Integrated control of neglected zoonoses: improving human health and animal production through scientific innovation and public engagement

Final Report Summary - ICONZ (Integrated control of neglected zoonoses: improving human health and animal production through scientific innovation and public engagement)

Executive Summary:
Globally, Neglected Zoonotic Diseases (NZDs) are disproportionately borne by communities in low resource settings, particularly in rural and peri-urban areas where socioeconomic activities maintain proximity to domestic or wild animals. Unlike ‘emerging’ zoonoses which attract considerable attention, the NZDs are normally omitted from major international and national policy frameworks, contributing further to
the cycle of neglect through lack of awareness of their impact and a subsequent lack of funding for control. The poor bear perhaps the heaviest burden of the impact of NZDs, given they are at great risk of both contracting these diseases and not having the resources to seek medical treatment. Given the important poverty buffer of livestock and animal products to poor – particularly rural – livelihoods, the dual burden of disease both in humans and animals increases the social and economic impact of the NZDs. The situation is further complicated in that both production and companion animals of significant societal value may act as reservoirs from which these diseases are transmitted to man.

The five year Integrated Control of Neglected Zoonoses (ICONZ) project brought together twenty-one European and African partners with the overall strategic objective of developing integrated control packages for eight key “neglected” zoonoses as defined by the World Health Organisation (WHO); anthrax, bovine tuberculosis, brucellosis, cystic echinococcus, porcine cysticercosis, leishmaniasis, rabies and zoonotic trypanosomiasis. Through a series of complementary and interdisciplinary actions, ICONZ outputs have – and will continue - to improve the political profile of this important group of diseases, whilst simultaneously benefitting both human health and animal production under the umbrella of a One Health approach. In the first three years, more than 22 000 animals and over 2000 households were surveyed in over 300 sites, in order to establish the baseline prevalence and socioeconomic impact of these eight diseases across Africa. This activity alone significantly contributed to the existing NZD knowledge base on continent, driving ongoing advocacy and policy activities as well as feeding into the design of the subsequent control interventions. The resulting quantitative and qualitative outcomes from the baseline surveys have been used to develop intervention case studies in the International Partner Co-operation Countries (ICPCs); Morocco, Mali, Nigeria, Uganda, Tanzania, Mozambique and Zambia. Through these field-based case studies, improved control and awareness of neglected zoonotic disease at both community and national/regional policy levels has occurred through the development and validation of packaged intervention strategies. These intervention strategies have been communicated through a variety of media including community meetings, peer reviewed publications, international stakeholder meetings and policy recommendations in affected countries and regions.

Project Context and Objectives:
The ICONZ concept centred on the requirement to develop and promote integrated control packages for NZDs in developing countries. It was anticipated that combining integrated, inter-programmatic, and inter-sectoral approaches to reach marginalized populations or geographic areas, based on risk stratification, should provide significant added value in terms of both improved human health and animal production. ICONZ successfully applied a matrix that considered the technical components of control of the eight NZDs in the context of broader requirements such as gap analysis, technology transfer and communications through a series of interrelated work packages addressing the following project objectives:

Objective 1: Map global research into neglected zoonoses

Work Package two, headed by the University of Liverpool, was tasked with mapping pre-existing regional and national linkages between global NZD research programmes and funders via development of a sustainable database. Through liaising with NZD researchers, donors and programmes such as the European Technology Platform for Global Animal Health (ETPGAH) and the FP7 DISCONTOOLS, WP2
was able to identify major gaps in the current global NZD research activities. An interactive database has been developed that can be electronically populated in order to maintain an up-to-date platform of knowledge of the gaps in research programmes, including cross-cutting issues relating to human health, sustainable agriculture and socio-economics.

Objective 2: Obtain knowledge and information on the neglected zoonoses in terms of disease, epidemiology and burdens

While many zoonoses have been well controlled or even been eliminated in industrialised countries, most developing countries do not currently have the capacity and the means to control them, or even know where they are. The first step in addressing the NZDs was therefore to assess the NZD burden to animals and humans in the case study countries, in terms of disease occurrence, livestock productivity losses and public health impact. This objective was designed under Work Package 3 (Swiss Tropical Institute of Public Health) to develop and test sustainable data collection and reporting systems for zoonoses in Africa. Geographic information systems (GIS) have been used to collate, analyse and display the information and enable risk mapping that builds on previous methods for integrated human-animal risk-based surveillance systems for the NZDs. Importantly, this objective builds on One Health through combining human and animal health within the broader societal and ecosystem context. Addressing under-reporting, a central feature of the limitations of NZD control, was a key point of this objective.

