1.* **Title of the project:**
Chagas R&D Accelerator Initiative: a coordination mechanism for accelerating the development of new health tools for Chagas disease

2.* **Submitted by:**
Left blank to facilitate impartial evaluation.

3.* **Target disease or health condition:**
*(Focus on type II and III diseases and special R&D needs of developing countries in type I diseases where there is an identified health technology gap.)*

Endemic throughout Latin America and the leading parasitic killer of the Americas, Chagas disease (American trypanosomiasis) is a highly important but little-addressed public health issue, not only in Latin America but also increasingly in non-endemic, developed countries, due to globalization and population flows. Chagas disease ranks among the world’s most neglected diseases (type III). Enormous gaps remain between the estimates of the number of people living with Chagas disease and those actually diagnosed and receiving treatment.

The only two existing drug treatment options, benznidazole and nifurtimox, remain limited and very often unsatisfactory, especially when used in adult chronic Chagas patients; they require long treatments and have numerous side effects. There is a consensus among physicians and researchers that new treatment options are urgently needed.

Also, a significant hurdle for the treatment of Chagas and the development of new drugs has been the lack of qualified early markers of therapeutic response. Indeed, no single reliable test of cure exists that can be used to monitor treatment efficacy in chronic patients in a timely manner. An important advance in recent years has been the standardization and optimization of PCR methodology, and evaluation of other biomarkers of treatment response in Chagas disease. Additional work is necessary for their validation and to fill the existing gaps.

4.* **The suggested health technology that project seeks to develop:**
*(e.g. medicine; diagnostic test; medical device; vaccine etc.)*

The project aims to coordinate and accelerate efforts to address the R&D gaps for Chagas disease in relation to:
- Development and registration of a PCR assay diagnostic kit
- Selection, qualification, and validation of new biomarkers of treatment efficacy
- Establishment of biobank portal
- New treatment options for patients with Chagas disease (see Questions 6 and 9)

5.* **Project summary:**
This proposal recommends as a Candidate Demonstration Project the creation of a coordinating mechanism based on open knowledge and innovation principles to accelerate the development and delivery of new tools to treat and control Chagas disease.
The last few years have seen positive progress in the R&D landscape for Chagas disease, with different actors involved such as not-for-profit and public research institutions, product development partnerships (PDPs), governments, universities, and pharmaceutical and biotechnology companies. Collaborations, scientific knowledge sharing, and a critical mass of expertise are being built around existing platforms related to the disease.

However there is a lack of targeted coordination (portfolio management) of promising R&D approaches and the political, technical, and financial support needed to translate research findings and clinical studies into new and better treatments for people living with Chagas disease. Therefore, a mechanism of focused coordination is needed for Chagas R&D to define priority drug candidates, prioritize projects with the highest chances of new-tool delivery, explore the use of new R&D incentive mechanisms, investigate innovative ways to finance R&D through country, regional, and international initiatives, and secure policy commitments for open innovation and patient access to newly developed products.

To address this need, we propose the establishment of a coordination mechanism for accelerating Chagas R&D called the Chagas R&D Accelerator Initiative.

The Coordination Initiative would be composed of representatives of the scientific community, key Latin American governments, PAHO/WHO, TDR, DNDi, treatment providers, and the International Federation of People Affected by Chagas Disease (FINDECHAGAS), supported by a secretariat housed in an existing institution. The Secretariat will need to be committed to minimizing overhead costs and achieving value for money.

The guiding principles of the Initiative are defined as:

- Open knowledge and innovation: institutions, companies and researchers from different Platforms and networks (e.g. Chagas Clinical Research Platform [CCRP], Nuevas Herramientas para el Diagnóstico y la Evaluación de Pacientes con Enfermedad de Chagas [NHEPACHA Network], and Integrated Chagas Disease Program [PIDC]) would sign a formal agreement ensuring open knowledge sharing.
- Sustainable funding: members of the committee, principally governments, would commit to secure the necessary funding for the identified priorities through different mechanisms.
- Equitable access: development of an access policy for funded projects requiring that new therapeutic and diagnostic tools be developed as public goods and ultimately available at affordable prices.

