Summary report on research accreditation

I. General information

Name of organization	**Institute of Phthisiopneumology "Chiril Draganiuc"**
Organization type (*to underline*)	Research institute Higher education institution Ministerial research institute
Research direction (s) of organization	Epidemiology, prophylaxis, diagnosis, treatment and medico-social recovery of patients with tuberculosis and nonspecific pulmonary diseases.
Correlation with strategic research direction (s) of activity in the field of science and innovation for 2013-2020	3. Health and Biomedicine
Evaluated period	2010-2014
Web of organization	www.ifp.md

II. Research capacity (annual average for evaluated period)

Total number of employees	**66.2**					
Number of scientific researchers	**48.6**					
Number of researchers who possess honorific titles, scientific degrees, scientific and scientific-didactical titles	ASM full members -	ASM corresp. members -	Professor **2.8**	Associated professor **21.4**	Dr.hab. **7.8**	Dr. (PhD) **20.4**
Number of researchers involved in international projects	European Commission programs **3.2**	United Nations programs and funds -	Bilateral programs financed from the national budget **2.4**	Others **15.4**		
Number of young researchers (under 35 years old)	PhD students **1.6**		Others **8.8**			
Financial resources - revenues (thousand MDL)	Public budget **2975.0**		Special means **676.5**			
Categories of special means (thousand MDL)	National **603.2**		International **73.3**			
Distribution of expenditures (thousand MDL)	Salary **2591.2**	Procurement of scientific equipment **707.1**	Traveling for scientific purposes (travel, accommodation, per-diems, etc.) **7.6**	Other **345.6**		

List of 3 basic research methods, equipments, technologies (per accredited field)	1. Equipment which enables the rapid diagnosis of tuberculosis by molecular-genetic methods and identification of Nontuberculous mycobacteria by pyrosequencing: GenoType MTBDRplus, GenoType MTBDR*sl*, Xpert® MTB/RIF, GenoType MTBDRsl, PyroMark Q96 ID instrument, PyroMark Q96 Vacuum Workstation; 2. Equipment for determining susceptibility to antituberculosis drugs of line I and II on liquid media: BACTEC ™ MGIT ™ 960. 3. Equipment for exploring the upper and lower respiratory tract, functional exploration complex respiratory: videobronhoscop, bodyplethysmograph.
List of provided scientific services	1. *M. tuberculosis* isolation and determination of resistance to anti-TB drugs of I and II line by using the classical method and liquid method; 2. Identification of *M. tuberculosis* directly from clinical specimens microscopic positive and negative and determination of resistance to anti-TB drugs of I and II line by molecular-genetic methods; 3. Bodyplethysmografy, Spirometry; 4. Bronchoscopy; 5. Immunological and histological examinations.
List of editorial activities	Co-founder of the journal "Buletinul Academiei de Ştiinţe a Republicii Moldova. Ştiinţe medicale", ISSN 1857-0011, category B, http://www.bsl.asm.ms

III. Distribution of the number of research projects and themes during the evaluated period

ASM institutional projects	2010 **6**	2011 **7**	2012 **7**	2013 **7**	2014 **7**
ASM projects in the frame of State Programs	2010 -	2011 -	2012 -	2013 -	2014 -
ASM technological transfer projects	2010 -	2011 -	2012 -	2013 -	2014 -
ASM projects for equipment procurement	2010 -	2011 -	2012 **1**	2013 -	2014 -
ASM projects for young researches	2010 -	2011 -	2012 **1**	2013 **1**	2014 -
ASM projects in the frame of bilateral programs	2010 **1**	2011 **1**	2012 **1**	2013 -	2014 -
International projects/grants	2010 **2**	2011 **2**	2012 **3**	2013 **4**	2014 **3**
List of 3 representative international projects/grants	**1. Program - Capacities** / Module III - Bilateral cooperation ROMANIA - MOLDOVA. "Preparation and physicochemical characterization of new tioureide of 2- (2-phenethyl) benzoic acid and the corresponding metal complexes as potential antimicrobial agents." Execution period: 01.06.2010 - 30.11.2012 **2. U01 AI077957-01. NIAID RFA-AI-08-001**"Rapid tests for assessing resistance and screening of tuberculosis with extensive resistance". NIAID				