Objective 3: To improve and develop control tools for the neglected zoonoses by identifying gaps and investing in the development of new tools needed to effectively control these diseases

The major limitations of many currently available diagnostics for the NZDs – both in terms of the capacity of local health systems and cost – is an important contributor to the under-reporting and misdiagnosis which contributes to ‘neglect’. The third objective, undertaken by WP4 led by the Institute of Tropical Medicine (ITM) was therefore to improve and/or further develop disease control tools that are locally and culturally acceptable to the countries and communities where they are most required. Disease control tools include all the components along the diagnosis-treatment continuum, including diagnostics, vaccines, pharmaceuticals, animal and human health policy (e.g. movement control, confinement of animals, culling, meat inspection, sanitation), decision support tools (e.g. epidemiological investigation and models, databases, GIS, expert systems) and messaging and publicity. Emphasis was given to the validation, improvement and distribution of existing candidate diagnostics, including the validation of the Rose Bengal and Loop-mediated isothermal amplification (LAMP) tests for brucellosis and HAT respectively, along with continuation with the development of a pen-side porcine cysticercosis test and specific biomarkers for Taenia solium.

Objective 4: To improve and develop integrated control and prevention strategies promoting the concept of ‘one health’. This involves dealing with health problems in people, their livestock and other domestic and wild animals they depend on for their livelihoods through the development of integrated ‘intervention packages’

Integrated intervention packages are at the core of ICONZ; developed to highlight the ‘packaged’ approach possible for both NZDs and other non-zoonotic diseases that impact the productivity of a
particular livestock species, and/or across livestock species within a particular community. In this regard, four work packages were developed to address control and prevention of NZD clusters in particular settings within each ICPC, with an emphasis on the development and validation of integrated intervention packages aimed at simultaneously addressing the various diseases in context with overarching social and economic considerations. The specific work packages were:

- **WP5** (University of Navarro, Spain): Neglected Bacterial Zoonoses Cluster (anthrax, bovine tuberculosis and brucellosis).
- **WP7** (Institute of Tropical Medicine, Belgium): Neglected Pig-associated parasitic zoonoses cluster (Porcine cysticercosis, human taeniasis and neurocysticercosis).
- **WP8** (Makerere University, Uganda): Neglected vector-borne Zoonoses cluster (zoonotic trypanosomiasis).

Tightly aligned with this objective was the requirement to simultaneously determine and compare the cost-effectiveness of the different types of intervention packages, leading to greater empowerment of both communities and policy makers to make informed choices for control and prevention. The activities under this objective have led to several significant operational research outputs which indicate the effectiveness, safety and impact of some of these integrated intervention packages, providing information and options for control suitable for use by governments and donor bodies.

**Objective 5:** To promote intersectoral collaboration in the control of neglected zoonoses

This objective was developed in order to address the issues arising out of the dual nature of zoonoses, where their control or elimination is only feasible through effective control in the animal reservoir. It is a reality that the veterinary sector is usually tasked with implementing these measures, however is reluctant – and in many cases does not have the resources - to bear the cost of control, particularly since the main benefits are seen in human health. However, in order to convince public health/medical bodies to contribute to the costs of NZD control, a high cost-effectiveness must be clearly demonstrated. Careful calculation and analysis of costs of different strategies have been shown to provide unexpected insights and thus greatly inform the choice of control strategy (e.g. Kayali et al., 2006, Lutumba et al., 2005 and Shaw and Cattand, 2001). Building on such cost analyses for the NZDs under ICONZ Work Package 9 (AVIA-GIS, Belgium) has contributed to the current knowledge of the cost effectiveness of different options for control and prevention, continuing to promote veterinary-medical collaboration.

**Objective 6:** To empower women in decision making related to control of neglected zoonoses in livestock through messaging cognisant of traditional knowledge and appropriate to the economic, sociological and cultural contexts of affected communities

Women are important beneficiaries of effective NZD control, and therefore key players in the implementation of control strategies. This is firstly because of their role as primary carers and those largely responsible for identifying illness in the family and seeking care for it. Secondly, interventions to stop transmission of many NZDs - for example tuberculosis, brucellosis, cysticercosis - takes place at the food
processing stage or involves the teaching of specific hygienic practices. An integral part of the development of appropriate control packages under ICONZ Work Package 10 (Sokoine University of Agriculture, Tanzania) has been via meeting with women in affected communities and discussing measures most practical for them and how they could be supported in implementing them and in extending them to their families.

