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| **Deliverable D2.2: Roadmap and recommendations for deployment – Focus on nanotechnologies for health** |



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# Abbreviations and acronyms

**Partner Acronyms:**

EURECAT Centre Tecnològic de Catalunya, Spain

REDINN Rete Europea dell’Innovazione, Italy

ION Institute of Nanotechnology, UK

MTV Malsch TechnoValuation, Netherlands

ZSI Zentrum für Soziale Innovation, Austria

VTT Technical Research Centre of Finland, Finland

RELANS Latin American Nanotechnology and Society Network, Brazil

MINCyT The Ministry of Science, Technology and Productive Innovation, Argentina

CIMAV-CONACYT Centro de Investigación en Materiales Avanzados, S.C, Mexico

MEC Ministry of Education and Culture, Uruguay

EUROCHILE Eurochile Business Foundation, Chile

**Abbreviations and acronyms used in this report**

AIDS Acquired Immunodeficiency Syndrome

CIATEJ Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco

CIMAT Centre for Advanced Interdisciplinary Research on Materials Science

CIMIS Centre for Integrative Medicine and Innovative Science

CINVESTAV Centre for Research and Advanced Studies

CNPq Brazilian National Council for Scientific and Technological Development

DiscoGnosis Disc-shaped point-of-care platform for infectious disease diagnosis

DOTS Directly Observed Treatment, Short-Course

EHS Environmental, Health and Safety

ELSA Ethical, Legal and Social Aspects

ELSI Ethical, Legal and Social Implications

ETPN European Technology Platform on Nanomedicine

EU European Union

EU-CELAC JIRI European Union and Community of Latin American and the Caribbean States’ Joint Initiative for Research and Innovation

EULANEST Promoting and Coordinating Research Co-operation among EU Member States and Latin American Countries

HIV Human Immunodeficiency Virus

HPV Human papillomavirus

ICP International Cooperation Partner

IMSS Mexican Institute of Social Security

INIFTA Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas

IPN Polytechnic Institute

ISO International Standardization Organization

ISO International Standardization Organization

KIT Royal Institute for the Tropics

LA Latin America

LAC Latin American and the Caribbean

LNN Laboratory of Nanomedicine and Nanotoxicology

MDGs Millennium Development Goals

MDR-TB Multidrug-Resistant Tuberculosis

MECESUP Higher Education Quality Improvement Programme

MIT Massachussets Institute of Technology

NanoCiTec Nanoscale Science and Technology Centre

NANOSUS Platform for nano-biotechnology projects for the Unified Health System (SUS)

NCDs Non-communicable Diseases

NGOs Non-governmental organizations

NIA Nanotechnology Industries Association

NIAID US National Institute of Allergy and Infectious Diseases

NMP Nanosciences, Nanotechnologies, Materials & New Production Technologies

NTDs Neglected Tropical Diseases

OIP Open Innovation Platform

PLUS Paris Lodron University in Salzburg

PodiTrodi Point-of-care Diagnostics for Tropical Diseases

Qdots Quantum dots

RNAi Ribonucleic acid interference

SDGs Sustainable Development Goals

siRNA Small Interfering RNA

SisNANO Brazilian National Nanotechnology Laboratory System

SMEs Small and Medium Enterprises

STD Sexually Transmitted Diseases

STI Science, Technology and Innovation

STI Science, technology and innovation

SUS Unified Health System

TB Tuberculosis

TNF-α Tumour necrosis factor alpha

UFC Federal University of Ceara

UFRJ Federal University of Rio de Janeiro

UN United Nations

UNAM Universidad Nacional Autónoma de Mexico

UNESP University of the State of São Paulo

UNIFESP Federal University of São Paulo

USP Universidade de São Paulo

WHO World Health Organization

WoS Web of Science

XDR-TB Extensively Drug-Resistant Tuberculosis

# Summary

This roadmap is addressed to stakeholders dealing with nanotechnologies, and especially with nanotechnologies for health, in Latin American countries. Considering the newness of the field and the early development stage of applications, the recommendations found here are more directed to policy-makers, academic experts and other experts dealing with knowledge transfer from university or research institutes to industry and promotion of start-up businesses. Among proposed actions of the OECD to address key challenges to the adoption of nanotechnology solutions is the development of area specific roadmaps. In the NMP DeLA project (Nanosciences, Nanotechnologies, Materials and New Production Technologies - Deployment in Latin American Countries), we therefore aimed to develop strategic roadmaps for the areas of health, water and energy, which include the complete system of research, industrial development and financial management.

The present roadmap on nanohealth is the product of a 2-year multi-stakeholder research process where we addressed the question of how nanotechnology-based solutions to health-related challenges (especially focusing on the Latin American context) should be produced in the future. The research approached five thematic clusters: (1) research, (2) policy making and funding, (3) education and training, (4) industry and investment and (5) ethical, legal and social aspects. In a previous step we ask the questions what is already there and how is nanotechnology currently deployed in Latin America in the context of health related challenges? The roadmap gives examples of existing good practices, as well as opening pathways and providing recommendations for efficient and responsible management of technological solutions. The aim of the roadmap is to guide stakeholders in the promotion of research and innovations that are meaningful, especially from a perspective that is driven by basic needs of Latin American societies and people. The diseases focused on are tropical infectious diseases, in particular tuberculosis, and cancer, which were selected because of the immense burden they bear on poor and vulnerable communities.

# Introduction

This roadmap is an important output of the NMP-DeLA project, which has the objective of developing a series of activities between European (EU) and Latin American (LA) countries, that aim to strengthen the local research and training potential as a way of facilitating the deployment of nano and advanced materials technologies in areas of major societal challenge in LA: energy, water and health. This document refers to the roadmap on the deployment of nanotechnologies for health in the context of Latin American countries, whereas the other roadmaps on water, energy and on general findings can be downloaded on the project website.

The target audience for this roadmap is composed of policy makers, academics, industrialists and practitioners, including non-governmental organizations (NGOs) and civil society, in the field of health, and especially in neglected infectious diseases, tuberculosis and cancer, which are the main focus of the analysis in this roadmap.

This roadmap details:

1. Training needs and research priorities including research, development and innovation (RD&I) themes and technology gaps, as well as industrial challenges,

2. The most successful and innovative NMP technologies used today in Europe and LAC, including a review of methodologies, good practices and trends in the pursuit of improving renewable energy (in particular photovoltaics, PVs), water treatment and healthcare,

3. Recommendations for potential collaborative research deployment.

The time horizon for the roadmap is the year 2025. Our main concern is how the deployment of nanotechnologies in the three focus areas can help realize the Millennium Development Goals[[1]](#footnote-2) and, therefore, address major societal challenges. These affect mostly the poor populations of developing countries, in this case those living in LA and, more specifically, the International Cooperation Partner[[2]](#footnote-3) (ICP) countries participating in the NMP-DeLA project (Argentina, Brazil, Chile, and Mexico) plus Uruguay. Due to similarities to be found in terms of problems faced by other countries in LA and the Caribbean (LAC) region, and the pervasive nature of nanotechnologies, we engaged other LAC countries in outreach activities where the roadmap was validated (expert workshops and summer schools).

This document then presents the methodology used for the construction of the roadmap; applications of nanotechnologies for health-related societal challenges and in particular in the area of tropical infectious diseases and cancer; and the main findings and recommendations for deployment in Latin America.

# Roadmap for Deployment of Nanotechnologies for Health

We used the criteria for governance of nanotechnologies proposed by (Roco et al 2011b), which states that it needs to be:

• Transformative – including a results or projects-oriented focus on advancing multi-disciplinary and multisector innovation

• Responsible – including environmental, health and safety (EHS) and equitable access and benefits

• Inclusive – participation of all agencies and stakeholders

• Visionary – including long-term planning and anticipatory, adaptive measures

Rocco et al (2011b) give examples of applications of nanotechnology governance functions (the ones mentioned above) in the United States. They emphasize that nanotechnology can be used as an example of how an emerging field has evolved in tandem with consideration of environmental, health and safety (EHS) aspects as well as ethical, legal and social implications (ELSI) or ethical, legal and social aspects (ELSA). Nanotechnology has been governed by an international commu-nity of professionals engaged in research, education, production and societal assessment of nano-technology, which has the potential to guide its applications for the well-being of different societies and the environment.

We also bear in mind that governance of nanotechnology has been said to be essential for realizing economic growth and other societal benefits, protecting public health and environment, and supporting global cooperation and progress. Besides the criteria for governance of nanotechnologies we also used Nussbaum’s adapted Capability approach[[3]](#footnote-4) (Malsch and Emond 2013) as foundations for the construction of the roadmaps, in order to support a needs-based perspective and to bring a multi-dimensional approach to the foresight exercise. The capability approach is a theory of human rights translated into a limited number of basic capabilities that each person anywhere in the world should be enabled to develop. Some of these capabilities are relevant to international cooperation in STI as well and they are discussed in the context of the deployment of the NMP-DeLA project:

* *Public engagement*: are all stakeholders represented in discussions on the roadmap?
* *National sovereignty*: is national sovereignty of LA countries, where the roadmaps should be deployed, respected? What resources do they have and are they willing to invest by themselves? This calls for the suggestion of integrating the roadmaps into existing national plans for STI.
* *Foreign investment*: will the roadmaps fit in the EU strategy for international cooperation under Horizon 2020? What about national strategies of EU Member States?
* *Private investment*: can we convince industrial companies and venture capitalists to invest their own resources in implementing the roadmaps?
* *Access to higher education and research jobs*: in the NMP-DeLA project we should follow an equal opportunity policy for selection of participants in the outreach activities as well as in the stakeholder workshops. In the roadmap we discuss education and training and equal opportunities policies for the organizations involved in implementing the roadmaps.
* *Target research to poverty and health-related problems*: this is the leading force in the development of the roadmaps.
* *Environmental sustainability*: take into account both EHS aspects of nanomaterials and expected environmental benefits (especially in energy and water).

## Methodology of Elaboration of the Construction of the Roadmap

Key research questions have been used as a tool in the roadmapping process. The roadmap has been built upon a needs-based perspective: improved healthcare, clean and sufficient water, sustainable energy in LA. The time frame for each roadmap is 10 years, up to year 2025.

The focus of the roadmap lies on those technologies/needs with possible important impact on poor populations in LA, and more specifically in Europe’s International Cooperation Countries (ICP) in LA plus Uruguay. In order to formulate very specific conclusions and recommendations, a choice of core topics was made, considering that not all technological developments nor the full range of societal needs can be addressed. The topics covered in this roadmap were tropical infectious diseases, tuberculosis, and cancer because these are considered to have largest impact on poor and vulnerable populations of the countries in the region.

It is important to note that a substantial amount of resources is needed to compile comprehensive roadmaps. The roadmapping exercise within the context of NMP-DeLA is limited in scope as the research relies on (a) a bibliometric analysis, (b) results of four one-day workshops on each topic and (c) expert interviews and focus groups.

### Research questions

The roadmap has been structured along key research questions to be explored by implementing different methodological approaches and participatory assessment methods. This section shows these approaches in more detail. Most of the assessment tools have been applied in the framework of NMP-DeLA events to use synergies and to save costs. Inter-connections between research questions have been exploited by means of joint organization by project partners of participatory events and focus groups, where a set of questions has been discussed with different stakeholder groups.

**Research question 1: What is already there?**

Objective: Identification of the state of the art of research and products/applications in nano-health.

Assessment tools:

* desk research
* bibliometric analysis
* expert consultation

Result: mapping of advanced materials deployment for societal challenges potential for innovations in the areas analysed.

Research question 2: How is NMP deployed (now) in the context of societal challenges in the fields of health?

Objective: Assessment of the extent to which nanotechnology research (and funding programmes) aims to address major health related societal challenges.

Assessment tools:

* participatory workshops
* focus groups
* individual expert interviews

Result: identification of good practices and recommendations for future actions

**Research question 3: How can solutions, technologies and applications be produced in the future?**

Objective: This question guided the formulation of recommendations and the innovation strategy, which aims at supporting successful commercialization of nanotechnology developments in the field of health in LA by looking at the drivers and challenges for commercialization and how infrastructure can assist small and medium enterprises (SMEs) and academia in commercialization efforts in LA. In order to achieve this, the innovation strategy will be largely based on the results of outreach activities in LAC, i.e. on surveys, interviews and discussions with stakeholders.

Assessment tools:

* desk research on international roadmaps for the deployment of nanotechnologies
* stakeholder consultation through the website
* survey with SMEs and academia in LAC
* participatory workshops

Result: Recommendations for deployment and innovation strategy[[4]](#footnote-5)

The roadmap construction process with research questions and criteria and capabilities is depicted in Figure 1.