The responsibilities of the Initiative would be to:

- Review and validate R&D priorities for Chagas disease
- Define priority treatment candidates and biomarker projects
- Oversee development of a Chagas disease biobank portal
- Develop and implement an equitable access policy
- Review and validate funding needs
- Identify potential funding mechanisms at country, regional, and international levels
- Review and validate proposals for innovative incentive mechanisms such as prizes
- Review and propose regulatory, financial, and procurement policies to facilitate access to final products
- Monitor project implementation and results
- Review and validate financial reports
- Facilitate information sharing with national programs and regional initiatives
- Appoint and have oversight of delegated activities of the Secretariat

The goal of this Coordination Initiative would be to accelerate R&D for Chagas disease, in order to deliver and support the scale-up of new treatment options (shorter treatment regimens, combinations of existing drugs, and brand-new drug therapies), as well as a new field-friendly PCR diagnostic kit and new qualified
biomarkers for assessing treatment response, within 5 years. Such new tools would be used to support control of Chagas disease worldwide.

The project should at the same time address research gaps, ensure effective coordination at all levels, secure resources for developing and delivering new health products, and demonstrate innovative mechanisms for long-term, sustainable, needs-driven R&D (see Questions 7 and 16).

6.* Public health need that the proposed project aims to address:
(Explain the public health need in terms of burden of disease; prevalence; incidence; fatality rate; geographical spread; current interventions and their limitations; and what proposed new technology would change in terms of disease prevention, control, diagnosis, treatment etc. If detailed information is not possible at present then please provide some basic level information)

Chagas disease, caused by the parasite Trypanosoma cruzi, is endemic in 21 Latin American countries, where PAHO estimates that 7.6 million people are infected and 108 million are at risk of the disease.¹ WHO estimates approximately 7 to 8 million people infected worldwide.² More than 10,000 deaths are estimated to occur annually from Chagas disease.³

Chagas disease causes the highest disease burden of any parasitic disease in the Western hemisphere,⁴ with an infection rate estimated at 1.4% in endemic areas,⁵ and wide geographic variation of 0.1% to 45.2%.⁶ Migration from Latin America to the United States, Canada, Europe, Japan, and Australia has resulted in the global spread of patient populations.

Even with a decreasing incidence of the disease, due to successful programs of vector control, the burden of Chagas-associated heart and gastrointestinal disease is expected to continue in the future as individuals already infected progress from the indeterminate to the chronic phase of disease.

Congenital infection (mother-to-child transmission) of Chagas also remains a public health issue. According to PAHO, approximately 1.8 million women of childbearing age (15-44 years) are infected, and a total of 14,000 cases of congenital Chagas infection occur each year.⁷ In a recent estimate,⁸ a total of 212,179 children under 5 years of age were reported to be infected in endemic countries, 16,683 below one year of age.

Through its impact on worker productivity, premature disability, and death, 430,000 disability-adjusted life years (DALYs) are lost annually because of Chagas.⁹ In the case of Brazil alone, losses of over $1.3 billion in wages and industrial productivity were due to the disabilities of workers with Chagas disease.¹⁰

The urgent public health needs due to Chagas disease are two-fold:

1. Improved and better tolerated treatments: The only two drugs available, benznidazole and nifurtimox, are therapies of long duration and are poorly tolerated, especially in adult chronic Chagas patients. Because the adverse events of these drugs are related to the length of treatment, the need to evaluate shorter treatment courses of these drugs is clear. The development of safe, effective, affordable new treatment options for the millions of people with Chagas infection, and the prevention of chronic complications, are recognized as key disease control priorities.¹¹,¹² The ideal drug treatment for Chagas disease, defined by its Target Product Profile (TPP), should be a safe, effective, oral, 30-day (maximum) course efficacious against all T. cruzi strains, in acute and chronic disease stage, as well as for all age groups. Other improved treatment options could be shorter treatment regimens of existing drugs in monotherapy or in combination.