ICONZ has highlighted where women are critical to the successful control of NZDs, both in terms of their role in protecting the health of their families, and their responsibility of farming activities. ICONZ surmised that if the importance of NZD and the burden they cause to animals and humans can be demonstrated to women, they are more likely to work effectively to implement control at a local community level. The important role of women in NZD control is reflected in broader health and development policy initiatives such as the Millennium Development Goals (MDGs), the Sustainable Development Goals (SDGs) and the European Parliament Resolution on Major and Neglected Diseases in Developing Countries (adopted in 2005) that all serve to remind us of the importance of women in primary health care and that women, children and people with disabilities need to be mainstreamed into health policies and related statistics and research.

7. To transfer technologies and build capacity in developing countries to control neglected zoonoses

It was an early recognition that without the effective transfer of technologies and capacity building, ICONZ project outputs would not be sustainable. Under Work Package 11 (University of Copenhagen, Denmark), ICONZ has provided significant technology transfer and training to the participating ICPCs in a variety of areas including statistics, epidemiology, GIS, research design, socioeconomics and social research methodologies. Coordinated stakeholder engagement and participant feedback has occurred at all levels since project inception. In addition to the capacity building which has occurred via short face to face and online courses, Over 70 PhD and MSc students have been trained across a large number of participating ICONZ institutes, with around 120 scientific publications ultimately expected. Students have come from a broad range of natural and social science backgrounds from a variety of medical, biological and human health sectors, providing a solid base for One Health and zoonoses awareness in the next generation of researchers and policy makers. Additionally, the production of innovative advocacy materials such as the ‘vicious worm’ tool [http://www.theviciousworm.org/] have contributed to the available community training and advocacy packages for livestock keepers and households.

8. To ensure maximum benefit from the project by a pro-active programme of dissemination aimed at all relevant stakeholders especially by raising the profile of the neglected zoonotic diseases both internationally and within affected countries

There is a lack of prioritisation by policy makers to control NZD as a result of various bottlenecks. Apart from the poor awareness of the impact of NZDs to both animals and humans in a number of communities, the lack of active involvement by both the veterinary and the human medical sectors is a secondary contributing factor. In order to ensure that the importance of zoonotic diseases is recognized by decision-makers and donors, effective advocacy, firmly grounded in evidence-based assessments of the burden of these diseases on people, animals and poor livestock-keeping communities, was prioritised by Work Package 12 (University of Edinburgh, UK) via this final objective. The ICONZ Advisory Council,
established at an early stage, played a role in raising the profile of the NZDs within various policy bodies through the strengthening of international and regional networks. Another area where advocacy remained central was at the level of district and community stakeholders; the dissemination report highlights the countless media and actors which have been sensitised to the NZDs and One Health as a result of ICONZ activities.

Project Results:
ICONZ consisted of 12 Work Packages, each with its own separate set of objectives. Successful achievement of the majority of these objectives has resulted in a significant portfolio of ICONZ outputs, culminating in an impressive number of postgraduate awards, publications and advocacy materials to promote the NZDs to both international and national decision-makers. The results and outputs of each individual Work Package are highlighted in the following pages.

Work Package 1: Project Management and Coordination
University of Edinburgh, United Kingdom

Work Package 1 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. Ensure the effective management of the project so that it meets its objectives
2. Networking and liaison within the consortium
3. Promotion of international partnerships

Early in the project, WP1 coordinated an appropriate governance structure, consisting of the Management Board (all Work Package and ICPC leaders, ICONZ Secretariat based at Edinburgh) and an Advisory Council (AC). The AC, chaired by Professor Paul Gibbs of the University of Florida, brought together representatives from the human, animal and environmental health sectors from a number of countries and high profile institutes including the FAO, WHO and Ugandan public health ministry. The primary purpose of the Advisory Council was to respond to requests for advice from Management Board on project direction and to make recommendations to ensure that the anticipated outputs of the project remained relevant and updated. The Advisory Council members were:

- Professor Paul Gibbs, BVSc, PhD, FRCVS (chair)
- Katinka de Balogh, FAO
- Dr Chioma (Chichi) Amajoh, Nigeria
- Dr. François-Xavier Meslin, WHO
- Dr. Speciosa Wandira Kazibwe, Uganda
- Prof Richard Kock, UK

WP1 has also successfully produced records of the ICONZ stakeholder meetings, including regular teleconferences, since 2009, resulting in a valuable archive of discussions and decisions regarding project direction and scientific findings. The interim and final scientific reports – including publishable and executive summaries – are also a source of information for both programme leaders and the public.