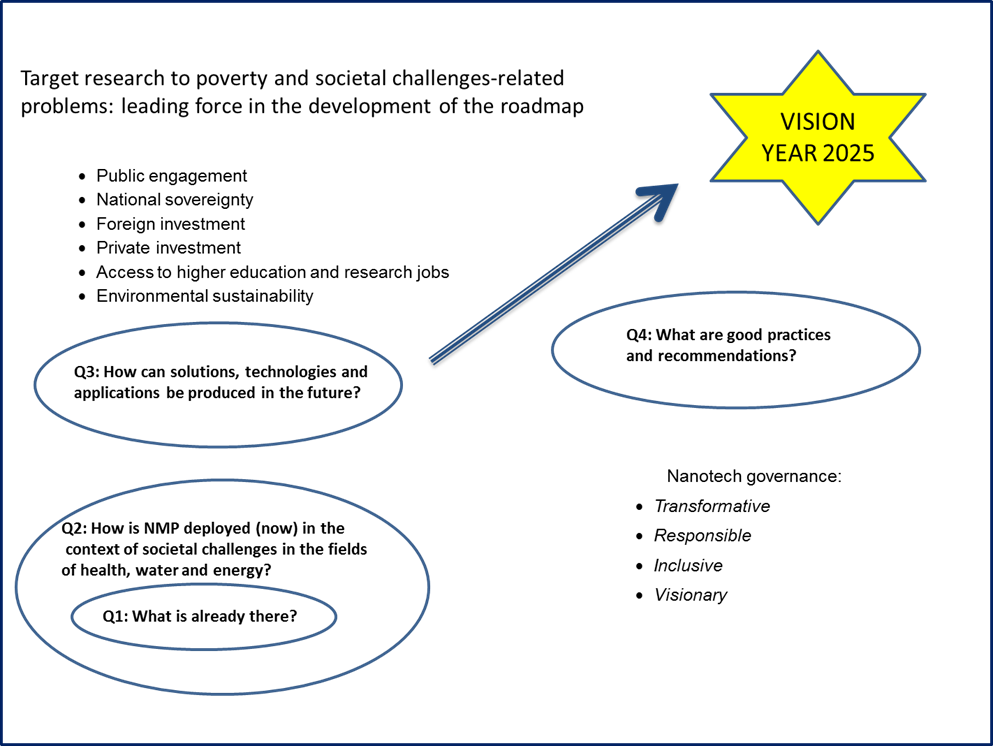


Figure 1: Research questions, criteria and capabilities in construction of NMP-DeLA roadmaps

# Nanotechnologies to Address Health-Related Societal Challenges

Nanotechnology is often classified as an emerging, enabling, and disruptive technology base that has potential (and confirmed) cross-industrial applications, besides being convergent (Romig Jr. *et al* 2007). Because of its multidisciplinary nature, developments in many scientific fields have allowed nanotechnology to become integrated in many disciplines and enlarge its application areas. It has been recognized as a revolutionary field of science and technology comparable to the introduction of electricity, biotechnology, and information and communication technologies (Roco *et al* 2011a) and is described as a broad-based, multidisciplinary field projected to reach mass use by 2020 and affecting education, innovation, learning and governance (Roco *et al* 2011a).

According to the International Standardization Organization (ISO 2010 online) nanotechnology is the application of scientific knowledge to manipulate and control matter in the nanoscale (referring to particles whose size ranges from approximately 1nm to 100nm) in order to make use of size- and structure-dependent properties and phenomena, as distinct from those associated with individual atoms or molecules or with bulk materials.

At the nanoscale materials acquire new characteristics that can be exploited in a wide range of novel applications. They include potentially cheaper and more efficient technologies that can benefit the world’s poor, such as water filters, efficient solar powered electricity, and portable diagnostic tests (Nano-Dev 2010).

The literature (e.g. Foladori and Invernizzi, 2005, Foladori and Invernizzi, 2008, NIA 2013, Aydogan-Duda 2012, ETPN 2014) generally speaks of nanotechnologies as being a useful means of tackling societal challenges, including those that affect populations of developing countries, therefore also creating, even if indirectly, means of inclusiveness and poverty alleviation. There is an abundant stream of bibliometrics-based analyses informing the different applications of nanotechnologies (e.g. Kostoff *et al* 2007) and specifically considering their applications in the context of developing countries and societal challenges and LA (e.g. Kay and Shapira 2009; Cozzens *et al* 2013; European Commission 2013).

Even though societal challenges are often preceded or associated with the words grand or global, meaning they are grand or global in scale, like climate change, for example, they may also have a global scale in the sense that problems that affect developing countries, such as famine, impacts of climate change, wars, epidemics, etc., may also affect developed countries. The societal challenges for developing countries are the visible object of the Millennium Development Goals (MDGs), implemented by the United Nations (UN 2000, UN Millennium Project 2005). The MDGs of relevance to this roadmap on nanohealth are listed below in Table 1. They serve as a guide for identifying the ways in which nanotechnology developments can be deployed to improve the lives of the world’s poorest people. Nonetheless, by focusing on health-related MDGs we do acknowledge the relevance of goals such 1) as eradicate extreme poverty and hunger; 2) achieve universal primary education; 3) promote gender equality and empower women; 4) ensure environmental sustainability. These ones as well are important to the achievement of proper health standards especially to poor people, they are just not on the focus of the present work.

Science, technology and innovation (STI) play a central role in understanding the phenomena of societal challenges and their interactions, risks and consequences, as well as developing solutions (OECD 2012). However, STI alone is not enough, as the development context of the countries have to be considered (Salamanca-Buentello et al 2005). Nanotechnologies could play an important role in the development of solutions, having impacts on the welfare of nations, knowledge assets and contributing to achieving and sustaining economic growth. It can, for example, enable many industries to produce products and services that are cheaper and lighter (Aydogan-Duda 2012a).

Significant for the deployment of nanotechnologies for the needs of developing countries are the findings of Salamanca-Buentello *et al* (2005). They ranked, with the help of experts, nanotechnology applications and their relationship to the achievements of specific MDGs. In here we focus on those health-related relevant applications.

The roadmap has been prepared taking into consideration the findings of Salamanca--Buentello et al (2005) because of the similarity of context in which we aim to advice for the deployment of nanotechnologies for health, the LA region, which is configured mostly of developing and emerging countries.

Table 1. MDGs of relevance for the roadmap on nanohealth

|  |  |
| --- | --- |
| **Goals** | **Target Indicators** |
| 4. Reduce child mortality | Reduce by two thirds the mortality of children under five |
| 5. Improve maternal health | Reduce maternal mortality by three quarters  Achieve universal access to reproductive health |
| 6. Combat HIV/AIDS, malaria and other diseases | Halt and reverse the spread of HIV/AIDS  Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it  Halt and reverse the incidence of malaria and other major diseases |
| 8. Develop a global partnership for development | In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries  In cooperation with the private sector, make available the benefits of new technologies, especially information and communications technologies |

Source: Based on United Nations (2000)

Table 2. Correlation between the top applications of nanotechnology for developing countries and the UN MDGs – Focus on health applications

|  |  |
| --- | --- |
| **Applications of Nanotechnology** | **Examples** |
| Disease diagnosis  and screening | Nanoliter systems (Lab-on-a-chip)  Nanosensor arrays based on carbon nanotubes  Quantum dots for disease diagnosis  Magnetic nanoparticles as nanosensors  Antibody-dendrimer conjugates for diagnosis of HIV-1 and cancer  Nanowire and nanobelt nanosensors for disease diagnosis  Nanoparticles as medical image enhancers |
| Drug delivery  systems | Nanocapsules, liposomes, dendrimers, buckyballs, nanobiomagnets, and attapulgite clays for slow and sustained drug release systems |
| Health monitoring | Nanotubes and nanoparticles for glucose, CO2, and cholesterol sensors and for in-situ monitoring of homeostasis |
| Vector and pest  detection and  control | Nanosensors for pest detection  Nanoparticles for new pesticides, insecticides, and insect repellents |

Source: Salamanca-Buentello *et al* (2005:385)

## Nanotechnologies for Health

General applications of nanotechnologies for health[[5]](#footnote-6) are within the fields of nanobiotechnology, nanomedicine and nanodevices (Frost & Sullivan 2008). According to the European Technology Platform on Nanomedicine (ETPN), nanomedicine is the application of nanotechnology to achieve innovation in healthcare (ETPN 2014).

*It uses nanometre scale materials and nano-enabled techniques to diagnose, monitor, treat and prevent diseases. These include cardiovascular diseases, cancer, musculoskeletal and inflammatory conditions, neurodegenerative and psychiatric diseases, diabetes and infectious diseases (bacterial and viral infections, such as HIV), and more* (Filipponi and Sutherland 2013:157).

According to Filipponi and Sutherland (2013), the potential contribution of nanotechnologies to medicine is extremely broad and includes: new diagnostic tools, imaging agents and methods, drug delivery systems and pharmaceuticals, therapies, implants and tissue engineered constructs. As many biological mechanisms in the human body are also nanoscale they allow nanoparticles and nanomaterials to potentially cross biological barriers to access new sites of delivery (directly to the targeted organ/tissue) and to interact with DNA or proteins at different levels, in different organs, tissues and cells (ETPN 2014). Nano-medicine is comprised of new applications for healthcare, in which nanomaterials and nano-electronics are being used for targeted drug delivery or for early detection of diseases (and in theranostics which combines detection and therapy).

The Nanotechnology Industries Association (NIA 2013) states that the deployment of nanotechnologies in medicine will positively impact the lives of populations in developing countries because it will allow the development of cost-effective and simple diagnostics devices for patients, and treatment of diseases affecting populations of developing countries.

A list of applications compiled by Aydogan-Duda (2012c) demonstrates the general applications of nanotechnologies in a variety of industries. Considering the purpose of this roadmap we focus on the applications for health, as can be seen in Table 3.

Table 3. Applications of nanotechnologies in the medicine and healthcare industry

|  |  |
| --- | --- |
| **Major challenges** | **Potential of nanotechnology applications** |
| * Long-time wounds of surgeries take to heal. * Damage cancer therapy can cause to other tissues. * Side effects of the trial and error method of drug delivery * Risk organ transplantation may result in crippling the entire immune system. * Health problems cannot be cured at all. | * The present practice to deliver chemicals into the body is via the bloodstream or to the stomach, and let it spread through the body[[6]](#footnote-7). For some chemicals like insulin, this is acceptable. But for others, such as chemotherapy drugs and some antibiotics, it is best to keep them as localised as possible. * Nanotechnology can assist in targeting therapies to where they are needed. * Nanomedicines and nanotech machines have created the possibility of diagnosing, treating, and preventing disease with the use of smart drugs and equipment that target specific organs or cells. |
| Side effects or damages to non-target cells | Nanotechnology has the potential to engineer particles to be used for detecting and treating diseases or injuries within target cells, thereby minimizing the damage to healthy cells in the body |
| * Unnecessary damage to other cells while treating a particular cell * Infection during surgery or in wounds * Untargeted diagnostics, treatment, and drug delivery | * Nanocrystalline silver is already being used as an antimicrobial agent in the treatment of wounds * Very useful devices using nanotechnology and other nanoproducts are under development which include:   + Quantum dots (Qdots), which can coated with specific targeting molecules to identify the exact location of cells (e.g. cancer) in a body   + Nanoparticles that deliver drugs directly to cells to minimize the damage to healthy cells   + Nanoshells that heat up when they absorb infrared light and destroy cancer cells selectively (as they are more sensitive to temperature rises)Nanotubes, which can provide a scaffold for new bone material to grow on |
| * Costs and operability of diagnostics | * Portable diagnostic kits are being developed, based on nanotechnology, that can deliver rapid results on blood chemistry or some other physiological marker without the need to send samples to a lab |

Source: Based on Aydogan-Duda (2012c)

## Diseases focused on the NanoHealth Roadmap

In this roadmap we look more closely at diseases which are considered a greater burden to poor populations in LA with the aim of contributing to achieving the MDGs. As with any new technologies, often the developed countries, and well-off sections of society of developing countries, reap the benefits before they can be used or accessed by poorer members. As the debate about the deployment of nanotechnologies in general pays more attention to the issue of an international divide between rich and poor, developed and developing countries, we aim to address these issues as well by means of discussing governance and the adaptive capability approach, as mentioned earlier in Chapter 5.

