Implementation of WHA 66.22: Summary of candidate demonstration projects
Implementación de WHA66.22: Resumen de propuestas para proyectos de demonstración

Organización Panamericana de la Salud
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ITLE	Summary	Area/disease	Country	Target output	PAG (pdf)
1. DETERMINACIÓN DEL EFECTO BIOLÓGICO DE COMPUESTOS FENÓLICOS DE LA MORA TROPICAL DE ALTURA (*RUBUS ADENOTRICHOS*) EN MODELOS CELULARES, TISULARES Y ANIMALES	El proyecto "Caracterización de la actividad biológica *in vitro* de tres especies vegetales de interés científico nativas de Costa Rica" permitió identificar que el jugo de la mora tropical de altura (*Rubus adenotrichos*) posee gran potencial anti-carcinogénico, específicamente como agente quimiopreventivo contra el cáncer de piel. La presente propuesta pretende realizar una caracterización molecular más detallada de la actividad biológica de la mora tropical de altura, con el fin de identificar en dos fracciones químicas cuáles son los compuestos específicos responsables de la bioactividad, así como dilucidar claramente la vía celular involucrada. En etapas posteriores, se desarrollará la fase de escalamiento, de manera que se pueda trabajar en formulaciones de productos que puedan ser eventualmente comercializados por una casa farmacéutica de origen costarricense.	Cancer	COR	Cancer treatment	1
2. CEIBA CONSORTIUM FOR POPULATION PHARMACOGENETICS TO IMPROVE DRUG SAFETY AND EFFICACY IN LATINAMERICA	Despite Hispanics constitute one of the largest groups in the world, including in the United States of America there is a paucity of pharmacogenetics studies. The ethnic background of Hispanics mostly derives from an admixture over the past five centuries of local Ancient Amerindians, Backs and Europeans. The Ibero-American Network of Pharmacogenetics and Pharmacogenomics (RIBEF) Network was created in 2006 with the purpose of promoting collaborative pharmacogenetic/genomic research and clinical implementation aspects in Hispanics form Latin America and the Iberian peninsula. Among current RIBEF activities, the CEIBA.FP Consortium aims to study the variability of phenotypes and genotypes in Hispanics that are relevant to pharmacogenetics (**Rodeiro I. et al., 2012**). In sum, drug metabolic capacity need to be determined in vivo and its correlation with a given genotype must be reanalyse for a given population. Specifically the CEIBA Consortium is aimed at analysing the frequency of relevant drug metabolizing enzymes pheno and genotypes in Hispanics populations, and ultimately to design a "Predicted Phenotypes from Genotypes" for Hispanics.	Drug metabolism	Multicountry CEIBA consortium	Biomarker panels to prevent pharmacogenetically mediated drug-drug interactions in LAT populations	9

3.	MEDICAL DEVICE DEVELOPMENT FOR EARLY DIAGNOSIS OF NEOPLASIAS BY MEANS OF TISSUE CHARACTERIZATION USING ELECTRICAL IMPEDANCE TECHNIQUES	This project proposes the development and tuning of an acquisition system for electrical characterization of living tissue, using impedance measurement techniques in order to support the early diagnosis and localization of tumors. The research hypothesis assumes that healthy tissue presents electrical characteristics (normal) and that the disease tissue has different electrical characteristics (pathological). To move from one condition to another should exceeded some threshold, small change some parameter, some trends, etc, which could be controlled to generate early warnings.	Cancer	VEN	Medical device based on thechniques for measuring electrical impedance in order to characterize the living tissue as a support for early tumors diagnosis	30
4.	USO DE LA CONGELACIÓN LENTA EN EL ALMACENAMIENTO DE LOS ALIMENTOS EN EL ÁREA DE COCINAS DEL SISTEMA HOSPITALARIO CON EL FIN DE IMPLEMENTAR EL PROCESO DE TRANSFORMACIÓN DE LOS ALIMENTOS VEGETALES Y ANIMALES A FORMAS TERAPÉUTICAS EN EL TRATAMIENTO DE LAS ENFERMEDADES DEGENERATIVAS. (NUEVA TECNOLOGÍA)	La implementación del proyecto es conocido como Tisuloterapia con alimentos sometidos a congelación lenta, Alimentos en crioterapia, Crioterapia de los alimentos, Terapia Nutricional o Dieta del Dr. Javier Urrutia García.	Enfermedades degenerativas y otras		Transformacion de alimentos a formas terapeuticas	36
5.	ORGEX (ÓRGANOS Y EXTREMIDADES)	Actualmente tratamos de desarrollar innovación en tecnología para conservación de órganos y extremidades para trasplante y/o rescate en el caso de extremidades, la intervención propuesta es en conejo .La técnica sería intervenir a 30 conejos para retirarles un riñón y someterlos a la	Discapacidad y trasplante.		1) Solución conservadora-oxigenadora-nutrititva 2) Bolsas de	45

	técnica de conservación normo-térmica (solución modificada y bolsas de conservación) con circulación artificial, para posteriormente volver a reimplantárselos y valorar si funcionó la conservación (esto retirándoles el otro riñón sano). Si vemos que funciona escalar a modelo porcino la misma técnica. Dentro de estas actividades también probaremos un recirculador y bolsas para conservación. El objetivo principal es llegar a establecer un banco de órganos, y poder salvar extremidades. Y mencionando que si está técnica funciona escalaremos el proyecto para probar un tratamiento endovascular quirúrgico de mínima invasión para la ateromatosis, así como un sistema para el tratamiento endovascular para el trauma craneoencefálico.			conservación 3) Dispositivo para recirculación artificial.	
6. "DESARROLLO DE ESTRATEGIAS PARA LA REDUCCIÓN DE LA MORTALIDAD MATERNA A PARTIR DEL ANÁLISIS DE GOBERNANZA Y PARTICIPACIÓN SOCIAL EN PROGRAMAS DE SALUD MATERNA EN GUATEMALA"	Con el objeto de desarrollar estrategias para la reducción de la mortalidad materna con la aplicación de indicadores de gobernanza en los programas de atención materna, se propone un proyecto de investigación demostrativa que evaluará con el uso de indicadores de gobernanza y participación social, los niveles y tendencias de la política de atención materna. Para tal objetivo, se tomará a los actores sociales que interactúan en los distintos niveles de los programas y política de atención materna tendente a la reducción de la mortalidad materna como unidad de análisis.	Salud Reproductiva. Morbi-mortalidad Materno	GUT	Resultados: año 1 productos de la investigación servirán como insumos para formular las estrategias de gobernanza y participación en la atención materna tendente al abatimiento de la mortalidad materna; en los años 2, 3 y 4 se aplicará la estrategia en los municipios seleccionados, en el primer semestre del año 3 se compararan 3 los resultados de proceso, luego en el primer semestre del año 5 se realizará una evaluación comparativa con base a los criterios de gobernanza y	49