Work Package 2: Mapping Global Research on Neglected Zoonoses
Work Package 2 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To provide a clear picture of current worldwide research into diagnosis, burdens and control of neglected zoonoses.
2. To evaluate and analyse the information gathered to identify significant gaps in the research into NZ.
3. To encourage networking among the key workers on neglected zoonoses targeted in this call.

The major result achieved by Work Package 2 in meeting these objectives was the development of the Neglected Zoonoses Research Database (NZR Database), available through the dedicated web site at www.zoonoses.ac.uk/iconz. The NZR Database includes three components; the Research Projects Component containing information from researchers on their current projects, the Publications Component covering publications cited within PubMed for the period 1950 to 2012 and the Funders Component covering the period 2006 to 2012, developed from reviews of funders’ own databases. In order to encourage networking between researchers with common interest, WP2 undertook a survey of researchers who had published papers on the NZDs in order to assess their priorities for research and potential for linkages with other researchers in the same field.

Detail of the NZR Database:

i) The Research Projects Component contains information on research commencing from 2006 that includes work related to the eight zoonoses. Initially information was actively solicited from researchers on their current projects and classified into the seven categories, however the database has developed to a point where researchers can now enter information on their own research projects. Information was also made available by ICONZ partner institutions and was also retrieved from the publically available datasets of other European Union projects; for example the Global Network for Animal Disease Research (STAR-IDAZ) database, which also contains information generated by the Emerging and Major Infectious Diseases of Livestock (EMIDA), and Animal Health and Welfare ERA-Net ((ANIHWA) projects.

ii) The Publications Component has been developed as an adjunct to the research projects database, in order to enable access and assessment of research outputs that are not reliant upon voluntary contributions of information. It contains details of published papers held in the PubMed citations index relating to each of the 8 neglected zoonoses for the period 1990 to 2012, accessed at www.ncbi.nlm.nih.gov/pubmed/. The PubMed citation index was interrogated using search phrases within published titles and abstracts to identify publications concerning both disease control and aspects of the pathogen. The resulting publications data can be mined and interrogated to provide a range of outputs such as the names of experts, research institutes, grant information, funders and other relevant summary statistics including the temporo-spatial distribution of research. This component provides information on the nature and volume of work for each of the diseases published over a specified period. The database also allows historical analysis of research into the 8 zoonoses, allowing current work and output to be put into perspective. Users of the website are able to access outputs from the publications component.
The Funders Component currently covers the period 2006 to June 2012, however has potential to be continuously updated, particularly regarding the top 20 human and animal health research funders given their funding allocations in terms of programmes and projects are usually visible in the public domain. The main organisations funding research into the eight neglected zoonoses were identified using a combination of searches such as google, funder’s name and, where known, their institutional or project websites. Funders’ databases were scrutinised via their web sites and details extracted in relation to the diseases along with full details of the projects which are being funded. In the initial phase, 68 funders making awards in the field were identified and full details for the projects being funded were entered into the database. A series of charts are available on the web site which provides a summary of the funding awards identified in relation to the 8 neglected zoonoses. Full details of those funding bodies which were identified as having provided funding for research on at least one of the 8 neglected zoonoses are provided in a grid. This can be interrogated using a search function similar to that used by many spreadsheet programs to obtain information on the projects being funded by each organisation. This provides a number of options for searching and filtering the data presented.

Email survey: An email survey was distributed in February 2013 and repeated in 2014 to authors who had published or received relevant NZD funding in the preceding three years. This email also highlighted the presence of the NZR Database and invited recipients to contribute their perceived priorities for research funding for the eight diseases. In order to maximise response rates, detailed information was not requested in the survey, and responses were anonymised. The volume of responses and the systematic nature of their collection resulted in the collection of useful basic information regarding the nature and volume of current research, providing a means by which to identify ongoing funding priorities via continuous evaluation of the research picture for each disease.