Considering the prominent findings of the bibliometric mapping and diseases affecting the most vulnerable populations of LA,the nanohealth roadmap will cover both communicable and non-communicable diseases, more specifically *tropical diseases,* with attention given to *tuberculosis*, and in addition to *cancer*.

### Tropical Infectious Diseases

Tropical diseases are often preceded by the adjective ‘neglected’, because they are poverty-related diseases, affecting mostly people who often cannot afford to pay for the treatment they need, and are therefore not subject to as much research and development by major pharmaceutical laboratories and donor agencies. Some recent exceptions include initiatives to eradicate malaria, tuberculosis and HIV/AIDS being carried out by the Gates Foundation and partners. These diseases are endemic in tropical and subtropical regions. Finding means for better diagnostics and treatment of tropical diseases will greatly impact the overall health, social and intellectual achievements and economies of the populations affected, therefore contributing to the achievement of other MDGs. Nanomedicine can provide solutions for tropical diseases, following up developments, such as nanotechnology-based molecular diagnostic platforms, nanoscale drug delivery systems and medicines.

We could not identify in the mapping exercise or actions of major international organizations dealing with tropical diseases, such as World Health Organization (WHO), Global Network for Neglected Tropical Diseases, Bill and Melinda Gates Foundation, the use of nanotechnologies as a strategy to fight NTDs. Despite this, we decided to focus on these diseases because they cause immense burden worldwide (about one billion people) and in LAC (about 180 million vulnerable people and with widespread distribution across the region).

The typology of tropical diseases refers to a medically diverse group of infections caused by a variety of infectious agents and pathogens such as viruses, bacteria, protozoa and helminths (Souza *et al* 2010). There are tropical diseases endemic in all (tropical) regions concerned and some that are prevalent and endemic in specific countries. The main infectious tropical diseases by pathogen type (ASTMH 2014) are comprised of: viruses (Dengue fever, Yellow fever, Rotavirus, HIV/AIDS, Ebola, Lassa fever), bacteria (Cholera, Escherichia coli, Tuberculosis, Hansen's disease/Leprosy), parasites (Malaria, Leishmaniasis, Trypanosomiasis/Chagas Disease, African trypanosomiasis or "sleeping sickness", Schistosomiasis, Filariasis, Onchocerciasis or "river blindness"), enteric protozoa (Cryptosporidiosis, Giardiasis, Amebiasis), other protozoa (Toxoplasmosis, Trichomononiasis), other helminth parasites (helminthiasis caused by Necator americanus and Ancylostoma duodenale, Ascaridiasis Trichuriasis, Strongyloidiasis, Taeniasis/neurocysticercosis). Besides these, there are still tropical diseases of “local” concern such as Chlamidiasis, Norovirus, Sapovirus and poisoning due to toxins transmitted by bites of venomous animals, as in the case of Brazil (Souza *et al* 2014).

The WHO has listed seventeen tropical diseases, considered to be neglected, as targets of special actions by the WHO and other concerned organizations. The list with the seventeen neglected tropical diseases, their causes, distribution and impacts are provided in Annex 3. It has to be said that there is a lack of uniformity in the data presented in Annex 3, as they were compiled from WHO (2013a) making clear cases of under-reporting and lack of data on burden of the diseases as well as on impacts of use of available prophylactic and preventive therapeutics. By many accounts, Brazil is the country most affected when it comes to prevalence of tropical diseases in LA.

Annex 3 also illustrates many reasons for concern about neglected tropical diseases regarding their distribution, impacts, burdens (health, economic, social and psychological) and the potential of co-infection and co-morbidity, especially in individuals suffering from HIV/AIDS (WHO 2013a). They have also been detected in poor areas of developed countries, such as the United States, according to accounts from ASTMH (2014) and Hotez (2013), and in Europe due to migration and re-emergence of diseases (WHO 2013a). These undermine poor people’s achievements and represent a burden in their countries, as well as being related to the effects of natural and anthropogenic devastations and climate change (as in the cases of rabies, dengue, malaria and yellow fever).

Considering LA, the regional focus of NMP-DeLA project, it can be seen that most of the tropical diseases are endemic in the region, as highlighted in Annex 2. In LA there are about 50 million people living in a state of extreme poverty (with an income of less than one dollar a day), and about 180 million below the poverty line, out of a total population of about 597 million. The majority of these people live in conditions favouring a greater burden of disease. These people are often members of vulnerable groups, such as indigenous populations, rural inhabitants, the elderly, women living in poverty and children.

Below we take a look in more detail at Tuberculosis, an infectious disease that is endemic in tropical regions, and has seen resurgence in the form of resistant strains and co-infection with HIV/AIDS all over the world.

### Tuberculosis

Tuberculosis (TB) is caused by the bacterium *Mycobacterium tuberculosis* and is spread from person to person through air. TB usually affects the lungs (pulmonary TB) but can attack other parts of the body as well. Most people infected with the *Mycobacterium tuberculosis* bacterium will not develop TB and do not usually transmit the bacteria, however, a small proportion of people will have active TB with symptoms. With proper treatment the prognosis for TB is good.

TB is an infectious disease with a continued, high global burden, despite being preventable and mostly curable. TB is found in all parts of the world and is one of the leading causes of adult deaths. In 2012, 8.6 million people fell ill with TB and 1.3 million died from the disease. In 2011 South America accounted for two-thirds (67%), Mexico and Central America 17%, the Caribbean 11% and North America 5.1% of all incidences of TB cases in the Americas. The total number of new TB cases in the area was estimated to be 268,400 (PAHO 2013).

Multidrug resistant TB (MDR-TB) is a form of TB which does not respond to standard treatments. The primary cause of MDR-TB is the incorrect or inappropriate use of anti-TB drugs. MDR-TB is prevalent in practically all countries surveyed by WHO (WHO 2014a). In LAC most of the estimated MDR-TB cases among notified pulmonary TB cases in 2011 were found in seven countries: Peru (2100), Brazil (1100), Mexico (470), Ecuador (350), Argentina (350), Dominican Republic (320) and Haiti (310). Extensively drug-resistant TB (XDR-TB), which is a more severe form of TB, is also prevalent. It has been reported to be found in 11 countries in LAC (PAHO 2013).

HIV and MDR-TB have a large impact on TB control. People infected with HIV have 20 to 30 times higher probability of developing TB. It is estimated that 1.1 million of the 8.6 million globally infected people in 2012 were HIV positive. In 2011, Brazil, Mexico and Haiti accounted for most of the HIV-positive TB cases in LAC. At a country level the highest prevalence of HIV-co-infection with TB were found in Belize, Trinidad and Tobago, and Suriname (PAHO 2013).

Diabetes may become the next challenge for global TB control. Diabetes has a proven relationship with TB and people with diabetes have been found to have as much as three times a higher risk of developing TB compared to people without diabetes. Diabetes is a growing health burden worldwide and especially in low- and middle-income countries (Shaw 2009; WHO 2011). In a study conducted by PAHO (2008), it was estimated that diabetes was a major contributor to the TB burden of the region. The study recommended that TB was routinely screened for among those with diabetes.

TB and poverty are connected; TB can be seen as both a result of poverty and a factor creating poverty. Lack of access to health care services, poor nutrition and inadequate living conditions contribute to increased susceptibility to TB. The economic burden of TB on families can be severe. The disease affects mainly people in their most economically productive years (between ages of 15 to 59 years) and is one of the main causes of mortality for women between 15 and 44 years of age. There are around 10 million orphaned children as a result of adult deaths (WHO 2013d).

In 1993, WHO declared TB as a global public health emergency. This was followed by publishing a five-point action plan called Directly Observed Treatment, Short-Course (DOTS)[[7]](#footnote-8) to guide national efforts in TB treatment (WHO 2014c). Most countries have adopted the recommended approach and much progress has been achieved since. TB mortality rate has dropped 45% since 1990 and incidence rates are decreasing, although at a slow rate (2% per year) on a global scale (WHO, 2013d). In 2011, Brazil, Peru, Mexico and Haiti were the leading countries for the number of TB cases in the Americas, and the four countries accounted for 60% of all cases in the area. Globally, Brazil ranks 17th on the number of TB cases, however, it should be noted that there has been a substantial reduction in new cases of TB in Brazil over the past twenty years (PAHO 2013).

The UN MDGs have a target (6C) of reversing the incidence of TB by 2015. The “Stop TB Strategy” of WHO adopted the MDG target and set global targets of halving TB prevalence and mortality rates by 2015 from the level in 1990. The year 2050 was set as a target to eliminate TB as a public health problem (< 1 case per million population). These targets have been supported by the Stop TB Partnership, which is an international body hosted by the WHO and with almost 1100 partners involved in the fight against TB in over 100 countries. A global post-2015 tuberculosis framework strategy is under development that will contain milestones for 2025 and targets for 2035, with the goal of ending the TB epidemic (WHO 2014b).

The target of halving TB mortality rate globally by 2015 is within reach. Two WHO regions -the Americas and the Western Pacific Rim- have reached the 2015 targets concerning reduced incidence, prevalence and mortality. However, African and European regions are not on track to achieve targets (WHO 2013d).

### Cancer

The world health landscape is changing as more people live longer. Life expectancy in many LAC countries has risen substantially in the past decades and the LAC economies are currently in different phases of demographic transition to ageing populations. Demographic transition is related to epidemiological transition with a decline in infant mortality and shift from communicable, maternal and perinatal diseases to chronic conditions. The share of non-communicable diseases (NCDs), including cancer, has grown and become the main cause of mortality in the region, with NCDs as the cause 74% of all deaths in the Caribbean and accounting for 69% of all deaths in Latin America (PAHO 2014). It is estimated that 1.8 million new cases of cancer will be diagnosed in LAC in 2030 and over 1 million cancer deaths will take place (Ferlay *et* *al* 2012).

As economies in LAC are growing rapidly, the standard of living is rising and the lifestyles of people are changing. Demographic changes and industrialized lifestyles contribute to the growth in cancer rates. Physical inactivity, unhealthy diets, smoking and high alcohol consumption are major risk factors for cancer. Tobacco use, which is the single major cause of cancer, is highest among adult populations in Chile, Bolivia and Uruguay in LAC, whereas, obesity has been found highest in English-speaking Caribbean countries (PAHO 2014b).

Exposure to sun and environmental carcinogens are also identified risk factors for cancer. Worldwide, three billion people cook and heat homes with open fires using solid fuels (i.e. wood, coal, charcoal, animal dung, crop waste). Cooking and heating in poorly ventilated houses may expose people to indoor smoke levels that are 100 times higher than acceptable for small particles. Most of the affected people are poor people living in low- and middle-income countries. In LA, many indigenous people live in remote areas and use biomass fuel for cooking and heating. These people have been found in a number of cases also to live on environmentally degraded lands. Examination of cancer incidence and mortality of indigenous populations in LA is difficult, owing to a lack of data (WHO 2014, Goss 2013).

At the moment there are fewer cases of cancer in LAC than in Europe or the United States[[8]](#footnote-9). However, the all-cancer mortality-to-incidence rate for LAC is notably higher[[9]](#footnote-10) (Ferlay *et al* 2012). Higher mortality rate in LAC is due to diagnosing cancers at advanced stages and also partly related to poorer access to care. Worldwide, cancer incidence rates are still highest in more developed regions, whereas, cancer mortality is relatively higher in less developed countries. This is due to late diagnosis and poor access to treatment facilities (IARC 2013).

In LAC, cancer deaths in men are mainly caused by prostate cancer, followed by lung, stomach and colorectal cancers; whereas breast cancer, followed by cervical, lung and colorectal cancers are the main causes of mortality in women. Cancer incidence and mortality for men and women in LAC are depicted in Figure 2. It is interesting to note that, although in the United States prostate cancer is by far the most common cancer for men and breast cancer for women, it is lung cancer that has the highest mortality rate for both sexes (Ferlay *et al* 2012).

|  |  |
| --- | --- |
| Incidence and mortality of different cancers in LAC | |
|  |  |

Figure 2. Incidence and mortality of different cancers in LAC.

Source: Ferlay et al (2012)

As depicted in Figure 2, breast cancer is the most common type of cancer in women both in terms of new cases and deaths in LAC. Mammography screening and early treatment has decreased breast cancer mortality in developed countries, whereas, in LA, breast cancer mortality has been increasing for the past two decades (Goss 2013). In women under 65 years of age breast cancer mortality is much higher in LAC (57%) than in North America (41%) (PAHO 2014c).

Around 17% of cancers in LA are estimated to be attributed to infections. Viral hepatitis infections are the main cause of liver cancer and 82% of all liver cancers in LA have been found to be caused by viral hepatitis infections (Goss 2013).