					participación social; en el segundo semestre del año 5 se realizará la abogacía para la sostenibilidad de las estrategias positivas con los actores sociales de todos los niveles involucrados en la atención materna.	
7.	E-DOCTOR MÓVIL.	Comprendiendo y utilizando el significado de Tecnología Sanitaria como: amplia gama de productos para el cuidado de la salud y que, en una u otra forma, se utilizan para diagnosticar, vigilar o tratar cada enfermedad o condición que afecta a los seres humanos. Estas innovadoras tecnologías (aplicación de la ciencia y la tecnología). El Ministerio de Salud Pública y Asistencia Social de Guatemala (MSPAS) a través del plan de e-health se plantea la idea de implementar el proyecto "e-Doctor Móvil", que fortalecerá al recurso humano de los servicios de salud en la capacitación constante, el realizar medidas de prevención, la toma de decisiones clínicas correctas, el diagnóstico oportuno y manejo adecuado de los casos de pacientes que se compliquen con hemorragia y/o trastornos hipertensivos en el embarazo.	Hemorragia obstétrica y trastornos hipertensivos en el embarazo	GUT	Convirtiéndose esta plataforma en un Doctor Virtual, quien asistirá al personal encargado de la atención de las pacientes embarazadas o el posparto a detectar los diferentes síntomas, signos de las pacientes y a la vez dar un probable diagnostico en base a los hallazgos encontrados, indicando al personal de salud el manejo adecuado (medicamentos, tratamientos y/o traslado) de la paciente según sea el caso, la ventaja de poseer "e-Doctor Móvil", es que	89

					podrá tener acceso a las comunidades más retiradas de Guatemala y poder hacer uso de la tecnología móvil, como lo puede ser SMS encriptados (Mensajes de Texto Seguros), 3G, para el envió de información en línea de la paciente.	
8.	**PRODUCTION OF LIPOSOMAL AMPHOTERICIN B FOR THE TREATMENT OF VISCERAL LEISHMANIASIS**	The Brazilian Ministry of Health has a current strategic project for establishing a productive development partnership (PDP) for the local production of the active pharmaceutical ingredient and medicine Liposomal Amphotericin B (lyophilised injectable powder 50 mg), in order to attend the demands of SUS (Brazil´s National Health System) to fight visceral leishmaniasis (VL). The government uses its purchasing power and promises to buy the drug over the period of five years from a specific laboratory. In return, this same lab transfers the technology used to produce the drug to a State lab. This way, an important drug such as this one used to fight visceral leishmaniasis can be produced at a lower cost locally by a State lab, increasing the population´s access to the medication and reducing the country´s dependence on private international laboratories. The project being proposed aims to leverage from the knowledge gained from this Brazilian project and implement a regional Latin American PDP, so more countries may benefit and offer this medicine to their population, helping to fight visceral leishmaniasis.	Visceral leishmaniasis	BRA (MOH)	API and formulation of Amphotericin B	108
9.	**ESTABLISHMENT OF PUBLIC-PRIVATE PARTNERSHIP FOR THE DEVELOPMENT OF A DIAGNOSTIC KIT FOR PRENATAL AND POSTPARTUM**	The Ministry of Health of Brazil established the Productive Development Partneships (PDP), with a view to ensure the supply of strategic products for the Brazilian Unified Health System (SUS) . In Brazil, there is already a pilot project using a PDP for development, registration, production of an industrial platform for multiplex diagnostics and point of care for prenatal and postpartum. This project aims to develop a diagnostic kit to use the Programs of Public Heath for prenatal and postnatal care, in the context	Pre and postpartum care/diagnosis infectious diseases	BRA (MOH)	A point-of-care and diagnostic plataform, using immunodiagnosis, capable to diagnose 11 pathogens for prenatal and for postpartum.	121

	of the "Stork Network Strategy". The proposal in question is to develop, validate and produce antigens for immunological diagnosis for 11 pathogens, in which 8 are virus, 2 are protozoa and 1 is bacteria, namely, HIV-1 and HIV-2 virus, which are the cause of the acquired immune deficiency syndrome; HTLV-I and HTLVII, related to diseases such as Adult T-cell leukemia/lymphoma and the Tropical Spastic Paraparesis (TSP)/myelopathy; HBV and HCV virus, the cause of viral hepatitis B and C; Rubella Virus, Cytomegalovirus (CMV), Treponema pallidum, the causative agent of syphilis, Tripanosoma cruzi, the causative agent of Chagas disease and Toxoplasma gondii, which causes toxoplasmosis. In the case of HIV-1 and HBV, besides the antigens to detect the presence of antibodies against such diseases in serum from tested patients, it is also required the antibodies to detect, respectively, the viral proteins p24 (HIV-1) and HBsAg (HBV). This project foresees six (06) phases: 1. development of the antigens and the antibodies; 2. development of polymer 3. production of the integrated circuit (chip); 4. development of production techniques; 5. development of fluorophore; and 6. validation. In Brazil, the entities involved in the process of research and production development are the public institution Fundação Oswaldo Cruz (Instituto Carlos Chagas - ICC /Fiocruz Paraná) and private laboratories.				
10. DEVELOPMENT AND REGIONAL PRODUCTION OF L-ASPARAGINASE FOR THE TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)	Acute Lymphoblastic Leukemia (ALL) is, at a global level, the most frequent childhood cancer, being the most commonly encountered type of leukemia in children . Most of children diagnosed with ALL are enrolled into clinical research studies, or treated in accordance with protocols spread ans standardized troughout the world . The numbers of ALL around the World are estimated in 75.000 new cases per year, and in developed countries 80% of them are cured, after a 2 to 3 years treatment, which is based in compliance with the protocols Patients living in poor, and developing countries, or in unfavorable socioeconomic and cultural conditions, with poor access to health services, treatment, misuse of medications, and in noncompliance with the protocols by any of the partners of it, health professionals, family, and patients increases the chances of relapses. In 2002, the number of children without treatment around the world were estimated in 60.000 cases per year, mostly because lack in access to treatments, and due to the costs related to it.	Acute Lymphoblastic Leukemia (ALL)	BRA (MOH)	Local production of L-Asparaginase	135