	Global Consortium for Drug Resistant TB Diagnostics - GCDD. University of California, San Diego. The term of execution: 01/10 / 2009-31 / 06/2014 **3. FP7-HEALTH-2007-B.** "The clinical trial of drug-resistant TB in Europe." WHO Collaborating Centre for Tuberculosis and respiratory diseases, foundation "Salvatore Maugeri" Research Institute of Trade, Italy. The term of execution: 01/01 / 2009-31 / 12/2013.				
Research contracts	2010 **13**	2011 **13**	2012 **14**	2013 **13**	2014 **10**
List of 3 representative research contracts	1. Two scientific contracts concluded in 2013 with the State University of Medicine and Pharmacy "N. Testemiţanu" for immunological services. 2. Scientific Contract concluded with the Institute of Chemistry of the AMS from 22/05/2013 for microbiological services. 3. Scientific Contract concluded with the State University of Medicine and Pharmacy "N. Testemiţanu" on 02.01.2014 for immunological services.				

IV. Scientific publications

Total number of publications abroad	Books -	Chapters in books -	Journal papers **4**
Total number of publications in ISI journals and books	Books -	Chapters in books -	Journal papers **8**
Total number of publications in the country	Books **1**	Chapters in books -	Journal papers **102**
Total number of conference abstracts	International abroad **157**	International in the country **26**	National **21**
List of 5 representative publications (per accredited field)	1. CRUDU, V.; STRATAN, E.; ROMANCENCO, E.; MORARU, N.; TURCAN, N.; ALLERHEILIGEN, V.; HILLEMANN, A.; First Evaluation of an Improved Assay for Molecular Genetic Detection of Tuberculosis as Well as Rifampin and Isoniazid Resistances. *Journal of Clinical Microbiology*. 2012, v. 50, nr. 4, 1264–1269. ISSN: 0095-1137. **IF: 4.153.** 2. LANGE C., ABUBAKAR I., ALFFENAAR J.-W.C., BOTHAMLEY G., CAMINERO J. A., CHANG K.-CH., CODECASA L., A CORREIA A., CRUDU V., DAVIES P., DEDICOAT M., DROBNIEWSKI F., DUARTE R., EHLERS C., et all. Management of patients with multidrug resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. *Eur Respir J*. 2014 Jul;44(1):23-63. ISSN: 0903-1936**. (IF:7.125).** 3. JENKINS, H.E.; CRUDU, V.; SOLTAN, V.; CIOBANU, A.; DOMENTE, L.; COHEN, T. High risk and rapid appearance of multidrug resistance during tuberculosis treatment in Moldova. *Eur Respir J.*, 2014, 1385-1390. ISSN: 0903-1936. **(IF:** 7.**125).** 4. RODWELL, T.C.; VALAFAR, F.; DOUGLAS, J.; QIAN, L.; GARFEIN, R.S.; CHAWLA, A.; TORRES J.; ZADOROZHNY V.;		

