [Draft]. WHO/UCN/NTD/2020

Meeting of the International Task Force for Disease Eradication, April 2018. WHO. Wkly Epidem Rec Nos. 1/2, 2019, 94, 1-16

Alencar CH, Ramos AN, do Santos ES et al. Clusters of leprosy transmission and of late diagnosis in a highly endemic area in Brazil: focus on different spatial analysis approaches. Trop Med Int Health. 2012 Apr; 17 (4): 518-25

Bakker MI, Scheelbeek PFD, van Beers SM. The use of GIS in leprosy control. Lepr Rev (2009) 80, 327-331 Barreto JG, Bisanzio D, de Souza Guimarães L et al. Spatial analysis spotlighting early childhood leprosy transmission in a hyper-endemic municipality of the Brazilian Amazon Region. PLoS Negl Trop Dis. 2014 Feb: 8(2): e2665

BCG vaccines: WHO position paper – February 2018. WHO. Wkly Epidem Rec No. 8, 2018, 93, 73-96

Zhao Q, Sun Y, Liu H et al. Prevention and Treatment of Leprosy – China, 2009-2019. CCDC Weekly. (2) 4, 53-56

Chen X, Sun L, Zhao Q et al. Development and evaluation of a droplet digital PCR assay for the diagnosis of paucibacillary leprosy in skin biopsy specimens. PLoS Negl Trop Dis. 2019 Mar: 18, 13 (3): e0007284

Framework for Zero Leprosy in the Maldives "100 Leprosy Free Islands by 2023". Health Protection Agency, Ministry of Health, Maldives and WHO Country Office for Maldives.

Lee J, Kim JP, Nishikiori N et al. The decline of leprosy in the Republic of Korea; patterns and trends 1977-2013. Lepr Rev (2015) 86, 316-327

Larrea MR, Carreno MC, Fine PEM. Patterns and trends of leprosy in Mexico: 1989-2009. Lepr Rev (2012) 83, 184-194

Suárez-García I, Echevarría JRG, Cervera FM et al. The decline of autochthonous leprosy in the Valencia Region of Spain: patterns and trends 1940-2015. Lepr Rev (2017) 88, 162-173

Koba AI, Ishii N, Mori S et al. The decline of leprosy in Japan: patterns and trends 1964-2008. Lepr Rev (2009) 80, 432-440

GPZL Reports on Research Priorities. Lepr Rev (2019) 90, 237-289

Annex 1: List of participants

Country representatives

Dr Raisa Caridad Rumbaut Castillo Ministry of Public Health Havana, Cuba

Mr Vusi Lokotfwako Ministry of Health Mbabane, Kingdom of Eswatini

Dr Douglas Edgardo Avelar Aguilar Secretariat of Health Tegucigalpa, Honduras

Dr Ruy López Ridaura Ministry of Health Mexico City, Mexico

Professor Mario Martínez Gonzáles National Autonomous University of Mexico Mexico City, Mexico

Dr Fátima Leticia Luna López Ministry of Health Mexico City, Mexico

Dr Martha Angélica García Avilés Ministry of Health Mexico City, Mexico

Dr Patricia Guadarrama Pérez Ministry of Health Mexico City, Mexico

Dr Irais Lizbeth Rodríguez Montes Ministry of Health Mexico City, Mexico

Dr Iris Estrada-García National Polytechnic Institute Mexico City, Mexico

Dr Vladimir Henánez Sosa Ministry of Health Santa Cruz Xococotlán, Oaxaca, Mexico Dr Manuel Sandoval Días Ministry of Health Jalisco, Mexico

Dr Eduardo Antonio Jiménez Suazo Ministry of Health Managua, Nicaragua

Dr Kenturah Edwin-Tobias Ministry of Health and Wellness Castries, Saint-Lucia

Dr Bernadina Rasnik Favotto Ministry of Public Health Montevideo, Uruguay

Unable to attend:

Dr Fathimath Nazla Rafeeq Ministry of Health Male', Maldives

Technical experts and partner agencies

Dr Silmara Penninia Alfredo da Matta Foundation Manaus, Brazil

Dr Vijay Kumar Pannikar (remotely) WHO Technical Advisory Group on Leprosy Hosuru, India

Professor Paul Fine London School of Hygiene and Tropical Medicine London, United Kingdom of Great Britain and Northern Ireland