There are wide health disparities among countries and within countries in LAC. The challenge for countries in the region is to develop sustainable health care systems that cover treatment for NCDs and provide social protection, especially for poor people. Health insurance is restricted in many countries to higher-income populations and public health care services are focused on communicable diseases. Treatment of NCDs has poor health care status and may need to be paid out-of-pocket. For the poorest families, costs prohibit the possibility to benefit from preventative and health-protective measures. In LAC the rural poor are even more disadvantaged than the urban poor. There is greater poverty in rural areas and poorer access to cancer treatment services. Regional health disparities and differences between public and private hospitals can be found in the distribution of early and advanced-stage disease (Goss 2013).

A review on the present state of care for breast cancer in Brazil identified regional and socioeconomic disparities in access to public mammography screening, diagnostic accuracy, availability and quality of equipment in use for treatment, access to therapies and cancer awareness (Lee 2012). According to a study made in the Amazone project, more advanced stages in breast cancer were found in those working in public institutions than in the private sector; 36.9% of patients in public system were diagnosed with stage III and IV compared to 16.2% in the private sector (Simon 2009).

Clinical trials are essential to the process of developing new cancer treatments. In LAC participation in clinical trials can be an attractive option for patients as trials provide access to medical therapies which would not otherwise be available for patients. Mexico, Brazil and Argentina have been the most established countries in clinical research (Virk 2009).

As the incidences of cancer continue to grow, this will pose a major health and economic threat to LAC and other low- and middle-income countries. Hospitalisation accounts for the highest share of direct costs of cancer, while drug costs are a small portion. From the economic point of view, avoidance of advanced (IV) stage of cancer is important for reducing costs (Goss 2013). Investment in prevention, timely and adequate diagnosis and treatment of cancer are important measures in reducing cancer burden in LAC.

## Nanomedicine for tackling of Tropical Infectious Diseases

Tackling of NTDs can be done through public-health measures, such as vector control, education, treatment and prevention (for example through vaccination). These measures are often not enough, as poor countries stricken by NTDs often lack health facilities and capabilities for diagnosis, and treatments may require strict adherence and still have harsh adverse effects. Many of the diseases have not been in the research and development agendas of the pharmaceutical industry, and the lack of financial resources to acquire medicines either by infected people or their governments, as well as political willingness in some cases, has limited impact.

Look *et al* (2010) call attention to the technological deficiency of available and effective therapeutics that prevent or alleviate disease progression and propose the use in the near future of nanomedicines to tackle tropical infectious diseases in the developing world by promoting more effective immunotherapy to prevent or clear pathogen infection. According to them, nanoscale vehicles are particularly adept at facilitating immunotherapeutic approaches because they can be engineered to have different physical properties, encapsulated agents, and surface ligands. Furthermore, point-of-care diagnostics containing nanostructured materials offer new alternatives for portable and sensitive health monitoring that can guide the use of nanoscale immunotherapies. New vaccines and therapeutics will also improve patient compliance with treatment, avoiding the potential generation of drug resistant pathogens, and nanoparticles used as novel immunotherapeutic platforms are attractive for several reasons: these systems can encapsulate a high density of bioactive compounds that can stimulate immunity; they can be fabricated from materials that can release encapsulated compounds in a sustained fashion over several days to months; they can be extensively modified to enhance their bioactivity or transport to specific cells and organs within the body and because of the flexibility over their synthesis and formulation (Look et al 2010: 381).

As an example of achievements in delivery of nanoscale therapeutics Look et al (2010) cite the possibility of nanocarrier-based systems to deliver drugs that are administered in several doses in the course of long periods (such as the treatment of visceral leishmaniasis with antibiotic paromomycin in Bihar state in India by the Institute for One World Health). Other advantages of encapsulating therapeutic agents inside nanoparticles, is the potential to improve their stability during transport across extreme temperature environments and to enhance the agent’s bio-distribution within the body after its administration. Still, the authors emphasize that there are opportunities for further improvement using nanoscale drug delivery systems.

Focusing on preventive strategies, there are still two approaches on how nanoparticles can be used to create new generations of versatile and potent prophylactics: 1) innate immune stimulators and microbicides for short term protection against pathogen transmission in the event of known potential exposure and 2) vaccination strategies that attempt to elicit immunological memory responses to prevent infection, for long term protection.

The application of nanomedicines for therapy of tropical diseases is illustrated in Table 4. Need to emphasize you are not preventing any prophylactic-related strategies.

Regarding diagnostics, Look *et al* (2010) emphasize that solutions to be deployed in developing countries need to be clinically accurate and reliable, cheap, quick and simple to use. Diagnostic solutions can be deployed in “lab-on-a-chip” devices. Diagnostic solutions specific to tropical diseases exemplary of note are the following EU-funded projects: Point-of-care Diagnostics for Tropical Diseases (PodiTrodi) and Disc-shaped point-of-care platform for infectious disease diagnosis (DiscoGnosis). PodiTrodi ended in 2011 and aimed to analyze proteins and DNA –strains of tropical disease pathogens using advanced point-of-care technologies. DiscoGnosis runs until October 2015 and its objective is to develop a platform for detection of malaria and similar pathogenic diseases in a rapid, multiplexed and non-invasive way. According to Smit (2013) the estimated time to market is 6 - 8 years.

There is still a risk of a “nanodivide” regarding the deployment of nanomedicines for the well-being of poor populations around the word. As there was no mention of deploying nanotechnologies for treatment of NTDs in WHO’s accounts (WHO 2013d), this may be an indication that political desire advocating for developing advanced technologies for the treatment of these diseases is still weak. Although the extent of nanotechnology deployment and its increasing scientific visibility are not exhaustively discussed here, the burdens represented by these diseases and the claims for the MDGs and its transition to Sustainable Development Goals (SDGs) may be important enough to push for the introduction of nanotechnologies for their treatment.

Table 4. Selected strategies for chronic infection treatment

|  |  |  |  |
| --- | --- | --- | --- |
| **Chronic condition** | **Current treatment strategy** | **Therapy duration** | **Example of NMP strategies** |
| HIV/AIDS | Highly active anti-retroviral therapy (HAART) | Life-time; daily oral dose | Dermavir patch  Antiretroviral pediatric formulation1 |
| Leishmaniasis | Pentostam  Glucantime amphotericin B  Amphotericin B  Paromomycin | 30 days; daily i.v. | AmBisome-liposome formulation with Amphotericin B |
| Tuberculosis | Rifampicin  Isoniazid  Pyrazinamide  Ethambutol | 6–9 months; three oral doses per week | Aerosolized rifampicin-PLGA;  aerosolized IFN-γ emulsions |
| African trypanosomiasis | Suramin  Pentacarinat  Melarsoprol[[10]](#footnote-11)  Ornidyl | 10–20 days; daily i.v. injection, up to 4 times/day | Lipid-drug nanoparticles |
| Chagas disease | Nifurtimox  Nitroimidazole  Benznidazole | ≥60 days; 2–3 daily oral dose | PEG-PLA ( Pegylated poly(lactide) and poly(lactide-co-glycolide) nanoparticles) nanoparticles  Novel benznidazole lipid-based drug delivery systems 2 |
| Schistosomiasis | Praziquantel | 1 oral dose | Lipid emulsion  Pediatric pharmaceutical suspension via miniemulsion polymerization 3 |
| Malaria | 4-aminoquinolines  8-aminoquinolines  4-Quinolinemethanols  Artemesinin  Atovaquone  Antibiotics | variable; typically 3–7 days for acute phase, followed by  daily dose with Primaquine for 2 weeks | Lipid emulsion of Primaquine |

Source: Based on Look *et al* (2010:11); 1Marques (2015); 2 approach of BERENICE project (2014) 3 da Fonseca et al (2013)

#### Treatment of Tuberculosis

Currently Tuberculosis is treated with a six-month course of antibiotics (WHO 2014a). MDR-TB needs a longer treatment time with second-line drugs that are more expensive and have more side-effects. For treatment of XDR-TB there are fewer options available as second-line drugs are not effective (WHO 2013d).

Sputum smear microscopy, culture of MTB bacilli, detection of MTB nucleic acids and clinical symptoms are used to diagnose active TB. For latent TB, a tuberculin test skin test and interferon gamma release assays are used. It is important to diagnose not only active TB cases but also latent TB cases, because 10% of the latent individuals can later develop active TB. If the immune system of a latent TB person is weakened, the probability of falling ill with TB will grow (Wang 2013).

Low specificity of clinical diagnosis, lack of availability of diagnostic testing in developing world laboratories and incapability to monitor patient compliance with the 6-9 months therapy, are reasons that are limiting TB diagnosis globally (Wang 2013). In 2011, the percentage of new PTB cases in LAC that were bacteriologically confirmed by any laboratory method varied between 53% (Guyana) and 98% (Trinidad and Tobago) (PAHO 2013).

Sputum smear microscopy is the most widely used diagnostic test for TB (WHO 2013d). However, sputum smear microscopy has a poor sensitivity, meaning that many people with active TB are not found. Also, people with advanced HIV infection are often not detected by sputum smear. Low cost and rapid results are the reasons for the wide use of sputum smear microscopy. Sputum cultures have a higher sensitivity, but also higher costs and obtaining results takes around 3-4 weeks. Rapid diagnostic tests have been developed, and some are already in use, for example Xpert MTB/RIF, which is able to detect the TB bacterium reliably within several hours (TB Online 2011).

## Nanotechnology in cancer treatment

The use of nanotechnology in the fight against cancer offers promising possibilities, from cancer diagnostics and imaging to therapy and drug delivery. Nanotechnology can be used for finding small tumours through imaging, and nanoparticles can deliver anticancer drugs to the tumour. With nanoscale therapeutics, precise targeting of tumours with minimal damage to healthy tissue is possible, as well as identification and elimination of cancerous cells at an early phase before forming tumours.

In traditional cancer treatment, drugs that are toxic to tumour cells are often toxic to healthy cells, thus causing undesirable and dangerous side effects to patients. Difficulty in localizing therapy to tumour sites, issues of drug toxicity, short drug circulation times and tumour resistance to drugs are problems in current cancer treatments. Compared with unmodified drugs, nanotechnology-based therapeutics have enabled more effective imaging and drug delivery in preclinical trials, with benefits such as, improved half-lives, retention, targeting efficiency and fewer patient side effects (Ho 2014).

In preclinical trials, several nanomaterial formulations have been promising. Different nanomaterials can act as vehicles for drug and imaging agent delivery. These include lipid-based vehicles (liposomes, solid lipid nanoparticles, and micelles); polymer carriers (hydrogels, polymersomes, dendrimers, nanofibres); metallic nanoparticles (gold, silver, titanium); carbon structures (nanotubes, nanohorns, nanodiamonds, graphene) and inorganic particles (silica). It has been discovered that different classes of materials are optimal for specific applications. For example, metallic particles have been found promising as photothermal (heat up in response to electromagnetic radiation, usually infrared) therapeutic agents (Chow 2013).

Some nanoparticle-based drugs are already on the market, for example, doxorubicin, a liposome-based drug for many types of cancers (including leukemias, lymphomas, and breast, uterine, ovarian, and lung cancers) and protein-bound paclitaxel for breast and other types of cancer.

### Examples of nanomedicines under development

Cancer nanotechnology is a vast field with ongoing development for diagnosis, prevention and treatment of cancers. Below are several examples of *ongoing* developments in the area.

Nanoparticles which are able to specifically attack cancer cells and bypass healthy cells have been demonstrated by researchers. Targeted nanoparticles for cancer treatment are based on the idea that drugs can be inserted into biodegradable polymeric nanoparticles with the surface of the nanoparticles coated in a protein (ligand) that binds to specific proteins (tumour antigen) on the surface of the cancer cell. BIND-014 is a drug candidate that is composed of a biodegradable nanoparticle containing a ligand that targets a specific protein present in prostate (and also in many other) tumours, and the chemotherapy drug docetaxel, which is widely used in the treatment of e.g. breast cancer. BIND-014 has recently entered phase 2 clinical trials (Dana-Farber 2014, BIND 2014).

Other therapies make use of potent anti-cancer proteins found within the body. For example, tumour necrosis factor alpha (TNF-α) is released by immune cells within the body to stimulate inflammation (and therefore destroy damaged or diseased tissue, including cancer). Promising research has combined TNF-α with gold nanoparticles, and targeted this to tumour cells where it stimulates their destruction. TNF-α has proved to be most effective with other chemotherapy drugs (Cytimmune 2014).

