1. Identification of the Research Unit

1.0 Reference

4413

1.1.Name of the R&D Unit

Global Health and Tropical Medicine

Saúde Global e Medicina Tropical

1.2. Acronym

GHTM

1.3. Coordinator

Paulo Ferrinho

1.4 Multidisciplinar/interdisciplinary R&D Unit

yes

Scientific areas

Diagnostic, Therapies and Public Health

Biological Sciences or Environmental Biology

Sociology

1.5 Profile of the R&D Unit

30 % Basic research

70 % Applied research and/or Experimental development

1.6 Keywords

Infectious diseases

Vector born diseases

Implementation Research

Health Development

1.7 Link to the Research Unit´s page on the Internet

http://GHTM.ihmt.unl.pt

2. Institutions and their Roles

2.1. Instituição de Gestão Principal - Main Host Institution

Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa

2.2. e 2.3 – N/A

2.4. Institutional commitment

(Recursos humanos e meios técnicos (espaço e materiais) que a(s) instituição(ões) de gestão, coincidente(s) ou não com as instituição(ões) participante(s), se compromete(m) a disponibilizar/Human and technical resources that host institution(s), coincident or not with the participating institutions (s), are committed to provide) - 3000 Caracteres (3000 characters)

The host institution for the Center is the Instituto de Higiene e Medicina Tropical (IHMT) (www.ihmt.unl.pt), an academic unit of the Universidade Nova de Lisboa (UNL). It offers postgraduate training, research and expertise, mainly in a context of health development cooperation.

IHMT has 56 PhD level researchers/lecturers and 41 support staff. It offers 6 MSc and 4 PhD programs and currently has a total of 224 students [148 Portuguese and 76 (34%) foreigners: 52 from Portuguese Speaking African Countries – PALOP, 13 from Brazil and 11 from other countries].

The research infrastructure comprises an accredited animal house for small rodents and insectaries for rearing and manipulating disease vectors such as mosquitoes, tsetse flies and sand flies. IHMT also has a centralized computer service, up-to-date laboratory facilities (partly renovated in 2012) and two level-3 biosecurity laboratories (BSL-3). A centralized support service is in place and it is responsible for common support-infrastructures such as a cleaning and sterilization unit. Access to cutting-edge modern equipment is possible through an extensive network of national and international collaborations.

Other IHMT infrastructures include a Communication Office, responsible for the implementation of a comprehensive strategy for communication and marketing.

Project management is ensured by a financial department and an office for project support (Gabinete de Apoio a Projetos) that actively looks for financing opportunities, disseminates information among researchers and supports proposal submission, project negotiations and reporting.

IHMT's active and prominent presence within national and international institutions and research networks provides it with a comparative advantage among Portuguese institutions to host the research programs in the field of international/global health that are proposed for the Center.

IHMT has a successful track record of research project management and resource mobilization. Between 2009 and 2013 it has attracted competitive funding from Portuguese and European funding agencies, totaling 40% of its total budget.

IHMT is highly supportive and committed to the success of the proposed Center and will put the above workforce and infrastructure at the disposal of the Center.

3. Research Unit Description and Achievements

3.1. Description of the R&D Unit

(Descrever os objetivos estabelecidos no período 2008-2012 e a forma de organização estabelecida para os atingir/ Describe the objectives for 2008-2012 and the organisational structure established to achieve them) - 7000 caracteres (7000 characters)

N/A

3.2. Major achievements

(Apresentar os principais resultados alcançados pela unidade no período 2008-2012 e listar as 10 publicações mais importantes da equipa / Present the main achievements produced by the unit for the period 2008-2012 and list 10 key publications) - 7000 caracteres (7000 characters)

GHTM is a new R&D Center that brings together researchers from IHMT with a track record in tropical medicine and International/Global Health. In this section we present some of our major achievements, published in international journals and organized by our traditional areas of expertise, highlighting the potential for transversal collaboration.

Research in international public health has focused mainly on health systems, human resources for health and health of vulnerable groups with a geographical focus on Portugal, Europe, and on the Community of Portuguese-speaking Countries (CPLP). Research includes health workforce studies; economics of human resources for health; analysis of the determinants of access to health services by vulnerable populations, namely migrants in Portugal, mothers and children in low-income countries; and management and organizational change in the health sector. The Group's approach to these issues covers policy, as well as socio-economic, environmental and epidemiological dimensions.

This research has produced reports such as "The scaling up the Stock of Health Workers", "Migration of healthcare workers in WHO European Region", "The state of the health workforce in the 5 Portuguese-speaking African countries (PALOPs)". The designation of IHMT as WHO Collaborating on Health Workforce Policy and Planning in 2011 is the recognition of its leadership and achievement in this field. Two members of the group are founding Editors of the Human Resources for Health Journal, which has evolved to an Impact Factor of 2.05 and ranking, 1st in the Industrial Relations and Labor category of the Thomson Reuters Journal Citation Report (JCR).

Tropical and Traveler's Medicine addresses issues related to the health status of migrants from Africa, South America and Eastern Europe and the risk of travel acquired infections. The group showed that 38% of travelers did not deliberately comply with malaria chemoprophylaxis due to side the effects of the drugs used. It has expanded its activities to research on *Mycobacterium tuberculosis* multi-drug resistance following the longstanding contribution of IHMT to the resolution of the pulmonary TB problem of Lisbon, generating complete case reports within 15-20 days for 10 Hospitals of the TB Task Force of Lisbon since 2000. MDRTB rates have dropped from 25% in 2000 to less than 1% in 2012 (Portugal has had the highest rates of XDR among MDRTB in Western Europe). Research on alternative therapies for antibiotic resistant infections such as M/XDRTB and methicillin-vancomycin resistant staphylococcal infections using non-antibiotic adjuvants has also been carried out.

Studies in the epidemiology of **opportunistic diseases** such as pneumocystosis, or cryptosporidiosis, microsporidia traditionally carried out in Portuguese AIDS patients, are being extended to migrants and travelers.

Field and hospital studies to determine the **association between prevalence of intestinal parasitosis/infections, nutritional status**, and socio-cultural factors have been carried out in Lisbon (City Hall Health education project), Angola (pre-school and school children), Mozambique (under-five children) and in São Tomé and Príncipe (STP) (pre-school children). Major advances have been made to understand the mechanisms of Rotavirus pathophysiological associated with severe diarrhea. A Rotavirus molecular epidemiology and surveillance project was implemented in STP: preliminary results show a high prevalence of infection (36.9%). Rotavirus studies in pre-school children in Angola have contributed to the introduction of a rotavirus vaccination policy for pre-school children.

Medical entomology at IHMT has been traditionally worldly renowned, having moved forward from classical to innovative approaches; A genome scan revealed 4 divergent regions between recently separated species of the malaria vector *Anopheles gambiae* which are likely to contain genes involved in reproductive isolation. In the same vector, continent-wide sequencing analyses revealed that mutations conferring insecticide resistance arose multiple times in both species. Microarray based analyses have shown that malaria infection in *An. gambiae* induces regulatory variations in genes encoding antioxidant proteins of which some have been also associated with insecticide resistance.

Monitoring of the mosquito *Aedes aegypti*, before and after the dengue outbreak in Madeira, determined that it probably originated from Brazil or Venezuela and had high levels of insecticide resistance. Insecticide resistance being a problem with most mosquito species, constituents of a series of plants were analysed and evaluated for insecticidal properties.

Industry collaborations led to development of textiles with nano-encapsulated repellents or insecticides.

Malaria researchers have shown for the first time *Plasmodium vivax* infects in Duffy-negative individuals from West Africa. This questions previous tenets that Duffy-negative people were protected against vivax malaria but also highlights that this parasite is able to use receptors other than Duffy to invade erythrocytes. Using genome wide approaches to uncover the molecular basis of resistance to artemisin, we produced new molecular markers of resistance, in a rodent malaria model and validated in natural *P. falciparum* populations where clinical response was assessed. The Integrated Control of Malaria in the Chokwé Region project, Mozambique (Project Santé-Health/2006/105-398, EU) has significantly contributed to an increase in the coverage of the indoor residual spraying in the region between 2008 and 2011.

IHMT has been involved in **vaccine development** for Leishmania infections, either testing vaccine candidates in a canine model, or characterizing the immune response revealing new information on the role of Treg cells. Novel approaches for drug development and delivery have been tested showing that trifluraline liposomal formulation are leishmaniacidal, while simultaneously exerting a protective immune response to *L. infantum*. The prevalence of feline and canine Leishmania infections was compared in the zoonotic focus of Lisbon and the first national canine leishmaniasis serosurvey revealed an overall prevalence of 6.3%. An international consortium involving Portugal/Brazil showed that parasites from both continents have the same genetic signature in association with the host type.

New phylogenetic methodologies for **HIV characterization** were designed and international guidelines for application in criminal investigation were drafted. The origin, spread and genetic diversity of HIV-1 and HIV-2 in Africa, Portugal and Europe were investigated. Patterns of HIV infection were found to be distinct across Portuguese speaking African countries (PALOP). The pathways of HIV-2 resistance to atazanavir were established and an algorithm for the interpretation of HIV-2 resistance to drugs was agreed upon.

Key publications (max 10)

1. Abecasis AB, Geretti AM, Albert J, Power L, Weait M, Vandamme AM. 2011. Science in court: the myth of HIV fingerprinting. Lancet Infectious Diseases. 11:78-9. IF: 19.966
2. Dias S, Gama A, Cargaleiro H, Martins MROM. 2012. Health workers' attitudes toward immigrant patients: a cross-sectional survey in primary health care services. Human Resources for Health 10:14. IF: 2.05
3. Dujardin JC, Campino L, Canavate C, Dedet JP, Gradoni L, Soteriadou K, Mazeris A, Ozbel, Y, Boelaert M. 2008. Spread of vector-borne diseases and neglect of leishmaniasis, Europe. Emerging Infectious Diseases 14:1013-1018. IF: 5.993
4. Dyer NA, Furtado A, Cano J, Ferreira F, Afonso MO, Ndong-Mabale N, Ndong-Asumu P, Centeno-Lima S, Benito A, Weetman D, Donnelly MJ, Pinto J. 2009. Evidence for a discrete evolutionary lineage within Equatorial Guinea suggests that the tsetse fly Glossina palpalis palpalis exists as a species complex. Molecular Ecology 18: 3268-3282. IF: 6.275.
5. Esteves F, Gaspar J, de Sousa B, Antunes F, Mansinho K, Matos O. 2012. Pneumocystis jirovecii multilocus genotyping in pooled DNA samples: a new approach for clinical and epidemiological studies. Clinical Microbiology and Infection 18, E177-E184. IF: 4.578.
6. Etang J, Vicente JL, Nwane P, Chouaibou M, Morlais I, do Rosário VE, Simard F, Awono-Ambene P, Toto JC, Pinto J. 2009. Polymorphism of intron-1 in the voltage-gated sodium channel 1 gene of Anopheles gambiae s.s. populations from Cameroon with emphasis on insecticide knockdown resistance mutations. Molecular Ecology 18: 3076-3086. ISI IF: 6.275.
7. Machado D, Perdigao J, Ramos J, Couto I, Portugal I, Ritter C., Boettger EC, Viveiros M. 2013. High-level resistance to isoniazid and ethionamide in multidrug-resistant Mycobacterium tuberculosis of the Lisboa family is associated with inhA double mutations. Journal of Antimicrobial Chemotherapy 68: 1728-1732. IF: 5.338
8. Mendes C, Dias F, Figueiredo J, Gonzalez VM, Cano J, de Sousa B, do Rosário VE, Benito A, Berzosa P, Arez AP. 2011. Duffy negative antigen is no longer a barrier to Plasmodium vivax – molecular evidences from the African West Coast (Angola and Equatorial Guinea). PLoS Negl Trop Dis 5: e1192. IF: 4.569
9. Nogueira PJ, Machado A, Rodrigues E, Nunes B, Sousa L, Jacinto M, Ferreira A, Falcao, JM, Ferrinho P. 2010. The new automated daily mortality surveillance system in Portugal. Eurosurveillance 15: 21-34. IF: 5.491
10. Sousa CA, Clairouin M, Seixas G, Viveiros B, Novo MT, Silva AC, Escoval MT, Economopoulou A. 2012. Ongoing outbreak of dengue type 1 in the Autonomous Region of Madeira, Portugal: preliminary report. Eurosurveillance 17:20333 IF: 5.491

3.3. External Advisory Committee Reports

(Principais relatórios do período 2008-2012, máx. 5 documentos / Main reports for 2008-2012, Max. 5

documents)

N/A

3.4. Composition of the External Advisory Committee

(Listar os elementos que integram atualmente a Comissão Externa de Acompanhamento / List the member of the current External Advisory Committee)

N/A

3.5. Brief description of the output indicators of the research team(s) of the new unit that support the vision and objectives of the strategic program

7000 caracteres (7000 characters)

In the period 2008-2012, GHTM researchers published 483 articles in international peer-reviewed journals indexed to ISI Web of Knowledge and Scopus, yielding an average of 2.01 articles per doctorate member-year (48 members) and 57 books or book chapters. During 2013 GHTM members had 63 on-going projects of which 10 were EU financed.

Advanced training has been a major component of the group's activity. Research-driven advanced training enables students and healthcare professionals with research skills, in updating their knowledge in biomedical sciences and promoting multidisciplinary interactions within the various research areas of the proposed R&D Center (GHTM). It has included graduate and postgraduate training programs receiving foreign students (e.g. Erasmus and Leonardo da Vinci) and courses at IHMT and in developing countries. During the five years, 46 students completed their PhD studies supervised by GHTM members. Currently the members supervise 104 PhD students.