Dr Mauricio Lisboa Nobre WHO Technical Advisory Group on Leprosy Natal, Brazil

Dr Rosa Castália Soares Working Group on Monitoring and Evaluation, WHO Strategic and Technical Advisory Group on NTDs Salvador, Brazil Dr David Blok Erasmus Medical Centre Rotterdam, The Netherlands

Professor Furen Zhang (remotely) Shandong Provincial Institute of Dermatology and Venereology Jinan, People's Republic of China

Mr Geoff Warne International Federation of Anti-Leprosy Associations Châtelaine, Switzerland

Dr Wim van Brakel Until No Leprosy Remains Amsterdam, The Netherlands

Ms Courtenay Dusenbury Global Partnership for Zero Leprosy Decatur, United States of America

Professor Hiroyoshi Endo Sasakawa Health Foundation Tokyo, Japan

Ms Aya Tobiki Sasakawa Health Foundation Tokyo, Japan

Ms Arielle Cavaliero Novartis International AG Basel, Switzerland

World Health Organization

Mr Cristián Morales PAHO/WHO Country Office for Mexico Dr Erwin Cooreman Global Leprosy Programme WHO Regional Office for South-East Asia

Dr R Santiago Nicholls PAHO/WHO Regional Office for the Americas

Dr Maria Jesus Sanchez PAHO/WHO Country Office for Mexico

Dr Nestor Alejandro Vera Nieto PAHO/WHO Regional Office for the Americas

Dr Abate Beshah WHO Regional Office for Africa

Dr Md. Jamsheed Ahmed WHO Regional Office for South-East Asia

Dr Albis Gabrielli WHO Headquarters

Unable to attend:

Dr Luis Gerardo Castellanos PAHO/WHO Regional Office for the Americas

Dr Isabelle Rogers PAHO Regional Leprosy Programme PAHO/WHO Country Office for Brazil

Dr Supriya Warusavithana WHO Regional Office for the Eastern Mediterranean

Dr Elkhan Gasimov WHO Regional Office for Europe

Dr Rahevar Kalpeshsinh WHO Regional Office for the Western Pacific

Annex 2: Programme

Time	Session	Presenter			
Day 1 – Monday 10 February 2020					
08:30 – 09:00 hrs	Registration				
09:00 – 09:30 hrs	1. Session I: Inauguration				
	I.1. Welcome remarks	Mr Cristián Morales			
	I.2. Opening remarks	Dr Ruy López Ridaura			
	I.3. Self-introduction of participants				
	I.4. Objectives and expected outcomes	Dr Erwin Cooreman			
	I.5. Statements by partners: GPZL, ILEP, Novartis, SHF	Ms Courtenay Dusenbury, Mr Geoff Warne, Ms Arielle Cavaliero, Ms Aya Tobiki			
	I.6. Announcements				
09:30 – 10:00 hrs	Group picture and tea/coffee				
	2. Session II: Overview of leprosy control				
10:00 – 10:30 hrs	II.1. Current global leprosy situation	Dr Erwin Cooreman			
10:30 – 11:00 hrs	II.2. History of leprosy control	Dr V K Pannikar			
	3. Session III: Elimination of leprosy as a public health problem				
11:00 – 11:30 hrs	III.1. Generic framework for control, elimination and eradication of NTDs	Dr Albis Gabrielli			
11:30 – 11:45 hrs	III.2. WHA Resolution, definition of leprosy as a public health problem and global progress	Dr Erwin Cooreman			
11:45 – 12:00 hrs	III.3. From control to elimination as a public health problem: experience from Mexico	Dr Fátima Leticia Luna López			
12:00 – 12:30 hrs	III.4. Validation of elimination as a public health problem: how it is done for other diseases	Dr Santiago Nicholls			
12:30 – 13:30 hrs	Lunch break				
13:30 – 14:00 hrs	III.5. Validation of elimination of leprosy as a public health problem: outcome of consultation in PAHO	Dr Santiago Nicholls			
14:00 – 15:45 hrs	III.6. Group work: discussion on way forward				
15:45 – 16:00 hrs	Tea/coffee break				
16:00 – 16:30 hrs	III.7. Feedback from group work	Rapporteurs			
	4. Session IV: Other business				
16:30 – 17:00 hrs	IV.1. Introduction of GPZL	Ms Courtenay Dusenbury			
17:00 – 17:30 hrs	5. WHO Secretariat meeting (secretariat members only)				