WP3: Knowledge and Information on Neglected Zoonoses
Swiss Tropical and Public Health Institute, Switzerland

Work Package 3 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To provide essential epidemiological and sociological information on each of the neglected zoonoses
2. To develop a standardized and accepted methodology for quantifying the burdens and costs of neglected zoonoses
3. To utilise these methodologies to quantify the overall burden of neglected zoonoses targeted in the call in humans and animals

The first notable research result from WP3 was the development of a standardised methodology for quantifying the burden of NZD, including various disease-specific DALY parameters such as disability weighting factors, in collaboration with the International Food Policy Institute and the World Bank (Narrod et al 2012). Initial ICONZ meetings held with WP9 highlighted the lack of information on how to measure losses to human life for zoonotic diseases (necessary for estimating DALYs), which before ICONZ started only existed for brucellosis, rabies and echinococcosis. A general protocol (blue print) is now available which is representative and considers clustering and variable density of hosts (sampling proportional to size). However, we recognized that such study designs need to be contextualized and adapted to
particular countries. The sampling frame, sample size calculation process and study design from the Morocco and Mali case studies served as a model for this comprehensive template, which has been tested in a variety of differing geographic, systemic and population contexts to date. The publication has attracted significant attention from the scientific community, having been cited 13 times to date. A report on this deliverable can be found at: http://www.iconzafrica.org/Document.mvc/Download/3/535.

In conjunction with AVIA-GIS (WP9), work to determine the livestock productivity losses and costs associated with NZDs has been ongoing throughout the project lifetime through integration of this component within ICPC case studies, and is still continuing. Livestock productivity losses are quantified by extending demographic models of livestock populations to incorporate stochastic parameter specifications using an existing bio-economic model called Livestock Development Planning System (http://www.fao.org/agriculture/lead/tools/livestock0/en/). The uncertainty of parameter values can be formally addressed by using Monte Carlo simulation. Additional worksheets have been added to this model to include stochastic parameter information, prices for commodities and economic outputs such as the asset value of livestock and the net present value of livestock products. A book chapter published with WP4 in the Handbook of Zoonoses describes the best practices for diagnostic tests and the livestock productivity losses due to brucellosis and summarises the methodology of assessment for this particular disease. A collaboration with ILRI has also done the same for bovine tuberculosis (Tschopp et al 2012), and described in chapter 12 of the recently released textbook entitled One Health: The theory and practice of integrated health approaches, edited by Jakob Zinsstag and other members of WP3.

Significant progress towards understanding the existing levels of NZD underreporting has been made, for example the underreporting of anthrax across Africa (Tafah 2010). Similarly, Yvonne Muthiani (2012) compared the data obtained through ICONZ ICPC case studies with the official national and international reports of these diseases, concluding that the lack of standardisation in current national and international surveillance and reporting systems warrants improvement. In the absence of a functioning reporting system epidemiological, medical and veterinary scientists play an important role to keep these diseases in the public health policy agenda. The analysis also demonstrated the usefulness of comparing representative field studies – such as that undertaken within the ICONZ ICPCs - with official figures to estimate the level of underreporting, which indicates this task could also be undertaken by research projects studying neglected diseases in alternative contexts worldwide in order to improve our understanding of the true NZD burdens. In cases where epidemiological field studies were few or unavailable, hospital based studies have been shown to play an important role in documenting the disease in patients seeking treatment in hospitals (e.g. 14 retrospective studies discussing echinococcosis in Morocco).

With additional support from WHO-FERG (Working Group on Food Borne Zoonoses), systematic reviews on the burden of brucellosis and bovine tuberculosis have been conducted and are already published or currently under review (Dean AS et al. 2012, Müller B et al. in press, Dürr S et al. under peer review). Additional publications include practical recommendations on the surveillance of rabies and brucellosis, appearing in two chapters of the recently launched One Health textbook (Lechenne et al. 2015 Chapter 16 - Integrated rabies control, Zinsstag et al. 2015 Chapter 12 - Brucellosis surveillance and control: a case for One Health).
WP3 was also tasked with identifying the main determinants of transmission between animals identified in case countries. Although the deliverable focuses on transmission between animals, the prevalence and risk factors for zoonotic infections in humans in several countries are also important to understand. Such risk based surveillance is becoming increasingly popular especially in veterinary surveillance and particular in the context of zoonotic diseases. Although many guidelines and recommendations are available (e.g. FP7 RiskSur project) almost all focus an early detection of exotic diseases or on demonstrating freedom from disease. Risk based surveillance for monitoring of endemic diseases has been neglected so far. To fill this gap, recommendations and practical implications of risk based surveillance of zoonotic diseases in endemic and resource limited settings have been summarised in a scientific publication which is currently under peer review (Hattendorf and Zinsstag 2015). Some special aspects of surveillance, e.g. surveillance of antimicrobial resistance and joint disease surveillance are presented and discussed in a further book chapter (Schelling and Hattendorf 2015 Chapter 10 - One Health study designs. Almost the ground level, almost 2000 animal keepers have been interviewed across the ICPCs with regards to biological and behavioural risk factors. Analyses have been presented in numerous theses, international conferences and many scientific publications; for example from Mozambique (Moiane et al. 2014), Tanzania (Mwakapuja et al. 2013), Uganda (Muhanguzi et al. 2014a, Muhanguzi et al. 2014b), Mali (Mauti et al 2015), Nigeria (Ducrotoy et al. 2015) and Zambia (Chitwambi et al. 2015).