An important component of the training has been the delivery of courses in endemic countries. In 2011/2012, applied courses on Parasitology and Entomology were held in Angola and Brazil as well as Public Health and health services management courses in Angola, Cape Verde, Guinea-Bissau and Mozambique. These were specific thematic training actions with a strong operational component and with a diverse audience, ranging from graduate students (PhD, MSc), university lecturers, to front-line health workers. Since 2008, a program for training lab technicians and researchers from the community of the Portuguese-speaking countries (CPLP) on TB and TB Control Programs has been implemented with more than 50 trainees certified for Tb laboratory diagnosis (see http://fordilab-tb.ihmt.unl.pt/index.html).

Other examples of formal training have been the PROCAPS (Programa de Capacitação de Recursos de Saúde) doctoral program held in Angola and the preparation of the future inter-institutional, International doctoral program between IHMT and the Fundação Oswaldo Cruz (FIOCRUZ Brazil) in Health Sciences. A Biomedical PhD program is being negotiated with the Centro de Educação Médica (CEDUMED) of Angola. Distance learning masters programs in biostatistics, epidemiology and medical microbiology are being negotiated with Angola and Mozambique. IHMT's public health researchers collaborate in an inter-institutional doctoral program with the Escola Nacional de Saude Publica (ENSP) and the Faculdade de Ciência Médica (FCM) of UNL and the Institute of Public Health from the University of Porto (ISUP). Our courses make use of videoconference and e-learning tools.

As regards cooperation for development, GHTM members have been committed to principles defined in 2009, aligned with the Paris, Accra and Busan Declarations. The main axis of this cooperation for development have included scientific and technical sustainable capacity building in resource-limited countries and regions (in terms of human and infrastructure resources),

support to disease prevention and control programs to the CPLP member states and services to the community/civil society.

The host institution (IHMT) and consequently its members, is Portugal's major presence in global health organizations such as IHP+ (International Health Partnership), COHRED (Council on Health Research for Development), GAVI Alliance (Global Alliance for Vaccines and Immunisation), WHO (World Health Organization), TDR (Tropical Disease Research program); CPLP and IANPHI (International Association of National Public Health Institutes).

Networks have been established at the European (e.g. "Collaborative HIV and anti-HIV drug resistance network", "Europe network for infectious diseases surveillance", I COST actions), Iberian (e.g. Iberian Platform for Malaria network) and CPLP (e.g. RINSP – Network of National Public Health Institutes, RETS – Network of National Health Technical School) level, as well as with their UNASUL (Union of South American Nations) counterparts, enabling North-South and South-South collaboration with African and South-American partners. Collaboration with Latin America (Brazil, Colombia and Cuba), Africa (PALOP), Asia (Taiwan, East Timor, Macao) and Europe is sustained by international projects, supporting R&D activities and short-term training courses.

Per year, IHMT's clinical services respond to about 11 000 travel medicine and 500 tropical medicine consultations (including tropical pediatrics and tropical dermatology), supported by reference laboratory services.

Science communication and dissemination to the general public through the mass media and to high-schools (*e.g.* the Ciência Viva program led by FCT) is assisted by the local production of information materials and by encouraging the integration of young students in R&D activities through participation in scientific projects and other initiatives for science initiation (e.g. small projects to be developed by young high-school students).

A newly approved Elsevier Foundation project for 2014-15, will create a Network of Portuguese Speaking women in Tropical Health, which will allow the IHMT to support the scientific development of women, mostly associated with a network of lusophone African faculties of medicine and by extension all, scientists in African Portuguese speaking countries.

Consultancy services are provided to enterprises and Governments in our areas of expertise. Hence, national health workforce policies in Angola, Guinea-Bissau and Mozambique were developed by teams coordinated by GHTM researchers.

4. Funding 2008/2012 (€)

Description	2008	2009	2010	2011	2012	Total
Pluriannual Programme/Strategic project	542,181.70	367,829.56	529,835.91	227,384.66	226,412.32	**1,893,644.15**
FCT-funded projects	498,401.09	297,426.54	239,592.95	435,245.86	371,857.32	**1,842,523.76**
European Commission-funded projects	136,933.48	252,083.01	135,699.84	260,503.23	156,442.24	**941,661.80**
Other international projects	5,609.62	22,500.00	647,787.74	694,037.74	217,830.42	**1,587,765.52**
Other national projects	154,158.51	167,104.30	254,662.08	60,643.30	116,053.62	**752,621.81**
National industry projects	16,315.11	12,019.87	0.00	15,626.44	3,758.60	**47,720.02**
International industry projects	0.00	0.00	0.00	0.00	0.00	**0.00**
	1 353 599,51	**1 118 963,28**	**1 807 578,52**	**1 693 441,23**	**1 092 354,52**	**7 065 937,06**

5. General Indicators 2008/2012

5.1.

Description	2008	2009	2010	2011	2012	Total
No. of researchers	38	43	44	45	45	**215**
No. of integrated researchers	38	43	44	45	45	**215**
No. of technicians and administrative staff						
PhD theses under the supervision of integrated members	6	11	13	15	1	**46**
Publications in international peer reviewed journals	86	83	110	102	102	**483**
Books and book chapters of international circulation	9	6	12	14	16	**57**
Models	-	-	-	-	-	-
Patents	-	-	-	-	-	-
Prototypes	-	-	-	-	-	-
Industry research contracts	2	1	-	1	1	5
Research contracts with national or international bodies	15	13	25	21	16	90
Other research outputs	-	-	-	-	-	-

5.2. Overall description of indicators and research outputs/Highlights (6000 characters)

Over the past 5 years (2008-2012), members of our team have published a total of 483 research papers in indexed international journals; 128 during 2013. The median ISI Web of Knowledge 2012 impact factor of the journals in which the group has published was 2.72, a value above the median impact factor of our reference subject areas (Entomology: 0.88; Parasitology: 2.15; Tropical Medicine: 0.94; Microbiology: 2.40; Public, Environmental & Occupational Health: 1.56; Health Care Sciences & Services: 1.635) and also in line with those of more generalist areas (Evolutionary Biology: 2.75; Infectious Diseases: 2.61; Genetics & Heredity: 2.58). These papers have an average of 9,60 citations per article. In the same period 57 book or book chapters were also published. On the whole, 46 PhD theses were completed under the supervision of team members.

The international acceptance of our research is translated by the ability to compete for research funds. Over the past 5 years, our research team was involved in 90 funded projects covering the different areas of research. Of these, 60 were led by members of our Center as PIs. The Portuguese Foundation for Science and Technology has been our main funder but international funding represents 36% of our project-funded budget. Our major international funding agencies have been mainly the European Commission (FP6 and FP7 programs), but also the Gates Foundation, Ministry of Health Angola, CPLP and the industry. All this effort has been obtained

with a relatively small amount of researchers (48 members), who have been able to obtain an average of 1,413,187€/per year representing circa 29,500€ per year per researcher and to publish 2.01 papers/researcher/year in ISI index journals /per year in the last 5 years

The major research topics in Biomedical Sciences included:

- Molecular epidemiology and genetic diversity studies have been conducted on *Plasmodium spp*., *Leishmania spp*., opportunistic parasites (namely *Cryptosporidium spp*., microsporidia and *Pneumocystis jirovecii*) and veterinary parasite populations, particularly to unveil prevalence levels and to associate specific strains with virulence and transmission intensity. In this context, we have published the first report of *Plasmodium vivax* infection in Duffy-negative individuals from West Africa;
- Studies of human genetic factors to assess determinants of disease outcome have identified a new variant of the pklr gene that was found to be highly frequent in endemic regions for malaria but absent in non-endemic regions;
- Genome-wide scans have been successfully applied to detect genes or genomic regions associated with: i) anti-malarial drug resistance; ii) divergence between closely related mosquito taxa; ii) candidate genes modulating parasite invasion in the mosquito;
- Behavioral and genetic studies of insect vectors have been carried out in the field to determine key features of disease transmission, the genetic structure of vector populations and the potential impact of environmental changes in these populations;
- Developments were made in the selection and testing of new candidate compounds for malaria treatment (e.g. triterpenoids), as well as in the detection of new therapeutic targets (e.g. cystein proteases);
- Research on host-parasite interactions included: i) iRNA-based experimental research on pathways of parasite recognition in the mosquito vector; ii) evaluation of the protective role of neotropical Leishmania antigens towards an effective vaccine for tegumentar leishmaniasis; iii) experimental assays of vector competence in leishmaniasis.
- Molecular epidemiology and genetic diversity studies have been conducted on HIV and TB, either in a global scale or in a regional scale, with incidence in Portuguese speaking countries. Description of the molecular determinants for drug and multi-drug resistance in HIV and TB and characterization of new alternative drug targets and alternative compounds & therapies focused on drug resistant forms of these infections and their interaction with the human host. Host genetic determinants for susceptibility, new markers for infection and disease progression, new phylogenetic methodologies, new diagnostic procedures and new drugs have been described in high-impact international scientific literature and incorporated in international guidelines from major health organizations.

Major research topics in population health, policies and services have included:

- The identification of health needs of travelers, migrants and vulnerable populations and their determinants;
- The characterization services and resources available to travelers, migrants and vulnerable populations in terms of the various economic, cultural, organizational dimensions of their accessibility;
- The identification of service and resources needs – with a special focus on human resources for health;
- The analysis of the policy framework which affects the development of the health workforce and the mapping of stakeholders positions;

- The study of alternative pathways to train health personnel, with a special emphasis on managers, to adjust to the changing needs of the population and to reduce the absolute gap of health workers globally and in all portuguese speaking countries;
- The characterization and study of PALOP health systems to design policies and planning for universal health coverage.

6. Componente Científica - Programa Estratégico 2015/2020 - Scientific Component – Strategic Programme 2015/2020

6.1. Abstract in Portuguese for publication

6000 caracteres (6000 characters)

Portugal tem estado na vanguarda do processo de globalização desde o século XV, criando uma longa herança de experiências bem-sucedidas em conviver com a diversidade social, em saber promover a integração equilibrada da e na diversidade multicultural e em responder eficazmente a fluxos migratórios. As formas modernas de globalização criaram problemas novos e complexos a serem resolvidos pelos países e a investigação científica aplicada é uma importante ferramenta estratégica para os resolver. O controlo de endemias, a prevenção de epidemias e pandemias, a qualidade da saúde e as questões sociais associadas a fluxos migratórios e grupos marginalizados, as mudanças sociais e económicas e as restrições devido às mudanças climáticas e ainda as políticas de saúde inadequadas, são velhos desafios ainda a serem enfrentados, que necessitam agora de ser abordados numa perspetiva global.

Os Objetivos de Desenvolvimento do Milênio (ODM) revelaram-se um importante mecanismo social e organizacional para manter o apoio político na promoção de metas de desenvolvimento globais comuns, criando um consenso sobre conceitos-chave para os resolver. A Organização das Nações Unidas (ONU) começou em 2012 discussões sobre quais devem ser, a partir de 2015, os novos ODM. No final de 2013, a ONU afirmou claramente que as metas pós- 2015 devem concentrar-se em melhorar a vida de grupos marginalizados e basear-se nos princípios dos direitos humanos, da igualdade de gênero e do Estado de direito, independentemente do seu estado de desenvolvimento. A agenda de desenvolvimento pós -2015 irá reforçar o compromisso da comunidade internacional para a erradicação da pobreza e o desenvolvimento sustentável, através da implementação das melhores políticas para a integração dos grupos mais vulneráveis, promovendo a ligação intrínseca entre a erradicação da pobreza e a promoção do desenvolvimento sustentável.

Estes grandes desafios a serem propostos e o debate sobre a agenda de investigação da União Europeia (EU), sob o quadro do programa Horizonte 2020, consubstancia o programa de investigação e desenvolvimento (I&D) aqui proposto e intitulado - Saúde Global e Medicina Tropical (SGMT) - que está organizado em torno de duas linhas temáticas (LT) : 1) os desafios da saúde de viajantes e migrantes e suas consequências para a saúde pública, sistemas de saúde e profissionais de saúde , 2) doenças emergentes e mudanças ambientais e climáticas, a emergência ou reemergência e circulação de doenças transmitidas por vetores e outros agentes patogénicos de alto impacto na saúde num contexto global de mudança (ambiental, social , demográfica, política e económica) .

A equipa que constitui a proposta SGMT está numa posição única para criar valor acrescentado a estes LTs, tirando proveito da sua associação exclusiva com as redes nacionais e internacionais de I&D em saúde e o mundo acadêmico, sobretudo no contexto da Comunidade de Países de Língua Portuguesa (CPLP). Somamos uma combinação multidisciplinar única de conhecimentos e de competências de investigação em ciências médicas e biomédicas, ciências sociais e cooperação para o desenvolvimento e avaliação de políticas de saúde. Esta proposta está cimentada na longa tradição de investigação aplicada em medicina tropical e trabalho de colaboração com as organizações de saúde globais, como a OMS (Centro Colaborador em Políticas de Saúde) e a Associação Internacional de Institutos Nacionais de Saúde Pública, entre outros. A equipa do SGMT irá realizar, em colaboração com estes parceiros e redes,

investigação aplicada para construir conhecimento e produzir informação relevante para as políticas de saúde através da integração e transversalidade dos três Grupos de Investigação propostos - 1) Doenças transmitidas por vetores; 2) TB, HIV e outros agentes oportunistas e 3) Saúde das Populações, políticas e serviços.