2. Tests for therapeutic response: The currently accepted standard method of measuring treatment response (clearing of infection) is seroconversion, which is not suitable for drug development, let alone broader public health use, since it requires a long, multiyear period of follow-up and cannot be easily performed in
resource-poor settings. Thus, qualified tests of therapeutic efficacy are critically needed to accelerate clinical drug trials by reducing time and costs and assessing patient cure, which can help assure people living with Chagas that a given treatment works, so helping with treatment compliance.

7.* Explain which new and innovative approaches and mechanisms to supporting financing and coordination of R&D this project would demonstrate?

(This is a very important part to be filled. The idea of these demonstrations projects is “to address identified gaps that disproportionately affect developing countries’ particularly the poor, and for which immediate action can be taken” (WHA66.22).

66th WHA considered these demonstration projects as part of the efforts to “take forward action in relation to monitoring, coordination and financing for health research and development”. The assembly decided to identify such projects that: “(a) address identified research and development gaps related to discovery, development and/or delivery, including promising product pipelines, for diseases that disproportionately affect developing countries, particularly the poor, and for which immediate action can be taken; (b) utilize collaborative approaches, including open knowledge approaches, for research and development coordination; (c) promote the de-linkage of the cost of research and development from product price; and (d) propose and foster financing mechanisms including innovative, sustainable and pooled funding; (2) The demonstration projects should provide evidence for long-term sustainable solutions.”)

Coordination

The Chagas R&D Accelerator Initiative will demonstrate that Chagas R&D can be accelerated through focused coordination of promising R&D projects, collaborative Platforms, equitable access to new products, and sustainable funding secured through existing and new funding mechanisms. It will demonstrate that countries in Latin America can collaborate on R&D priorities based on open innovation principles, focused on a disease of regional importance. It will also demonstrate that endemic countries can collaborate on funding directly and through in kind access to facilities and expertise. Such R&D collaboration, including with stakeholders and public and private funders from any region, would establish an important precedent within the region and internationally, and provide opportunities to evaluate whether such collaborations would be of benefit in other disease areas.

To address identified R&D gaps for Chagas, the Coordination Initiative would focus on the following proposed R&D project areas of high patient need (see Question 9): a new PCR test kit, new biomarkers to measure treatment response, a biobank portal, new administration strategies of existing drugs in monotherapy or in combination, and proof of concept of new drug compounds.

The new coordination mechanism would demonstrate collaborative approaches to Chagas R&D primarily through already established networks, or Platforms, focused on Chagas disease such as:

- **Chagas Clinical Research Platform (CCRP):** coordinated by DNDi and gathers more than 80 institutions from over 20 countries. Its objective is to provide new medicines for treatment of *T. cruzi* infection through a flexible, needs-driven, knowledge-sharing platform delivering concrete support for R&D.

- **NHEPACHA (Nuevas Herramientas para el Diagnóstico y la Evaluación de Pacientes con Enfermedad de Chagas):** network of 11 institutions managed by CRESIB (Centro de Investigación en Salud Internacional de Barcelona), with a focus on the development and improvement of new tools and biomarkers for Chagas disease.

- **PIDC (Integrated Chagas Disease Program):** coordinated by FIOCRUZ, in Brazil, this program gathers researchers from the different FIOCRUZ units, promoting internal cooperation through thematic networks in order to increase institutional research efficiency and strengthen fundraising capacity for relevant R&D initiatives.
Despite ongoing interactions and collaborations among these networks, more focused coordination of promising R&D projects is needed to accelerate their completion. Open knowledge sharing would be made an integral part of this Coordination Initiative through the signing of a formal agreement with existing platforms and R&D networks ensuring data transparency and publications of results (whether positive or negative) through existing avenues (e.g., CCPR web forum, WIPO platform, open access peer-reviewed journals).

The Initiative will implement a policy of equitable access to new therapeutic and diagnostic tools, based on agreed-upon principles ensuring that the products developed via the coordinated funding are done so as public goods, with affordable pricing, thus supporting de-linkage of R&D costs from final product prices. To ensure sustainable access, the coordination mechanism will regularly review and propose enabling regulatory, financial, and procurement policies.