Photothermal therapy with nanoshells (a silica core covered with a thin shell of gold) uses heat to kill cancer cells. By changing the size of the core and the thickness of the gold shell, it is possible to tailor the nanoshell to respond to a specific wavelength of light. Nanoshells convert near-infrared light into heat, which destroys tumour cells (which are more sensitive to heat than normal cells). The conversion of light to heat is very localized and does not affect nearby healthy tissues. The therapy is broadly applicable to most solid tumour types, and clinical trials for head and neck cancer, as well as, primary and/or metastatic lung tumours are being carried out (Nanospectra Biosciences 2014).

Iron-oxide nanoparticles can be heated using an alternating magnetic field and in a similar way to the silica nanoshells destroy tumours. An additional benefit is that the destruction of the cells can activate an immune response that attacks tumours elsewhere in the patient who have not had the heat treatment. It is envisioned that with the technique the immune system could be trained to attack unrecognised metastatic tumours (Dartmouth 2014).

Ribonucleic acid interference (RNAi) is a promising mechanism for silencing cancer-causing genes. RNAi is a biological process that is important in normal cell development and differentiation (to switch off specific gene expression). As a therapeutic device it has shown potential in shutting down genes that have become hyperactive through cancer. High specificity and potency as well as reduced toxicity are advantages of small interfering RNA (siRNA) compared to conventional small molecule or protein-based drugs. With detailed analysis of each tumour, RNAi-based therapies make it possible to choose the most appropriate anticancer drug for each patient (Bora 2012).

In the development work, the challenge has been to safely deliver therapeutically effective doses of small interfering RNA (siRNA) into tumours and avoid healthy cells. Delivery of siRNA to the target tissues and stability in serum are the focus of current research and development work (Bora 2012). An example is a novel drug, consisting of RNAi molecules and lipid nanoparticles, that has been tested in a first clinical trial with patients that have advanced liver cancer, with promising safety and clinical utility results (Tabernero 2013, Vall d’Hebron Institute of Oncology 2013).

# State of the Art in Nanotechnologies for Health in LA

The results of the mapping of the deployment of nanotechnologies for health in LA has been used to substantiate the construction of the roadmap, as it has identified enabling programmes and initiatives, scientific output, key institutions and researchers and international cooperation targeting advanced materials deployment for health applications (see Invernizzi et al 2015, NMP-DeLA website).

Whenever needed we refer directly to the mapping exercise (Invernizzi et al 2015), therefore we present only a summary of the findings of that main document here. Data was gathered through bibliometric study techniques, using the two major international citation databases available, Thomson Reuter’s Web of Science (WoS) and Elsevier’s Scopus, and through desk research, searching public databases on R&D groups, institutions and on public funds allocated by topic in each country. It is important to note that access to information on public policies, funding, research groups, institutions, laboratory facilities and companies involved in research, development and production in the area of nano-health was very uneven among the countries.

Based on the gathered information and key research questions, a questionnaire (See Annex 1) was developed and distributed online and also used for in-depth interviews. Altogether 14 people were interviewed (8 from Latin America and 6 from Europe). In addition, information from 13 speakers during the NMP-DeLA workshop in Buenos Aires on 19 May 2014 was incorporated. Results from the interviews are presented in Chapter 8. The list of interviewees can be found in Annex 2.

Several LA countries have started promoting nanotechnology over the last decade, and included it as a strategic area in their STI Plans. The process has been led by Brazil, Mexico and Argentina, not only as the largest economies in the region, but also as the countries that have historically accumulated the more advanced scientific capabilities. Other LA countries have followed.

The main results of the publication and co-publication analysis in the field of nanomedicine (Invernizzi et al 2015) using WoS and Scopus databases are:

• Publications on nanohealth in LAC have increased since the year 2000. The area of greatest development in the region is drug delivery, which has seen exponential growth since 2005, followed by *in vivo* imaging and biosensors according to WoS data. Other areas are still at an early stage of development.

• The data obtained after performing both methodologies showed a strong concentration of publications in Brazil and Mexico, and to a lesser extent, Argentina. The Universidade de São Paulo (USP) and the Universidad Nacional Autónoma de Mexico (UNAM) are the two top research institutions.

• Co-authoring is another important trend. Authors from the EU are present in approximately one quarter of the publications according to data taken from the Scopus database, but are less representative according to the WoS database. In both studies, Spain, France and Germany stand out as the most common partners in EU-LAC collaborations. Such collaborations have intensified since the mid-2000s, according to the Scopus data, following the general increasing trend in research funding and publications.

• Cooperation among Latin American countries, assessed by co-publications, is weaker and concentrated on bilateral collaborations between Mexico and Cuba, Brazil and Cuba, and Argentina and Brazil. Five Latin American countries do not have any such collaboration.

• A list of leading authors, groups, institutions and main international collaborations, portrayed in the bibliometric mapping, identified relevant experts and potential participants in future project activities.

Desk research by country added some important qualitative and quantitative information, which can be summarized as follows:

• There are strong inequalities between countries regarding research infrastructure, human resources, and funding. Brazil and Mexico have the strongest capabilities, followed at a considerable distance by Argentina. This presents a regional gap.

• All the countries have research groups in nanohealth with specialization on different topics: Brazil (mainly drug discovery and therapies and drug delivery), Mexico (materials for diverse applications in nanomedicine, drug discoveryand therapies, and drug delivery), Argentina (drug delivery and tissue engineering), Chile (drug discovery and therapies), Colombia (nanotechnology applied to cancer research), and Uruguay (small group of research scattered among different areas);

• Research groups in most countries have some degree of cooperation with international research networks, within and outside the region. In Brazil and Argentina, the research organization in networks has been heavily induced by STI policy.

• Research funding in all countries comes mostly from public funds. Even companies carrying out R&D rely heavily on public funds. In the case of Brazil more than one third of the nanotechnology projects granted to companies, with non-refundable funds, were directed to promote nanomedicine. Furthermore, around one third of the funding directed towards research networks was secured by nanomedicine related projects. The Brazilian Ministry of Health also allocated funds directly to this area. In Mexico, a study of several calls for research showed that around 5% of the budget was aimed at nanotechnology research; and of that only 10% had the aim of fostering nanomedicine.

• There is small number of companies with R&D and commercial activities in nanomedicine in the LAC region. Brazil has the largest number, with 30 of them in the area of pharmacy and health. In Mexico, only 2%, of 101 companies with activities in nanotechnology, and these are looking at applications in the following areas: medical and dental devices, biomedicine and pharmaceuticals. No information was available for the other countries.

• It is not an easy task to distinguish what research in the area of nanomedicine could be of social relevance for the Latin American region. On the one hand, most of the research is very basic in nature; so the potential applications and benefits are very difficult to envisage. On the other hand, several Latin American countries have crossed the “epidemiological transition” and present a very similar pattern of diseases and causes of deaths to most developed countries. Although some typical diseases, such as tropical diseases, are still of importance, most research seems to be directed to the global landscape of medical issues. However, it may be possible to mine data that researchers already have, to identify possible opportunities for collaboration. For example, a more detailed bibliometric analysis could identify groups that have been using techniques, such as genomics and proteomics, and would have data of relevance to other groups developing therapies or diagnostic platforms.

A national strategies implemented by Brazil, which address nanomedicine ,worth mentioning here is the National Nanotechnology Laboratory System (SisNANO), a platform for nano-biotechnology projects for the Unified Health System (SUS) called NANOSUS. This platform, formed by various partners, aims at developing, validating and prototyping nanobiotechnological processes and products for the SUS, which is the public health system of Brazil. Although SUS has universal coverage, the majority of its clients are concentrated in the middle and low income classes.

## Nanomedicine for tropical diseases

## Research

In general, few examples exist of research on nanomedicine targeting tropical diseases in LA and in general besides those presented in Table 4 and mentioned in this report.

The mapping of deployment of nanotechnologies for health (Invernizzi et al, 2015) not identify significant research, by means of bibliometric studies, addressing the topic of tropical diseases and scientific cooperation between LA and Europe. On the positive side, some international cooperation networks already exist. In particular the SABIN institute hosts the Global network on neglected tropical diseases (NTDs). The US National Institute of Allergy and Infectious Diseases (NIAID) could also be open to international cooperation with European and Latin American partners.

The interviews revealed that several NMP-DeLA community of interest members are working on nanotechnology for tropical diseases in international cooperation. For example, at the Paris Lodron University in Salzburg (PLUS), the Immunology and Allergy Division at the Department of Molecular Biology is working on nanomaterials in medicine and nanodrug delivery for allergy therapy. This can be applied to selecting active drug compounds through the effect on the immune system. They already have Brazilian contacts. In the project Promoting and Coordinating Research Co-operation among EU Member States and Latin American Countries (EULANEST), nanomedicines are being developed for topical treatment against Leishmaniasis in cooperation with partners from Argentina and the University of Berlin. The Royal Institute for the Tropics (KIT) in the Netherlands is working on nanodiagnostics, for more rapid detection of Tuberculosis. They are cooperating with partners from research and industry in the Dutch programme NanoNextNL and from developing countries. Also in the Netherlands, The National Institute for Public Health and Environment RIVM, at Maastricht University, University Medical Centre Utrecht and the company Enceladus are studying interactions of nanomedicine with the immune system. This is relevant to applications of nanotechnology to tropical diseases.

## National activities

In Brazil, several projects have been funded by the Department of Science and Technology of the Ministry of Health, in association with the Brazilian National Council for Scientific and Technological Development (CNPq) from 2004 to 2010 on “controlled drug delivery systems” directed to leishmaniasis treatment. The Brazilian National Institute of Nanobiostructures and Nanobiomolecular Simulation at Federal University of Ceara (UFC) specializes in the biotechnological applications of crystals (of amino acids, DNA, RNA and proteins) including the engineering of crystals for drug development for neglected diseases. At the Federal University of São Paulo (UNIFESP), the Department of Ocular drugs and Therapies works on nano for therapies for neglected ocular diseases. The recently created Laboratory of Nanomedicine and Nanotoxicology (LNN) at the Physics Department of the University of the State of São Paulo at São Carlos (UNESP-São Carlos) has as one of its priorities the development of new materials for detection of biological substances and biosensors for diagnostics of several health conditions, including neglected diseases. At the Federal University of Rio de Janeiro (UFRJ), research is ongoing on drug delivery and vaccines that target leishmaniasis through transdermal drug delivery. At USP, priorities in nanomedicine research include Leishmaniasis and Chagas disease.

This low level of research activity focuses the need and relevance of political involvement in order to address such ailments that impact the lives of mostly disadvantaged populations in LAC. Look et al (2010) also call attention to the technological deficiency of available and effective therapeutics that prevent or alleviate disease progression.

## Policy and funding for tropical diseases

Funding for research and product development on tropical diseases is very limited. The WHO and Bill Gates Foundation fund research on tropical and neglected diseases, including parasitosis. Recently, the WHO called upon its member states to invest more in tropical diseases (Holmes 2015). At global level, the Global Fund invests in projects proposed by countries combating HIV/AIDS, Malaria and Tuberculosis. It is not clear if this includes R&D on new drugs and diagnostics in general, let alone nanomedicine.

## Pharmaceutical and medical devices industry and investment targeting tropical diseases

Liposomal nanomedicine is available and can in principle be applied to the parasite Leishmaniasis. The drug is 1000x more effective after incorporation in a liposome. According to an interviewee it is still not available on the market for three reasons:

* the costs of development and testing are too high
* treatment costs are projected to be US$10-12 instead of US$0.10 per pill
* the drug would have to be injected in hospital while the existing drug can be administered orally.

Nanotechnology is not used in most existing products for tuberculosis treatment, but offers opportunities for new point-of care diagnostics in the future.

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#### Nanomedicine for cancer

### 7.2.1 Research

While cancer is not a priority topic in nanomedicine research in LA, the bibliometric study carried out in NMP-DeLA has identified some groups and individuals working on this, per country.

In **Brazil**, the Department of Science and Technology of the Ministry of Health, in association with the CNPq, has, from 2004 to 2010, funded several projects on “controlled drug delivery systems” directed to cancer[[11]](#footnote-12). Such research targeting cancer has been carried out at the Federal University of Rio de Janeiro (UFRJ).The recently created Laboratory of Nanomedicine and Nanotoxicology (LNN) at the Physics Department of the University of the State of São Paulo at São Carlos (UNESP-São Carlos) includes research on the toxic effects of nanoparticles and carbon nanotubes on healthy and cancer cells. The Centre for Nanotechnology and Tissue Engineering at USP produces nanostructured photo-activated drugs for skin cancer treatment. It cooperates with the Excellence Centre for the Treatment of Cancer in Belém do Pará, Brazil.