A instituição de acolhimento, o IHMT / UNL, a equipa e esta proposta pretendem abordar a saúde global como um campo de investigação que aborda a saúde das populações, transcendendo mas não negligenciando as preocupações de cada país. Inspira-se na experiência de médicos, biomédicos e especialistas em ciências sociais. A partir de diferentes perspetivas multidisciplinares, centra-se sobre os determinantes e formas de distribuição da saúde num contexto global. Uma perspetiva epidemiológica identifica e caracteriza os principais problemas de saúde globais. A perspetiva médica descreve as patologias das principais doenças globais, promove a prevenção, o diagnóstico e o tratamento com o auxílio de novas abordagens biomédicas com base em nanotecnologias (eg. electronics in paper e nanogoldbioprobes), desenvolvidas na FCT/UNL. Uma perspetiva economica enfatiza a relação custo-efetividade e o custo-benefício destas abordagens, a produção de conhecimento e o desenvolvimento de ferramentas e sistemas que os indivíduos, as comunidades e os países precisam a fim de melhorar os cuidados de saúde.

Ambicionamos alargar a nossa liderança como uma instituição de I&D nesta área da saúde global, sendo a ponte entre as instituições de saúde da CPLP em I&D de modo a posicionarmo-nos conjuntamente no mundo como um parceiro privilegiado para a cooperação e I&D em saúde, respeitando o nosso legado de vanguarda nos desafios societais criados pelas migrações e pelo desenvolvimento global e a globalização - alinhados com os conceitos-chave das novas metas do milênio, da declaração de Busan e dos desafios do Horizonte 2020.

Em conclusão o SGMT visa produzir evidência científica para melhorar os resultados no combate às ameaças globais em saúde, através de intervenções baseadas em evidências, fortalecendo o papel e o futuro de Portugal como um dos principais parceiros no desenvolvimento e implementação de uma agenda de investigação aplicada em saúde global.

6.2. Abstract in English for evaluation

6000 caracteres (6000 characters)

Portugal has been in the forefront of the globalization since the fifteenth-century, creating a longstanding inherited know-how to face social diversity, multicultural integration and migratory fluxes. The modern forms of globalization created new and complex problems to be solved by countries and applied research is an important strategic tool to solve these problems. A number of health issues in relation to the global challenges such as control of endemic diseases, prevention of epidemics and pandemics, health and social issues associated to migratory fluxes and marginalized groups, social and economic changes and constraints due to climate changes and inadequate health policies are old challenges still to be tackled, that now need to be addressed on a global perspective while remaining locally relevant.

The Millennium Development Goals (MDGs) revealed to be an important societal and organizational mechanism to maintain political support for common global development goals, creating consensus on key-concepts to address these problems. The United Nations (UN) started in 2012 discussions on what should be the new MDGs, from 2015 onwards. In late 2013, the UN clearly stated that the post-2015 goals should particularly focus on improving the lives of marginalized groups and be based on the principles of human rights, gender equality and the rule of law worldwide, independently of the development status of the country. The post-2015 development agenda will reinforce the international community's commitment to poverty eradication and sustainable development, by implementing the best policies to integrate the most vulnerable groups, promoting the intrinsic linkage between poverty eradication and promotion of sustainable development.

These challenging issues and the debate on the EU research agenda, under the frame of the

Horizon 2020 program, have consubstantiated the research program of the proposal - Global Health and Tropical Medicine (GHTM) - which is organized around two thematic lines (TL) : 1) Health challenges of travelers and migrants and their consequences for public health, health care systems and for the health workforce; 2) Emerging diseases and environmental changes, addressing the emergence or re-emergence, growth and circulation of Vector-Borne diseases and other high-impact pathogens in a global context of change (environmental, social, demographic, political and economic).

The GHTM-research-team is uniquely placed to provide added value to these TLs, by taking advantage of its unique association with networks within the international development community, within Portugal and the community of Portuguese speaking countries (CPLP) health and academic world. To these we add a multidisciplinary combination of expertise and research capacity in fundamental, clinical, social sciences and policy development and evaluation. The ground where this program will be built-in stands in the long tradition of research on tropical medicine and collaborative work with global health organizations such as WHO (Collaborating Center on Health Workforce Policy and Planning) and the "International Association of National Public Health Institutes", among others. GHTM will conduct, in collaboration with these partners and networks, research to build knowledge and produce a relevant evidence basis with the input of three Research Groups - 1) Vector-borne Diseases; 2) TB, HIV and Opportunistic Pathogens and 3) Population Health, Policies and Services.

The host institution, Instituto de Higiene e Medicina Tropical da Universidade Nova de Lisboa (IHMT/UNL), the research team and this proposal intend to address global health as defined as a research field that addresses the health of populations, transcending but not neglecting, the concerns of individual nations. It draws on expertise from medical, biomedical and social science disciplines, including demography, economics, epidemiology, political economy and sociology. From different disciplinary perspectives, it focuses on determinants and distribution of health in a global context. An epidemiological perspective identifies and characterizes major global health problems. A medical perspective describes the pathology of major global diseases, and promotes prevention, diagnosis and treatment with the assistance of state-of-the art biomedical and biotechnological approaches that the in-vitro diagnosis based on cheap and clean nanotechnologies allow, namely the e-paper electronics and the nanogold-bioprobes developed by our partners at FCT/UNL. An economic perspective emphasizes the cost-effectiveness and cost-benefit of these new approaches at both individual and population level, producing knowledge, developing tools and strengthening systems, which individuals, communities and countries need in order to improve their health status through the promotion of excellence in research, training and systems implementation.

Our vision is to extend our leadership as a R&D institution in this specific field of global health and tropical medicine, addressing present and future health problems, bridging across CPLP R&D institutions in a worldwide context, becoming a privileged partner for health cooperation and development, respecting our national heritage of being in the forefront of the new development and societal challenges related with globalization – aligned with the key-concepts of the new millennium goals, the Busan declaration and the societal challenges of the Horizon 2020.

In conclusion GHTM, as a R&D Center devoted to global health and tropical medicine, aims at producing scientific evidence to improve health outcomes related to global health threats, through evidence-based interventions, strengthening Portugal´s role and future as a leading partner in the development and implementation of a global health research agenda.

6.3. Strategy and vision of the unit and future management

*(Apresentar a **estratégia e a visão** da unidade a desenvolver no decurso dos 6 anos /Strategy and vision for the next 6 years and management of the Research Unit. 7000 caracteres (7000 characters)*

BACKGROUND

A Center devoted to global health and tropical medicine (GHTM) is a natural extension of our institutional efforts to congregate expertise and focus on specific areas of excellence, already existing within the host institution (IHMT) and its network of international partners. IHMT has a long tradition of research on tropical medicine and currently, is also Portugal's main presence on global health organizations such as TropEd (Network for Education in International Health), IHP+ (International Health Partnership), COHRED (Council on Health Research for Development), GAVI Alliance (Global Alliance for Vaccines and Immunization), WHO (World Health Organization), TDR (Tropical Disease Research program); CPLP (community of the Portuguese-speaking countries) and IANPHI (International Association of National Health Institutes). Traditionally, the geographical focus has been the PALOPs (Portuguese-speaking African countries), but now encompasses Portugal and the European Union, other African and Mediterranean countries and Brazil.

The Millennium Development Goals (MDGs) have proven to be a powerful mechanism to maintain political support for development. Even so the post-2015 development agenda raises important questions about what should be the next development goals and how they should be implemented. These, and the debate on the EU research agenda and the Horizon 2020, have set the motto to define the research program of GHTM, which is organized around thematic areas for which the GHTM-research-team is uniquely placed to provide added value, by taking advantage of: 1) its unique association with networks within the international development community, within Portugal and the community of Portuguese speaking countries (CPLP) health and academic world; 2) a multidisciplinary combination of expertise and research capacity in fundamental, clinical, social sciences and policy development and evaluation; 3) the complementarity between programs within the host Institute, such as that of the WHO Collaborating Center on Health Workforce Policy and Planning, the emerging network of medical faculties in the PALOPs and the CPLP Network of National Public Health Institutes (RINSP).

VISION

Our vision is to reinforce our leadership as a R&D institution on global health and tropical medicine, to be able to address present and future health problems, bridging across CPLP R&D institutions in a worldwide context, becoming a privileged partner for health cooperation and development.

MISSION

Our mission is to produce knowledge, develop tools and strengthen systems, which individuals, communities and countries need to improve their health status through the promotion of excellence in research, training and systems implementation.

STRATEGIC AIMS

GHTM aims to generate scientific evidence, to develop expertise in its areas of knowledge and to improve health outcomes through evidence-based interventions. We aim to consolidate a R&D Center devoted to global health and tropical medicine, strengthening Portugal´s role as a leading partner in the development and implementation of a global health research agenda.

The GHTM will address European economic/societal concerns about human health, particularly regarding the threat of reintroduction of tropical diseases in Europe and the challenge resulting from large population movements due to travel and migration. We expect to have an impact on European and global health, along with significant opportunities to correct the problems of, *inter alia*, decrease of quality of life, lack of sustainability of health systems, emerging antimicrobial resistance and Vector-Borne diseases.

The main areas of activity are research, education and knowledge translation, setting the context for the three strategic operational aims of the GHMT, namely:

to generate scientific outputs on key areas of the IHMT´s expertise – vector-borne diseases (VBD); tuberculosis, HIV and opportunistic infections (THOP); and population health, policies and services (PPS) - through high quality interdisciplinary research;

to make the evidence of these outputs available to decision-makers, facilitating its translation into relevant interventions;

to develop technical & scientific expertise and strengthen local and regional research capacity.

HOW ARE WE GOING TO BUILD UP ON THIS SET OF EXPERTISE AND INTERNATIONAL NETWORKS TO ACHIEVE THOSE AIMS?

GHTM will conduct, in collaboration with its partners and networks, research to build knowledge and produce relevant evidence basis for two Thematic Lines (TL) with the input of three Research Groups (RG).

The TLs adopted address major challenges globally and for Portugal's health system and focus on:

1) Health challenges of international travelers and migrants (HCTM) and their consequences for public health, health care systems and for the health workforce;

2) Emerging Diseases and Environmental changes (EDEC), addressing the emergence or re-emergence, growth and circulation of VBD and other high-impact pathogens in a global context of change (environmental, social, demographic, political and economic);

Both TL will operate in a matrix that cuts across the R&D activities of the three Research Groups (RG): 1) Vector-borne Diseases (VBD); 2) TB, HIV and Opportunistic Pathogens (THOP); and 3) Population Health, Policies and Services (PPS).

THE GOVERNANCE STRUCTURE

A Management Board (MB) will set the strategic direction of the GHTM and will be composed of a Director (the IHMT Director), a Scientific Coordinator and an Administrator (the IHMT Administrator). The Director of the IHMT is elected by the IHMT Board of Trustees (Conselho do IHMT) composed of IHMT members elected by the staff, and external members nominated by the UNL Rector. The MB will meet at least once every quarter.

A Scientific Committee (SC) will assist the MB in its decisions. The SC will be led by the Scientific Coordinator and will include the three RG-Leaders and two TL-Leaders. The SC will be responsible for the strategic plan implementation and monitoring of productivity. The SC will meet at least once a month.

RG and TL leadership will promote activities where GHTM has potential impact and can generate high quality results through these complementary and interacting groups.

An Advisory Committee (AC) of 5 internationally renowned scientists and experts on the areas of Intervention and Research of the Center will advise the Director on the selection of the Scientific Coordinator based on her/his program and CV; will advise on recruitment of research staff; on opening new research groups or thematic lines or on the closure of existing ones; will evaluate the progress of the GMTH scientific activities and the overall performance of members, research groups, and thematic lines. The AC will meet at least once per year.

6.4. Laboratory intensity level of the unit

(Choose from one of the three levels of laboratory intensity below)

Elevada

Laboratory intensity level Justification

(3000 characters)

The intensity level is justified by the amount of experimental laboratory-based work expected from two of the RG and one of the TL proposed. This laboratory work includes:

- Molecular-based epidemiological surveys (including drug and insecticide resistance) and monitoring disease evolution
- Genetic characterization of human, intermediate hosts, pathogen and vector populations
- Development of new diagnostic tools
- Design and testing of new tools for disease control

6.5. General objectives

Present the general objectives to develop over the 6-year period of the strategic programme (7000 characters)

In a context of political, economic, social and climatic changes with significant impact worldwide, we aim to consolidate a R&D Center devoted to global health (GH) and tropical medicine (TM), strengthening Portugal´s role as a leading partner in the development and implementation of a GH research agenda.

The activities of the three RG - Vector-borne Diseases (VBD); TB, HIV and Opportunistic Pathogens (THOP); Population Health, Policies and Services (PPS)] will contribute with practical solutions to solve global health problems, mostly of tropical origin, with a special focus on health problems associated with mobility of human and vector populations and emerging neglected diseases.

The RGs have specific objectives that are either particular for the Group or shared by different Groups. All Groups share the following objectives that will be tackled in different angles:

1) To assess the risk/impact of new technologies and new policies in health care systems;
2) To evaluate the costs of scaling-up the current health workforce in selected low-income Portuguese speaking countries to address health needs in general and in particular those related to VBD and THOP.

Infectious pathogens and their vectors will be addressed by the VBD and THOP Groups that share the following objectives:

3) To assess VB infections and THOP in migrants and travelers and early detection and management of imported diseases;
4) To characterize host-pathogen interactions and host susceptibility;
5) To develop implement and validate new tools for diagnosis, namely: biomarkers and molecular targets for early detection of diseases and drug resistance traits;
6) To develop markers and ecological-biochemical-molecular targets for vector control and prevention of environmental-human transmission;
7) To develop community-based infectious diseases monitoring strategies.

Central to the control and elimination of VBD are their vectors, thus the VBD Group has the following specific objectives:

8) To characterize vector competence;
9) To develop community-based vector monitoring;
10) To develop or improve risk maps for the major VBD that can potentially threaten Portuguese territory and southern European countries.

