WHO Collaborating Centre
Prevention and treatment of Human Echinococcosis

ANNUAL REPORT – May 2015 to May 2016
1. Please briefly describe the progress made in the implementation of your agreed workplan as WHO collaborating centre during the past 12 months (or the reporting period listed above). Please report on how each work plan activity was implemented, if any outputs have been delivered, if any results have been achieved and if any difficulties have been encountered during this time. If an activity has previously been completed, has not started yet, or been placed on hold, please indicate this.

**Activity 1:**
**Development of imaging methods and procedures, molecular and immunological tools for improvement of echinococcosis diagnosis and follow-up**

*Responsible persons: Oleg Blagosklonov and Frederic Grenouillet*

- **To develop imaging methods in order to improve the detection, the treatment and the follow-up of human echinococcosis**

The development and validation of accurate animal model for preclinical functional imaging is still the main goal. The tests are in progress in collaboration with Swiss colleagues to that end (Bern University - Parasitology Institute, University hospital of Lausanne – Department of Nuclear Medicine). New partners joined the workgroup; and French-Tunisian project on the development of radiotracers of CE/AE for nuclear medicine was submitted for funding (Utique 2017 program). The harmonization of imaging procedures was identified as an issue during the EuroEchino workshop (Besançon, April 2015). International group of experts was formed to prepare the recommendations for the interpretation of computed tomography (CT) and magnetic resonance (MR) images.

- **To develop new molecular tools to detect infected patients and to assess immune response in patients**

The development of new biomarkers for diagnosis and follow-up of AE has been continued (Echino-Vista Project (ongoing hospital clinical research project: 2012-2016); unfortunately, the joint project between Chinese NSFC (National Natural Science Foundation of China) and French National Research Agency could not be funded, despite excellent scientific appreciation (project submitted for funding: 2015-2018), but collaboration with Bern University - Parasitology Institute/ Pr B Gottstein, is always doing well and fruitful (cf. common publication below). Inclusion of new patients in EchinoVista Project was just closed in June 2016 (52 patients included). Long term follow-up of this cohort is actually ongoing (4 year follow-up, will be completed in May 2018).

Using a label free mass spectrometry proteomics approach coupled to immunopurification of vesicular fluid proteins, we have identified seven proteins which seem promising as biomarkers for evaluation of ABZ response of the patients. Further experiments using recombinant proteins for ELISA analysis of a larger panel of patients will permit us to evaluate discriminant power of these proteins; sera from patients of the French EchinoVista cohort, as well as sera from Chinese and Swiss cohort will be used for assessment of this new tool for treatment monitoring.
We also investigated the interaction between *Echinococcus multilocularis* vesicular fluid (*Em*-VF) and human cells from healthy blood donors. Exposure to *Em*-VF had bearing on both differentiation and maturation of MoDendritic cells (DC), as a decrease in the expression of co-stimulatory molecules was observed. PBMC exposed simultaneously to *Em*-VF and LPS induced a significant increase of TGFβ (p < 0.05, Wilcoxon signed-rank test). Further experiments showed that TGFβ production was lymphocyte-dependent. We recently showed that NK cells stimulated with *Em*-VF had a significant decrease in proliferation and activation (p < 0.05, Wilcoxon signed-rank test).

PD-1 is a cell-surface receptor expressed on T cells that regulates the adaptive immune response. Engagement of PD-1 with PD-L1 leads to the inhibition of CD3-mediated T cell proliferation and cytokine production. It has been hypothesized that the PD-1/PD-L1 pathway may be involved in the immunity escape of *E. multilocularis*. Based on this hypothesis, and in collaboration with our colleagues of Bern Institute (Pr B Gottstein, J Wang), we are performing experiments where mice are infected with *E. multilocularis* eggs orally and treated with PD-1 to block AE development; results will be confronted to those obtained with *E. multilocularis*-infected mice knock-out for the PD-1/PD-L1 pathway. These innovative experiments are still ongoing.