In **Mexico**, the Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco (CIATEJ) is working on a chip containing nanoparticles of gold for early detection of cancer. At the Centre for Research and Advanced Studies (CINVESTAV) of the National Polytechnic Institute (IPN), research is ongoing targeting nanomaterials for treating cervical cancer and precancerous cellsn the Mexican Institute of Social Security (IMSS) there is research on new diagnostic methods for cancer and other diseases. In addition, researchers the Institute for Biotechnology, University of Sonora, are investigating cancer.

In **Argentina**, the Laboratory of Highly Reactive Species at the Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas (INIFTA) works on nanomaterials, toxicity and cancer. The faculty of Exact Sciences of the National University of Rio Cuarto works on photo-assisted cancer therapy. Instituto Leloir works on nanomedicine for cancer. The Laboratory’s gene therapy designs and applications are patented. They apply Camelid (Llama) anti-bodies found in LA. They cooperate with INIS Biotec, Instituto Leloir technologies incubator. Through their Argentinean partner company, Immunova, they are in touch with Ablynx, which is in the business of screening Llama antibodies against therapeutic targets, and received US$20 billion investment from Merck. They also cooperate with Argentinean family laboratories.

In **Chile**, the Centre for Advanced Interdisciplinary Research on Materials Science (CIMAT) at the University of Chile works on magnetic nanoparticles for cancer treatment and the Centre for Bioinformatics and Molecular Simulation at University of Talca, in cooperation with the Fraunhofer Institute, works on cancer treatment. The Centre for Integrative Medicine and Innovative Science (CIMIS) at Andrés Bello University and University of Santiago in Chile are cooperating in the Higher Education Quality Improvement Programme (MECESUP) project. This applies modelling to early detection of cancer cells. Other applications are in neuroscience, pain treatment, and drug release of antibiotics. They host the best computer facility in Chile.

In **Colombia**, the interdisciplinary network of the Nanoscale Science and Technology Centre (NanoCiTec) works on cancer and nanotechnology. Overall, Colombia´s research groups have a strong focus on nanotechnology applied to cancer research.

### Pharmaceutical and Medical Device Industry

Several nanoscale drug delivery products are on the market, mainly for cancer. The interest of industry is more in prolonging the patent life of anti-cancer drugs, according to some NMP-DeLA Community of Interest members. In a collaboration between Israel and Brazil, the Nanose diagnostic devices has been developed that can diagnose different cancers in the body.

#### Responsible research and innovation aspects

Clinical trials are essential to the process of developing new cancer treatments. In LA participation in clinical trials can be an attractive option for patients as trials provide access to novel and otherwise unattainable medical therapies. Mexico, Brazil and Argentina are the most established in clinical research (Virk, 2009). Such clinical trials in developing countries are a sensitive issue that has been the topic of a report of the European Group on Ethics to the European Commission in 2003.[[12]](#footnote-13) In European funded projects, proposed trials are subject to ethical review before funding is approved.

# Recommendations

The below recommendations are regarding the production of nano-based solutions, technologies and applications targeting tropical diseases and cancer, developed in Europe and LA with a view to fostering international cooperation. They include solutions needed, timeframe for implementation and action steps (at national, EU and LAC level) for developing applications in LA.

Some general observations are presented first because they are related to the topic of policy-making, funding, ELSA and nanosafety, which are umbrella to all the discussions regarding deployment of nanotechnologies worldwide and locally for LA.

**Policy**

NMP-DeLA community members recommended that a wider network of stakeholders be engaged in discussions of topics related to nano for health. These stakeholders should include government, NGO and private sector stakeholders that are interested in health issues, including non-profit foundations/organizations, epidemiology vigilance institutions, programs dedicated to evaluation of population differences in non-transmissible diseases. At regional level, nanotechnology should be included in the EU-CELAC Joint Research and Innovation (JIRI) policy dialogue.

Governments and organizations working on legal and intellectual property issues in LA should develop rules on industry-university cooperation, as well as providing unified standards on contractual issues between LA and EU partners. The LA governments should all join the Patent Cooperation Treaty, invest in infrastructure and equipment and offer investment for technology transference. A common policy by government agencies fostering nanoeducation is needed.

Countries across the globe are drafting biosimilar regulations to reduce the cost of biological therapeutics testing, and to improve patient access to low-cost drugs for cancer and other diseases. At a global level, the WHO has included nano in its Healthy Workplace Programme in the form of occupational health and safety regulation/guidelines for nanomaterials. Government departments across the globe should apply occupational health safety rules, manage production, educate workers, fund risk assessment, and discuss social issues.

The model of the Brazilian initiatives SIsNANO and NANOSUS should be studied by other countries in LA, as well as any other country in the world considering its level of newness, and be replicated. Means of doing this could be by forum discussions in representative institutions, such as WHO, especially in its LA chapter PAHO.

## Funding

In order to establish networks, intensive work should be done to establish linkages between the research groups in LA and in Europe, the USA, Asia and Oceania. It is important to provide funding to the research networks to work in projects that have a long term perspective. Funding is also needed to promote the participation of large companies that are performing R&D in Europe. Funding should be targeted to individuals with the right technical expertise, not just institutions. Individuals should be willing to contribute their expertise for 2-3 years.

By 2025, a common funding strategy should be elaborated in LA for nanomedicine. It would be useful to have similar programmes in all of LA with a common interest and a common policy to determine that the money will be granted to specific priorities. The biggest challenge will be to create a programme that is independent of the economic and political situation in each country. In general, there is a lack of funding for research on health problems.

For nanosafety, countries in LA other than Brazil should fund longer term collaborations. This should consider the selection of experts, and have clear objectives, dissemination and training activities, and fund specific R&D projects.

Investors are needed for start-ups and incubators in Latin America. International financial institutes such as the World Bank and IMF should be encouraged to include expert researchers and industrialists from LA (and EU) in their review and impact assessment panels, and to focus in particular on societal impacts.

**Nanosafety**

A group of stakeholders in nanosafety should be defined that includes regulatory agencies, industry associations and experts performing safety relevant research. These should be brought together through a physical meeting to start with and a white paper drafted that details how to proceed with the integration of European and LA efforts. In the longer term, LA nanosafety experts should be offered access to infrastructure and equipment and training, e.g. in the European facilities. Priorities in research include the following:

* Study exposure to nanomaterials throughout the life cycle of consumer products
* Study chronic profiles and different exposure routes (e.g. inhalation)
* Study exposure to food that contains nano-structured ingredients
* Study links between exposure to nanoparticles and diseases for different groups (workers, consumers, adults, children, etc)
* Develop new methods for epidemiology

**Ethical, Legal and Societal Aspects**

Opportunities for contributing to Ethical, Legal and Societal Aspects of NMP are two-fold: in organizing dialogue about these issues, and in targeting projects towards improving societal benefits. The ETP Nanomedicine already offers a platform for elaborating questions and answers in the grey zone of ELSA of nanomedicine. An example is the discussion about the ethical aspects of nanomedicine coming from the EU projects and the experiences of the Institut Pasteur in this field, when implementing nanomedicine. There is interest in extending this network to LA partners. Furthermore, Horizon 2020 calls require that funded projects consider means by which the benefits of the research can be shared equitably with populations that do not have access to such medications.

## 8.1 Tropical Diseases-related recommendations

## Research

In general nanomedicine is not included in current international strategies for combatting tropical diseases. There appears to be a gap between the stakeholders interested in tropical diseases and the stakeholders in-terested in nanomedicine.

However, NMP-DeLA community members mentioned the following opportunities for targeting their research to tropical diseases in cooperation with Latin American partners.

* + Work at Fiocruz Brazil on nano-diagnostics and drug delivery could be focused on HIV, Malaria and TB. However, this is expensive to develop and calls for global initiatives.
  + The Department of Biology, Chemistry, Pharmacy of the Institute of Chemistry and Biochemistry, at the Freie Universität in Berlin has expertise on drug targeting (dendritic polymers), that could be ap-plied to neglected diseases: leishmaniasis, chagas. This could be achieved through adapting the same nanoparticles they are preparing, by changing the ligands at their surface for instance. They are currently working with groups in Spain and at the Massachussets Institute of Technology (MIT).
  + Paris Lodron University’s research on asthma and allergies could be targeted to investigating why Latin American countries such as Brazil and Peru have a higher allergy incidence than other countries. In addition, it could focus on parasitosis, because allergies arise as result of the body’s anti-parasite system being activated by mistake. By extension, it could be possible to bring the substantial R&D effort on allergies in industrialised countries to bear on the work being performed in the tropics on parasites.

## Policy and funding

Due to the risk of a “nanodivide” regarding the deployment of nanomedicines for the well-being of poor populations around the word, as mentioned previously, deploying nanotechnologies for prevention and therapy of neglected tropical diseases, the issue should be approached by policy-makers as well as be taken into account in significant fora, such as UN: At the international level, the negotiations on the Sustainable Development Goals with a time horizon until 2030 that should be adopted in September 2015 by the UN General Assembly are converging on a proposed list of 17 Goals supported by 69 UN Member States. The proposed Goal 3. “Ensure healthy lives and promote well-being for all at all ages” includes a tentative point 3.3 “by 2030 end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases”. Even though the way forward to achieving this goal is not specified down to the level of specific technological solutions such as nanotechnology, the goal can function as a benchmark helping to coordinate efforts of the stakeholders including those interested in nanomedicine.

## Pharmaceutical and medical devices industry and investment

In general, WHO recommends building on successes through public private partnerships to develop new medicines, vaccines, diagnostics and vector control methods. “Public and private sector incentives must be set up to encourage NTD research and development using appropriate collaborative measures that can allow exchange of expertise and scientific knowledge through:… a variety of measures including corporate responsibility schemes and platforms such as the Uniting to Combat NTD coalition, to encourage innovative incentives (Holmes 2015: 65)”

NMP-DeLA community members mentioned some opportunities for developing products targeting tropical diseases.

* Current activities at FIOCRUZ, Brazil, on nanoparticle for diagnostics could be focused on three or four tropical diseases, e.g. schistosomia, leishmaniasis, and malaria. This fits with the existing Brazilian pro-gramme on treatment and diagnosis of Leishmaniasis.
* An Argentinean start-up, LATINER, is working on nanoparticles for tropical diseases including Chagas disease and possibly also Leishmaniasis. This is a public-private enterprise. Projects are funded by government subsidies until the platform technology is mature and then patented and licenced.
* In Europe, the NANOFACTURING project supports the development of antiviral dengue fever nanopharmaceuticals at the Italian foundation for Cancer Research’s Institute of Molecular Research.

As news about development of the outcomes of the above-mentioned projects PodiTrodi and DiscoGnosis are not yet known, it is recommended their further development and commercialization, for which it might be useful to speed it up by means of public-private partnerships, in case funding is a hindrance to the development.

## Research on nanomedicine for cancer

In most countries cancer is one of the promising application areas of nanomedicine, but not the subject of a separate strategy. The US National Cancer Institute’s (NCI) Alliance on Nanotechnology in Cancer has been implementing such a strategy targeting nanotechnology for cancer since 2005, including Centers of Cancer Nanotechnology Excellence, Cancer Nanotechnology Platform Partnerships, Cancer Nanotechnology Training Centers, Pathway to Independence Awards in Cancer Nanotechnology Research and Nanotech-nology Characterization Laboratory.

The ETP-Nanomedicine White Paper Nanomedicine 2020 includes cancer as one of its target diseases, but does not include a separate chapter dedicated to cancer.

A sound strategy for collaboration should be the inclusion of nanomedicine targeting cancer into health strategies of national governments in LA as well as the developing of joint work with Europe and USA in order to foster deployment.

**Policy and funding for cancer**

While the EU does not have a specific programme targeting nanomedicine for cancer, the current workpro-gramme 2014-2015 in Horizon 2020 includes one call targeting nanomedicine therapy for cancer. It foresees an investment of 6-9 million euro per project.

Countries across the globe are drafting biosimilar regulations to reduce the cost of biological therapeutics testing and improve patient access to low-cost drugs for cancer and other diseases. While the EU has al-lowed biosimilars for several years, the first biosimilar drug is only entering the US market in 2015, sur-rounded by controversy.

# Conclusions

The specific case of Latin American (LA) countries provides an interesting and challenging object of study regarding nanotechnologies for health. On the one hand, diseases and medical conditions endemic to this area, such as tropical infectious diseases, demand well-targeted specialized measures. On the other hand, health problems that are common worldwide manifest themselves differently in LA. For example, tuberculosis, which has been largely eliminated in developed countries as a preventable disease, remains a major burden in LA. Similarly, the prognosis for cancer patients in developed countries is nowadays fairly optimistic due to early detection and advanced treatment, while in LA mortality rate is significantly higher mainly because of the less efficient functioning of the healthcare system.