	SOO KIM M.; HOSHIDE M.; CATANZARO D.; JACKSON L.; LIN, G.; DESMOND, E.; RODRIGUES, C.; EISENACH, K.; VICTOR, T.C.; ISMAIL, N.; CRUDU, V.; GLE, M.T.; CATANZARO, A. Predicting Extensively Drug-resistant Tuberculosis (XDR-TB) Phenotypes with Genetic Mutations. *Journal of Clinical Microbiology*, 2014, 52(3):781-9. ISSN: 0095-1137, **(IF: 4.232).** 5. VARZARI, A.; BRUCH, K.; DEYNEKO, I.V.; CHAN, A.; EPPLEN, J.T.; HOFFJAN, S. Analysis of polymorphisms in RIG-I-like receptor genes in German multiple sclerosis patients. *J Neuroimmunol*, 277(1-2), 140–144. ISSN: 0165-5728**. (IF: 3.062).** 6. TROLLIP, A.P.; MOORE, D.; CORONEL, J.; CAVIEDES, L.; KLAGES, S.; VICTOR, T.; ROMANCENCO E.; CRUDU, V.; AJBANI, K.; VINEET, V.P.; RODRIGUES, C.; JACKSON, R.L.; EISENACH, K.;, GARFEIN, R.S.; RODWELL, T.C.; DESMOND. E.; GROESSL, E.J.; GANIATS, T.G.; CATANZARO, A. Second-line drug susceptibility breakpoints for Mycobacterium tuberculosis using the MODS assay. *Int J Tuberc Lung Dis*, 2014, Feb,18(2):227-32. **ISSN:** 1027-3719. **(IF:2.756).**
List of 5 citations	1. CRUDU, V.; STRATAN, E.; ROMANCENCO, E.; MORARU, N.; TURCAN, N.; ALLERHEILIGEN, V.; HILLEMANN, A.; First Evaluation of an Improved Assay for Molecular Genetic Detection of Tuberculosis as Well as Rifampin and Isoniazid Resistances. *Journal of Clinical Microbiology*. 2012, v. 50, nr. 4, 1264–1269. ISSN: 0095-1137. **IF: 4.153.** 67 citations 2. LANGE C., ABUBAKAR I., ALFFENAAR J.-W.C., BOTHAMLEY G., CAMINERO J. A., CHANG K.-CH., CODECASA L., A CORREIA A., CRUDU V., DAVIES P., DEDICOAT M., DROBNIEWSKI F., DUARTE R., EHLERS C., et all. Management of patients with multidrug resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. *Eur Respir J*. 2014 Jul;44(1):23-63. ISSN: 0903-1936**. (IF:7.125).** 67 citations 3. VARZARI, A.; BRUCH, K.; DEYNEKO, I.V.; CHAN, A.; EPPLEN, J.T.; HOFFJAN, S. Analysis of polymorphisms in RIG-I-like receptor genes in German multiple sclerosis patients. *J Neuroimmunol*, 277(1-2), 140–144. ISSN: 0165-5728**. (IF: 3.062).** 3 citations. 4. TROLLIP, A.P.; MOORE, D.; CORONEL, J.; CAVIEDES, L.; KLAGES, S.; VICTOR, T.; ROMANCENCO E.; CRUDU, V.; AJBANI, K.; VINEET, V.P.; RODRIGUES, C.; JACKSON, R.L.; EISENACH, K.;, GARFEIN, R.S.; RODWELL, T.C.; DESMOND. E.; GROESSL, E.J.; GANIATS, T.G.; CATANZARO, A. Second-line drug susceptibility breakpoints for Mycobacterium tuberculosis using the MODS assay. *Int J Tuberc Lung Dis*, 2014, Feb,18(2):227-32. **ISSN:** 1027-3719. **(IF:2.756).** 10 citations. 5. MARTINIUC, C.; BRANISHTE, T. The use of beta-blocker Nebivilol

	in patients with chronic pulmonary disease in association with arterial hypertension. *Revistă medico-chirurgicală.* Iasi, Romania. 2012, 116(1), 218-221. ISSN 0048-7848. 6 citations.