Collaboration with Algeria allowed to perform a genotyping study of CE cysts from this country (humans, animals cysts), which was completed and just published in *Parasitol Research* (Zait et al. 2016). It highlighted that *E. granulosus* sensu stricto, genotype G1, remain the most prevalent genotype in Algeria and confirmed that *E. canadensis* G6 was identified in South Algeria, in humans and camels cases.

- **Organization of an external quality assessment (EQA) in laboratories involved in *Echinococcus* serology (*E. multilocularis* and *E. granulosus*).**

  Last EQA program was organized in 2014 and involved twenty-six laboratories, located in France (n=21), Switzerland (n=3), Germany (n=1), and Czech Republic (n=1). It was not renewed in 2015, due to moving of parasitology lab of Besançon University Hospital to a new building and restructuring of some of its activities with other labs. Following renewal of our accreditation to ISO 15189 standard, for serological analysis, we plan to organize a new EQA program for *Echinococcus* serology in autumn 2016 at the European and Chinese level. Discussion with EQA specialized organization (Probioqal, CTCB) is also ongoing, to support logistical concerns of such program.

  Similarly, few European labs are able to monitor albendazole sulfoxide (ABZ-SO) in blood samples and no EQA program for this measurement actually exists. Thus, an Inter Laboratory Comparison (ILC) program focused on ABZ-SO measurement is currently discussed between labs from France, Switzerland and Germany.

  - **To perform and to develop pharmalogical monitoring of albendazole treatment**
    **Study of albendazole concentration in parasitic and liver tissue**

    We conducted a pilot study (2008-2013) to validate pre-analytical conditions required for albendazole sulfoxide (ABZ-SO) determination in per-operative specimens, at surgery. It allowed us to measure ABZ-
SO in specimens from thirteen patients with AE liver lesions without involvement of neighboring organs or metastasis. ABZ-SO was detectable in AE lesion from 12 out of 13 patients. ABZ-SO concentrations were significantly higher in AE lesion tissue than in non-infected liver (p=0.02; Wilcoxon test). These results were confirmed by the analysis in 2014-2015 of 44 new operatives specimens, from 11 patients included in the EchinoVista study. The manuscript of the paper on this study is currently in the process of writing.

**Articles**


**Communications**


**Invited lectures**

Laurence Millon - IV International Conference on Analytical Proteomics, - Lisbonne 7-9 sept 2015. Identification of immunoreactive microbial proteins in the field of allergic and parasitic diseases, and application for serodiagnosis

Laurence Millon - XXVIth World congress on Echinococcosis– Bucharest 1-3 Oct 2015. Advances in immunological diagnosis and follow-up of Alveolar Echinococcosis
Activity 2:  
Implementation of clinical studies  
*Responsible persons: Carine Richou and Bruno Heyd*

- To elaborate and implement clinical studies

**Prospective follow-up of patients with AE in clinical reference centres in France and China: Echino-VISTA project.**

The objectives of this prospective multicenter study have been already described in a previous annual report. The study started in June 2012 and involved 6 clinical centres from Eastern France. The expected number of inclusions (50 patients) has been exceeded, with 54 AE patients included (32 followed in Besançon clinical centre); among them, 19 were in the surgical group and 35 in the non-surgical group. The same follow-up is conducted in Urumqi, China, with a similar protocol. The subsequent clinical, biological and radiological courses of these patients through June 2016 (end of follow-up) will be analyzed.

**Long term-outcome in inoperable alveolar echinococcosis patients under benzimidazole therapy.**

We assessed the long term outcome of 23 patients followed in Besançon with non-resectable AE under benzimidazole therapy. We evaluated the relationship between clinical outcome and specific serology and 18F-FDG-PET. This work has not been submitted yet because a new standardized commercialized kit for serology using the Em18 antigen will be soon available. The results obtained with this serology will be compared to those obtained with the serology using Em2+ antigens.

**Interventional endoscopy survey**

This retrospective European study focused on the usefulness of endoscopic stenting of the biliary ducts for AE with biliary obstruction. This work is now completed and has been presented at the ESCMID training course on parasitic zoonoses in Pavia in May 2015. Doctor Sylvain AMBREGNA, hepatogastroenterologist at Besançon University Hospital, presented his MD Thesis on this work on Aug 2015. The corresponding scientific paper is at the end of the preparation step and will be submitted soon.