In general, socio-economic factors such as poverty, living conditions and access to health care pose serious obstacles in LA, and the supply side of health care services suffers from similar challenges. Availability of health care, and related infrastructures as well as knowledge-related capabilities is still largely lacking despite recent progress. The opportunities with nanotechnologies for health in these settings could have a major positive contribution. Nanotechnologies applied to drug delivery systems, health monitoring and disease diagnostics and screening are beginning to enter the market, and gradual progress is expected towards 2025. The main advantages of nanotechnology-derived solutions include more effective and cost-efficient treatment with less unwanted side effects. Nanotechnologies allow health care solutions to be developed that are more affordable and easier to use, transport and store.

Against this background and the opportunities described in this report, we present next the main conclusions and recommendations to promote and advance the development and uptake of nanotechnologies for health in LA towards 2025.

**Establishment of knowledge networks**

The first step in promoting nanotechnologies for health in LA involves strengthening of existing knowledge networks and extending them in terms of stakeholders and topics involved. Networking, knowledge transfer and collaboration are essential both within LA countries as well as globally. In the short-term, the focus of knowledge networks should be on research and education, e.g. linking existing research communities in LA to address similar and complementing nanotechnology topics or promoting mobility of experts between LA and Europe. In the medium- to long-term the focus of networking extends from research towards industry and markets.

**Strategic commitment**

A prerequisite to advance nanotechnologies for health is, especially addressing problems in LA, political commitment and support. National governments in LA countries as well as international organizations in the topics of health, nanotechnology and research funding need to acknowledge and align nanotechnologies for health on their agendas, and commit long-term support and funding. Technology development needs to be monitored and assessed in a timely manner in order to inform decision-making and strategic planning so that political goal setting and funding for research, development and innovation activities is available.

In regards to cooperation with Europe the topic of nanotechnologies, and nanotechnologies for health in particular, should be included in the European Union and Community of Latin American and the Caribbean States’ Joint Initiative for Research and Innovation (EU-CELAC JIRI) policy dialogue. As this policy dialogue focuses on a diverse set of topics of common interest to both regions, and since it has already a working group on health, nanotechnologies for health could be incorporated into the agenda of this working group.

**Innovation ecosystems**

Related to the establishment of knowledge networks, the build-up of stakeholder ecosystems around the innovations in nanotechnologies for health is essential in the medium- to long-term. By this we mean bridging the gap from basic research firstly towards applied research and then to product development and commercialization as technologies mature. Along this process a shift from public funding towards industry involvement and investment should take place. Stakeholder ecosystems and partnerships between research and technology organizations, and businesses and companies in the health sector need to be established within LA and globally. Involvement and growth of local markets and businesses should be especially encouraged.

**Fair operational environment**

Throughout the short- to long-term considerations, in order to ensure that nanotechnologies for health can contribute to the improvement of the settings in LA, strategic planning needs to address ethical and safety related issues amongst others. Research and business communities in nanotechnology should follow mutually agreed nanosafety principles, and healthy market competition should avoid, e.g. ethical conflicts regarding patenting. Capacity and capabilities of local health care structures in LA countries should be strengthened to take the lead role, with the aim of providing better access for timely and affordable treatments for all demographic groups.

The ultimate conclusion of this research on nanotechnologies for health is that the field looks promising in terms of providing market-ready medical solutions in the medium- to long-term. The short-term considerations should therefore focus on strategic and political support to ensure collaboration in the research and development phase and sufficient funding. Medical and health issues characteristic to the LA region and functioning of the health care system in general should be highlighted in the development agendas of partnerships within LA as well as partnerships across continents.

In order to summarize the recommendations and conclusions of this roadmap we present some milestones, which stimulate in the short, medium and longer term research, development and innovation in Nanomedicine in Latin America. The presented milestones are no prediction of the future, but a compilation of recommendations, which resulted from our 2-year multi-stakeholder research process where we addressed the question of how nanotechnology-based solutions to societal challenges in the area of health should be produced in the future. Long term developments shall eventually flow into the achievement of the Sustainable Development Goals related to health, such as Goal 3 “Ensure healthy lives and promote well-being for all at all ages” including tentative point 3.3 “by 2030 end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases”.

We focus mostly on milestones at short and medium-term, reaching up to 2025, as this has been the timeframe for the roadmap. The long-term milestones are assumed to be envisioned consequences of the implementation of previous activities.

As key actors for the implementation of the milestones we would see policy makers, researchers, pharmaceutical industry, health care personnel, regulatory bodies, non-government organizations, regional, and international organizations. Of utmost importance for the implementation process is the full integration of all stakeholders in deciding priorities in the research agenda, in the transfer of research results into applications and standards and in the evaluation of the progress achieved based on the goals of the regional strategy, as recommended by Savolainen et al (2013).

For the monitoring of progress and impact of defined actions and strategy, we give extensive options of outcome and impact indicators in the general NMP DeLA Roadmap (download from [www.nmp-dela.eu](http://www.nmp-dela.eu)). The suggested indicators may be used as a basis for the developing of Nanomedicine specific key indicators for impact evaluation.

Table 5. Timeline for implementation of Nanohealth roadmap recommendations

|  |  |  |  |
| --- | --- | --- | --- |
| **Topic** | **Short term (by 2020)** | **Medium term (2020-2025)** | **Long term (2025-2030)** |
| **Research** | ETP-Nanomedicine is considering opening up to third countries, and has a bilateral agreement with Argentina as the first test case.  Start of activities for the creation of a Latin America Society of Nanomedidine. | Establishment of a Latin American Association for Nanomedicine as a regional member of the International Society for Nanomedicine. |  |
|  | Generation of a cross-national database of epidemiological records including cross-referencing to NMP-enabled treatments. | Benchmarking of national initiative on nanomedicine in public health (take SisNANO and NANOSUS from Brazil as role model). |  |
| **Funding** | National or regional fuding. | Use World Bank funds to finance. |  |
| **Infrastructure** | Generation of a database of Nanomedicine organizations and personnel in LA (resource inventory). | Set-up of a LA Nanomedicine Association as the regional hub in the International Society for Nanomedicine. | Establishment of joint infrastructure programs and funding mechanisms for nanohealth by LA governments. |
| **Technology Transfer** | The European Technology Platform (ETP) Nanomedicine invites additional LA members.  The European Technology Platform (ETP) Nanomedicine opens up to other LA countries | Good practices of technology transfer are implemented following model of the biotechnology in LA to the nano-health sector. | Established public-private partnerships for development of solutions (medicines, diagnostics, vaccines, etc.). |
| **Policy making** | Establishment of a regional working party to make recommendations on occupational health and safety issues to national governments. | Implementation of recommendations on occupational health and safety issues by national governments. | Developed strategy for leadership in treatment and prevention of NTDs. |
| **Capacity building** | (UNESCO) Bioethics Network[[13]](#footnote-14) is invited to play a coordinating role in building capacity for governing nanobiomedical ethics issues related to Nanomedicine in LA.  Establishment of a regional WG to discuss implementation of a curriculum for education on nanotechnologies both for vocational and university degrees. | Establishment of regional guidelines, and joint educational initiatives, on nanotechnologies. | Joint issuing of degrees on nanotechnology. |
| **RRI** | The ELSA board of the ETP Nanomedicine opens up to LA experts and stakeholders in cooperation with other national initiatives. | Creation of a network of correspondents in the field of ethical aspects of Nanomedicine applications in LA. |  |
| **Cooperation** | Inclusion of nanotechnology as a priority topic in the EU-LA Joint Initiative for Research and Innovation (JIRI). | LA Nanomedicine institutes engage with regional (IDB, WHO/PAHO, South American Institute of Government in Health, Brazil-Argentina Nanotechnology Institute) and international (e.g. WHO, WB, ETP-Nanomedicine) actors. |  |
|  | Nanomedicine academic, research and industrial organizations engaged in the ELAN (EU-LAC network of technology based business). | Companies and research institutes engage in technology transfer activities. | Nanotechnology-based business for health are operational. |

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# Annexes

## Annex 1: Questionnaire for consultation with experts

* What expertise and resources can your organization/research group contribute to deployment of nanotechnologies, materials and production technologies (NMP) for health in Latin America?
* Are you or is your organization already working with partners in Europe and Latin America in the field of nanotechnology and its applications in health? If so, could you expand on that? If not, are you aware of any plans of your organisation for such cooperation in the future?
* Which steps should be taken to develop NMP for applications for health in Latin America by 2025?
* What contributions should be made by which other partners to these developments?
* Could you suggest other organisations and contact persons who should be involved?
* Could you describe any market opportunities for the nano-enabled health technologies in your organisation’s innovation strategy for nanotechnology?
* Could you describe any societal challenges for the nano-enabled health technologies in your organisation’s innovation strategy for nanotechnology?
* Do you experience international cooperation as a driver for NMP deployment or is it rather hindering a need-driven research approach by dictating global research agendas?
* Is there anything you consider relevant to our innovation strategy and roadmap which I did not ask?

## Annex 2: List of Interviewees for NanoHealth Roadmap

**List of interviewees**

* Prof Dr Marcelo Calderon, Department of Biology, Chemistry, Pharmacy / Institute of Chemistry and Biochemistry, Freie Universität Berlin, Germany <http://www.bcp.fu-berlin.de/en/chemie/chemie/forschung/OrgChem/calderon/index.html>
* Dr Françoise Roure, CGEIET, Min Economie & Finances, France <http://www.cgeiet.economie.gouv.fr/>
* Prof Dr Albert Duschl, Paris-Lodron University Salzburg, Austria, <http://www.uni-salzburg.at/index.php?id=25707>
* Prof Dr Teresa Fernandes, Heriot-Watt University, UK, <http://www.sls.hw.ac.uk/staff-directory/teresa-fernandes.htm>
* Dr Henry Andrade, Universidad Pontificia Bolivariana, Medellin, Colombia, <http://www.upb.edu.co/portal/page?_pageid=1054,51984264&_dad=portal&_schema=PORTAL>
* Dr Miryam Asuncion, NanoGune, Spain, <http://www.nanogune.eu/en>
* Dr Henri Heussen, ArboUnie / COSANTA BV, Netherlands, [www.stoffenmanager.nl](http://www.stoffenmanager.nl)
* Dr Gabriela Canziani, Ph.D, Fundación Instituto Leloir, Argentina, <http://www.leloir.org.ar/>
* Dr William Waissmann, Fiocruz, Brazil, <http://portal.fiocruz.br/>
* Dr Rossana Madrid, UNT (Univ. Tucuman) Bioengineering department, Argentina, <http://www.unt.edu.ar/>
* Dr Mario Cisneros, Patent expert
* Dr Luis Velasquez, CIMIS, UNAB, Chile, cimis.unab.cl
* Professora Maria Espona, ARGIQ, Argentina, <http://www.argiq.com.ar/>
* Prof Dr Alvaro Duarte Ruiz, UNAL, Colombia unal.edu.co
* **Participants in the NMP-DeLA workshop Nano for Heath, 19-20 May 2014** [**www.nmp-dela.eu**](http://www.nmp-dela.eu)**:**
* Prof Dr Eder Romero, Associacion Argentina de Nanomedicinas
* Dr Ricardo Alvarado, Lanotec, Costa Rica
* Prof Dr Alvaro Duarte Ruiz, UNAL, Colombia unal.edu.co
* Prof Dr Juan Claudio Benech, MEC / IIBCE, Uruguay [www.iibce.edu.uy](http://www.iibce.edu.uy)
* Dr Pedro Cazes / Dr Marcelo Kaniuki, LATINER, Argentina
* Dr Carla Silva, CENTI, PT [www.centi.pt](http://www.centi.pt)
* Dr Richard Anthony, KIT, NL, [www.kit.nl](http://www.kit.nl)
* Dr Paula Queipo Rodriguez, PRODINTEC, Spain, [www.prodintec.es](http://www.prodintec.es)
* Dr Helvecio Rocha FIOCRUZ, Brazil, <http://portal.fiocruz.br/>
* Dr Monica Silenzi, MINCYT, AR
* Dr Santiago Sacerdote, CONICET, AR
* Dr Daniel Lupi, FAN, AR
* Dr Carlos Renaldi, CNEA, AR
* Dr Hector Pralong, MINCYT, AR