Collaboration and open and equitable access policies would be incentivized by the availability of funding and access to the in-kind resources provided by members of the coordinating committee, such as expertise and facilities. This funding and use of resources would be tied to agreement by the recipients to the open innovation and access policies.

The Initiative would also explore the use of specific awards or prizes to researchers and engineers who openly publish and share their research contributing to Chagas R&D. This research would include results, data, materials, and technology made available either in the public domain or through open, non-remunerated licenses.

**Funding**

While some current Chagas R&D projects already have some funding, little coordination exists among the funders and developers regarding prioritization of the most promising approaches and funding needed to move health-product candidates into preclinical and clinical trials. A coordinating Initiative could pull public and private funding into a virtual fund to support priority projects identified by the Initiative, which could be taken forward at national level or within multicity sites. To ensure sustainable funding, members of the Initiative, particularly governments, would need to commit the necessary funding to first support the establishment of the Initiative and to support the identified R&D priorities. An estimate of total funding needs is $53.58 million over 5 years, with $2.1 million for the Chagas R&D Accelerator Initiative and a virtual fund of $51.48 million to support priority R&D projects (see Question 17).

Some funding sources already exist in the region that could be leveraged and targeted in new ways to support this Initiative, including ministries of science and technology, ministries of health, national research agencies, national development banks (e.g., BNDES in Brazil), and regional philanthropic foundations, using financial instruments in these bodies that support socially responsible projects, innovation, and national industries.

8.* Evidence of market failure/research landscape:

(Explain why there has been no investment in this technology or why investment has not resulted in access to the health care product.)

People living with Chagas disease are predominantly poor, marginalized, and do not pose a profitable market for the pharmaceutical industry. Because of this lack of lucrative financial potential, little to no R&D has typically been carried out for Chagas disease.

Historically the market-driven, patent-based R&D framework has often failed to address public health needs in developing countries. According to the G-FINDER 2012 Report, in 2011 only 4.3% of the total R&D funding for neglected diseases was dedicated to kinetoplastid diseases (Chagas disease, sleeping sickness, and leishmaniasis), with a declining trend in funding since 2009. Of the $137.3 million spent on R&D for kinetoplastid diseases in 2011, $17 million was directed towards Chagas disease, with an increase of its share of total kinetoplastid funding from 8.1% in 2007 to 18.7% of total funding in 2011. The public sector
was the major funding source (73.3%), followed far behind by philanthropic funding (17.3%) and industry (9.5%). Among public funders, the Ministry of Health of Brazil ranked 11th, with average funding of $2.4 million/year over 5 years, and in 2011, the Ministry of Science, Technology and Productive Innovation in Argentina increased its funding by 210.6%.

Factors that have led to the historic lack of investment in Chagas R&D include the erroneous theory that Chagas disease is autoimmune in nature, which hampered research on antiparasitic mechanisms; predominant focus in past decades by endemic countries on control of vectorial transmission and blood bank screening procedures, with ongoing need to reinforce attention to screening and treatment of infected populations; and disputes about the therapeutic benefits of the current drugs, despite evidence showing that antiparasitic chemotherapy is beneficial for patients with chronic Chagas disease.\textsuperscript{xiv}

In the last few years, some progress has been made in Chagas R&D, including the development of a new pediatric dosage formulation of benznidazole (DNDi/LAFEPE), the start of several clinical trials testing new drug candidates in Latin America (DNDi-sponsored E1224, Merck/McMaster University-sponsored STOPCHAGAS) and Spain (Merck/ICS-sponsored CHAGAZOL), the upcoming results of the TRAENA and BENEFIT studies evaluating efficacy of treatment of adults with chronic disease, and the start of a second production source of benznidazole (Abarax, ELEA) in Argentina. But in order to deliver new tools, from both ongoing projects and R&D initiatives waiting to be launched, coordination and prioritization of the most promising R&D approaches, securing open innovation and access policies and funding mechanisms are needed.