**The XUUB study: Xining-Ulm-Urumqi-Besançon study**

The aim of this study is to compare Chinese and European patients with AE at diagnosis, to compare Chinese and European therapeutic strategies after diagnosis and staging. Imaging (CT, MRI and PET) will be reviewed in terms of differential diagnosis and treatment indication and outcome. A new unified international staging system of AE could be proposed and then endorsed by WHO if possible. A meeting will be held in China on June 24-26, 2016, including clinicians, radiologists and biologists from Besançon, Ulm, Xining and Urumqi to work on this project. For this purpose, we retrieved 127AE patients followed in Besançon diagnosed between 2003 and 2015. The following data have been recorded: gender, age at diagnosis, circumstances of the diagnosis, PNM classification, imaging, treatment (medical, surgical), and type of surgical treatment (curative, palliative...). A detailed re-assessment of these cases and similar cases recruited in the other 3 centres will be performed.
**Articles**


**Communications**


Activity 3:  
**Epidemiological survey of human cases, studies on human exposure, on wildlife and domestic animals.**  
*Responsible persons: Jenny Knapp, Francis Raoul & Patrick Giraudoux*

- To help organize and coordinate national, continental and worldwide eco-epidemiological surveys of human cases

**From Franchechino to the EurEchino Database**

The national reference center records all the new cases of AE for epidemiological and medical data. Recently the data were transferred to a database management system using the CleanWEB system, an integrated solution for the electronic management of clinical trials, as a user-friendly interface. Data from AE patients are now recorded with more security, traceability and the database can be connected to other systems in an interoperable setup. In order to use our experience in AE data collection, an extension of this new system was proposed to colleagues of other European countries who collect AE cases (EurEchino Database). This system based on the French database was available for European partners in March 2016. This system will provide homogenization of the data collected in Europe on AE cases and could help develop new clinical and research studies. The possibility of adapting the system for the collection of Chinese AE cases is currently under discussion, and will be evoked in June 2016 at the AE International workshop in Xining.

- To strengthen links between studies on wildlife, domestic animals and human exposure

**Transmission ecology of *E. multilocularis* in China and central Asia.**

A team including members of the WHO collaborating center, the Lanzhou Veterinary Research Institute of the Chinese Academy of Agricultural Sciences (LVRI), and the Lanzhou University joined in Zhang and Min counties, Gansu, China from May 13 to 20, to assess dog contamination in an historical hotspot. 257 dog faeces were collected in 26 villages between 2300 and 2700 m of altitude [http://gdri-ehede.univ-fcomte.fr/spip.php?article27#2015](http://gdri-ehede.univ-fcomte.fr/spip.php?article27#2015). Samples were pre-processed during an internship of Li ShuangNan (LVRI) at the Chrono-environment lab (WHO CC, Besançon) ([http://gdri-ehede.univ-fcomte.fr/spip.php?article46](http://gdri-ehede.univ-fcomte.fr/spip.php?article46)).

The feeding ecology of *E. multilocularis* definitive hosts in Kyrgyzstan and Gansu province (China) was explored within a Master internship (Justine Mariotte). The diet of dogs and foxes was investigated using a DNA-metabarcoding approach that allowed identification of prey items DNA extracted from faeces collected in the field (foxes) or from dog owners at a fine taxonomical resolution (species level in most cases). In parallel, *E. multilocularis* diagnosis was done using qPCR. Preliminary results suggest that: (i) *E. multilocularis* was not detected in dogs in Gansu whereas they predate small mammals; (ii) in Kyrgyzstan, *E. multilocularis* prevalence in dogs and foxes significantly vary among villages and areas, respectively; (iii) higher *E. multilocularis* prevalence in dogs is associated with higher number of species among the predated small mammals.
Assistance has been provided to the Key Lab of Fundamental Medical Research on Echinococcosis and first teaching hospital of Urumqi, Xinjiang, China. One research technician benefited from a 2 month internship in the Chrono-environment lab (WHO CC, Besançon) to train on epidemiological methods applied to *E. multilocularis*/*E. granulosus* transmission ([http://gdri-ehede.univ-fcomte.fr/spip.php?article44](http://gdri-ehede.univ-fcomte.fr/spip.php?article44)).