The overall aim of the PPS Group is to produce relevant evidence, which will contribute to help design adequate policies and support decision-makers to steer health systems towards universal health coverage (UHC). The group will focus on two target populations: (1) travelers and migrants (including refugees), and (2) women and children in low-income environments, both in Portugal and in the Portuguese-speaking African countries (PALOP). The Group's specific research objectives are:

11) To identify health needs of travelers, migrants and vulnerable populations and their determinants – in general and, more specifically, in relation to VBD and THOP;
12) To characterize services and resources available to travelers, migrants and vulnerable populations in terms of the various economic, cultural, organizational dimensions of their accessibility;
13) To identify, design and evaluate management strategies to mitigate obstacles to the access of populations to health services;
14) To identify service and resources needs – with a special focus on human resources for health – with the ultimate aim to progress towards UHC;
15) To analyze the policy framework which affects the development of the health workforce and the mapping of stakeholders positions;
16) To study alternative pathways to train health personnel, with a special emphasis on managers, to adjust to the changing needs of the population and reduce the absolute gap of health workers in Portugal and Portuguese speaking countries.
17) To characterize and study health systems in PALOP, to design policies and planning for primary-care reform, to address health promotion and sustained universal health care.

The RGs will implement two thematic lines (TL) that require multidisciplinary approaches and are important for Portugal's Health System and for Global Health. The objectives of the TL are as follows:

1- Health challenges of travelers and migrants (HCTM), will focus on understanding the health and health systems implications of travel and migration and on informing the development of better policy, service delivery and clinical practice strategies, aiming at:

- Characterizing disease health patterns of traveling and migrant populations;
- Defining transnational epidemiology of diseases in traveling and migrant populations;
- Developing and validating new technologies for early detection and appropriate combinational therapeutic regimens to increase effectiveness and prevent the emergence of acquired drug resistance;
- Characterizing the profile of health service utilization of migrants in Portugal and PALOP, overcoming barriers to the use of the health services, thus empowering and improving health literacy among migrants and travelers.

2- The **Emerging Diseases and Environmental changes** (EDEC), will focus on the impact of environmental and climatic changes on the emergence of infectious diseases and the geographic distribution of disease vectors, aiming at:

- Characterizing the epidemiological dynamics of emerging infectious diseases (EID) as consequence of environmental changes and/or climatic changes;
- Building and updating risk maps concerning the presence and dissemination of VBD in Portugal, as an entry point to/from southern Europe;
- Assessing the effects of immunosuppressive conditions in the susceptibility to pathogens and their implications to social and health systems;
- Characterizing molecular mechanisms responsible for the development of drug resistant strains and the vectorial factors responsible for competence to transmit pathogens;
- Developing and validating easy-to-perform diagnostic tests based on nanotechnology for the early detection of pathogens and determine their drug susceptibility.

The integrated development of the proposed TL will provide means for the development of new and improved strategies for the management and control of some of the major infections that are global health concerns, identifying at the same time system level bottlenecks to the adoption, scaling up and access to new technologies. Different infections will be addressed in a concerted approach, from the laboratory level (using shared experimental approaches and assessment tools), to the health system level (adopting implementation and evaluative research methodologies), focusing on specific human populations (migrants, international travelers and health workforce).

6.6. Implementation

(Plan for implementation of the strategic programme) 10000 caracteres)

In order to meet its aims and objectives – as specified on section 9.1 and contextualized in section 6.5 (General objectives) - the Center will depend on strong collaborations within RG and across TL at the IHMT but also on functional collaborative networks, both national and international.

The objectives will be fostered through annual implementation plans, following the strategic planning framework that follows. This framework builds on existing activities of the IHMT as identified in section 3.2.

The AC and SC once constituted will meet to validate it and further advise on their operationalization, under the guidance of RG, TL and team leaders.

Within the RG and TL, research teams will be composed by a leading PI with active funded projects and team elements working on a specific research topic that will contribute to the RG/TL objectives. Each research team will be responsible for: i) developing high-standard research work within the framework of the RG/TL's objectives and in line with the team's expertise; ii) integrating activities and sharing resources with other research teams within the RG/TL and with the other RG/TLs of the Center; ii) seeking funding by means of project submissions and other sources; iii) accommodating PhD and MSc students; iv) promoting networking and internationalization; iv) contributing for outreach and dissemination actions.

The RG leader will prepare the reports and represent the group in the GHTM scientific commission. He will be responsible for the monitoring of the research teams productivity in light of the objectives of the group. He will manage the Center funds attributed to the RG, including its distribution among the research teams according to their productivity and the support to strategic investments (e.g. common equipment, workshops).

The focus of the RG leadership will be to identify knowledge gaps, to define research questions/hypothesis/objectives, to develop methodological responses and to look for funds with the support of team leaders.

The role of the TL leadership will be to harness the contributions of the different RG into crosscutting initiatives of all RG and research teams, binding the Center into a coherent whole. The TL leader will also promote interaction among the research teams by means of regular meetings and specific actions (e.g. strategic transversal/multidisciplinary research project proposals).

Results will be assessed against predefined targets and indicators following yearly contracts with groups. Indicators will cover the assessment of technical deliverables and managerial efficiency and the source of verification. An external midterm review will be conducted from the start of the third year of implementation.

The implementation will lead to:

1- **Knowledge creation** - through basic research to unveil: aspects of the biology of pathogens, vectors and hosts; immune and genetic traits of the target human populations; socio-economic profiling of the target human populations; patterns of human mobility and bottlenecks to health system performance.

A combination of different tools will be used:

- Phylogeography and molecular epidemiology;
- Genomics, proteomics and transcriptomics approaches, molecular modeling and engineering, and *in silico* approaches. Anti-microbial and immunostimulating molecules will be studied and new delivery systems strategies using micro- and nano-scale materials will be developed in order to achieve novel mechanisms of treatment and disease control;
- Clinical epidemiology based on:
    - Disease monitoring in migrant populations;
    - Molecular epidemiology and early detection of emerging, neglected and opportunistic infections based on the development, and implementation of new multi-disease detection platforms based on molecular biology and nanotechnology and microfluidics;
    - Early detection of drug and insecticide resistance, as well as the underlying molecular mechanisms and potential ways to circumvent it;
    - New combinational therapeutic regimens to increase effectiveness and prevent the emergency of acquired drug resistance

    - Social epidemiology to determine biological, behavioral, economic, social, and political determinants of migrant health needs and health care seeking behavior;
- Epidemiological studies, mixed methods research, action research, economic studies and policy analysis to assess the validity, cost-effectiveness and relevance of new interventions.

These activities will extend through the 5 years and will involve R&D activities such as field based surveys; laboratory based experimental work, production of databases, and assessment of health systems needs and evaluation of their performance.

The success of these actions will be evaluated through Publications, Patents and more importantly, by the establishment of Industrial Partnerships for Product development and through the capacity to attract financial resources from the private sector.

2- **Knowledge translation**- Basic research question may respond to the needs of primary knowledge users, but project findings can have greater impact depending on the extent to which the results are transferable to other contexts, namely the users. Through the development of methodologies and tools for diagnostics, molecular epidemiology, disease control and health policies. Field-based experimental trials will allow testing the efficacy and accuracy of these new products. Liaison with health systems and industry will be guaranteed.

A combination of different tools will be used:

- Standard diagnostic methods will be used while new methodologies for pathogen detection will be developed and tested using the same framework;
- Standardized system of data collection will be implemented at the health center level and the travel medicine clinic at IHMT and others for the surveillance of neglected and tropical disease;
- Monitoring of demand for care in travel clinics (including IHMT) and other health services catering to migrant populations, in Portugal and PALOP;
- Health Workforce Observatories will channel information regarding health worker, motivations, expectations and needs to policy-makers;
- Health systems performance evaluation;
- Guidelines for knowledge translation including integrated and end-to-grant evaluation.

The activities will extend through the 5 years, scaling up after the 2nd year of the work program.

The success of these actions will be evaluated through the number and evidence of new/improved tools, case-management, strategies and/or policies resulting from GHTM activities, by the amount of peer-reviewed publications and gray literature used for health system/service development and by the establishment of political partnerships for policy development and implementations and funding from foreign government clienteles.

3. Advanced training through PhD and MSc programs and technical capacity building

A combination of different actions will be explored:

- New methodologies and contents specially through e- or blended-learning;
- Development of joint degrees with other institutions, including relocating some courses to PALOP and Brazil countries.

These activities will encompass the total duration of the work program.

The success of our education programs will be evaluated through the number of students attending the courses and graduated and their successful integration into the labor market; collaboration with other graduation programs; expansion of the formal education and training Portfolio (PhD, MSc and Short Technical Courses)

In terms of deliverables we expect:

- A more comprehensive understanding of the health patterns of migrants and travelers including their major infections and epidemiological indicators, from the country of origin to the recipient country;
- New diagnostic tools using innovative molecular supports (such as paper or gold particles), particularly for early detection of tropical and neglected diseases, such as extensively drug-resistant TB (XDR-TB), malaria, dengue, Human African Trypanosomiasis (HAT), pneumocystis, and leishmaniasis.
- Characterized drug and insecticide resistance mechanisms and potential ways to circumvent them;
- Preventive strategies for enteric viral or parasitic infections such as rotavirus and giardia/cryptosporidium, in order to mitigate the effects of these on the nutritional status of the populations at risk.
- New tools and standardized procedures that will allow rapid assessment and response in case of vector/disease's introduction.
- Knowledge basis necessary for the development of appropriate human resources for health (HRH) regulatory frameworks;
- Specialized training, leading to effective technology and skills transfer;
- Stronger educational institutions, better understanding of transnational issues (such as health worker migration) and stronger health systems, including global HRH governance as well as continuous monitoring of the health labor market in Portugal and PALOP countries.

6.7. Contributions for the regional strategy

(Integration and coordination of the unit's strategy with the specialisation strategy of the region(s)) 3000 characters)

FCT is currently working on the elaboration of a national strategic plan towards the formulation of a Research and Innovation Strategy for Smart Specialization as required from the Innovation Union and the new European Cohesion Policy flagship initiative.

The final document has not been finalized, and when FCT was inquired the following links were provided and assessed on the 18th December 2013 (FCT contribution to the National Strategy for Smart Specialization http://www.fct.pt/esp_inteligente/; for the Lisbon region: https://www.fct.pt/esp_inteligente/docs/Workshop_11122012_EduardoBritoHenriques.pdf - a presentation on R&D institutions – a description of the R&D situation in the region and its national context)

Having in mind those documents we expect to contribute for the regional specialization through: Generation of specialized knowledge with applications at regional, national and international level,

namely on the challenge imposed on the health system by migrants, and other travelers, and the effect of global changes on the health of individuals and populations).

Portugal, through its privileged relations with CPLP countries, is not only a port of entry of migrant populations from those countries into the European space, as well as maintaining a regular flux of workers, and other travelers, both from those countries into Portugal and vice versa. Such fluxes of people, and their goods, can bring about the introduction of pathogens, or their vectors. This can be further aggravated through the climate changes that affect the southern European and Mediterranean regions, where such introductions have already occurred with registered outbreaks (e.g. dengue and/or chikungunya in Italy, France and Croatia, and malaria in Greece). On the other hand, the recent increased outflow of workers from Portugal to the PALOP, demands for higher specialization in travel medicine with pre- and post-travel follow up in outpatients travel medicine clinics such as we have in IHMT, contributing to scaling up of skills much needed in the European region.

Liaison with industry and national health systems (in Portugal, other European countries and countries in our areas of influence - PALOP, Brasil, East Timor and Mediterranean basin) will be conducive to translation of global knowledge into locally relevant interventions, which can create local/regional health & wealth.

Advanced specialized training will generate career opportunities, and new chances to identify and start of business ventures.

6.8. Opportunities for advanced training

3000 caracteres (3000 characters)

Our host institution provides four PhD and six MSc programs and all members of our team are engaged in both teaching and student supervision under these programs. IHMT is also a founding member of the ***TropEd*** (http://www.troped.org) network, collaborating in the International Health MSc Program, with various courses/modules accredited by this association. In addition, our capacities in e-learning training expand the target audience of our courses giving it a global reach. GHTM advanced training will build on the currently existing post-graduate trainings to support MSc and PhD students thesis under the supervision of the Center's members. Furthermore, GHTM will be able to host PhD students for other advanced training programs interested in developing theses in our areas of expertise.

More recently, a joint international program in collaboration with the *Instituto de Investigação Científica Tropical* (IICT), Portugal and Fiocruz, Brazil on Tropical Diseases and Global Health was developed and will be implemented in the academic year 2014/2015. The joint international program, which is aligned with the GHTM strategy, will bring together the two most influential CPLP countries and their network of scientific and health system institutions, allowing students to access a network of resources with a large geographic implementation and solid international scientific reputation. The program combines know-how of three institutions in an integrated approach that includes basic research, socio-economic, cultural, ethics, infectious and chronic disease research, public health, health systems and human resources for health, food security and safety converging into the main areas of medical microbiology/parasitology and global health and development.

We have also extensive experience in implementing training actions in endemic countries. These courses and workshops address specific thematic areas with a strong applied and operational component. They accommodate a diverse audience, ranging from graduate students (PhD, MSc) to health technicians. To strengthen institutions in the South, GHTM will support PhD and MSc programs being developed with University Institutions in Angola, Cape Verde and Mozambique.

GHTM support to these actions is a priority, given their importance for the improvement of health in endemic countries and for establishing closer overseas collaborative relations. Also, this framework will provide young European scientists the opportunity to work with experts in various scientific disciplines, building capacities whilst enrolled in IHMT/UNL PhD and MSc programs, consistent with the scope of the European PhD programs, the promotion of R&D, young people employment and active contribution to society in Europe as forecasted by the Horizon 2020 EU program.