9. The scientific and technical feasibility:
(Describe the scientific and technical basis for the proposed technology in terms of the state of the art e.g. candidate molecules; biomarkers; pipeline; previous efforts, if any, to develop same or similar technology etc. Include some risk analysis)

1. A new PCR test kit:
PCR has increasingly been used as a tool for diagnosis and monitoring of treatment response in investigational settings. WHO/TDR sponsored a landmark study for standardization and laboratory validation of qualitative PCR testing for \textit{T. cruzi}. Further work on optimization and validation of the PCR technique has been recently published. Despite recent progress, additional work is needed to increase sensitivity and reproducibility and to develop a user-friendly diagnostic kit, which would provide an important public health tool for scaling up diagnosis, treatment evaluation, and support of disease control.

A mix of incentives will be the best way to achieve this objective. Push mechanisms (through grants) and a pull mechanism such as milestone prize could be considered.

2. New biomarkers for testing therapeutic efficacy:
New biomarkers of Chagas are needed to complement assessments of therapeutic efficacy using PCR. Although several studies on Chagas markers of treatment response in humans have been published in the last few years and are ongoing, additional work is needed to fully validate and qualify these as useful biomarkers of treatment efficacy that can be used in Phase III clinical trials and accepted by regulatory authorities. Coordination is needed to define priority biomarker candidates, set the R&D pathway, and secure new sustainable funding mechanisms to accelerate and support this development.

Research in this area could be transformed by creating targeted new incentive mechanisms such as a grants or a milestone prize that prioritizes research projects with the highest chances of delivering biomarker(s) suitable for translation into a test.

A milestone prize would be particularly suitable for the Initiative to explore for the acceleration of the identification and validation of new biomarkers, as several potential pathways to a biomarker are currently being researched. Unlike grant funding alone, which is only able to target one potential research group at a time, a milestone prize allows several promising research proposals to be taken forward by paying out at
regular milestones on the achievement of results. This means that several different approaches can be tried simultaneously. Prizes only pay for results, so if nothing significant comes forward, resources will not be wasted. A milestone prize is also suitable for academic researchers, as the design of the milestone prize is such that it combines a grant approach with a final prize payout approach. By making funding available to researchers throughout the research process, they can pay for the next stage, but only on the achievement of results at each stage. A milestone prize has already been successfully used in the biomarker field with the award of the $1 million Prize4Life for a biomarker for amyotrophic lateral sclerosis (ALS). The winner had preexisting grant funding, but the prize helped accelerate the research approach into the mainstream where it is now being used in drug development.

3. Biobank portal:
Research on biomarkers and on a test for therapeutic efficacy would be highly facilitated by access to biological samples collected from patients with Chagas disease, before and after treatment over the course of their follow up. For example, the WHO HAT biobank is a pivotal tool to facilitate research on new diagnostics for sleeping sickness (human African trypanosomiasis). Several biobanks for Chagas disease exist and have been proposed, but as yet there has been no mapping of current samples or sample gaps, no common access policies, and no single entry point for searching these sample banks, thus leading to delays and increased transaction costs for researchers and developers. The creation of a common-access portal to these biobanks, with agreement of common open access policies for research teams with credible biomarker research projects, would facilitate access to relevant biological resources and associated data. Such a biobank portal would provide access in an efficient and ethically and legally compliant manner and reduce fragmentation through harmonization of procedures, implementation of common standards, and potential fostering of collaboration. Part of the development of the portal should also be explicitly focused on supporting capacity building in countries with less developed biobanks, thereby contributing to strengthening research capacity in Chagas-endemic countries. The Initiative would decide which institution would host the biobank portal.

4. Alternative administration of existing drugs in monotherapy or combination, and proof of concept for new drug candidates:
Recent evidence suggests high efficacy of benznidazole, but broader use of this drug has been limited by safety and tolerability concerns and poor patient compliance. Duration of treatment for Chagas disease has not been evaluated systematically. Current treatment regimens and dosing intervals have been derived from decades-old patient series with limited direct comparisons.

New pharmacokinetic and pharmacodynamic data of existing drugs in monotherapy, and evidence of positive interactions between benznidazole and azoles, suggest that shorter treatment courses, different dosing regimens, and combinations with benznidazole should be assessed to improve Chagas treatment. At the same time, new azole derivatives (E1224, posaconazole) are currently being assessed in clinical trials, and a new drug candidate (fexinidazole) has entered clinical evaluation. Also, basic research is being conducted to identify potential new lead compounds.