WP3 in conjunction with AVIA-GIS has undertaken an impressive amount of spatial data analyses, which has enabled the creation of baseline maps of disease prevalence and other important geographical and land use data at both the country and study area levels of the ICONZ ICPCs; a first step in the analysis of spatial factors. Maps showing prevalence data for historical studies have also been created such as for rabies cases in Bamako (2000 - 2011), where the relative risk of disease is presented as the number of reported cases per 1,000,000 inhabitants on a 1 km resolution.

WP4: Improvement and Development of Disease Control Tools
Institute of Tropical Medicine, Belgium

Work Package 4 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To identify currently available disease control tools in relation to diagnosis, vaccination, treatment and policy for each of the neglected zoonoses listed in the call
2. To provide a detailed assessment of gaps in the disease control tools available
3. To facilitate the development of new and improved tools
4. To demonstrate the scientific validity of control tools for neglected zoonoses

In collaboration with the FP7 DISCONTOOLS project, WP4 led an expert consultation to identify a catalogue of currently available diagnostic tools for the 8 NZDs, resulting in a list of commonly agreed 'optimal' diagnostic tools being used for the ICPC case studies that led to the successful standardisation of diagnostic techniques and subsequent comparison and interpretation of results. In addition, a gap analysis has been performed of those diseases currently lacking readily available or effective control tools [http://www.iconzafrica.org/Document.mvc/Download/4/482]. There are several new and improved tools which are in the process of being validated and field tested, including adaption of the existing pen-side

The second major research result from WP4 was the development of a list of new or improved disease control tools which have been validated under laboratory conditions with contributions from ICONZ. For brucellosis, cysticercosis and tuberculosis, field validation of these diagnostic improvements has also been undertaken in the ICONZ ICPCs. The outcomes of this work for each disease as follows:

a) Anthrax - Quality Assurance system for locally produced vaccines:

The Gamma-phage test is the ‘gold standard’ test to assess the quality of locally produced vaccines, however field validation of this method as not able to be implemented.

b) Echinococcosis - Antibody-ELISA for sheep, recombinant E. granulosus vaccine for dogs:

Validation of the FTA Micro card sampling system was undertaken at the ANSES Nancy laboratory (Umhang et al, 2011, deliverable document 6.2). Positive results in ELISA correspond to exposure to the parasite, not to current infection, however detection of infection in the liver can still only be done by ultrasound or at meat inspection. The Echinococcus granulosus vaccine is in development, but is not yet commercially available.

c) Brucella - Field identification and typing kit:

A brucellosis enrichment-PCR method was developed and tested in the laboratory using 26 milk samples of seropositive animals from the Morocco case study. Direct inoculation of the enrichment broth was compared with the classical protocol based on inoculation of Farrell’s and CITA media plates. Both protocols yielded the same results (i.e. 4 positive samples), suggesting that the safer, simpler and cheaper enrichment broth can substitute for Farrell’s and CITA media. However, the multiplex PCR applied directly to the broth failed to identify the Brucella species. Further work would be necessary to improve the detection method.