6.9. Internationalisation

(Networks or other forms of participation at the international level 3000 characters)

GHTM research activities will be conducted primarily in Europe, CPLP member states and their bordering countries and the Mediterranean Basin, where collaboration with academic institutions and health departments is well established. Collaboration with national and international partners is conducted at various levels, from specific project participations to the establishment of formal institutional networks. Networks constitute an excellent means for system strengthening, technology transfer, data sharing, development of joint research projects and training actions.

Research networking through competitive joint funding in the CPLP space will be a primary priority of the Center activities. The main objectives of networking will be i) to establish national, regional and international sustainable networks, ii) to promote human resources, equipment and technology sharing and transfer with emphasis on mobility in the context of research-driven training, and iii) to translate this into institutional capacity building, scientific productivity gains and economic growth.

The networking process in itself is useful to leverage the Center capacity to lead and support regional/thematic (European, Iberian and CPLP) research activities and enable North-South technology transfer, especially to African and South American partners. The host institution has already formulated a number of cooperation protocols that facilitate integration of activities and concentration of resources and the access to field-based laboratories stations in Angola, Mozambique and Guinea-Bissau, involving multiple stakeholders, and including Faculties and National Institutes of Health. Research collaborative projects have been successful leading, to shared research agendas and activities, training courses and workshops in Europe, Africa and Brazil. The host institution is involved in 14 networks, with different scopes, funding and timescales, ranging from EU COST actions to a Brazilian Amazon network on malaria (http://www.ihmt.unl.pt/?lang=pt&page=investigacao&subpage=redes).

International capacity and visibility is fundamental for the implementation of innovative methodologies, technologies and cross-disciplinary approaches, as for training highly skilled researchers. Internationalization involves the implementation and the success of joint projects and activities. Although the members of the GHTM have been able to attract international projects (EU and others) and international students (34%), it is our priority to further facilitate the participation in international projects of other relevant institution, governmental and non-

governmental, through specific actions such as supporting project preparatory meetings, participation in international fora, summits, and topic-specific scientific meetings and mobilizing the participation and support of scientists with high international recognition, further attracting collaboration, students and young international scientists.

6.10. Knowledge transfer

(Registration and exploitation of patents, commercialisation activities of Science and Technology and development of prototypes) 3000 caracteres)

The development of new tools for diagnosis, treatment and control of the target diseases will open opportunities for new patents and prototypes. There will be an especial concern in involving the private sector at an early stage of the development of these tools to ensure its commercial potential. In addition, because some of the tools will be primarily targeting poverty-related infections and vulnerable groups, care will be taken to seek for support from funding institutions and their applicability in low income settings.

Translational aspects arising from this research will consist on the development of new tests as Point-of-care (POC) devices for:

a) Quantification of anti-HIV-2 antibodies, CD4+ T-cells count and viral load from whole blood samples, as a mean to reduce the costs currently involved in the diagnosis and monitoring of HIV-2 infection. (eg. See patents - WO2007084021 (A2) — 2007-07-26 and WO2007141650 (A2) — 2007-12-13 by JMMarcelino et al);

b) Early detection of TB and MDR-TB using gold-nanoprobe technology for the direct detection of targets and mutations. The main targets will be for 1st and 2nd line drugs from M/XDR-TB strains circulating in Portugal. We aim at translating the nanoprobes and paperfluidics technology and develop prototypes for their diagnosis to be produced and commercialized under the portuguese biotech diagnostics market and applied in low-resource settings and developing countries (eg. Paper based nanoprobe platforms developed in collaboration with the CENIMAT/Elvira Fortunato's Lab/FCT/UNL);

c) Early detection and identification of clinically relevant yeast species in culture and biological samples by fluorescence *in situ* hybridization (see patents from JInácio - WO2008135931 (A2) — 2008-11-13 and - EP2097541 (A2) — 2009-09-09 – partnership with industry –STAB VIDA and MIACOM DIAGNOSTICS GMBH);

d) Early identification of *P. jirovecii* haplotypes correlated with drug resistance and PcP poor outcome (to be developed with the above described nanobased platforms);

e) Gathering and analysis of molecular epidemiology for prediction modeling of spread, phylodynamics and phylogeographics (eg . see analysis software developed by AMVandamme)

f) Provision of new assessment tools and effective implementation strategies for the rollout and implementation of new technologies in the national health systems using the conceptual matrix of the Grading of Recommendations Assessment, Development and Evaluation system;

g) Development of new combinational therapies against multi-drug resistance mediated by efflux systems based on natural products and synthetic molecules that inhibit these transport systems. (eg. see Handzlik, Jadwiga and MViveiros patent - WO2013151450 (A1) — 2013-10-10).

6.11. Ethical issues

(Descrição de questões éticos relacionados com a atividade de investigação ou a utilização dos resultados produzidos pela unidade 3000 characters)

Many of the research lines will comprise experimental procedures involving animal models and/or human subjects. Ethical clearance is therefore a requirement that needs to be fulfilled according to the current channels available for these purposes. In this context, IHMT's multidisciplinary Ethical Committee will have a critical role in establishing guidelines and in the approval of experimental protocols to ensure best practices.

Specific projects involving human subjects and animals must be submitted and approved by IHMT and other local (when applicable) ethical committees. IHMT Animal House is accredited for animal experimentation and researchers who work with animals are certified by the national competent body – Direção Geral de Veterinária (DGV).

Whenever required, consultation of experts and external ethical committees will be carried out.

7. Expected Indicators of the 2015/2020 Strategic Programme

Description	2015	2016	2017	2018	2019	2020
Publications in peer-reviewed international journals	112	123	136	149	164	181
Patents and performing patents				1	1	1
Books and book chapters of international circulation	18	19	21	23	26	28
PhD theses under the supervision of integrated members	40	44	49	54	60	67
Conference proceedings	92	101	111	122	135	148
New materials, devices, products and processes			1		1	
Software, computer code and algorithms						
Books, including single-authored works (including scholarly editions of oral or written texts and translations with introduction and commentary)						
Edited special issues of journals, with substantial research input on the part of the researcher	1			1		
Chapters in books, including contributions to conference proceedings, essays in collections						
Creative writing (to the extent that it embodies research)						
Encyclopedia entries (to the extent that they embody research)						
Audio/visual and electronic/digital materials	5	5	5	5	5	5
Other categories, including web-based resources; video and audio recordings (to the extent that they embody research)						
Performances and exhibitions to the extent that they embody research						
Industrial research contracts	1	2	2	2	2	2
Research contracts with national or international bodies	24	27	30	34	38	42
Other research outputs						

8. Equipa de Investigação Proposta - Proposed Research Team

8.1. Criteria adopted by the R&D unit for the definition of integrated member, if different from FCT's reference table

(Lista de critérios e justificação para adoção dos mesmos/List of adopted criteria and justification) 3000 Caracteres (3000 characters)

The criteria adopted for defining a Unit's member took were based on the recommendations of FCT. However, GHTM members had to fulfill stricter scientific productivity criteria to be considered integrated members of the Center, as follows:

A) If holding a PhD for more than 5 years

Then a member must have at least seven scientific papers indexed to Scopus or Web of Knowledge in the last five years. International book/book chapter can replace two of those. Two indicators may be accepted, as long as they relate to a publication in a top 10% international peer-reviewed journal in the area of research.

Members should also have at least one funded project and 2 PhD or MSc supervisions.

B) I(f holding a PhD for less than 5 years

Then a member must have at least three scientific papers indexed to Scopus or Web of Knowledge in the last five years. International book/book chapter can replace one of those. One indicator may be accepted, as long as it relates to a publication in a top 10% international peer-review journal in the area of research.

List of Integrated Members / 10 nuclear CVs

(Integrated members of the proposed team with 10 nuclear CV)

#RG		Members´names	PI - RG	Nuclear CV	PI - TL
1	PPS	Paulo Ferrinho	s	s	
2	PPS	Cláudia Conceição			
3	PPS	Cláudia Istrate			
4	PPS	Filomena Pereira			
5	PPS	Gilles Dussault		s	
6	PPS	Giuliano Russo			
7	PPS	Inês Fronteira			
8	PPS	Isabel Craveiro			
9	PPS	Luís Lapão			
10	PPS	Maria Rosário Oliveira Martins			
11	PPS	Sónia Centeno Lima			
12	PPS	Sónia Dias		s	s
14	PPS	Zulmira Hartz			
1	THOP	Miguel Viveiros Bettencourt	s	s	
2	THOP	Ana Barroso Abecasis			
3	THOP	Anne-Mieke Vandamme		s	
4	THOP	Celso Cunha			
5	THOP	Francisco Esteves			

6	THOP	Isabel Couto			
7	THOP	João Inácio			
8	THOP	João Piedade			
9	THOP	José Maria Marcelino			
10	THOP	Maria Luísa Costa Lobo			
11	THOP	Maria Luz Martins			
12	THOP	Olga Maria Guerreiro de Matos		S	
13	THOP	Rita Castro			
1	VBD	João Pedro Soares da Silva Pinto	S	S	
2	VBD	Aida Maria Simões			
3	VBD	Ana Isabel A. Gonçalves Domingos			
4	VBD	Ana Paula Martins dos Reis Arez			
5	VBD	António Paulo Gouveia Almeida			
6	VBD	Carla Alexandra Soares Maia			
7	VBD	Carla Alexandra Sousa			
8	VBD	Dinora Maria da Silva Lopes Ferreira			
9	VBD	Gabriela Santos-Gomes			
10	VBD	Henrique Manuel Condinho Silveira		S	
11	VBD	Isabel Larguinho Mauricio		S	
12	VBD	Jorge Luis Marques da S. Atouguia			
13	VBD	Jorge Beirão Almeida Seixas			
14	VBD	Lenea Maria Campino		S	S
15	VBD	Luis Varandas			
16	VBD	Mª de Fátima Carvalho Nogueira			
17	VBD	Marcelo de Sousa da Silva			
18	VBD	Maria Odete Afonso			
19	VBD	Maria Teresa Novo			
20	VBD	Patricia Isabel Rosa Salgueiro			
21	VBD	Ricardo Manuel Parreira			
22	VBD	Sofia Júdice da Costa Cortes			

9. Proposed Research Groups

List of Research Groups

(Acesso às subsecções do grupo de Investigação / Access to subsections of the research group)

	Referência	Designação do RG	IR do RG
1	RG-4413-2777	Vector-Borne Diseases (VBD) Doenças Transmitidas por Vetores	João Pinto
2	RG-4413-2778	TB, HIV and Opportunistic Pathogens (THOP) TB, HIV e Organismos Patogénicos Oportunistas	Miguel Viveiros
3	RG-4413-2779	Population Health, Policies and Services (PPS) Populações, Politicas e Serviços de Saúde	Paulo Ferrinho

No total de grupos: 3

10. Proposed Thematic Lines

List of Thematic Lines (if applicable)

(Acesso às subsecções das Linhas Temáticas / Access to subsections of the Thematic Lines)

	Referência	Designação da TL	Investigador Responsável da TL
1	TL-4413-1507	**Health challenges of travelers and migrants (HCTM)** Saúde do Viajante e do Migrante	Sónia Dias
2	TL-4413-1508	**Emerging Diseases and Environmental changes (EDEC)** Doenças Emergentes e Alterações Ambientais	Lenea Campino

No total de linhas temáticas: 3

11. Budget for the 2015/2020 Strategic Programme

Overall budget

Rubrics	2015	2016	2017	2018	2019	2020
Human Resources	202 944,71	276 752,85	276 752,85	276 752,85	276 752,85	202 944,71
Missions	22 500,00	22 500,00	22 500,00	22 500,00	22 500,00	22 500,00
Consultants	8 500,00	8 500,00	8 500,00	8 500,00	8 500,00	8 500,00
Service Procurement and Acquisitions	45 000,00	75 000,00	15 000,00	15 000,00	15 000,00	15 000,00
Patent Registration	0,00	0,00	0,00	5 500,00	35 000,00	0,00
Adaptation of Buildings and Facilities	0,00	0,00	0,00	0,00	0,00	0,00
Overheads	74 788,94	106 550,57	64 550,57	65 650,57	71 550,57	49 788,94
Total Current Expenses	353 733,65	489 303,42	387 303,42	393 903,42	429 303,42	298 733,65
Equipment	95 000,00	150 000,00	0,00	0,00	0,00	0,00

[1] Valor limitado a 10% do financiamento solicitado. [2] Valor limitado a 20% das despesas diretas do financiamento solicitado.

12. 2015/2020 Strategic Programme Budget Rationale

12.1 Overall budget rationale

(Overall budget justification and specification of requirements for human resources and equipment in specific field) (5000 characters)

Although based on its current core competencies, RG and TL are planning to implement relatively fresh approaches to their research areas. In order to do so the PPS group will have to strenghten their critical mass on aspects of **social science** and **clinical epidemiology**. VBD and THOP groups need to consolidate and expand their expertise areas by strengthening skills in transversal innovative areas such as **bioinformatics** and **geography**,. The workload with travel, tropical and migrant health care needs to be harnessed systematically into systems that combine clinical data for care with data collection for research, hence the need to recruit a **senior clinical** researcher with medical training and experience on clinical trials that will develop a working team fundamental for GHTM field implementation.

In order to acquire skills and critical mass for developing research and attracting research grants in these areas core funds are requested to hire personnel to strengthen the multidisciplinary profile of GHTM, and equip them with starting grants to develop their thematic lines. This new staff will be ‘grant-holding fellows’ and possess the skills required to bridge the gap between the

RGs aiming at working across the TLs; the respective starting grants will be aimed at starting their research activity but most importantly at leveraging larger funds within the thematic lines.