**Original/review/opinion articles.**

Articles were coauthored with foreign partners about *E. multilocularis* transmission in Kyrgyzstan (Afonso et al. 2015), landscape and prey/predator relationships shaping Em transmission (Liccioli et al. 2015), a new *E. multilocularis* focus discovered in Gansu (Han et al. 2015), the link between hosts trophic ecology and behavior and the transmission of *E. multilocularis* in wildlife and domestic definitive hosts (Raoul et al. 2015, Baudrot et al. 2016, 2016a), the landscape epidemiology of Echinococcoses (Cadavid Restrepo et al. 2016) and remote sensing methods to describe intermediate host distribution (Marston et al. 2016)

**Sabbatical of Dr. Alessandro Massolo at UFC.**

Dr. A. Massolo, from the Dept. of Ecosystem and Public Health, Faculty of Veterinary Medicine, Univ. of Calgary (Canada), spent a 6 month sabbatical at Chrono-environnement research unit. He reinforced existing collaborations (see Liccioli et al 2015) and implemented new ones around the following research topics: (i) the interplay of toxicant and immunity in the wild: transmission of *E. multilocularis* mediated by toxicants in meso-predators; (ii) retrospective study of alveolar echinococcosis in Alberta, Canada, (iii) modelling the significance of early detection of parasitic DNA in livers of intermediate hosts, (iv) linking processes, properties and patterns across space-time scales for trophically transmitted parasites, (v) parasitic alteration of predator – prey relation in the *E. multilocularis* system. Also, he gave lab staff and students several seminars and courses about the transmission ecology of *E. multilocularis* in the urban settings of Canada.

**Detection of *E. multilocularis* in carnivore faeces : development of a copro-qPCR protocol**

The contamination by the parasite *E. multilocularis* is often described to be due to direct or indirect contact with red foxes, harbouring the adult worms. However domestic animals such as dogs and cats could play an important role in the transmission even if low prevalences are often reported in these animals. Molecular tools were developed in order to quantify the parasite in the carnivore faeces, combined to a host faecal PCR test, to confirm the morphological description. A system of PCR inhibitor control was added to this kit to assess the presence of disrupting elements in PCR and to have a quality control of the results. In total in the kit, faeces from dog, cat, red foxes, badger and stone marten can be assigned, together with *E. multilocularis* quantification and confirmation, while ensuring PCR inhibitors control. This study was published in Applied and Environmental Microbiology in May 2016 (Knapp et al., 2016). These tools permit epidemiologists and ecologiststo better characterize the risk of parasite transmission from the wild and domestic reservoirs to human.

**CECURE 2015: urban and rural spreading of *E. multilocularis* in France**

The project CECURE (Contamination of the environment, urban and rural circulation of *Echinococcus multilocularis*) was started in 2014 in order to assess the presence of the parasite in French rural and urban areas by the detection of the parasite DNA from copro-samples (foxes, dogs, cats and mustelids) by using the qPCR protocol developed in our laboratory (Knapp et al., 2014), and improved by using a sequencing step and PCR inhibitor control (Knapp et al., 2016). Three towns in a highly endemic region in France and urban parks and cities around Paris were investigated. In 2015, a total of 557 samples were collected (304 feces is rural areas, 253 in urban areas), with 89% of the panel workable for analyses. The
parasite was detected by qPCR only in the rural areas, in 46% of the fox feces (56/123), 86% confirmed by sequencing, in 3% of dog feces (2/74), 50% confirmed by sequencing and 10% of cat feces (6/63), 50% confirmed by sequencing. In the urban areas, no copro-samples were confirmed as positive by sequencing. The data obtained in this study will be combined with the data obtained in 2012 to 2014 to be published.