	Today, the numbers are quite the same, and the challenging is still the same, make accessible the treatments, through the protocols, and medicines needed to the success of an international strategy, which would make possible for children living in poor, and developing countries to be treated. Brazilian Ministry of Health has a current strategic project for establishing a Productive Development Partnership (PDP) for the local production of L-Asparaginase, the enzyme, made through biological route in order to improve the access to treatment in United Health System (SUS). This strategy is based in the power of health sector in Brazil to enhance the lack of investments needed to develop drugs like that.. This way, an important drug, such as this one used to fight ALL, can be produced at a lower cost locally by a State lab, increasing the population´s access to the medication and reducing the country´s dependence on private international laboratories. The project aims to reduce countries' technological dependence through local capacity for production of a biological product. More importantly, the project aims at benefiting local children who have been neglected by research and development efforts.				
11. DEVELOPMENT OF A VACCINE AGAINST SCHISTOSOMIASIS BASED ON THE RECOMBINANT SM14 A MEMBER OF THE FATTY ACID BINDING PROTEIN: CONTROLLING TRANSMISSION OF A DISEASE OF POVERTY.	The Brazilian Sm14 Schistosomiasis Vaccine Platform was launched and strongly pushed in the context of a formal WHO program, specifically structured towards the Development of Anti Schistosomiasis Vaccine. Main outcome of this initiative was the selection of 06 priority antigen candidates out of which Sm14 continued to be developed. With strategic support of WHO, Fiocruz move forward, to final development of Sm14 as the unique Schistosomiasis Vaccine emerging from an endemic country such as Brazil in the most important scientific institution, Fiocruz, directly linked to Brazilian Ministry of Health. The project on the development of a vaccine against schistosomiasis based on Sm14 recombinant protein is a long term project, emblematic, complex and has the major challenge of developing, in Brazil, a human vaccine against schistosomiasis that is an outcome of basic research at FIOCRUZ, with strong innovative and educational components both in the adopted methodology as in its strategic design aiming to benefit and protect humans living in endemic area. The rSm14 molecule was selected from a mixture of adult schistosome components obtained from living worms, previously shown to protect mice against infection. It was identified on the basis of a long-	Schistosomiasis	BRA (Fiocruz)	Schistosomiasis Vaccine	148

	term investigation focusing on vaccination experiments in populations of outbred animals. Specifically, two distinct animal models (SW mice and NZ rabbits) were developed with the parasitological approach of high and low susceptibility to cercarial infection; vaccination schedule parameters that influence protection were assessed in the strict context of animal models and minimum protection levels were established to optimize experiments and define immunization route and scheme (number of doses, dosage of antigen protein, adjuvants). Innovative methodology was used for protection assessment and we believe this has been critical for the selection not only of native rSm14 but also the identification of a mutant form which was constructed by site directed mutagenesis selected for its higher stability as compared to the native protein sequence. We have recently successfully accomplished Phase 1 clinical trial with the Sm14 vaccine in 20 healthy male volunteers. The vaccination schedule, based on Hepatitis B vaccine, consisted of 03 IM injections of of GMP -Sm14 +GLA vaccine protein produced at the Ludwig Institute for Cancer Research –Cornell Univ facility ,Ithaca , NY, in monodosis presentation. Results, attested safety with almost no side effects. Immunogenicity was evaluated by Elisa with anti IgG ab also showed vaccination to be highly immunogenic mostly after the second dose. In collaboration with IDRI, we are presently assessing the immunological signature of vaccination by screening cells and sera from the human volunteers sent to IDRI.				
12. POINT OF CARE PLATFORM FOR DIAGNOSTICS OF CHAGAS DISEASE, APPLICABLE TO OTHERS TROPICAL DISEASES AND POTENTIALLY ON ONCOLOGY	The diagnosis and discrimination of infectious diseases such as Chagas, malaria, leishmaniasis, dengue, or HIV in geographic regions with poor or low-density medical infrastructure is of high socioeconomic importance. While so-called “rapid in-vitro diagnostic tests” for single diseases are already on the market, more complex analytical protocols are necessary to clearly identify a certain tropical disease and to determine the status of the disease - the latter being crucial for proper treatment. Such complex analytical protocols include liquid handling as well as sample preparation and amplification (PCR) of the nuclei acid of the specific pathogen. These sample preparation steps are currently only available for laboratory settings and have not yet found their way in mass-producible, integrated	Chagas and infectious diseases/diagnosis	BRA (Fiocruz)	Point of care platform for diagnostics of Chagas disease, applicable to others tropical diseases	163

	point-of-care (POC) diagnostic tests. Furthermore, PCR technology use in POC devices is still elusive, although PCR has long been accepted for diagnostic purposes. This situation happens because PCR equipments are bulky and demand a stable supply of electrical power. Additionally, PCR reagents are temperature sensitive, and the great majority of neglected disease cases occur in tropical, poor countries where basic infrastructure is not always present. Our proposal aims to develop a diagnostic solution that comprises a portable, low-cost equipment and a single-use silicon-based PCR microchip. The instrument is equipped with fluorescent sensors and is controlled by a small computer (netbook or tablet). The microchip will contain the PCR reagents, which will be designed specifically for the target pathogens and stabilized for room temperature (or refrigerator) transportation. The technology is relatively simple, and the platform is being designed with the Brazilian Health System in mind (where very little infrastructure and very few skilled personnel are available), so we are confident that the platform could be easily applied to other conditions in developing countries. Due to Fiocruz's expertise, we propose the first test to be developed to be for Chagas disease, followed by malaria and leishmaniasis. Preliminary studies are being planned to develop tests also for tuberculosis, trachoma and filariosis.				
13. **PROYECTO INTEGRAL DE INVESTIGACIÓN Y EDUCACIÓN, SOBRE PARASITOSIS INTESTINALES, MALARIA Y CONOCIMIENTO TRADICIONAL EN ESCUELAS RURALES DE BOLIVIA-ECUADOR-PERÚ"**	La Red Andina de Investigación y Desarrollo de Plantas Medicinales de la Amazonía (RAPMA), conformada en el 2009, pretende aunar esfuerzos y optimizar el uso de las capacidades instaladas y los recursos disponibles en centros de investigación existentes en Bolivia, Ecuador y Perú, a través y llevar adelante estudios de investigación de especies amazónicas antiparasitarias, poco estudiadas, utilizadas para el tratamiento de la malaria, la leishmaniasis y los parásitos intestinales, seleccionadas a partir de farmacopeas tradicionales, con el fin de validar los usos tradicionales. Adicionalmente, de manera paralela, pretendemos compartir los conocimientos generados en estos centros y llevar adelante estudios de desarrollo de nuevas formulaciones y de preparaciones galénicas caseras, de tratamientos antiparasitarios a base de especies medicinales que ya han sido validadas, mediante estudios químicos, biológicos y de eficacia.El Proyecto tiene hasta tres componentes diversos: **Trabajos de Campo** (Diagnóstico y Seguimiento) Este permitirá identificar	Parasitos intestinales, malaria	BOL PER ECU	Diagnóstico coproparasitológico sobre incidencia de parásitos intestinales en niños de escuelas rurales, entre inicial y quinto de primaria con edades entre 5 y 12 años. Diagnóstico sobre malaria en las zonas de estudio y documentación de casos adversos o fracasos terapéuticos. Este trabajo inicial de	176