Three starting grants (30,000.00) will be needed in relation to the work of each fellow to enable the development of their work, but also to leverage and access larger funds through travelling for business development and data collection visits to the field. Such grants will be linked with the fellows' job descriptions, and will cover missions, equipment and the purchase of goods and services for data collection purposes.

Although access to equipment is possible through stable collaborations, networking and service-sharing, new equipment is fundamental to maintain competitiveness, therefore we request funds for a high-throughput genotyping platform and for a flow cytometer, two pieces of equipment fundamental for up to date generation of data. To run this equipment, specialized laboratory technicians are required. Insect rearing and manipulation is an extremely important asset of GHTM, therefore, a Laboratory technician is requested to maintain this highly demanding infrastructure.

In summary funds are requested to hire 1 senior Scientists, 2 junior Researcher, 2 Post-docs, 2 Lab technicians and 1 administrative staff for 6 years each.

Travel funds are requested for: a) Data presentation by GHTM members at international meetings; b) networking activities; c) dissemination of scientific and training activities, to increase exposure to the scientific community and to the society; d) R&D and health-related activities developed at low income countries where tropical diseases are endemic; e) promotion of small scale meetings for international grant proposal preparation and submission.

Funds are requested for Advisory Committee activities and for accommodation of invited speakers, lecturers and scientists involved in joint research activities, courses and workshops organized by the GHTM.

Service procurement and acquisitions: funds are requested for bibliography acquisition and publication costs; maintenance of equipment and maintenance/adjustment of infrastructures; laboratory consumables and reagents for strategic activities (mainly training action), under the scientific strategy carried out by the GHTM; administrative consumables.

Overheads: 20% of the total project funding.

12.2 Human Resources rationale

3000 caracteres (3000 characters)

One junior researcher and one post-doctoral fellow will be required within the new PPS research group to cover the new areas of activity:

The first post will be for a Post-doc social science scientist to develop work on migrants communities and travelers' needs; this fellow will be expected to work across disciplines such as sociology, international relations and public health, and to have previous experience of research on disadvantaged groups.

A junior researcher will be required to come from a medical background and have expertise at practitioner level in epidemiology and on the public health implications of emerging diseases in high- and low-income countries.

In order to consolidate the international implementation of VBD and THOP the following profile of researchers are needed:

Bioinformatician: Post-doc fellow with experience in molecular epidemiology, will be responsible for setting research lines involving the establishment and analysis of databases (sequences, SNPs) and designing computational solutions for data management and monitoring (e.g. diagnostic and epidemiological assessment tools).

Geographer: junior researcher will be primarily devoted to the EDEC Research Line and will be responsible for mathematical modelling and risk map development. She/He will work in close association with the bioinformatician for the development of innovative approaches for predicting risk and responsiveness in user-friendly informatics platforms.

A senior clinical scientist: with experience in designing, conducting and implementing clinical studies and capable of developing innovative, and efficient research, consistent with the global GHTM R&D strategy and able to work collaboratively with GHTM members from all RG and both TL.

In addition, funds will be required to hire three laboratory technicians, to support research activities (genotyping platform, flow cytometry and insectary management), and one administrative officer to support management.

12.3. Equipment rationale

(Equipment needs) 2000 caracteres (2000 characters)

A high-throughput genotyping platform (Illumina iSCAN) will be essential for the development and implementation of new diagnostic tools, molecular epidemiology and population genetic-based studies.

Flow cytometry and cell sorting are a vital component of immunology and infectious disease research. With a four-color, dual-laser, bench top flow cytometry system high-speed biomarker cell analysis on up to four distinct populations will be possible. This equipment also includes an automated cell separator located within a class II biosafety cabinet that allows the separation and isolation of specific cell populations, or to analyze/quantify fluorescent-labeled microorganism.

13. Reviewers proposed by the research unit(s)

(Indicação de 3 peritos / List of 3 reviewers)

NOME	INSTITUTION	EMAIL	SCIENTIFIC AREAS
Michael Miles	London School of Higiene and Tropical Medicine, UK	Michael.Miles@lshtm.ac.uk	Biomedicine
Mário Dal Poz	Univesidade Estadual do Rio de Janeiro, Brazil	dalpozm@uerj.br	Diagnostic, Therapies and Public Health
Jonathan S Friedland	Imperial College London, UK	j.friedland@imperial.ac.uk	Immunology and Infection

9. Proposed Research Groups

List of Research Groups

(Acesso às subsecções do grupo de Investigação / Access to subsections of the research group)

	Referência	Designação do RG	IR do RG
1	RG-4413-2777	Vector-Borne Diseases (VBD) Doenças Transmitidas por Vetores	João Pinto
2	RG-4413-2778	TB, HIV and Opportunistic Pathogens (THOP) TB, HIV e Organismos Patogénicos Oportunistas	Miguel Viveiros
3	RG-4413-2779	Population Health, Policies and Services (PPS) Populações, Politicas e Serviços de Saúde	Paulo Ferrinho

No total de grupos: 3

9.1 Identification of the Research Group (RG-4413-2777)

9.1.1 Reference of the research group

RG-4413-2777

9.1.2 Name of the Research Group in Portuguese

Doenças transmitidas por vetores

9.1.3 Name of the Research Group in English

Vector-Borne Disease

9.1.4 Palavra(s) chave(s) - Keyword(s)

1 - Early detection diagnostic tools

2 – Emerging infections

3 - Vector monitoring

4 - Risk maps

9.1.5 Existiu no período 2008/2012 - Existed in 2008/2012

No

Instituição participante a que pertence o Grupo de Investigação - Participating Institution to which the Research Group belongs

Instituto de Higiene e Medicina Tropical

9.2 Members

9.2.1. List of Integrated Members / 3 nuclear CVs

Name	Principal investigator	Nuclear CV (s ou n)
João Pinto	s	s
Isabel Larguinho Mauricio	-	s
Ricardo Manuel Parreira	-	s

9.2.2 List of current PhD students

(PhD students of the proposed group)

Maria Armanda Viana Rodrigues

Maria de Aires Machado Pereira

Maria Luisa de Oliveira Feijao Monteiro Simoes

Sonia Pestana Ascensao
Cristina Isabel Rodrigues Mendes
Filipa Santana Ferreira
Gonçalo Filipe Rocha Seixas
Kinanga Kiaco
PEDRO RAFAEL DIMBU
Zoraima Naymbe da Silva Neto
Marisol Garzon Lozano
NUNO MIGUEL DA SILVA MARQUES
Tiago António Casaca de Rocha Vaz
Teresa Lobo Machado Sousa Nazareth
Diara Kady Monteiro Vieira Lopes Rocha
Jailson Fernando Brito Querido
Joana Isabel Figueira Ferrolho
João Pedro Costa Alvares Viegas Nunes
Lis Tavares Coelho Lobo
Sílvia Filipa Alves Beato
Teresa Maria Dias Costa de Miranda Baptista Fernandes
Sheila Marisa Cardoso
ANA MARIA BUTTLE DE MENDONCA MOURAO POSSIDONIO DE ARMADA
Diana Isabel Viana da Fonseca Campelo
Sónia Raquel Mota Faria

9.2.3 List of other researchers of the Research Group

(Other researchers of the group proposed)

	Nome	**Chave associação**
	Filomeno Fortes	J0252804TXT
	Derek	J025834KAT4
	Marietjie Venter	J58031128aqq

9.3 e 9.4

N/A

9.5 Organisational Structure and Objectives of the Research Group for 2015/2020

9.5.1 Structure of the Research Group (4000 characters)

The VDB group integrates researchers with diverse expertise and background to implement R&D through a multidisciplinary approach. Our major research interests comprise the following major areas: drugs and mechanisms of drug resistance; molecular epidemiology; evolutionary biology and population genetics of pathogens and vectors; host-parasite interactions and immune responses; vector biology and insecticide resistance; and environmental changes. Malaria, leishmaniasis and arboviral diseases have been the major vector-borne diseases in to which our research has been primarily focused. In addition, there has been an increasing interest in research on the field of emerging infections such as trypanosomiasis and tick-borne diseases.

At IHMT, our group members have access to equipped laboratories for implementing techniques for vector and pathogen identification, cellular and molecular studies, biochemical analysis and genetic profiling. Access to cutting-edge technologies (*e.g.* microarrays, genomic sequencing and mass-spectrometry) is granted by means of networking and project collaborations. An essential component of our capacities is the ability to perform *in vivo* assays using animal models. We have the capacity and expertise to establish the full life-cycle of malaria and leishmaniasis parasites. In our insectaries, we keep colonies of mosquito and sand-fly vectors, which are used for experimental infections and to test new products for vector control. Our animal facility provides the capacity to keep laboratory animals required to conduct *in vivo* experiments. Finally, we have biobanks of cryopreserved isolates of vector-borne pathogens, including reference strains (*e.g.* drug susceptible and resistant) and field isolates.

Members of our research team have extensive experience in field-based research, particularly in endemic regions of Africa (PALOP countries mainly) and South America (Brazil) and also in our own territory. These activities include epidemiological surveys, bio-ecological studies of vector populations, social studies and disease monitoring activities.

The VBD group with research teams coordinated by a Leading PI will function as described in section 6.6.

9.5.2 Objectives of the Research Group (4000 caracteres)

Challenges imposed by environmental changes and mobility have brought VBD back in to the scientific and political agenda. There is a growing concern that increased mobility of people and goods may result in the resurgence of vector-borne infections. Examples from recent past have highlighted the potential for this (re)emergence. Among these are the chikungunya virus outbreak in Italy 2007, and autochthonous Dengue cases in France and Croatia in 2010. The USA has had West Nile virus (WNV) outbreaks since 1999. In Europe, among the largest WNV outbreaks are those of Romania (1996) and Greece (2010). In the past decade, sporadic autochthonous cases of malaria have been reported in Spain, France, Italy and Greece it has occurred for 4 consecutive years since 2010

Portugal has not been invulnerable to vector-borne diseases. The country is endemic for leishmaniasis with prevalence in canine populations reaching up to 18%, and a mean 6.3% in the whole country. The most recent public health concern was the dengue epidemic in Madeira Island in Oct. 2012. A total of 1891 cases were reported in a population of ca. 270000 inhabitants, transmitted by a recently introduced Aedes aegypti population.

The VBD group will apply fundamental and translational research with the ultimate goal of effectively contributing for ameliorating the global burden of VBD. The group will develop research and advanced training actions to tackle specific questions under the thematic lines of the center. Our major research objectives are:

1. **Vector-borne infections in vulnerable populations**

We aim at identifying the major VBD in migrants, travelers or other vulnerable populations of Portugal, whether of zoonotic origin or not. Phylogeographic origins, profiles of virulence and drug resistance of pathogens will be analyzed. This will be crucial for identifying major VBD either autochthonous or that may be introduced in the country.

2. Vector competence, vector-pathogen interactions and insecticide resistance

We aim at characterizing the receptivity of Portuguese vector populations for transmission of exotic pathogens and also to contribute with new knowledge on molecular determinants of infection in vectors, as well as insecticide resistance. This information is critical for development of innovative control strategies.

3. Human host susceptibility

The outcome of an infection is greatly influenced by the genetic background of the human host. In non-endemic regions, the risk of disease is greatly enhanced by an immunological naïve population, increasing the potential for severe epidemics. We will combine immunological and human genetics approaches to assess determinants of susceptibility to vector-borne infections in Portuguese and migrant populations.

4. Community-based vector monitoring

In spite of the existing vector surveillance systems, people exposed to insect bites are often the first to detect newly introduced vectors. We aim at developing research and training actions towards the establishment of a community-based sentinel vector monitoring system with the aid of GIS, complementary to the surveillance already in course in Portugal.

5. Molecular tools for diagnostics

We aim at developing rapid tools for diagnostic of VBD. This covers a need shared not only by low-income endemic countries where these diseases are often misdiagnosed due to lack of resources and trained personnel, but also by non-endemic countries with low awareness and experience in the diagnostics of imported diseases. We propose to develop a multi-diagnostic VBD tool that combines clinical data with a multi-pathogen identification platform and a bioinformatics application to help in differential diagnosis.

6. Improved risk maps

The information obtained by developing objectives 1, 2 and 3 will be used to established and validate new or improved risk maps for the major vector-borne diseases that can potentially threaten our territory and the southern European region.

9.1 Identification of the Research Group (RG-4413-2278)

9.1.1 Reference of the research group

RG-4413-2278

9.1.2 Name of the Research Group in Portuguese

TB, HIV e Organismos Patogénico Oportunistas

9.1.3 Name of the Research Group in English

TB, HIV and Opportunistic Pathogens

9.1.4 Palavra(s) chave(s) - Keyword(s)

1- Opportunistic diseases

2- Early detection and diagnosis

3- New nanotechbased tools for detection

4- Drug resistance and new therapies

9.1.5 Existed in 2008/2012

No

9.1.6 Participating Institution to which the Research Group belongs

IHMT/UNL

9.2 Members

9.2.1. List of Integrated Members / 3 nuclear CVs

	Nome do investigador	Principal investigator	Nuclear CV (S ou n)
	Miguel Viveiros	s	s
	Olga Maria Guerreiro de Matos	-	s
	Anne-Mieke Vandamme		s
	João José Inácio Silva		
	Isabel Maria dos Santos Leitão Couto		
	Ana Barroso Abecasis		
	Celso Vladimiro Ferreira de Abreu Cunha		
	Francisco Vaz de Carvalho Esteves		
	João Mário Brás da Piedade		
	José Maria Marcelino		
	Maria da Luz Marques Martins		
	Maria Luísa Lobo Ferreira da Costa		
	Rita Maria Rodrigues Teixeira de Castro		

9.2.2 List of current PhD students

(Alunos de doutoramento do grupo proposto/ PhD students of the proposed group)

Diana Isabel Oliveira Machado
Elsa Maria dos Viveiros Fortes Gabriel
Mónica Susana Claudino Nunes
Joana Sustelo Sequeira Cavaco Silva

9.2.3 List of other researchers of the Research Group

(Outros investigadores do grupo proposto / Other researchers of the group proposed)

	Nome	**Association Key**
	Marta Sofia Martins	J0139360649
	Liliana Isabel Rodrigues	J0326169C00V

Total: 2

9.3 e 9.4

N/A

9.5 Organisational Structure and Objectives of the Research Group for 2015/2020

9.5.1 Structure of the Research Group (4000 caracteres)

The research of the TB, HIV and Opportunistic Pathogens Group (THOP) will be focused on the epidemiology, diagnosis and control of opportunistic diseases (ODs), and the clarification of basic aspects of the interactions between microbes and their hosts and how drug resistance develops.