A Brucella field ID and typing kit was developed and included among the training materials of WP5. Two reviews of the available brucellosis diagnostic tools and their applicability in the context of ICPCs/developing countries have been developed, along with a book chapter reviewing the available brucellosis vaccines and their applicability in the context of developing countries. Finally, a paper on the validation of the Rose Bengal test for the diagnosis of human brucellosis has been published (Díaz et al. 2011), with a similar paper in progress for animal brucellosis.

d) Bovine tuberculosis - Interferon gamma test, lateral flow immunochromatography and chip for fast screening:

The chip and lateral flow immuno-chromatography platform testing revealed these diagnostic methods were not sensitive enough, however newly developed nano-technology has proven to be 1000-10000 times more sensitive than the former platforms. The interferon gamma test (BOVIGAM®) however
became available and was implemented in the Mozambique case study (see deliverable 5.2). In addition to this major achievement, spoligotyping was undertaken of 400 M. tuberculosis strains and several M. bovis strains from Mozambique, and the tuberculin test was validated and compared with other diagnostic methods under African conditions.

In order to do this, comparison of TB diagnostic techniques were undertaken in a TB positive cattle herd of Jersey and Holstein-Friesian breeds from Manica province, Mozambique. Validation of the immunological diagnostic tests requires the determination of the true infectious state of the individual reactor animal as determined by isolation of the infectious pathogen M. bovis, which requires post-mortem samples. Due to ethnic tradition and custom, smallholder cattle owners were not willing to sell reactor animals for slaughter and isolation of the bacteria in sufficient numbers (and the costs of buying reactors would have exceeded the project budget), hence it was not possible to test on local cattle breeds. The following suite of comparative BTB diagnostic tests were undertaken on 106 cattle: antibody test (IDEXX ELISA), Gamma interferon release assay (Bovigam), Single intradermal cervical comparative skin test (SICCT), postmortem inspection at slaughter and bacterial culture and species identification by means of PCR.

The results showed that whilst SICCT detected 77.5% of animals as positive reactors, IDEXX ELISA detected 38.6%, and IGRA only 27.2%. Post mortem inspection revealed suspect lesions in 93.6% of the slaughtered animals, bacterial growth was observed in approximately 75.6% of the cultured samples. This means that meat inspection showed the highest sensitivity to detect suspect animals. Analyzing the accordance between different methods, SICCT detected 74.4 3% and IDEXX ELISA 41.2% of meat inspection-positive animals. Culture-positive animals had been positive at 78.2% by meat inspection, at 79.3 % by SICCT and at 100 % by IDEXX ELISA. Despite the biased selection samples, these preliminary data clearly demonstrate the advantage of ELISA and IGRA to handle the animals only once is contrasted by the far higher sensitivity of SICCT. Thus, at present SICCT is still considered the most appropriate method to detect bTB in cattle.

e) Rabies - direct rapid immunohistochemical test

A direct rapid immunohistochemical test became available relatively early in the ICONZ project, allowing for the identification of rabies antigen in brain tissue. This sensitive, specific and cheap test, gives reliable results on fresh specimens within a few hours in more than 95–99% of cases.

f) Leishmaniasis - rK39 immunochromatographic test

The rK39 immunochromatographic test is available through InBios International Inc., Seattle, USA, along with a protocol for isolation of Leishmania strains via in vitro cultivation in NNN medium.

g) Cysticercosis - pen-side test for detection of pigs with viable cysticerci, efficacy and safety of oxfendazole, diagnostic test for taeniasis

i) Establish T. solium biomarkers

To improve the diagnosis of porcine cysticercosis, it is important to find biomarkers (proteins) that are
uniquely produced by Taenia solium and not by other Taenia species of parasite. In a first step towards that goal, a high throughput proteomic analysis of the excretion/secrection proteins (ESPs) from T. solium metacestodes from naturally infected pigs in Peru and Zambia (5 pigs per country) was started. A major bottleneck for proteomic analysis of cestodes however is the incompleteness of protein databases due to the lack of genomic information and comprehensive expressed sequence tag (EST) libraries. Therefore, we relied on homology to other helminth species to supplement the T. solium database with protein sequences, composing our own protein database via a self-written Perl script to extract protein sequences from all Taenia, Echinococcus, Schistosoma and Trichinella species from the National Center for Biotechnology Information non-redundant (NCBInr) database. Combining these two innovative solutions we were able to report 27 already described T. solium proteins, 17 host proteins and 32 proteins likely to be of T. solium origin, but identified using sequences from other helminths.