	la situación de las infecciones parasitarias, al punto de partida del programa y los controles sucesivos, permitirán evaluar el adelanto, así como los problemas, en las mejoras de las condiciones de salud entre los niños en las escuelas rurales. Este trabajo permitirá compartir el uso de protocolos comunes consensuados (Campo), facilitando la interpretación de los resultados y la toma de acciones en las zonas de trabajo.**Trabajos Académicos e Investigación** (Pregrado/Postgrado) Este aspecto permitirá formar recursos humanos al máximo nivel, ya que las investigaciones de campo y laboratorio, involucran estudiantes en programas académicos existentes en cada uno de los países. Este trabajo permitirá utilizar protocolos comunes (Laboratorio), facilitando los procesos de transferencia y adaptación de metodologías entre los laboratorios involucrados.**Trabajos sobre la Biodiversidad** (Conocimiento Tradicional). Este componente del proyecto, pretende documentar el uso tradicional de especies medicinales (en las zonas de acción) y permitirá aislamiento y la caracterización química y biológica de los derivados naturales activos, (Cabezas de Serie), mientras que al mismo tiempo se definirán aspectos relacionados a posibles mecanismos de protección de estos conocimientos y sus aplicaciones a los derivados potenciales para desarrollo local.			diagnóstico y seguimiento en el campo, y continuo a lo largo del proyecto, permitirá seleccionar el tratamiento más adecuado, entre los niños, de las escuelas, de acuerdo a diagnóstico y condiciones poliparasitismo.	
14. WIPO RE:SEARCH CONSORTIUM	Infectious diseases have a disproportionately devastating impact on individuals living in poverty. New products are desperately needed, yet due to a lack in market incentive, innovation in this field has been limited. By creating partnerships between pharmaceutical and biotechnology companies with assets and scientists with complimentary research interests and capabilities, WIPO Re:Search accelerates the discovery and development of promising new solutions for diseases of poverty. WIPO Re:Search is not a funding organization, yet when funding is needed, BVGH provides Members with access to its Funders Database. This Database is a comprehensive database of all open funding opportunities relevant to neglected disease research. The database summarizes and categorizes funding opportunities' critical information, including program description, disease and product focus, stage of R&D, researcher and institute eligibility requirements, geographic restrictions, deadline, contacts, and URL. By providing a single location that presents all relevant	NTD, malaria and TB	BIO Ventures for Global Health (BVGH)	seeks to accelerate the development of new drugs, vaccines, and diagnostics for NTD, malaria and TB	190

	funding opportunities, the novel, sortable database allows scientists to more efficiently search for the essential funding required to continue their much-needed research. Minimizing time spent identifying funding opportunities enables the researcher to direct his or her focus to other important laboratory activities. Through the combination of providing access to IP assets, proactive partnering, and support for identifying funding opportunities, the WIPO Re:Search consortium offers the WHO and its member nations with an opportunity to accelerate the development of much-needed products for diseases of poverty.				
15. DEVELOPMENT AND EVALUATION OF AN INTEGRATED PROJECT TO TREAT PATIENTS WITH ADVANCED, UNRESECTABLE LUNG CANCER IN THE VILLA CLARA PROVINCE.	The project aims to develop a complex intervention for comprehensive treatment of advanced lung cancer, including the introduction in the medical practice of novel biotechnology products:- LeukoCIM , granulocyte colony stimulating factor (G -CSF) It is used in the treatment of cancer patients to accelerate recovery from neutropenia after chemotherapy, allowing higher intensity of treatment regimens.- EPOCIM : Recombinant Human Erythropoietin (r -HuEPO)It is used in the treatment of anemia in cancer patients.- CIMAher is a humanized monoclonal antibody that in combination with radiotherapy objective response is increased and there are no severe clinical evidence of toxicity .- CIMAvax -EGF is a therapeutic cancer vaccine that induce an immune response of specific antibodies that recognize the EGF and inhibits it binding with its membrane receptors. CIMA-vax EGF is the first and the only cvaccine for treating non-small cell lung cancer (NSCLC), which increases the survival of patients with advanced-stage disease.- Vaxira : vaccine preparation that induces the production of antibodies specific Ab3 IgG and IgM isotype against NeuGcGM3 ganglioside, capable of recognizing this antigen and cause lysis of tumor cells that over express the same (antibodies with cytotoxic capacity) . It increases the survival of patients with non-small cell lung cancer (NSCLC) in recurrent or advanced stages (IIIB / IV) compared to patients treated with best supportive care. The complex intervention is aimed to contribute to early diagnosis, improve the comprehensive treatment and impact in reducing the mortality of patients with lung cancer . It is proposed aimed at increasing survival and quality of life of patients by combined actions in secondary health care (SHC) and primary health care (PHC) . The intervention will	Lung Cancer	CUB	Complex intervention for comprehensive treatment of advanced lung cancer	203

	have 5 components: 1) Organization and management structures , 2) care for cancer patients diagnosed with advanced lung cancer, 3) Capacity Building , 4) Communication and 5) Evaluation				
16. EL VIRUS DEL PAPILOMA HUMANO Y LA RESPUESTA INMUNE EN EL CONTROL DEL CÁNCER DE LARINGE.	**El cáncer de cabeza y cuello ocupa el sexto lugar de incidencia en cáncer y representa el 4% de las neoplasias malignas a nivel mundial. Las cifras indican que cada año alrededor de 650,000 personas reciben el diagnóstico de cáncer de cabeza y cuello y 350,000 mueren por la enfermedad. La edad de aparición es en general por encima de los 40 años y existe una relación causal de consideración con la ingestión de bebidas alcohólicas y hábito de fumar, mientras que el consumo de frutas y vegetales modula parcialmente los efectos carcinogénicos del alcohol y el tabaco. La relación del virus del papiloma humano (HPV) con este cáncer se investiga por mas de 20 años dado que la detección del virus oscila entre 0-100% de los pacientes.El estudio propuesto daría información para un tratamiento personalizado en los pacientes lo que posibilita una mejor utilizacion de los recursos disponibles. La importancia indiscutible de este aspecto se amplifica en países de ingresos limitados donde la incidencia de cancer es similar a la de los países con condiciones económicas favorables pero la prevalencia y la mortalidad son superiores.**	Cáncer de Laringe	CUB	Este proyecto procura realizar un diagnóstico más integral del cáncer de laringe, considerando los parámetros que inciden en la decisión terapéutica y por consiguiente en el curso clínico.	216
17. LOS MICROARNS 21, 129-5P, 155 Y 200C COMO MARCADORES PRONÓSTICOS Y PREDICTIVOS EN EL LINFOMA DIFUSO DE CÉLULAS B GRANDES	**El estudio de posibles biomarcadores en las muestras de tumores incluidos en parafina permite realizar análisis retrospectivos y asociar estos con la respuesta a tratamiento y la evolución clínica. Los microARNs son ARNs no codificantes que regulan post-transcripcionalmente la expresión génica, son muy estables y se encuentran bien conservados en bloques de parafina. Pueden ser exacta- y reproduciblemente extraídos y cuantificados a partir de estos bloques y proporcionar una información valiosa que correlacione su concentración con la evolución clínica, siendo posible utilizarlos como marcadores pronósticos y predictivos. En este proyecto retrospectivo, analítico y observacional proponemos utilizar el PCR a tiempo real para cuantificar los niveles de miR21, miR129-5p; miR200c y miR-155 en bloques de parafina de 200 pacientes diagnosticados con LDCBG entre los años 2007-2012 y correlacionar dichos niveles con variables clínicas y anatomo-patológicas así como con el resultado del tratamiento. La**	Cáncer. Linfomas No Hodgkin.	CUB	Prueba pronóstica y predictiva	223