V. Innovation outputs

Total number of patents	Registered in the country **3**	Registered abroad -	Implemented **3**
Total number of new developed methods and technologies	Registered **8**	Non-registered -	Implemented **8**
Total number of new scientific products	Registered **15**	Non-registered -	Implemented **15**
List of 5 representative innovation outputs (per accredited field)	1. A method for preventing superinfection of samples during testing the susceptibility of *M. tuberculosis*. 2. A method for assessing the leukocyte index of allergy. 3. The new version of the molecular genetic method for the detection of tuberculosis and rifampicin and isoniazid resistance (Line Probe Assay Genotype MTBDRPlus Ver2.0). 4. Criteria for determining disability at patients with chronic bronchial disease. 5. Improvement of classical microbiological method of isolating M. tuberculosis in nutrient liquid medium (MODS).		

VI. Other outputs

Total number of scientific outputs for central and local authorities (draft of law, strategies etc.)	**2**		
Total number of scientific outputs for educational institutions	Handbooks for high education -	Handbooks for pre-university institutions -	Number of researchers – supervisors of license and master theses **4**

VII. Major scientific and innovation achievements

Short description of main scientific results and their confirmation (by awards, citations, development of international projects etc.)	1. A diagnostic algorithm was developed by applying rapid tests for assessing resistance and screening of tuberculosis with extensive resistance. The results were appreciated by the Certificate of Honor from the Global Consortium for Drug resistant TB Diagnostics, USA, 14/03/2014. 2. The scientific results contributed to the development of national TB control programs 2011-2015 and 2016-2020 (2011-2015 - approved by Government Decision no. 1171 of 21.12.2010, 31.12.2010 Published in the Monitorul Oficial no. 259 -263, art Nr: 1316). 3. For the first time, the immunological reactivity and the preimmune resistance in pulmonary tuberculosis associated with *Toxocara canis* was studied. 4. It was optimized the tuberculosis treatment of pulmonary MDR TB by