Genetic dataset for *E. multilocularis* typing
The parasite *E. multilocularis* presents a low genetic diversity amongst strains described in humans and animals, while different phenotypes can be described amongst the metacestode lesions. The microsatellite EmsB, a tandemly repeated DNA sequence was studied to better describe the genetic diversity from non-coding and repeated DNA sequences in *E. multilocularis*, because of its high polymorphism. In order to share the data related from this genotyping, the EWET project (EmsB website for *Echinococcus* Typing) was implemented in 2015. A database will contain a data set that will be used as an open data source with *E. multilocularis* isolates. For each isolate, information about the geographical position, the EmsB genetic profiles, and the hosts will be available. Researchers will have the possibility to download all or part of the data set and perform genetic distance calculations, maps and genetic trees. The project will be presented in an international publication, which is under writing process and the website will be released in the second semester of 2016.

- To develop new modelling methods (statistical, deterministic, SMA, etc.) for risk assessment of echinococcosis in a spatial context and simulation tools

Mathematical modeling of the predator-prey interactions in a context of multiple resources and of the consequences in terms of *E. multilocularis* transmission.
The PhD work of Virgile Baudrot, at Chrono-environnement research unit, was aimed to develop of a mathematical framework to model the predation of one predator on several prey (multi-species functional response-MSFR), which is the situation in the field for *E. multilocularis* hosts, and to use this MSFR in an eco-epidemiological model for trophically transmitted parasite such as *E. multilocularis*. This leads to: (i) the conclusion that the preference of the fox towards a given small mammal prey species depends not only on the relative importance of this given species within the small mammal community (frequency-dependence) but also on the total abundance of the small mammal community (density-dependence) (Baudrot et al. 2016a); (ii) the construction of a deterministic one predator-two prey model, based on MSFR, hosts community composition and competence, to explore the disease risk (R₀) of the cestode; results of the study show that the pattern of feeding interactions changes the relationship between disease risk and prey community composition (Baudrot et al. 2016b).

**Articles**


Communications


Activity 4: Training and Education

Responsible persons: Solange Bresson-Hadni and Laurence Millon

- To provide health professionals with specialized training / To provide expert advice to professionals for the management of patients with cystic and alveolar echinococcosis

Dedicated AE or CE patients’ file discussion in multidisciplinary meetings/
Organization and management of a monthly multidisciplinary clinical meeting to discuss AE and CE patients’ files (open to all centres requesting advice; and including young professionals’ training)

Most of the files of patients for whom an advice is requested are presented and discussed during a specific multidisciplinary meeting, dedicated to difficult AE or CE patients’ files. It allows all experts from the WHO Collaborative Center (hepatologists, interventional gastro-intestinal endoscopists, liver surgeons, parasitologists, pharmacologists, radiologists, nuclear medicine specialists) to join for multidisciplinary discussions. Difficult cases from France or other countries (mostly from Switzerland) have been discussed at these meetings. It is also open to young fellows from all these medical specialties, offering in addition an excellent opportunity for training. Five multidisciplinary meetings have been held under the coordination of Dr C.Richou and Pr S.Bresson-Hadni (19/06/2015; 09/10/2015; 18/12/2015; 05/02/2016; 18/03/2016; 17/05/2016).

Expert advices and consultations:
From June 2015 to May 2016, Pr Solange Bresson-Hadni, Pr Dominique Vuitton, Pr Laurence Millon, Dr Carine Richou and Frédéric Grenouillet regularly gave advices about patients from distant places, and difficult AE or CE cases, either from France or other countries [advices for 46 French patients; 5 advices for patients living in other countries, including 4 AE cases from Switzerland and one patient with multiple atypical liver lesions living in Chicago (USA)]. Advices are also regularly given on risk factors for AE or CE in various regions of the world and prevention measures.

Expert advice was given on the diagnosis (including serology and image files transferred by the requesting physicians) and on the treatment, both for AE and CE (72% for AE cases and 28% for CE cases). For difficult CE cases, additional expert advice was, if necessary, obtained from Dr E. Brunetti, WHO Collaborating Center in Pavia (Italy).