	inclusión de los microARNs propuestos en este proyecto como posibles biomarcadores permitiría el diseño racional de novedosos regímenes terapéuticos aumentando la probabilidad de obtener mayores tasas de respuesta, mayor duración de las mismas e incluso superar la resistencia debido a la heterogeneidad tumoral.				
18. EVALUATION AND PREPARATION FOR DEPLOYMENT OF A NEW SINGLE DOSE LIVE ATTENUATED ORAL CHOLERA VACCINE	The general goal of this project is to prepare for the deployment of a single dose oral cholera vaccine effective against cholera caused by the vibrios of the o1 serogroup. The live attenuated strain Vibrio cholerae 638 will be the vaccine active ingredient. The ingestion of fresh cultures of 638 by Cuban healthy adults was demonstrated to be safe, immunogenic, fecally shed and protective against cholera in controlled volunteer studies. Phase I – II studies with pilot GMP vaccine lots demonstrated its safety, immunogenicity and fecal shedding of the active ingredient in healthy adults from Cuba and in apparently healthy adults from Mozambique. In this project we plan to conduct a phase I study with the vaccine in children (≥5) and teenagers (≤18) and a phase I-II study on HIV seropositives. Intensive parallel basic research will be conducted to obtain a novel thermostabilized vaccine formulation provided in a new pharmaceutical form, with the concurring advantages of being lighter to transport than traditional formulations and easier to administer without the need of buffer. A bridge study with the new formulation/presentation will be conducted on healthy adults, which will be pivotal to an intermediate phase ii – iii demonstration study on the value of the cholera vaccine as an adjunct control measure during cholera outbreaks. A new GMP dedicated facility for the manufacture of this oral biological will be constructed; the vaccine will be prequalified and provided worldwide via WHO.	CHOLERA CAUSED BY VIBRIOS OF THE O1 SEROGROUP.	CUB	SINGLE DOSE ORAL CHOLERA VACCINE.	232

19. MICOPLASMAS UROGENITALES Y CÁNCER EN CUBA: ENFOQUE INTEGRAL PARA LA PREVENCIÓN Y CONTROL EN LA SALUD PÚBLICA	En la última década numerosas investigaciones han estado enfocadas a la relación entre los micoplasmas urogenitales y los procesos cancerígenos. En este sentido ha quedado establecido a nivel internacional la existencia de asociación entre la colonización de diferentes tumores por especies de micoplasmas y el fallo de las quimioterapias en el tratamiento de estos pacientes, lo que incide directamente en la progresión de la enfermedad, así como en el gasto de recursos médicos y económicos para sustentar dichos tratamientos. En Cuba son muy pocos los estudios realizados sobre micoplasmas asociados a infecciones en el humano, por lo que el Laboratorio Nacional de Referencia sobre Micoplasmas del Instituto de Medicina Tropical ”Pedro Kourí” propone desarrollar un proyecto donde se incluyan sistemas de diagnóstico para especies de micoplasmas en muestras clínicas de pacientes con sintomatología urogenital y pacientes con cáncer, seguido de análisis integral clínico y epidemiológico para conocer la prevalencia de estos microorganismos en grupo de pacientes vulnerables, así como el análisis de valores de susceptibilidad antimicrobiana y caracterización genotípica, que permitan con ello establecer pautas para tratamiento y control en población susceptible y brindar conclusiones científicas al Sistema Nacional de Salud.	Infecc por Micoplasma	CUB	El diagnóstico microbiológico y clínico junto a estudios epidem. para la prevención y control de infec. urogenitales causadas por micoplasmas que derivan a enfermedades malignas.	240

20. AFFORDABLE DIAGNOSTIC TESTS FOR CANCER	Among the "special R&D needs of developing countries in Type I diseases where there is an identified health technology gap" is the need to develop better and more affordable cancer diagnostic tools. There is an opportunity to test open source de-linkage approaches to the development of new tests for cancer, and there are projects that are feasible, realistic, and likely to demonstrate success within a five year period. There are many types of cancer for which existing diagnostic tools are inadequate and specific cases or needs that will be appropriate to treat as priority projects. The proposal is to create a fund for open source diagnostics for cancer that are affordable and appropriate for use in low infrastructure settings, allocating resources into different reward systems that offer different opportunities to improve cancer diagnostics. The project will focus in particular on diagnostic tools that provide more affordable and more useful options in developing countries to provide (1) early detection of cancer, and/or (2) that identify useful bio-markers or other criteria that are beneficial in determining treatment options, such as determining whether breast cancer patients are candidates for treatments associated with amplification or over-expression of Human Epidermal Growth Factor Receptor 2 (HER2). This may include modifications to existing technologies, or entirely new technologies. There are a vast array of diagnostic needs for cancer in general, and particular challenges associated with patients that have low incomes, and/or when testing is conducted in resource poor settings with poor infrastructure. The project would set up two different innovation funds, each implemented in connection with different types of prizes, an open source dividend, and open licensing of intellectual property rights associated with the innovation for use in cancer diagnostics.	Cáncer	COL (MOH and Administrative Dept. of Science and Technology) Knowledge Ecology International (KEI)	Affordable diagnostic test for cancer	250