Securing agreement on open innovation and access principles and having early involvement of regulatory authorities in the selection of clinical candidates are needed, as are funding and incentive mechanisms to accelerate this research.

10. Reasons for proposing:
(Provide details if any priority setting and/or selection criteria that has underpinned the consideration to take up this area of technology for development.)

Chagas disease has been considered a priority disease for countries in Latin America, and the needs for new treatments and better coordination have been recognized in regional and international resolutions:

11. **Who could potentially develop the technology/carry out the research?**

*(Provide known details: individual researcher? Group of researchers? Research/coordination organization including PDPs? Group of research organizations working together? Combination of these; What would be the process of selection of developers?)*

(see questions 5 & 7)  

(100 words)

12. **Who could potentially manufacture the final product?**

*Multinational company? Local production? Joint venture? How the decision will be made about the producer?*

Producers selected for priority R&D projects would need to commit to the equitable access and IP policies set by the Initiative including that products will be registered in all endemic countries; to production and supply at cost, plus a minimal margin, in all endemic countries, regardless of income level; open licensing of any IP and the possibility of technology transfer to encourage capacity building and entry of alternative suppliers.

(100 words)

13. **What could be the role of WHO, if any, in this demonstration project to bring this venture to fruition?**

WHO/PAHO would be a member of the Coordinating Initiative, and specific roles in collaboration with Initiative members would include the following:

**Scientific input:**
- Commitment to review target product profiles (TPPs) and update the guidelines;
- Links to Platforms and research data on PAHO Regional Platform on Access and Innovation for Health Technologies (PRAIS);
- Advice on establishment of biobank portal based on the experience of the WHO HAT biobank

**Access input:**
- Interface with national Chagas disease control programs, catalyzing rapid translation and adoption of new technologies into public health use;
- Advise on pooled procurement mechanisms, such as the PAHO Strategic Fund;
- Estimate Chagas treatment needs of endemic countries and report on the outcomes of these demand forecasts to assist manufacturers in scaling up production, planning distribution, and timely delivery.
  - PAHO with the Brazilian Ministry of Health organized a meeting to estimate the needs of the existing treatments for Chagas (benznidazole and nifurtimox), which was attended by representatives from 14 endemic countries and manufacturers. This precedent should be followed yearly in order to provide better guidance and coordination to manufacturers regarding new treatment regimens to help ensure the optimization of time and sufficient quantities are produced.
- Promote collaboration among national regulatory authorities on new product registrations, by working through the Panamerican Network for the Medicines Regulatory Harmonization (PARHF Network) and the PAHO National Regulatory Authorities of Americas.
14. Please outline a timeframe and projected milestones for the project covering the first 5 years. This should also highlight the immediate actions that need to be taken?

Step 1: Establish the Coordination Initiative. Organize a meeting of representatives of the Chagas Clinical Research Platform, NHEPACHA, PIDIC, FINDECHAGAS, Latin American governments, TDR, and WHO/PAHO in order to agree on the coordination Initiative’s responsibilities, select members, and identify the chair and the hosting institution of the secretariat.

Step 2: First working session of the Coordination Initiative to formally commit to the guiding principles of open knowledge and innovation, sustainable funding, and equitable access, and agree on the technology projects to pursue for development (see Questions 5 and 7)

Step 3: Series of working sessions on R&D priorities and funding mechanisms:
- Agree on funding needs and identify sources of public and private funding to pool into a virtual fund for use overall and per R&D project
- Step 3A: For PCR kit, establish and validate existing Target Product Profile (TPP), defining the objectives and the minimum-acceptable and ideal requirements for the diagnostic test, and identify the most appropriate developers and industrial partners for this test
- Step 3B: Define and validate existing TPP on biological markers of therapeutic efficacy
- Step 3C: Establish implementation plan for biobank portal and agree on hosting institution
- Step 3D: Update and validate existing TPP on new drug candidates, and identify priorities among current and planned clinical trials (including proof of concept progression to Phase III)
- Identify the most appropriate push and pull mechanisms to incentivize priority R&D projects, such as initial grants and milestone prizes