Collaboration: Xinjiang Medical University and Qinghai Medical University 1st Teaching Hospitals, China (Depts of Hepatology and Hepatic Surgery). DA Vuitton spent 1 week in Sept 2015 and 2 weeks in May 2016 for scientific training, discussion on research projects, on drafts of scientific papers with young scientists and physicians. Links regarding the application of the team in Urumqi as WHO-Collaborating Centre are reported below.

The common project on the comparison between European and Chinese cases of AE (XUUB study) has been presented in the Activity 2. section. It is anticipated that our collaboration with the First Affiliated Hospital of Qinghai Medical University will be closer in the next months/years. In the past, most of the collaboration with Qinghai province, certainly the province with the highest number of echinococcosis casesin China, both CE and AE, mostly concerned epidemiology and transmission, or through training of
young professionals in Besançon (in parasitology and in clinical pharmacology) or in Qinghai (WHO-supported training courses of the local CDC). More direct collaboration on the care management of patients is planned with the departments of Hepatic Surgery and Radiology.

- **To provide information to professionals and to the public**

**Participation of P Giraudoux and DA Vuitton in the Global Water Pathogen Project of the UNESCO.**

The project is defined on the website http://www.waterpathogens.org/ : To improve sustainable access to basic sanitation and safe drinking water, GWPP will update knowledge on water pathogens using advanced information technologies by publishing and disseminating a state-of-the-art reference resource on water-related disease risks and intervention measures and create an online open-access database and knowledge platform. GWPP will provide an updated review of the efficacy of sanitation technologies and serve as a compendium of waterborne pathogen information and quantitative data to support risk assessment to protect water safety. Work will also be conducted with the World Health Organization to support its Sanitation Guidelines.

The specific contribution of our WHO-Collaborating Centre passes through the participation of P Giraudoux and DA Vuitton in the redaction of the chapter on “Echinococcus sp” (http://www.waterpathogens.org/node/169); DA Vuitton will also attend the meeting of the “Helminths” group of experts in Sept 12-13, 2016 in Barcelona, Spain.

**Cooperation with the patients’ association AIREA**

The annual meeting of the AE patients’ association, AIREA (Association for Information and Research on Alveolar Echinococcosis) was held November 15th, 2015 at the Besançon University Hospital, with the participation of Pr G Mantion, who gave a talk about surgical treatment of Echinococcosis, and Dr J Knapp, who gave a talk about data reported by the FrancEchino network in 2015. Prof S Bresson Hadni, Prof L Millon and Prof D Vuitton also participated in this meeting and answered questions from patients about various subjects (diagnosis, treatment, research).

**Participation of all experts from our WHO CC in national academic training and continuing education on echinococcosis in their respective fields as well as invited lecturers at national or international meetings to provide updated information on AE.**

Pr S.Bresson-Hadni gave a lecture on alveolar echinococcosis with current data on the management of AE patients at the annual French post-graduate meeting of private hepato-gastroenterology (Paris, France, December 4th 2015) and at the annual postgraduate course organized by the Swiss Society of Hepato-gastroenterology dedicated to Swiss private and public hepato-gastroenterologist (Brunnen, Switzerland, April 7-9th 2016).

Pr F.Grenouillet gave 2 invited lectures: 1/ "Epidemiology and biological diagnosis of alveolar echinococcosis in France" at the 16th annual meeting of the French National Society of Infectious Diseases (SPILF) (Nancy, France, June 11th 2015) ; 2/ « Alveolar echinococcosis : Epidemiology, diagnosis,
management and initiation of a European registry for human cases». Infectious Diseases Seminar, Université Libre Erasme, Bruxelles (Belgique), March 2nd 2016.

Pr F.Grenouillet gave invited lectures at the Faculty of Medicine in Saint-Etienne (France) in 2 Master 1 courses: 1/ “Echinococcosis : from environmental approach to Humans pathology”, in collaboration with Pr F.Boué, November 12th 2015.2/“Alveolar echinococcosis”. Master 1 “Physiopathology of transmissible diseases”. March 8th 2016.


Pr P.Giraudoux and Dr J.Knapp gave a public lecture on alveolar echinococcosis at the « Maison de la Réserve », Remoray, Doubs Department, France, October 4th 2015.