21.	**DEVELOPMENT OF CLASS D CPG ODN (D35) AS AN ADJUNCT TO CHEMOTHERAPY FOR CUTANEOUS LEISHMANIASIS AND POST KALA-AZAR DERMAL LEISHMANIASIS (PKDL)**	Cutaneous Leishmaniasis (CL), also known as button d'orient, chiclero's ulcer, Aleppo sore, Delhi's boil, etc., is a neglected disease that is characterized by disfiguring skin lesions. Worldwide, an estimated 1.5 million suffer from different forms of CL and Post Kala-azar dermal Leishmaniasis (PKDL) every year (1), but only a small percentage receives treatment. Currently there is no vaccine for Leishmaniasis and little R & D is aimed at alleviating the suffering of millions of CL cases, mostly children. However, CL & PKDL are disfiguring diseases that result in stigma, economic loss and affects mainly unprivileged populations with limited resources. Scars from CL lesions last for a life time and particularly on the face severely affect the whole life of afflicted individuals, particularly girls and women. PKDL is strongly believed to act as a reservoir of visceral leishmaniasis (VL) which underscores the need to develop an effective treatment. CL and PKDL patients require weeks or months of daily antimonial injections (toxic, painful, expensive). The objective for this demonstration project is to develop a short, safe, affordable and field-friendly treatment that are efficacious at least for CL caused by *L. tropica* and *L. braziliensis* (but which would ideally also work for CL caused by other organisms) and for PKDL. This project will allow demonstrating the effective use of delinking of the price of R&D and the price of the product though equitable or humanitarian licensing for global access, which ensures a low price of the final product given that the US-FDA has no intent to recover the investment in R&D as part of the Agency's mission. Development will require pooled funding from member countries. The time from manufacture to license is estimated at 7-8 years. But a new coordinated and collaborative approach with involvement of National Health authorities , National Regulatory Authorities and other relevant international and national stakeholders would foster a more efficient and faster process for making this medicine available and affordable to populations in need in target countries.	Cutaneous leishmaniasis and post kala-azar dermal leishmaniasis (PKDL)	USA (USFDA)	Treatment for Cutaneous leishmaniasis and post kala-azar dermal leishmaniasis (PKDL)	264

22. DEVELOPMENT OF HERCEPTIN'S BIOSIMILAR/BIOBETTER ANTIBODY, FOR USE IN BREAST CANCER	Cancer is a leading cause of death worldwide. In the last years, treatments with monoclonal antibodies (MAbs) have improved the life expectancy of patients. In particular Herceptin (humanized Ab, IgG1, recognizes the HER2 molecule and registered for adjuvant and metastatic treatment of breast cancer, marking a significant difference in survival in the treatment of this kind of tumor. But the production of these molecules is very expensive, so its use is not easily accessible to all patients, mainly in developing countries. Biosimilars/biobetters antibodies, are molecules obtained by recombinant DNA techniques, with manufacturing complex, so in many cases, it is possible to obtain similar but not identical molecules comparing with innovative products. The expiration of patents on recombinant proteins reduces the risk of legal disputes for infringing patent laws. Once expire the same, the first limiting factor for obtaining these molecules will be in the domain of the industrial technology and the availability of production capacity for products that require higher cell expression and scaling of fermentation of these industrial level. Only few countries with previous development in this field will have sufficient capacity to meet demand. In the case of countries like Cuba that have such capacity, the real limitation is the increasing regulatory barriers imposed by the transnational biotech, and which has become a heated debate, so that the products remain unique to the same current production companies with very high prices and access to patients for therapeutic efficacy of these drugs will remain very limited.The MAbs registered and widely used in the therapy of diseases such as cancer, are protected by patents (including Herceptin), which have begun to expire. In this project the CIM proposes develops together with PAHO, the production of a variant biosimilar/biobetter of Herceptin. Our center has technology and experience in research, development and production of MAbs, but lack the financial resources to develop a project from production and characterization of MAbs to Clinical Trials (Ecs) with regulatory requirements such that they must be comparative to the original product, the cost would exceed one million dollars. From the scientific point of view, despite the CIM has a proprietary technology platform should be developed cell lines with high levels of expression, as well as large-scale production and in parallel develop Abs against the	Breast Cancer	CUB	Herceptin's biosimilar/biobetter antibody	296

same target therapeutic but with improved biological functions (increase biological activity or decrease immunogenicity and increase half-life or higher levels of production and new formulations as subcutaneous.The final goal of this project is to develop accessible product for their costs to Cuban patients with a technology for local production transferable to other Latin American countries. The success of this project depends on its speed, by the urgent medical need for patients to have the product

23. ECOSYSTEM FOR FINANCING DEVELOPMENT OF AN OPEN SOURCE MULTIPLEX POINT OF CARE (POC) DIAGNOSTIC TESTS FOR THE DIFFERENTIAL DIAGNOSIS OF FEVER OR SEPSIS. HENCEFORWARD, THIS WILL BE REFERRED TO AS THE OPEN SOURCE FEVER DIAGNOSTIC PROJECT	The project is a multi-government collaboration to fund a low-cost multiplex point of care (POC) diagnostic test for the differential diagnosis of fever/sepsis. The motivation is to improve the diagnosis of patients suffering from fever in low-resource settings, thus enhancing treatment options, and also, reducing inappropriate use of antibiotic drugs. While motivated by the need for tests in resource-poor settings, the innovation will be also useful in non-resource poor settings and high-income countries, increasing the global social value of the innovation to donors. The project begins with the identification of an innovation need, and then proposes a method of financing investments to achieve the needed diagnostic services. The voluntary plurilateral funding by governments will be used in a combination of push and pull funding mechanisms, implemented with full de-linkage of R&D costs from product prices. The cost of the project is between US$70 million to $200 million, depending upon the level of donor support. The value of a successful innovation vastly exceeds the high end of the project funding, and the bulk of the funding would be in the form of obligations to only reward successful innovations, substantially lowering the risks and improving the expected cost benefit of the project to donors. The Target Product Profile (TPP) being developed for this test is targeted for use at the minimum in district health settings for patients (neonates, children and adults) presenting with fever syndromes. Because the causative pathogens of fever will differ by clinical setting and geographical region, one key feature of this diagnostic test is the flexibility to integrate epidemiological data of fever pathogens in various settings into the test. The final selection of the pathogens that need to be included in the test should be informed by the particular geographical and clinical setting for which the fever diagnostic test will be used. In order to meet the needs in resource-limited settings, the specifications are in accordance with previously established WHO ‘assured’ criteria for the test to be ‘affordable, sensitive, specific, user-friendly, rapid, robust, equipment-free and deliverable to end-users.’The governance of the project would include a Donor Committee, which would set high-level policies and enter into a contract with one or more entities to manage a portfolio of grants and innovation prizes. We anticipate that the Special	Fever of unknown origin	Multi (Doctors without Borders)	Low–cost, open source, multiplex point of care (POC) diagnostic test for the differential diagnosis of fever/sepsis	305

Program for Research and Training in Tropical Diseases (TDR), UNITAID or the World Bank would be among the entities that could manage the grants and/or prizes portfolio. Medical need: Fever is the most common presentation of infections. Fever without focal signs and symptoms is one of the most common reasons for admission to hospitals in low-income countries. [1,2] While accurate malaria diagnosis is now possible with the availability of a rapid diagnostic test (RDT)[3], there still remains a lack of diagnostic microbiology services for bloodstream infections and other common causes of fever despite efforts in improving laboratory capacity The intellectual property rights from the grants and innovation prizes would be conditioned upon the open licensing of intellectual property, data and technology transfer, possibly within a field of use, to insure open and competitive access to research outcomes. The program would include four different types of innovation prize funds. *(1) Biannual best progress prizes,*(2) *Milestone prizes*. (3) *End Product Prizes. (4) Open source dividend.*.The flexibility to use either grants and contracts or competitive prize contests is an important aspect of this project. Each of the mechanisms, grants and research contracts, milestone prizes, best progress prizes, end product prizes and the open source dividend, have strong points, but also gaps and weaknesses. The project embraces an ecosystem approach, using multiple mechanisms to advance and acquire development of new technology for fever diagnosis. In this sense, the sum is greater than the individual parts.