Timeframe for outputs:
- PCR diagnostic kit: achievable within 3 years
- Laboratory validation of selected biomarkers: achievable within 3 years, with at least one new biomarker validated for use in clinical trials within 5 years
- Establishment of biobank portal: 18 months, with support to establishment of two biobanks in endemic countries.
- New treatment options:
  - Proof of concept of alternative treatment regimens of existing drugs in monotherapy or in combination: 2-3 years
  - Proof of concept of a new chemical entity (NCE): 2-3 years
  - At least one new treatment option available and adopted within 5 years

15. What is the intellectual property (IP) landscape relative to this project? Is there any IP, e.g. patents that need to be licensed in to be able to develop and market the product in developing countries? How would IP and related intellectual assets, including knowhow, proposed to be managed in this project?

The proposed strategy of developing alternative regimens of existing drugs has limited IP implications, as current drugs are no longer under patent protection.

With regards to the development of new technologies, the equitable access policy established by the Coordination Initiative would include an IP policy that would be applied to all funded projects based on the following principles:
- Ensure ability to undertake further research based on the research findings in development of new tools or treatments
- Ensure treatments are ultimately affordable to the patients who need them and that access to these
treatments is equitable. Producers would have to commit to the production and supply at cost, plus a minimal margin, in all endemic countries, regardless of income level.

- Develop new drugs and tests as public goods. This would include open licensing of any IP and the possibility of technology transfer to encourage capacity building and entry of alternative suppliers.

In relation to the use of milestone prizes, the prize payment would be conditional on the winner agreeing to the IP policy.

16.* What would be the strategy to ensure access to the product once it is developed?

*(Access is an important dimension of these demonstration projects, it is important for the projects to begin with the end in mind, explain how this project would deliver the technologies to the needy patients i.e. price and affordability; modes of supply; storage; prescription; dispensing; and compliance; WHO will develop guiding principles for ensuring access to any products coming out of the demonstration projects)*

The early involvement and collaborative work of the Initiative with active participation of Chagas disease control programs, PAHO, and WHO, together with key research institutions, PDPs, and manufacturers, are seen as key components to minimise the time for translation and adoption of developed technologies.

Critical problems that would need to be solved to ensure proper product access:

- Poor demand quantification at country level, and poor aggregation of demand at regional and international levels
- Weak procurement practices
- Uncertain routes to market for new products or suppliers (e.g. lack of clear regulatory pathways)
- Reliance on single suppliers where alternatives are possible, raising concerns about price and supply security
- Lack of operational and human resources to deliver treatments in the field to ensure treatment scale-up

The Coordination Initiative would act as a forum to:

- Support the work of PAHO and others on demand forecasting (see Question 13) to assure producers of sufficient demand from countries to expand production capacity and encourage other suppliers to enter
- Assess needs and propose options for using innovative financial approaches, such as volume guarantees, Advance Purchase Commitments (APC), and pooled procurement, which may be required to scale up manufacturing of these treatments, ensure their affordability, and facilitate their delivery to patients
- Explore and facilitate innovative regulatory pathways to strengthen collaboration and mutual recognition between regulatory authorities
- Secure commitments from donors to tie funding to policies that require: products be registered in all endemic countries; commitments to production and supply at an affordable price; open licensing of any IP; and possibility of technology transfer to encourage capacity building and entry of alternative suppliers
- Have regular contact with national programs and regional initiatives to discuss how new tools could be integrated into their national strategy, and advocate to national governments that appropriate resources are committed to scale up treatment.

17. How could the project be financed paying particular attention to the need to demonstrate new and innovative forms of financing? Also provide an estimated cost of the project.

Proposed cost estimates:

The cost of the coordination Initiative and secretariat is estimated as follows: $300,000 for set-up (first
year), and $450,000 per year for operation/administration over next 4 years, assuming 1 to 2 permanent staff and office set-up and maintenance, as well as 3 in-person coordination meetings for the first year and 2 in-person meetings for the following years. The total cost estimate of the coordination Initiative over 5 years would be $2.1 million.