THOP brings together researchers with an extensive track record in microbiology, molecular biology, biochemistry, epidemiology, and immunology of Opportunistic Diseases and other diseases caused by pathogenic microorganisms, which will develop their research in complementary approaches, according to the following areas:

1. Pathogen/Host Cellular and Molecular Interactions and Targets

(A) Studies on the cellular and molecular interactions between the human microbiomes (skin, lungs, gut, blood, genital tract) and the human host under immunosuppression (HIV co-infection, cancer, chronic diseases). Four infectious disease models were selected for this research area - HIV, multidrug resistant bacterial infections, fungal infections and parasite infections based on the following rational: (i) major relevance of these diseases as opportunistic in the immunosuppressed patient and in the human health, in the developed and developing world; (ii) the extensive track-record of the IHMT/UNL on these infections and the access to biological samples for their diagnosis, which allows the optimization of tests for distinct biological matrices;

(iii) distinct approaches may be tested and optimized for early detecting infections (e.g. detection of antibodies, antigens or nucleic acids); (iv) extensive experience available at our team and partners on their gold-standard laboratory diagnosis and (v) existence of researchers working on these subjects in our Units and collaborators, namely young PhD and MSc students.

2. DEVELOPMENT OF RAPID DETECTION TOOLS/ DETECTION PLATFORM

(B) Tools development for the early detection of potential opportunistic diseases and monitoring its onset for rapid therapeutic response ; (C) Development of point-of-care detection platforms for detection of opportunistic pathogens; (D) Understanding spread of infections to guide containment strategies; (E) Assessment of putative biomarkers": from genetics to biochemistry and immunology.

3. RESEARCH ON NEW THERAPEUTIC APPROACHES

(F) High-throughput molecular approaches for epidemiology: identification of drug resistance and virulent subtypes; (G) Drug resistance mechanisms and effective therapies - The research to be carried out will focus on the evaluation of new natural and pharmaceutical candidates' products with new effective antimicrobial activity; development of immunomodulators and vaccines using genomics, proteomics and transcriptomics knowledge and new strategies to incorporate bioactive molecules in a delivery system using micro and nano-scale materials.

These three research areas will be connected by an aim-oriented framework according to the following major axis: Basic research → translation into deliverables → field application→ dissemination.

The THOP group with research teams coordinated by a Leading PI will function as described in section 6.6.

9.5.2 Objectives of the Research Group (4000 caracteres)

The microbiome constitutes the sum of all microbes, their genomes and their interactions with the particular environment(s) of the host (skin, lungs, gut, blood, genital tract, etc). This concept was postulated by Joshua Lederberg (Nobel Prize in Physiology/Medicine in 1958), who argued that microorganisms inhabiting the human body influence human physiology and should be included as part of the human "ome". The human body contains over 10 times more microbial cells than human cells and only in the late 1990's it was realized that this "personal environment with many ecological niches and a huge biodiversity" can have an overwhelming impact on human health.

The diversity of the human microbiome is an area of intense investigation because changes in the microbiome may be associated with the development or chronicity of many infectious conditions/diseases. It is well known that the aftermath of antibiotic administration often lasts for a long time after discontinuation of treatment, suggesting that a prolonged dysfunction is induced in the host's microbiota, that readily ends up in a severe infection, very often multidrug resistant relapses, especially when antibiotic treatment is associated with host immunodepression. HIV co-infection is, by far, the most cumbersome comorbidity/coinfection that influences many opportunistic microbial infections, especially when it progress to AIDS.

The onset of infections caused by pathogenic microorganisms present in the microbiomas of the immunosuppressed host or in the host with clinical or "social" prognosis of acquiring a potential opportunistic infection is a concern always present when susceptibility to infection is present in the anamnesis of the patient, especially the chronic patient. The early detection of these opportunistic agents, for implementation of preventive measures and rapid clinical response,

using new point-of-care easy to perform molecular platforms for detection of specific targets (nucleic acid targets and immune biomarkers) is the primary goal of this research group. Our primary “human host” to be under study, will be the migrant from PALOP countries, portuguese travelers and the minority populations of the /Portuguese societies that have to live with immunosuppressive chronic disorders/co-infections/diseases. For them, the early characterization of potential opportunistic microbial infections is of outmost importance and for the health system it is an important contribution for infection prevention, control and treatment.

In summary, the extensive background of this research group, gathered during more than 20 years of applied research and teaching in medical and biomedical sciences, will be applied on providing valid approaches to the following problems:

Human Health related problems:

a) Human infectious disease and the host system response – Biomarkers and molecular targets for early detection;

b) Human infectious disease and the global warming – Ecological markers and ecological-biochemical-molecular targets for vector control and prevention of environmental-human transmission;

c) Human infectious disease and the zoonotic connection/link – New tools for early detection and treatment/control for animal and food-borne infectious diseases.

d) Human infectious diseases and global travel & population migration - early detection and management of imported diseases.

Health System related problems:

a) Human infectious disease and the health system response – Early detection, rapid clinical response, rapid information management and epidemiological response;

b) Human infectious disease and the costs for the health system – impact assessment, impact evaluation, cost effect assessment;

c) Risk & impact assessment of new technologies and new politics in health;

d) Training and competence of human resources in health – foster the consolidation of the human resources for health sciences.

9.1 Identification of the Research Group (RG-4413-2279)

9.1.1 Reference of the research group

RG-4413-2279

9.1.2 Name of the Research Group in Portuguese

Populações, Políticas e Serviços de Saúde

9.1.3 Name of the Research Group in English

Population Health, Policies and Services

9.1.4 Palavra(s) chave(s) - Keyword(s)

1- Migrants

2- Travelers

3- Maternal and child health

4- Health workforce

9.1.5 Existed in 2008/2012

No

9.1.6 Participating Institution to which the Research Group belongs

IHMT/UNL

9.2 Members

9.2.1. List of Integrated Members / 3 nuclear CVs

	PI - RG	nuclear CV
Paulo Ferrinho	s	s
Cláudia Conceição		
Cláudia Istrate		
Filomena Pereira		
Gilles Dussault		s
Giuliano Russo		
Inês Fronteira		
Isabel Craveiro		
Luís Lapão		
Maria Rosário Oliveira Martins		
Sónia Centeno Lima		
Sónia Dias		s
Zulmira Hartz		S

9.2.2 List of current PhD students

(Alunos de doutoramento do grupo proposto/ PhD students of the proposed group)

Adriana Cunha Curado
ANA FILIPA DE MENDONÇA DA GAMA
Anabela Pereira Coelho
André Aurélio Marona Beja
ANTONIO PEDRO DA COSTA DELGADO
Artur Jorge Correia
Carolina Bastos Gasparinho Antero da Silva
Inês Ferreira Pita de Campos Matos
João Manuel Taborda de Matos Lopes
João Pedro Bernardo Gregório
José Alexandre Menezes da Silva
Lícia de Oliveira
Luciana Caroline Albuquerque Bezerra
Marica Ferri
MARTA ALEXANDRA FARTURA BRAGA TEMIDO
Marta Sofia Mano Moreno
MIE OKAMURA
Miguel André Fouto Pinho de Oliveira
Rui Miguel Neves Cortes

9.2.3 List of other researchers of the Research Group

(Outros investigadores do grupo proposto / Other researchers of the group proposed)

9.3 e 9.4

N/A

9.5 Organisational Structure and Objectives of the Research Group for 2015/2020

9.5.1 Structure of the Research Group (4000 caracteres)

The Population Health, Policies and Services (PPS) Group is a multidisciplinary team of researchers in fields ranging from policy analysis, health promotion, management of health services, clinical medicine and population health. Universal Health Coverage (UHC) is the group's inspiring principle, which is only achievable through a quality, motivated and adequately distributed workforce.

The Group has multiple and complementary focuses: health problems of travelers; health problems of migrants; health problems of women and children; health workforce issues; and bottlenecks in the planning and management of health services. The Group's approach to these issues will cover their policy, as well as their sociological, economic, epidemiological and clinical dimensions. These approaches include epidemiological surveys, qualitative studies, policy analysis, economic and organizational analysis, education needs assessment, discrete choice experiments, labor market analysis, satisfaction surveys, case studies and evaluative research.

At IHMT, our group members find support within the Department of Public Health and Biostatistics, the Department of Clinical Care of Tropical Diseases, the WHO Collaborating Center on Health Workforce Policy and Planning and the Travelers Health Clinic.

Group members have a long experience of collaboration with institutions in Portugal and Europe, in Portuguese-speaking African countries (PALOP), Brazil and East Timor. In the PALOP, they have contributed to the development of Institutes of Public Health, supported academic programs in several faculties of medicine, contributed to strategic health plans, informed policy on rotavirus vaccines and nutrition interventions in school and pre-school children, coordinated the development of human resources strategies, and contributed to the creation of training programs, such as the specialty in public health for physicians of the five PALOP and Timor-Leste. The publication record and the participation of members in collaborative research projects illustrate this engagement in international work and in translating knowledge into effective interventions. The designation of IHMT as WHO Collaborating Center on Health Workforce Policy and Planning in 2011 is a recognition of its leadership in that field. Members have also experience of work in international agencies, such as the World Health Organization and the World Bank.

In addition to their research activities, members of the Group are engaged in teaching at Masters and PhD level. As of December 2013, members of the Group were supervising 48 PhD students.

The Group and its research teams with a leading PI will function as described in section 6.6.

9.5.2 Objetivos do Grupo de Investigação -Objectives of the Research Group

The overall aim of the PPS group is to produce research evidence contributing to help health policy and decision-makers to steer health systems towards universal health coverage. The group will focus on three target populations: (1) travelers and migrants (including refugees), (2) women and children in low-income environments, both in Portugal and in the PALOP, and (3) health workers.

The PPS RG will support the activities of the other two RG - Vector-borne Diseases (VBD) and TB, HIV and Opportunistic Infections (THOP) – to contribute with practical solutions to solve global health problems associated with the mobility of vector and human populations and with emerging and neglected diseases. With the other two groups, PPS will contribute methodologically to the following objectives:

1) Assess risk/impact of new technologies and new policies in healthcare systems;

2) Evaluate the costs of scaling-up, quantitatively and qualitatively, the current health workforce in selected low-income PALOP countries to address health needs in general and in particular to address needs to target VDB and THOP within comprehensive health systems.

The specific research objectives are:

1. Identifying unmet health needs of travelers, migrants and vulnerable populations and their determinants;
2. Characterizing services and resources available to travelers, migrants and vulnerable populations in terms of the various dimensions of their accessibility (economic, cultural, organizational);
3. Identifying/designing/monitoring and evaluating management and program responses to mitigate obstacles to improved access to quality services;
4. Analyzing the policy framework affecting the development of the health workforce and stakeholders' positions;
5. Studying alternative ways to train health personnel adjusting to the changing needs of the population and reducing the absolute gap of health workers in portugal and in cplp countries;
6. Designing and validating workforce policies aiming at maximizing health gains for the target populations;

The sum of these research activities will contribute to informing policy development with a view to helping countries in their efforts to control VBD and THOP and to attain and sustain UHC.

10. Proposed Thematic Lines

List of Thematic Lines

	Referência	Designação da linha temática	Investigador Responsável
1	TL-4413-1507	**Health challenges of travelers and migrants (HCTM)** Saúde dos viajantes e migrantes	Sónia Dias
2	TL-4413-1508	**Emerging Disease and Environmental changes (EDEC)** Doenças Emergentes e Alterações Ambientais	Lenea Campino

No total de linhas temáticas: 3

10.1. Identification of the Thematic Line (TL-4413-1507)

10.1.1 Reference of Thematic Line

TL-4413-1507

10.1.2.Name of the Thematic Lines in Portuguese

Saúde dos viajantes e migrantes

10.1.3 Name of the Thematic line in english

Health challenges of travelers and migrants (HCTM)

10.1.4 Principal Investigator

Sónia Maria Ferreira Dias

10.1.5 Scientific área(s)

Seleção até 4 áreas científicas em qualquer domínio científico

1- Epidemiology

2- Health care services

3- Implementation Research

4- Policy frameworks

10.2 Description of the Thematic Line

10.2.1 Description of the Thematic Lines

(7000 characters)

In an increasingly globalized world, travel and migratory flows pose challenges to public health and health care systems. Modern transportation and tourism, business travel, and legal and illegal migration contribute to the dissemination of pathogens and genetic traits, changes in lifestyle, and vulnerability to abuse and exploitation. This changes the profile of burden of disease with repercussions for the health care system, which has to adapt to different needs and has to be responsive to an ever more multicultural clientele. The importance of mobility and migration for health and health systems is increasingly recognized. The migrant health agenda is receiving greater attention in Europe, particularly in the greater Mediterranean region, as well as in Africa, the Middle-East and the Americas. The European migrant health agenda has been supported by the World Health Assembly Resolution on the Health of Migrants of 2008, the EU political commitment, which is reflected in policies and legal instruments, and several recommendations of the Council of Europe.