24. ACCELERATING INNOVATION AND ACCESS TO MEDICINES FOR TUBERCULOSIS THROUGH OPEN COLLABORATION: A PUSH, PULL, POOL APPROACH ("THE 3P PROJECT")	In 2011, there were 12 million people who needed TB treatment worldwide; 95% of whom live in low--- and middle---income countries (L&MICs). Because the TB mycobacterium mutates quickly, it needs to be treated using drugs in combination. Multiple Drug Resistant TB (MDR---TB) infected over 310,000 people in 2011, and there are reports of Extensively Drug Resistant TB (XDR---TB) and even Totally Drug Resistant TB (TDR---TB). However, current TB medicines are over 50 years old. The first new TB medicine in 50 years was recently approved by the United States Food and Drug Administration (bedaquiline); however, it has mainly been tested with older medicines, and as yet no novel 'pan---TB' regimens (effective against drug---sensitive and drug---resistant TB) have been fully developed. In essence, while TB treatment has recently taken a step forward, the current R&D system has failed to deliver the giant leap forward that is needed – that is, a more effective, shorter and safe combination of multiple new TB drugs. Furthermore, a healthy pipeline is needed due to the expected emergence of drug resistance. However, there are not enough candidate drugs in the pipeline, and many of those that exist are stalled or moving forward too slowly. TB is not a high priority in commercial drug development, as it predominately affects patients in L&MICs and often vulnerable populations, such as the homeless, prisoners, migrants and those co---infected with HIV. The ultimate goal in TB treatment is a combination of medicines that effectively, safely and quickly treats all forms of TB in as few pills as possible (i.e., a fixed---dose combination). There is an urgent need to improve MDR---TB treatment: the current treatment for DS---TB takes 6 months and MDR---TB treatment takes 2 years, including daily injections for at least 8 months. MDR---TB treatment is particularly difficult, because many medicines are toxic with side effects, such as deafness, psychosis and severe nausea, and must be taken at precisely the same time each day to prevent resistance. Thus, MDR---TB patients have difficulty in completing their treatment, making them less likely to be cured of TB, exacerbating their drug resistance and left with very limited future treatment options.	Tuberculosis (TB):both drug-sensitive and drug-resistant (DR-TB)	Multi (Doctors without Borders)	TB medicines: single drugs, regimens, fixed-dose combinations, and pediatric formulations	321

	Today, existing incentives drive commercial drug developers to develop individual compounds in isolation. However, what is required is the simultaneous development of multiple compounds tested in combination with each other. We propose to transform R&D for new TB treatments through the "3P Project" – incorporating novel approaches to financing R&D (Push, Pull) and managing intellectual property (Pool) in order to accelerate innovation and achieve more equitable access to better medicines. In this open, collaborative framework, researchers and clinicians will be incentivized to share scientific data and clinical trial results, and to conduct medically appropriate research on multiple compounds. A Technical/Scientific Advisory Committee, which could be hosted by the WHO, will set technical priorities and define Target Regimen Profiles for MDR---TB treatment and ultimately for an improved treatment for all forms of TB. This system offers four benefits over the current system: 1) reducing the duplication of research efforts thereby saving time and money, 2) "de---risking" potential combinations as early and as affordably as possible, 3) accelerating drug combination development, and 4) reducing the risk of resistance to new compounds. In addition, the project will have three milestone prizes for combination regimens of TB medicines that progress through two major hurdles in the R&D process – entry into the beginning of clinical development (into Phase I) and establishment of proof of concept (success at end of Phase II), alongside a potential small prize for entering the open collaborative framework and discretionary grant funding. Other smaller incentives at various points in the R&D process may be added, as necessary, in order to address bottlenecks. Where such incentives are not sufficient, royalty---bearing licenses could be negotiated between the patent pool and the IP holder(s).				
25. EVALUACIÓN CLÍNICA DE UNA **VACUNA** ANTINEUMOCÓCCICA CONJUGADA HEPTAVALENTE	El proyecto persigue demostrar, como enfoque novedoso, que la vacunación con PCV en población infantil de 1 a 5 años tiene efectos directos e indirectos en la prevención de la enfermedad neumocócica y en la circulación de la bacteria; y que este grupo etario puede ser atractivo para realizar una vacunación antineumocócica complementaria a la que se	Vaccine/pneumo	CUB	vacuna conjugada antineumocócica	341

CUBANA EN LA POBLACIÓN INFANTIL DE 1 A 5 AÑOS DE PAÍSES EN VÍAS DE DESARROLLO, COMO ESTRATEGIA NOVEDOSA PARA REDUCIR LA CIRCULACIÓN DE LOS NEUMOCOCCOS Y EVITAR EL REMPLAZO DE SEROTIPOS.	realiza en los lactantes, para evitar seguir complejizando la vacunación en los lactantes. Partiendo de la disponibilidad de un candidato vacunal producido en condiciones GMP, con una fase de investigación pre-clínica y toxicológica culminada, con las primeras investigaciones Fase I de seguridad en adultos, niños preescolares (4-5 años) y lactantes 7-11 meses, donde el producto ha demostrado un perfil de seguridad similar a las vacunas comerciales, puede resultar atractivo financiar las etapas finales de investigaciones clínicas de este proyecto. Una vez demostrada la eficacia clínica de este candidato vacunal, será indudablemente una opción muy valiosa para el mercado de los países subdesarrollados, pues competiría en precio con las actuales vacunas comerciales, y se podrían realizar transferencias tecnológicas a países emergentes para incrementar la producción de la vacuna y su accesibilidad a los países que hoy no pueden introducir las actuales PCV por sus elevados costos. La hipótesis científica que se persigue demostrar, requiere diseñar y conducir ensayos clínicos de la vacuna cubana heptavalente en población infantil de 1 a 5 años, en aquellos países en vías de desarrollo donde aún no se haya introducido masivamente ninguna de las vacunas conjugadas y medir el impacto que esta vacunación tiene sobre la circulación del neumococo y en la prevención de las enfermedades neumocócicas. Si se demuestra que la vacunación en niños mayores de 1 año afecta sensiblemente la circulación del neumococo en la edad que es reconocida como la “incubadora” del germen, es de esperar que con una vacunación en estas edades contra los serotipos re-emergente no sea necesario seguir complejizando las vacunas del lactante, sino dejar en este grupo etario una vacunación básica de 7-10 valencias, complementada con una vacunación adicional en el período de 1-5 años de vida. El proyecto demandará también financiamiento para fortalecer los sistemas de vigilancia epidemiológica en determinados países o regiones, con la creación de facilidades para medir el impacto en la circulación y en la enfermedad. Se realizarán también los ensayos clínicos en lactantes que permitan obtener el registro sanitario para este grupo etario, donde el camino clínico está claramente definido por los organismos regulatorios y se prevé que para el 2015 se pueda tener registrada esta vacuna en	