To minimize costs, the secretariat is proposed to be hosted within an existing organization. Actual staffing and office costs will depend on the degree to which the secretariat’s functions are outsourced or provided by the hosting organization, which will depend on the competencies of the selected hosting organization.

**Priority R&D Projects**

These costs estimates will be reviewed and validated by the coordination Initiative. These are therefore indicative costs at this stage.

**PCR diagnostic kit:** Additional incentives for the completion of development of a PCR diagnostic kit is estimated at $3 million.

**Biomarker prize:** $1.33 million
- Prize purse: $1 million
- Review of feasibility and development of outline of prize proposal: $80,000
- Development and implementation of prize proposal: technical challenge design, formulation, and management: $150,000 first year, $100,000 for remaining 2 years

**Biobank portal:** $750,000
- Set-up: $150,000
- Annual operation cost of $200,000 for 3 years

**Biobank set-up and operation:** Additional costs for setting up and maintaining 2 biobanks is estimated at $2.4 million.

**Development of new treatment options:** Total cost of $44 million over 5 years is estimated taking into account the current Chagas R&D landscape, which includes current funding gaps and projected cost increases for drug-development projects that could be implemented by a number of institutions. The funders will decide which projects, institutions, and developers will receive this funding from the virtual fund.

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<thead>
<tr>
<th>Project Component</th>
<th>Cost Estimate, US$</th>
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<tr>
<td>Coordination Initiative and secretariat</td>
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<td>PCR diagnostic kit</td>
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<td>Biomarker prize</td>
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<td><strong>TOTAL</strong></td>
<td><strong>53,580,000</strong></td>
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Some flexibility is required in this budget estimate given the possibility of unknown cost factors. The coordinating Initiative will regularly review progress and budgets to produce revised expenditure forecasts and highlight challenges and opportunities that may impact the timetable.

To ensure sustainable funding, members of the Initiative, particularly governments, would need to commit the necessary funding to first support the establishment of the Initiative and to support the identified R&D priorities. Governments could also provide indirect funding through the provision of facilities and expertise. A coordinating Initiative could pull public and private funding into a virtual fund to support priority projects identified by the Initiative, which could be taken forward at national level or within multicountry sites.
Some funding sources already exist in the region that could be leveraged and targeted in new ways to support this Initiative, including ministries of science and technology, ministries of health, national research agencies, national development banks (eg, BNDES in Brazil), and regional philanthropic foundations, using financial instruments in these bodies that support socially responsible projects, innovation, and national industries.

18. How could the project be governed and coordinated paying particular attention to the need to demonstrate better way of coordination?

The Coordination Initiative would be composed of representatives of the scientific community, key Latin American governments, PAHO/WHO, TDR, DNDi, treatment providers, and the International Federation of People Affected by Chagas Disease (FINDECHAGAS), supported by a secretariat housed in an existing institution.

The Chagas R&D Accelerator Initiative will demonstrate that Chagas R&D can be accelerated through focused coordination of promising R&D projects, collaborative Platforms, equitable access to new products, and sustainable funding secured through existing and new funding mechanisms. It proposes a key role for endemic countries. There are few health R&D initiatives that have been conducted under the leadership of endemic countries, yet the sustainability of essential health R&D critically depends on developing countries involvement and leadership at all stages of the R&D process. It will demonstrate that countries in Latin America can collaborate on R&D priorities based on open innovation principles, focused on a disease of regional importance. It will also demonstrate that endemic countries can collaborate on funding directly and through in kind access to facilities and expertise, such R&D collaboration, including with stakeholders and public and private funders from any region, would establish an important precedent within the region and internationally, and provide opportunities to evaluate whether such collaborations would be of benefit in other disease areas.

(See questions 5 and 14 for more details).

19. Have any donor agencies/governments already indicated interest in supporting the project?

There are ongoing discussions with countries and institutions in the region who have expressed interest in principle in the project.

References


ii World Health Organization 2013. Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases.


vii PAHO/DNDi collaboration, Benznidazol Demand Forecasting, manuscript in preparation.