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<tr><td></td><td colspan="5">associating surgical methods, which resulted in minimal postoperative complications (4.4%) and debacilation in 100% cases. By surgery treatment combined with DOTS, plus regimens, yielded high cure rate (65.2%) of patients with MDR tuberculosis. The persistence of high activity of the inflammatory tuberculosis process is a direct indication for surgical treatment of limited tuberculosis lesions.
5. For the first time there were determined the clinical and microbiological aspects of pulmonary tuberculosis in cases of abandoning tuberculosis treatment.
6. There were determined the causes that contribute to the formation of contingents of patients with chronic forms of tuberculosis and proposed actions to prevent the development of chronic forms of tuberculosis.
7. For the first time in Moldova there were studied the dissemination, forming peculiarities and the clinical manifestations of pulmonary hypertension in patients with chronic obstructive pulmonary disease (COPD) and pulmonary hypertension correlation with the severity of hypoxemia, endothelial dysfunction, dysfunction of pulmonary ventilation and the diffusion capacity of pulmons, COPD stages. For the first time it was developed the classification of endoscopic bronchial signs, reflecting the peculiarities of the clinical course of COPD. There were optimized the methods of diagnosis and the regimens of the pharmacotherapy COPD complicated with pulmonary hypertension, intended for application in the phthisiopneumologist’s activity, family doctor and the functionalist.
8. For the first time, there were studied the secondary cases of tuberculosis outbreak, including specificities of development, clinical form, duration of tuberculosis development and the resistance spectrum of *M. tuberculosis*. Obtained data will contribute to the improvement of the Information System of Monitoring and Evaluation of Tuberculosis and will conduct to identifying and monitoring the outbreak of tuberculosis, thereby improving the epidemiological situation of tuberculosis.</td></tr>
<tr><td>Number of researchers invited as speakers at international conferences</td><td>2010
5</td><td>2011
3</td><td>2012
10</td><td>2013
8</td><td>2014
8</td></tr>
<tr><td>Short description of technological transfer and innovation results and their certification by implementation</td><td colspan="5">1. The criteria for determining disability in patients with chronic bronchial disease were used in the development of normative acts for Vitality Medical Expertise Commission's work in order to establish the percentage of working capacity of patients with chronic bronchial disease (certified by implementing Order no. 12/70 of 28.01.2013 on the approval of criteria for determining disability and work capacity of adults).
2. Computerized photoplethysmography for estimating the endothelial dysfunction in patients with chronic obstructive pulmonary disease was implemented in practice. The surveillance in dynamics of rigidity and reflection indices in patients with chronic obstructive pulmonary disease allows us estimating the effectiveness of treatment, condition and prognosis of vascular remodeling processes and the prognostic of the basic disease.
3. Complex methods of treatment of tuberculosis were implemented,</td></tr>
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<tr><td></td><td colspan="5">which contributed to the increase of the sensitive tuberculosis treatment success rate from 57% in 2010 to 78% in 2014 and multidrugresistant tuberculosis - from 49.3% in 2010 to 58% in 2013.
4. It was developed the curative technology of exudative pleural tuberculosis that includes administering corticosteroids and chemotherapy endolymphatic regional preparations, osmotic stimulation of the lymphatic drain. The proposed technological alternatives accelerate the stopping of exudation in the pleural cavity.
5. There were improved the classical microbiological methods of isolating of M. tuberculosis in liquid nutritive media - Microscopic Observation Drug Susceptibility assay (MODS). An assay based on detection of M. tuberculosis in a standardized liquid medium with concomitent evaluation of drug sensitivity. The average time of detection of MDR-TB is 7-12 days, which allows confirming quickly the diagnosis. The implementation of rapid isolation of liquid media by the use of MODS, helped to reduce the terms of delivery averaged 2-2.5 times and increased the significance of positivity percentage cultures to 25-30% by the classical method 45 - 50% MODS method.
6. It was developed in common with Hain Lifescience company, Nehren from Germany, a new version of molecular-genetic method for the detection of tuberculosis and rifampicin and isoniazid resistance (Line Probe Assay Genotype MTBDRPlus Ver2.0). The elaborated method allows the fast detection by genetic-molecular methods of M. tuberculosis from negative microscopic sputum and determines the resistance to Rifampicin and Isoniazid.
7. There were developed research methods of adverse reactions in patients with asthma and pulmonary tuberculosis: 1) obtaining information based on data leukocyte formula about the adaptive immune reactions of the body state and 2) method for assessing allergy leukocyte index, which facilitates the selection of patients with preclinical allergic condition for detailed examination.</td></tr>
<tr><td>Number of defended dr./dr. hab. theses per year</td><td>2010
-</td><td>2011
-</td><td>2012
-</td><td>2013
-</td><td>2014
-</td></tr>
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VIII. Present/further involvement in the Horizon 2020 (FP7)

The project "An evaluation study for the performance of the MTB-DNA Blood for the DNA-isolation from whole blood and detection of MTB by FluoroType MTB tests on HIV positive patients with suspected TB" was applied to a Horizon 2020 call (not selected).

IX. Accredited research field and its evaluation by the National Council for Accreditation and Attestation of the Republic of Moldova (very good/good/ satisfactory)

Phthisiopneumology - good

X. Category (A/B/C) attributed by the National Council for Accreditation and Attestation of the Republic of Moldova to the organization

X. Institutional development actions planned for the next 5 years (maximum ½ page).

- To optimize the rapid diagnosis of resistant tuberculosis by improving the methods of susceptibility testing.
- Complex multifactorial study of epidemiological situation in territories with different levels of TB incidence and proposing measures to improve the epidemiological situation.
- To determine the diagnostic and management features in tuberculosis with extensive resistance (XDR and XXDR).
- To study the immune peculiarities of patients with pulmonary tuberculosis with primary and secondary resistance.
- To study the medical and social, microbiological and immunogenetic factors, involved in the development of tuberculosis.
- To improve and adjust to current epidemiological conditions new treatment regimens for the resistant tuberculosis.
- To optimize the diagnosis and the treatment of nonspecific pulmonary diseases.
- To expand scientific collaboration relations by establishing partnerships with national and international scientific research centers.