## Annex 3: Causes, Distribution and Impacts of Neglected Tropical Diseases

|  |  |  |
| --- | --- | --- |
| **Disease and Cause** | **Distribution** | **Impact** |
| Dengue | Pandemic threat in more than 125 countries (Africa, Americas, South-East Asia, Eastern Mediterranean). Outbreak threat in Europe. **Hyperendemic** state in the **Caribbean, Central and South America** (but Chile, Uruguay and part of Argentina). | Estimations (Beatty *et al* 2008): 3.6 billion people living in risk areas; 230 million infections, millions of cases of dengue fever, over 2 million cases of the severe disease, and 21,000 deaths. Also major social impact in the case of large epidemics, which disrupt primary care for hospitalized patients. |
| Rabies | Endemic in Africa, Middle East, Central and South-East Asia and Western Pacific. Human rabies transmitted by dogs is widespread in **Cuba, The Dominican Republic, El Salvador, Guatemala, Haiti and Bolivia**; human rabies transmitted by vampire bats is concern in **South America** **(Brazilian Amazon, Colombia, Ecuador and Peru).** Moderate risk in other **LAC countries** (no cases in Chile and Uruguay). | Cause of tens of thousands of human deaths annually. |
| Trachoma | Estimated 325 million living in endemic areas. Blinding trachoma is hyperendemic in remote rural areas of Africa, Asia, Central and **South America** (mainly Brazil), Australia and the Middle East. In hyperendemic areas as much as 90% of school children may be affected. | More than 21 million people have active trachoma, 7.2 million need surgery for trichiasis, and 1.2 million are irreversibly blind.  Annual economic cost due to loss of productivity estimated between 2.9 and 5.3 US$ billion; increases to 8 billion if trichiasis is included. |
| Buruli ulcer | Detected mainly in tropical and subtropical climates. Historically reported in 33 countries, with a trend in increase in number of cases in Australia, Gabon and Ghana. Cases have been reported in in Japan as well. | Main problems are associated with long periods needed for healing (including hospitalization), disabilities, and deaths from sepsis and tetanus. |
| Endemic Treponemathoses  [Comprise yaws, endemic syphilis (bejel) and pinta]  Cause: bacteria of genus *Treponema* | Cases reported mainly in Africa, South-East Asia and Western Pacific regions. | Ulcers may get infected with secondary infections, such as tetanus. Yawns can cause disfiguring and crippling disabilities and deformities, preventing children from attending school and adults from working. |
| Leprosy (Hansen disease)  Cause: Mycobacterium leprae | In 2012, 106 countries from Africa, **Americas** (mainly Brazil), South East Asia end Easter Mediterranean and Western Pacific regions reported cases. | Disease with heavy social and economic impact as sufferers are stigmatized, isolated and sometimes displaced from their work and barred from social life. |
| Chagas Disease  Cause: protozoa *Trypanosoma cruzi* (vector blood-sucking triatomine bugs) | Estimation: about 7 to 8 million people infected worldwide. Endemic in **21 LAC countries**. Cases outside LAC (United States of America, Canada, Europe and some Western Pacific countries) due to population mobility. | High costs of treatment of symptoms associated to onset of disease. Disease can be cured if treatment initiated immediately after infection. As an example, estimated annual costs for Colombia in 2008: about US$ 267 million for medical care and US$ 5 million spraying insecticide in vector control. |
| Human African Trypanosomiasis (Sleeping sickness)  Cause: protozoa parasites of genus *trypanosoma* (vector tsetse flies) | Latest (2011) estimations situate the incidence of cases in about 20000 a year. Both chronic and acute forms of the disease are endemic in, respectively, 24 and 13 countries in Africa. | Sleeping sickness affects mostly impoverished rural areas of Sub-Saharian Africa, which creates a trap for the communities. |
| Leishamaniasis  Cause: protozoa parasites genus *Leishmania* (vector female sandflies) | There are three forms of leishmaniasis: visceral (also known as kala-azar and the most serious form), cutaneous (the most common) and mucocutaneous. The disease is prevalent in 98 countries and 3 territories on 5 continents.  Estimated 1.3 million cases occur annually, of which 300000 are visceral (90% of which occur in **Brazil**, Bangladesh, Ethiopia, India, Nepal, South Sudan and Sudan) and 1 million are cutaneous (occurring mainly in Afghanistan, Algeria, **Brazi**l, **Colombia**, Iran, Pakistan, **Peru**, Saudi Arabia, Syria and Tunisia) or mucocutaneous (mainly occurring in **Brazil, Peru and Bolivia**. | Estimated 20000 to 40000 people die from visceral Leishmaniasis annually.  Cutaneous Leishmaniasis has psychological burden on sufferers because of scars and deformities associated to it.  Cutaneous and mucocutaneous Leishmaniasis may lead to social exclusion as well.  Disease has negative effect on household income. |
| Cysticercosis/Taeniasis  Cause: Tapeworm *Taenia solium* | Endemic regions include **Latin America**, South and South-East Asia and sub-Saharan Africa. There are at least 50 million | Neurocysticercosis is the main burden caused by *Taenia solium* and is the most frequent preventable cause of epilepsy in developing countries. At least 50 million worldwide suffer from epilepsy, of which 1/3 of cases happen in regions where T. solium infection is endemic. Ex. In the case of Peru, 54% of the total annual minimum wage is spent in the first year of treatment and 16% in the second. |
| Dracunuliasis  Cause: *Dracungulus medinensis* (guinea worm), vector cyclopoid copepods | The disease is endemic of four countries in Africa (South Sudan, Ethiopia, Chad and Mali). The number of cases has been steadily decreasing since 1980s, when it was endemic in 20 countries. | There is no medicine or vaccine effective in treating of preventing dracunliasis, eradication is being achieved through public-health interventions. Eradication of the disease will save people from the burning that strike as worms emerge from their body, as well as may lead to an increase in 29% for the agricultural sector, once most affected people are small farmers, who become incapacitated during the course of the disease (about 5 weeks). |
| Echinococcosis  Cystistic echinococcosis (*Echinococcus granulosus*) and Alveolar echinococcosis (*E. multilocularis*) (intermediate hosts are farm and wild ungulates, rodents and small mammals) | Highly endemic areas are eastern part of Mediterranean region, northern Africa, southern and eastern Europe, **southern tip of South America (ex. Argentina, Peru)**, Central Asia, Siberia and western China. There are indications of re-emergence of Echinococcosis and its becoming a public-health concern. There are more of 1 million people worldwide affected. | Annual costs (treatment of cases and losses of livestock) associated with cystic echinococcosis are estimated to be US$ 3 billion. In human it can be life threatening if left undiagnosed and untreated. |
| Foodborne trematodiases  Cause: ingestion of food contaminated with metacercariae leading to clonorchiasis (*Clonorchis sinensis*), opisthorchiasis (*Opisthorchis viverrini* or *O. felineus),* fascioliasis (*Faschiola hepatica* or *F. gigantica*) and paragonimiasis (*Paragonimus spp.)* | There are reports of cases in more than 70 countries worldwide. Asia and **Latin America** are the most badly affected. Estimates from 2005 indicate that there were more than 56million people individuals infected, 7.9 million with severe sequelae and more than 7000 had died from foodborne trematodes infection. | Morbidity due to infection with foodborne trematodes are more severe after subsequent rounds of infection. Chronic infections with C. sinensis and O. viverrini are are strongly associated with cancer in humans. Economic losses are linked to losses in animal production (fish and livestock) leading to losses of income. |
| Lymphatic filariosis  Cause: infection with filarial nematode (species *Wuchereria bancrofti, Brugia malayi* or *B. timori*) (vector mosquitoes) | At least 40 million people have clinical manifestations of lymphatic filariasis; 1.39 billion people need preventive chemotherapy, and 70/72 endemic countries have initiated programs to eliminate the disease, which is endemic in Africa, South-East Asia, **Americas**, Eastern Mediterranean regional and Oceania. | Chronic manifestations of the disease cause impairment in occupation activities, educational and employment opportunities and mobility as well as to social exclusion due to stigma and discrimination of people with disfigurement of limbs and genitals. Economic benefits of tackling the disease were calculated at about US$ 24 billion for the years 2000-2007. |
| Onchocerciasis (River blindness)  Cause: filarial nematode (Onchocerca volvulus) trasmitted by blackflies | Disease is meso or hyperendemic in sub-Saharan Africa and hypoendemic in **Latin America (Venezuela, Brazil, Colombia, Ecuador, Guatemala and Mexico)** | River blindness has benefited from disease control programs. In the past it reduced economic productivity as the affected individuals could not work the land. It is estimated that there are about half a million blind people due to river blindness. |
| Schistosomiasis  Cause: *Schistosoma haematobium* (Urogenital schistosomiasis) intestinal schistosomiasis (*S. guineensis, S. intercalatum, S. mansoni, S. japonicum* and *S. mekongi*) (vector snails) | 249 million people worldwide were treated for schistosomiasis in 2012, and more than 779 million people live in endemic areas of the Middle East, **Caribbean**, **South America**, South-East Asia and sub-Saharan Africa. It is prevalent in poor communities without potable water and adequate sanitation. 25 million people live in endemic areas in **Brazil** (Allegretti *et al* 2012). | In children, schistosomiasis can cause anaemia, stunting and a reduced ability to learn, although reversible with treatment. Chronic schistosomiasis may affect work ability and in some cases can result in death, which in sub-Saharan Africa have been estimated to be more than 200000 per year. Urogenital schistosomiasis may cause bladder cancer as well as increase risk of HIV infection. |
| Soil-transmitted helminthiases  Common causes: *Ascaris lumbricoides, Trichuris trichiura, Necator americanus* and *Ancylostoma duodenale* | About 890 million worldwide need annual treatment with preventive therapy. Most affected countries are in Asia (India 27% of cases in the world), Africa, **Central and South America**. | Helminthiases affect mostly children in school age and infections may cause them learning difficulties and school absenteeism from school, as well as impacting earnings of adults and caregivers. |

Source: WHO (2013a)

1. It aims to address as well the sustainable development goals that will be integrated into the UN development agenda beyond 2015. Relevance to these MDG-plus goals will be incorporated to the final roadmap. [↑](#footnote-ref-2)
2. International Cooperation Partner Countries are (as defined for the EU's Seventh Framework Programme for Research and Technological Development - FP7) lower-income, low-income, lower-middle-income and upper-middle-income countries targeted by the European Commission to increase research cooperation (third countries). Organizations from these countries can participate and receive funding in FP7, providing that certain minimum conditions are met (see: http://wbc-inco.net/glossary/67). For the European program Horizon 2020, there are three categories of third countries: neighboring to the EU, industrial and emerging economies, and developing countries. See: http://ec.europa.eu/research/iscp/index.cfm?pg=strategy and http://ec.europa.eu/research/participants/portal4/desktop/en/opportunities/h2020/ftags/international\_cooperation.html#c,topics=flags/s/IntlCoop/1/1. [↑](#footnote-ref-3)
3. Originally published as chapter 5 in Ineke Malsch, Ethics and Nanotechnology, Radboud University Nijmegen, 2011, <http://repository.ubn.ru.nl/handle/2066/91234>. [↑](#footnote-ref-4)
4. The Innovation Strategy is published as a separate document available on NMP-DeLA website. [↑](#footnote-ref-5)
5. Nanomedicine refers to the application of nanotechnologies for health. In the roadmap exercise these concepts will be used interchangeably, unless precise definition is required. [↑](#footnote-ref-6)
6. Can also be introduced via nasal epithelium (sprays or inhalers) and dermal patches [↑](#footnote-ref-7)
7. DOTS has five major components: 1) political commitment and adequate funding 2) bacteriological case detection 3) standardized treatment regimen with patient supervision and support 4) regular, uninterrupted supply of quality-assured anti-TB drugs 5) reliable recording and reporting system [↑](#footnote-ref-8)
8. age-standardised rate of 177.0 per 100 000 in LAC, 255.4 in Europe and 318 in the United States [↑](#footnote-ref-9)
9. 0,54 for LAC, 0,44 for Europe and 0,33 for the United States [↑](#footnote-ref-10)
10. Since 2007, efforts have been made to switch to melarsoprol-free treatments for its toxic adverse effects. By 2009, 88% of cases were treated with melarsoprol-free therapy. Though, the use of this newest therapy option has caused financial burdens on programs (WHO). [↑](#footnote-ref-11)
11. It has also funded research targeting Leishmaniasis, as already mentioned earlier. [↑](#footnote-ref-12)
12. http://ec.europa.eu/archives/bepa/european-group-ethics/docs/avis17\_en.pdf [↑](#footnote-ref-13)
13. http://en.unesco.org/partnerships/partnering/bioethics [↑](#footnote-ref-14)