Time	Session	Presenter			
Day 2 – Tuesday 11 February 2020					
09:00 – 09:15 hrs	6. Recap of Day 1	Mr Vusi Lokotfwako			
	7. Session V: From elimination as a public health problem to interruption of transmission				
09:15 – 09:30 hrs	V.1. NTD Roadmap 2021–2030	Dr Albis Gabrielli			
09:30 – 10:00 hrs	V.2. Leprosy profile in NTD Roadmap and Post-2020 Global Leprosy Strategy	Dr Erwin Cooreman			
10:00 – 10:30 hrs	Tea/coffee break				
10:30 – 11:00 hrs	V.3. Conceptual framework: interruption of transmission and elimination of disease (20' presentation and 10' discussion)	Dr Albis Gabrielli			
	V.4. Possible strategies to achieve interruption of transmission				
11:00 – 11:15 hrs	V.4.1. Chemoprophylaxis with SDR: experience from Cuba	Dr Raisa Rumbaut			
11:15 – 11:30 hrs	V.4.2. Role of mapping	Dr Wim van Brakel			
11:30 – 11:45 hrs	V.4.3. Role of vaccines in leprosy	Dr Mauricio Lisboa Nobre			
11:45 – 12:30 hrs	V.4.4. Discussion				
12:30 – 13:30 hrs	Lunch break				
	V.5. Towards zero leprosy				
13:30 – 13:45 hrs	V.5.1. Finding the needle in the haystack: experience from Shandong, China	Professor Furen Zhang			
13:45 – 14:00 hrs	V.5.2. Maldives Roadmap for Zero Leprosy	Dr Md. Jamsheed Ahmed			
14:00 – 14:45 hrs	V.6. Defining interruption of transmission retro-actively	Professor Paul Fine			
14:45 – 15:15 hrs	Tea/coffee break	-			
15:15 – 16:00 hrs	V.7. Modelling to predict future trends	Dr David Blok			
	8. Session VI: Other business (contd)				
16:00 – 16:30 hrs	VI.1. Issues related to drugs (MDT, treatment of reactions, prevention)	Dr Erwin Cooreman			
16:30 – 17:00 hrs	9. WHO Secretariat meeting (secretariat members only)				

Time	Session	Presenter			
Day 3 – Wednesday 12 February 2020					
09:00 – 09:15 hrs	10. Recap of Day 2	Dr Douglas E Avelar			
	11. Session VII: From elimination as a public health problem to interruption of transmission (contd)				
09:15 – 09:30 hrs	VII.1. Elimination criteria for other diseases	Dr Md. Jamsheed Ahmed			
09:30 – 10:00 hrs	VII.2. Verification of elimination for other diseases – "Dossier"	Dr Santiago Nicholls			
10:00 – 10:30 hrs	Tea/coffee break				
10.30 – 12.30 hrs	VII.3. Group work				
	VII.3a Define criteria to declare elimination of disease/ interruption of transmission				
	VII.3b Define mechanisms to verify elimination				
	VII.3c Post-elimination surveillance				
12.30 – 13.30 hrs	Lunch break				
	VII.4. Feedback from group work				
13.30 – 14.00 hrs	VII.4.1. Group 1 (Topics a and b)	Rapporteur Group 1			
14:00 – 14:30 hrs	VII.4.2. Group 2 (Topics a and c)	Rapporteur Group 2			
15:00 – 15:30 hrs	Coffee/tea break				
15:30 – 16:00 hrs	VII.5. Research needs (epidemiological studies)	Professor Paul Fine			
	12. Session VIII: Other business (contd)				
16:00 – 16:15 hrs	VIII.1. Lucio Phenomenon	Dr Iris Estrada-García			
16:15 – 16:45 hrs	VIII.2. 2020 data collection	Dr Erwin Cooreman			
16:45 – 17:30 hrs	13. Session IX: Closing session				
	IX.1. Conclusions and recommendations	Dr Erwin Cooreman			
	IX.2. Comments/feedback from participants				
	IX.3. Closing remarks				
17:30 – 18:00 hrs	14. WHO Secretariat meeting (secretariat members only)				