	lactantes. Adicionalmente, como parte de este proyecto, se trabaja en el desarrollo de un segundo candidato vacunal heptavalente, que contiene los clásicos serotipos re-emergentes, con el objetivo de ser una vacuna complementaria en el período etario 1-5 años para los niños que hayan recibido PCV en la etapa de lactantes. Considerando el progreso del desarrollo de este producto, donde varias etapas de su desarrollo han sido vencidas satisfactoriamente, se aplica para este financiamiento necesario para culminar la fase de evaluación clínica de esta nueva PCV, la cual puede comercializarse por los mecanismos OPS/OMS con el objetivo de hacerla disponible para los países en vías de desarrollo.				
26. DESARROLLO DE UNA VACUNA TERAPÉUTICA PARA EL TRATAMIENTO DE LA ARTRITIS REUMATOIDE Y OTRAS ENFERMEDADES AUTOINMUNES	**Objetivo: El proyecto esta dirigido al desarrollo de una Vacuna terapéutica para el tratamiento de enfermedades autoinmunes, que contiene como antigeno la Interleucina-15 (IL-15). La IL-15 es una citocina que participa en la respuesta inmune innata y adaptativa y se le ha adjudicado un rol proinflamatorio en una serie de enfermedades autoinmunes donde su expresión no controlada contribuye a la patogénesis de la enfermedad, como la Artritis, enfermedad celiaca, enfermedades inflamatorias intestinales , y Diabetes. Hipótesis: El desarrollo de una formulación vacunal que genere una respuesta de anticuerpos policlonales neutralizantes en el paciente e inhiba la actividad proinflamatoria de esta citocina, puede ser útil en el tratamiento de estas enfermedades.Resultados: Como resultado de esta investigación se obtuvo la IL-15 recombinante en *E coli* y se estableció un proceso de purificación que permite obtener la proteína con más de 95% de pureza. Además se realizó su caracterización físico química, observando una especie homogénea con cambios en la extructura respecto a la proteína nativa y no activa biologicamente. Este tipo de vacuna anti citocina requiere la ruptura de tolerancia de celulas B a una proteína propia, en este caso la IL-15. Por ello se evaluó la capacidad del preparado vacunal para generar una respuesta de anticuerpos neutralizantes anti IL-15 humana en monos *Macaca fascicularis*, cuya IL-15 presenta un 97% de homología con la humana.** **El proyecto se encuentra en fase de transferencia al área de Desarrollo**	Artritis Reumatoide	CUB	desarrollo de una formulación vacunal	352

	para el escalado de producción de la proteína. También está en fase preclínica para evaluar su efecto en modelos de las enfermedades autoinmunes en que puede ser efectiva. Este proyecto está cubierto por una patente concedida en USA, Union europea y China				
27. **CHAGAS R&D ACCELERATOR INITIATIVE: A COORDINATION MECHANISM FOR ACCELERATING THE DEVELOPMENT OF NEW HEALTH TOOLS FOR CHAGAS DISEASE**	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 called the Chagas R&D Accelerator Initiative. 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. 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*	Chagas	Multi (DNDi)	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	362

	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.				
28. AFRICAN RESEARCH CAPACITY BUILDING PROGRAM	This project seeks to accelerate the development of drugs, vaccines, and diagnostics for the NTD, malaria and TB by providing developing world researchers with an opportunity to gain pharmaceutical discovery and development experience as well as providing developing world research institutions with much-needed biomedical research equipment.	NTD, Malaria and TB	BIO Ventures for Global Health (BVGH)	to accelerate the development of drugs, vaccines, and diagnostics for the NTD, malaria and TB	374
29. GLOBAL HEALTH INNOVATION QUOTIENT PRIZE	This project will address fevers of unknown origin caused by infectious agents, with a focus on children less than five years of age. Specific diseases include malaria and bacterial and viral infections. BVGH proposes a milestone-based prize to promote the development and launch of a multiplex point-of-care (POC) diagnostic test for the differential diagnosis of fever, targeted primarily at children less than 5 years of age. The Global Health Innovation Quotient Prize (IQ Prize) divides product development into successive parts—set at industry-recognized inflection points—and rewards successful completion of these milestones. In contrast with prize strategies that focus primarily on the result, the milestone approach used by the IQ Prize will help companies recover expended costs sooner and provide rewards for particular steps involving innovative risk. This approach provides an incentive for the private sector, and allows small- and medium-sized companies to participate by decreasing the required capital investment, as well as decreasing the risk associated with pursuing global health research and development (R&D). The IQ Prize will thus	Malaria, bacterial and viral infections in pediatric populations	BIO Ventures for Global Health (BVGH)	Point-of-care fever diagnostic	386

attract more interest and attention toward the development of diagnostics for global health-related infections. The IQ Prize includes a target product profile (TPP), detailing the sensitivity, specificity, time to read-out, price targets, and other relevant requirements to diagnose between parasitic, bacterial, and viral causes of fever in children in low resource settings. Two standards have been developed: “Core requirements”, reflecting the requirements the POC diagnostic must meet in order to have a significant health impact in the developing world; and “Optimal standards”, reflecting higher specifications as indicated by in-country health care workers. A developer must meet the core requirements in order to qualify for an award. The IQ Prize milestone structure rewards successful completion of key inflection points in the product development process and provides adequate commercial incentive to motivate industry participation. Sponsors would only award developers for the successful accomplishment of each milestone. These milestones include “platform technology proof of concept”, “platform build/prototype construction”, “clinical validation”, and “regulatory approval/CE mark”. Milestone award amounts reflect both costs and risk incurred by the developer at that particular stage of development. Risk premiums will be applied where achievement of milestones requires significant innovation and carries significant technical risk. A set number of awards will be made for each milestone. Determination of the number of awards is based on expected attrition rates at each stage of the competition. Estimates of likely attrition rates were gathered from industry stakeholders. Taken as a whole, the milestone approach used by the IQ prize constitutes a powerful tool to promote R&D investment in global health. In combination with other innovation incentives, the IQ Prize will help to make meaningful progress in the development of next-generation diagnostics and global health