Population mobility and migration are dynamic processes including multiple stages (departure, border crossing, arrival, return) each of which can impact health of communities of origin, transit and destination in complex ways. Health systems are only slowly waking up to the need to become more responsive to migrant populations by establishing appropriate and accessible health services. Ideally, the needs of migrants should be incorporated into all elements of health systems, including regulation, organization, financing and planning, to ensure non-discrimination, equitable access to and quality of health care.

Infectious diseases are well recognized and of particular importance. The characteristics and time of acquisition of infections depend on exposure in the original country, during migration, and in the resettlement environment. Indeed, the globalization of infectious disease epidemiology and of disease vectors will require the corresponding development of integrated programs to anticipate and manage these risks in response to the needs of an increasingly mobile population.

More recently the problem of chronic diseases and risk profiles among mobile populations has emerged as an area of public health significance that poses operational and financial challenges for service delivery and issues related to portability of social health protection.

HCTM will develop a knowledge and information base, grounded in scientific research, that will make it possible to (i) better understand the health and health systems implications of travel and migration and (ii) inform the development of better policy-, service delivery- and clinical practice strategies to address these – including empowerment of migrant populations to promote healthy behavior and appropriate curative and preventive health care uptake. It will address health issues associated with travel and both immigration into and emigration out of Portugal.

Particular attention will be given to the translation of the evidence into more effective and efficient policy and programmatic approaches targeted towards migration-associated health problems as well as to the development and testing of culturally adapted strategies for empowerment of migrant populations.

The research will build on the work of the RG in order to obtain their contributions towards: (i) understanding the epidemiology of health problems, distribution of health risks and determinants, and health outcomes among mobile populations; (ii) improving the knowledge about health care utilization patterns of these populations and the specific challenges this creates; (iii) supporting the development of efficient health care delivery response patterns; (iv) improving policy and regulatory frameworks affecting service response capacity.

These packages will require a multidisciplinary approach, ranging from biomedical studies, epidemiological analysis, clinical and social sciences approaches, including participatory research methods. The research will build on IHMT's well-established experience with applied research and teaching in biomedical, clinical and health systems sciences. It will take advantage of its clinical and academic networks of partners (governmental and non-governmental) in Portugal as well as in countries that are both sources and destinations of cross-border migration. It will include community-based and clinical surveys and studies in Portugal as well as in countries of origin and destination.

10.3 Research groups involved in the thematic Line

10.3.1

	Referencia	Designação do Grupo
1	RG-4413-2277	Vector-Borne Diseases
2	RG-4413-2778	TB, HIV and Opportunistic Pathogens(THOP)
3	RG-4413-2779	Health Policies and Services (HPP)

Total:

10.4 Organisational Structure and Objectives of the Thematic Line for 2015/2020

10.4.1. Structure of the Thematic Line

(4000 characters)

The Thematic Line HCTM will be supported by the three research groups that will interact in an integrated and sustained way, bringing multidisciplinary background expertise as well as a cumulative vast experience of research in the target populations and different countries (Portugal, PALOP countries, and Brazil).

The TL coordinator and the team/s congregated by her/him will be responsible for integrating activities and ensure collaboration with members of RG of the center, promoting applied learning opportunities, strengthening networking and internationalization and endorsing innovative dissemination activities. Specific activities on mobile or migrant populations' health research topic will be designed and implemented by these multidisciplinary teams (RGs and national/international collaborators) that will report to the TL Coordinator. Thematic Line leadership will facilitate fieldwork in migrants' communities of origin and destination as well as NGOs and public agencies that interact with mobile and migrant populations in a multidisciplinary approach involving RGs in their areas of expertise.

10.4.2 Objectives of the Thematic Line

(4000 characters)

HCTM will develop a knowledge and information base, grounded in scientific research, to (i) better understand the health and health systems implications and challenges of increasing cross-border travel and migration (in and out of Portugal) and (ii) inform the development of better policy-, service delivery- and clinical practice strategies to address these challenges.

The main research questions are grouped in 4 packages:

- The epidemiology of migrant health: What are the size, profile and characteristics of current and anticipated health problems (including emergent, neglected and opportunistic infections as well as chronic and non-communicable disease) and health risks associated with mobile and migrant populations? What is the differential susceptibility of mobile and migrant population in/out Portugal to prevailing health risks most prevalent in the host/destination countries? What are the specific biological, physical environmental, clinical, behavioral, socio-economic, and political determinants of health status
- Health care utilization patterns and challenges: What are the current utilization pattern and profiles in Portugal and in emigration-destination countries? What are the constraints on empowerment and health literacy among migrants, and how can they be oriented in support of healthy behaviors, prevention and adequate use of health services? What are the resource and outcome implications?
- Health care delivery response patterns: what are the current response patterns? What tools and technologies can be developed for early detection, improved combinational therapeutic regimens and prevention of acquired drug resistance? What organizational models are most appropriate to respond to the health challenges of migration? What are the health system implications (access, responsiveness, diagnostic, therapeutic, case-management) of scaling up response and increasing migration?
- Policy and regulatory frameworks. Research questions include: How do the current frameworks compare to other European approaches? What evidence-based recommendations can be made for improving the responsiveness of health systems in Portugal and partner countries?

This TL will be based on the research agenda of the three groups and its members' experience and expertise. The research will focus in the following issues:

1) The study of the transnational epidemiology of diseases in migrants and mobile populations' places of origin and of destination;
2) The analyses of migrants' state of health, the specific risks they may be exposed to and the corresponding health needs;
3) The development of tools for the early detection of emergent, neglected and opportunistic infections; as well as the uptake (and non-uptake) of appropriate diagnostic and therapeutic tools;
4) The development of new (technologies for early detection and) appropriate combinational therapeutic regimens to increase effectiveness and prevent the emergency of acquired drug resistance;
5) The understanding of the profile of health service utilization of migrant populations (supply and demand side, travel clinics, conventional health services), in Portugal and overseas, as well as overcome the barriers to access and use of health services;
6) The assessment of health service performance and evaluation of quality of care for migrant populations, including understanding of the effectiveness and efficiency of emerging models of care provision;
7) The empowerment and improvement of health literacy among migrants in order to support healthy behaviors, prevention and adequate use of health services.

The research as such is complemented with a translational component, designed to transform and disseminate the findings into relevant advice and dissemination among policy, managerial, professional and beneficiary stakeholders with a view of optimizing decision-making at the clinical, community, intra and inter organizational, and system level.

10.1 Identification of the Thematic Line (TL-4413-1508)

10.1.1 Referência da Linha Temática - Reference of Thematic Line

TL-4413-1508

10.1.2 Name of the Thematic Lines in Portuguese

Doenças Emergentes e Alterações Ambientais

10.1.3 Name of the Thematic Lines in English

Emerging Disease and Environmental changes

10.1.4 Name of the principal investigator

Lenea Campino

10.1.5 Scientific área(s)

Seleção até 4 áreas científicas em qualquer domínio científico

1- Epidemiological surveillance

2- Impact of environmental (climatic and human-made) changes on infectious diseases

3- Risk maps

4- Vector and vertebrate host susceptibility

10.2 Description of the Thematic Line

10.2.1. Description of the Thematic Line *(7000 characters)*

Economic growth, population dynamics (e.g. urbanization and migration) and industrial development over the past 50 years have resulted in changes in the natural environment and agricultural systems leading to persistence, emergence and re-emergence of infectious diseases. Climate change and climate variability, in part the consequence of atmospheric pollution are also responsible for this emergence. Infectious diseases are also associated with poverty mainly in developing countries, and with zoonosis, having an economic impact resulting from fatalities amongst high-value animals. These include African countries, namely the PALOP, and South America in which IHMT researchers have previous work experience and collaborations.

Emerging infectious diseases (EID) are dominated by zoonosis (60.3%), the majority of these originate in wildlife (e.g. West Nile virus), and are increasing significantly over time. In addition, over 50% of EID are caused by bacteria (e.g. *M. tuberculosis*) or rickettsia, reflecting a large number of drug-resistant pathogens, and more than 20% are VBD (e.g. Dengue) (Jones et al. (2008), 451: 990-4). In the last two decades a series of EID caused by bacteria, virus and parasites have re-emerged causing important public health problems, some of them becoming leading causes of morbidity and mortality.

Encroachment of human settlements and agriculture on natural ecosystems results in expansion of ecotones (transition zones between adjacent ecological systems), where species assemblages from different habitats get in contact. This provides new opportunities for pathogen spillover, genetic diversification and adaptation. Associations between disease emergence and ecotones

have been suggested for several diseases. Moreover, other factors, including economic development and land use, changes in human demographics and behavior and international travel, contribute to the emergence and re-emergence of infectious diseases. Almost all of these factors reflect in some measure the incursion of humans on the environment and on the microbial species that inhabit it, both physical and social. For example, increased urbanization has been associated with the geographic expansion of the mosquito vector *Aedes aegypti* and, consequently, of epidemic Dengue.

The recent technological advances in the area of genomics and proteomics, with which a pathogen can be fully sequenced within a matter of days, changed the paradigm of microbiology research. This capability is becoming critical to elucidate virulence factors and pathogenic mechanisms, as well as immune-evasion factors, receptors, and the immunodominant antigens to develop vaccines and therapeutic tools. The ability to sequence and annotate microbes now has taken its place at the forefront of how we deal with emerging and re-emerging infections.

This thematic line will contribute to biomedical research on infectious diseases, whether of zoonotic origin or not, and implementation of public and animal health measures, a principle consecrated in the “One Health Concept”. This will be attained with the use of technological advances, in particular, advances in genomics, proteomics and molecular epidemiology. This will help us to better understand mechanisms of pathogen virulence, transmission patterns, host immunity, drug resistance and further identification of new molecular targets useful for the development of diagnostic tools and new therapeutic approaches. In addition, population genetics and epidemiological surveillance will also be addressed. Thus, we will also contribute to the “One Health“ approach in clarifying the epidemiology of previously neglected and emerging zoonotic diseases which are increasingly being diagnosed either in European-Portugal or African-PALOP countries, and raise concern because of the impact on public health and economy of human and animal morbidity and mortality.

10.3 Research groups involved in the thematic line

10.3.1.

	Referencia	Designação do Grupo
1	RG-4413-2277	Vector-Borne Diseases
2	RG-4413-2778	TB, HIV and Opportunistic Pathogens(THOP)
3	RG-4413-2779	Health Policies and Services (HPP)

Total:

10.4 Organisational Structure and Objectives of the Thematic Line for 2015/2020

10.4.1 Structure of the Thematic Line

4000 caracteres (4000 characters)

The Thematic line “Emerging Diseases and Environmental Changes” (EDEC) will be supported by the three RG that will interact in an integrated and sustained way.

For each research topic, a framework involving basic research, multidisciplinary teams composed by elements of each RG will secure translational outcome and implementation at the health system level. The thematic line coordinator will ensure interaction between RG (and external

collaborators) by means of regular meetings, scientific activities to promote international collaboration and advocacy at national and international level. Progress reports will be elaborated and presented to the scientific commission of the Center.

There will be three main areas of activity to be promote by the TL Coordinator: i) epidemiological studies; ii) tools development (diagnostics, treatment, control); iii) risk maps, subjects that encompass the objectives of the RG. TL can act across the RG activities capturing the outcomes of RG helping in validating the original goals of the studies, that can serve as a basis for further work stemming from the research findings, thus bridging knowledge creation and its translation. For each specific activity multidisciplinary teams will design and developed R&D activities and the plans to achieve them.

10.4.2 Objectives of the Thematic Line

4000 caracteres (4000 characters)

The EDEC TL will address questions such as:

1. What is the impact of environmental and climatic changes on the emergency of infectious diseases?
2. What is the impact of climatic changes in the geographic distribution of Vector-Borne diseases?
3. What is the effect of encroachment of humans and wild settlements, due to social activities, on emerging diseases outbreaks?
4. What is the epidemiology of previously neglected and emerging zoonotic diseases
5. Which are the molecular mechanisms responsible for the development of resistant strains (e.g. in tuberculosis)?
6. What is the risk of introduction of exotic species (vectors/pathogens)?
7. Which are the implications of new strains and hybrid pathogens in the epidemiology of diseases?
8. Which are the effects of immunosuppressive conditions in the susceptibility to pathogens and their implications on social and health systems?
9. Which are the vectorial factors responsible for permissiveness to pathogens?
10. What is the role of population genetics in susceptibility and/or resistance of vectors to insecticides (e.g. Dengue´s vector)?

As for the other thematic line, this will also be based on the research of the three research groups, past and current work conducted by these groups at national and international level and also through members' expertise.

The research under this thematic line will focus on several issues:

1) The epidemiology dynamics of emerging infectious diseases (EID) addressed under the research groups, as consequence of environmental changes and/or climatic changes;

2) Epidemiological surveillance of VBD, whether zoonotic or not, in order to evaluate the dynamics, abundance and adaptation of proven and permissive vectors and or reservoirs, and the risk of introduction of exotic species (pathogens / vectors/reservoirs) due to climatic and human socio-economic changes and migrant fluxes;

3) Development of easy-to-perform diagnostic tests based on nanotechnology for the early detection of pathogens and to determine their drug susceptibility;

5) To build and /or to update risk maps concerning the presence and dissemination of VBD in southern Europe.

The interaction of this and the other thematic line, in conjunction with the researchers which will be integrated in the GHTM R&D Unit will contribute for a better understanding on pathogens and ways to control them, thus contributing for limiting the prevalence of infectious and opportunistic diseases and limiting the emergence of multi-drug resistant species/strains. In a broader sense, strategies for health improvement will be set, both for local populations and mobile populations.