Dr J.Knapp gave a training course on alveolar echinococcosis to students of the National Institute of Agricultural Medicine (INMA), Tours (France), November 27th 2015. During this seminar, she also conducted a practical training based on a questionnaire issued from the work of Belline Bourgeois (work for MD thesis) supervised by our group and recently published in Acta Parasitologica.

Articles

MD Thesis
Sylvain Ambrega - Prise en charge endoscopique des complications biliaires de l’échinococcose alvéolaire : une étude européenne. Franche-Comté University - August 28th 2015

• To help organizing congresses, workshops and roundtables

Co-organisation of the “XXVIth International Congress of Hydatidology”, Bucharest (Romania), 1-3 October 2015. Our WHO-Collaborating Centre was actively involved in the preparation of the scientific program of the World Congress, in close cooperation with Carmen Cretu, local organizer and Antonio da Silva, president of the International Society of Hydatidology. In the absence of designation of a coordinator of the WHO-Informal Working Group on Echinococcosis, the usual meeting of the WHO-
IWGE at this congress could not be held. On the initiative of our WHO-Collaborating center, it was replaced by an ‘International session’ dedicated to the public health aspects of echinococcosis, with a special video-lecture on Neotropical echinococcosis, a lecture on behalf of the PAHO, on the public health issues of echinococcosis in South-America, and a lecture on the European surveillance of zoonoses, and especially echinococcosis, by a representative of the ECDC.

2. Please briefly describe your collaboration with WHO in regards to the activities of the WHO collaborating centre during the past 12 months (e.g. means of communication, frequency of contact, visits to or from WHO). Please feel free to mention any difficulties

The re-designation form of our institution as WHO Collaborating with updating of TORs and Activities was submitted in March 2015, with the support of B Abela-Ridder. The designation of our institution as WHO Collaborating Centre has been validated in May 2015 and will be effective for a period of 4 years. (19/05/2015-19/05/2019).

Several phone conferences were held with B Abela-Ridder in the last 6 months about there-organization of the WHO Informal Working Group on Echinococcosis (WHO-IGWE). A call for nominations for a Chair of the WHO-IGWE coordination group was recently published, and we will be involved in the organization of the WHO-IGWE coordination group.

As mentioned above, our participation in the Global Water Pathogens Project is in the scope of UNESCO and WHO activities.

3. Please briefly describe any interactions or collaborations with other WHO collaborating centres in the context of the implementation of the above activities (if any). If you are part of a network of WHO collaborating centres, please also mention the name of the network, and describe any involvement in the network during the last 12 months

Interactions with the WHO Collaborating Center For Prevention and Care Management of Echinococcosis (Urumqi, PR China)

Our WHO-Collaborating Centre continued its support to the application of the Key-Lab on Echinococcosis, First Affiliated Hospital of Xinjiang University, China, as WHO-Collaborating Centre, by providing advices and making links with the group on Neglected Parasitic Zoonoses at WHO and its Head. Informal approbation by WHO authorities was obtained in April 2015 and final designation was effective in April 2016. Several members of WHO-CC Besançon (Prof S. Bresson Hadni, Prof E. Delabrousse, Prof L. Millon, Prof DA Vuitton, and Prof. G. Mantion) will participate in the first Working Meeting Notice of
WHO Collaborating Center For Prevention and Care Management of Echinococcosis, in Urumqi on the 30th of June 2016.

Interactions with the WHO Collaborating Centre for the Clinical Management of Cystic Echinococcosis (Pavia, Italy).

As usual, our links with the WHO-Collaborating Centre in Pavia are especially close regarding the clinical advices on CE care management; when a specific advice is asked by an international correspondent, the message/question is systematically transferred to Pavia, and a common answer is provided. Our links also concern the EurEchino database, in order to ensure inter-operability with the Herakles registry of cystic echinococcosis on the long-term.

4. Please briefly describe any type of technical, programmatic, advisory or other support received from WHO during the past 12 months for the implementation of the agreed activities listed above (if any)

No object