However, despite these creative solutions, the incompleteness of the T. solium protein database could never be fully circumvented and remains the main limiting factor in the wide-scale analysis of proteins expressed by the parasite. The draft genome of T. solium was published in April 2013. Until then, Cestoda (tapeworms) were the only class for which no genome sequence was available. The availability of the T. solium genome sequence is a major step forward, however, it is not sufficient for the current type of large-scale “omics” studies, which involve comparisons between species at the DNA, mRNA and protein level (e.g. in order to predict/avoid potential cross-reactions or to identify species-specific molecules). Therefore, it is of great importance to have genomic information on the other most important human Taenia species (T. saginata) as well as the non-zoonotic Taenia species that causes the most important cross-reactions in immunodiagnostic assays in pigs, namely T. hydatigena. ITM will explore other funding possibilities to have this work done and to make sure that the proteomic work on T. solium done in the framework of ICONZ can be valorised and ultimately result in the development of new performant diagnostic tools.

ii) Improved diagnostic test for human taeniasis:

Prior to ICONZ, the current limitations to the copro-Antigen testing for human taeniasis was its non-specificity, meaning positive samples had to undergo further DNA testing (PCR) in order to determine whether the positive sample was T. solium, or the relatively innocuous T. saginata/T. asiatica species. A set of monoclonal antibodies directed against T. solium adult tapeworm somatic antigens has been produced, where no cross reactions were found with T. saginata. Following biotinylation the antibodies that all are of IgM isotype were tested in a direct ELISA against antigen of T. solium and T. saginata and in a sandwich ELISA. The MoAb 3A12 gives a strong signal against T. solium antigen but not against T. saginata antigen. The test was partially validated on Zambian samples in late October 2014, with further validation work is being done on Tanzanian stool samples at UNZA.

iii) Assess safety and efficacy of oxfendazole for African pigs:

Oxfendazole has proven to be the most promising anthelmintic for treating Taenia solium cysticercosis in pigs; a single dose of 30 mg/kg has shown to have high efficacy against muscle cysts and be safe. However, at the onset of ICONZ the drug was not registered for use in pigs and it is currently not available in sub-Saharan Africa. Proper assessment of efficacy, effectiveness, safety and withdrawal time,
registration of thrug in a suitable pig formulation and availability of the drug in the endemic areas was recommended. Oxfendazole was tested in Mozambique (Mkupasi et al 2012).

iv) Development of a cysticercosis pen-side test for detection of pigs with viable cysticerci:

Development of a pen-side test for the detection of pigs with viable cysticerci (using lateral flow immunochromatography) has been ongoing, however specificity is still (too) low compared to the Ag-ELISA. Testing of different buffers and markers did not result in improvement.

h) Trypanosomiasis (T. b. rhodesiense) - existing PCR techniques adapted to LAMP format (Loop-mediated isothermal amplification)

Review of existing PCR techniques in comparison to LAMP (Loop-mediated isothermal amplification) is completed (Wastling et al, 2011). It was concluded that classical PCR is still the preferred method for molecular diagnosis of HAT (T. b. rhodesiense).

WP5: Improve and Develop Control and Prevention Strategies for Neglected Bacterial Zoonoses
University of Navarra, Spain

Work Package 5 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To improve and develop control and prevention strategies for the neglected bacterial zoonosis cluster (anthrax, bovine tuberculosis and brucellosis) in endemic developing countries, taking into account economic, sociological and cultural aspects related to the diseases as well as traditional knowledge.
2. To develop cost-effective disease control strategies for anthrax, bovine tuberculosis and brucellosis.
3. To develop integrated disease control packages for the neglected bacterial zoonosis cluster.
4. To provide information for incorporation under WP11 into materials to be used in training and capacity building activities.
5. To provide information for advocacy, and strategic options for control and prevention of neglected zoonoses to be disseminated under WP12 to governments, technical assistance agencies (e.g. WHO, FAO) and donor bodies.

WP5 research outputs were achieved via field activities and interventions on brucellosis and bovine tuberculosis in Morocco, Mozambique, Nigeria and Tanzania, resulting in comprehensive case studies on these bacterial zoonoses that incorporated a range of epidemiological, socioeconomic, advocacy and training aspects. The intervention elements (education, brucellosis vaccination, and test and slaughter) were proposed to the target communities and evaluated for acceptability and potential impact in Tanzania and Morocco (see deliverable 5.4 and 5.6). Data on costs of BTB and brucellosis and of the benefits of brucellosis diagnosis and vaccination in Morocco contributed to WP9 outputs. The following section outlines the specific outputs and accomplishments in each ICPC:

a) Morocco
The Moroccan case study involved farmers of the Province of Sidi Kacem, investigating brucellosis and BTB in both cattle and small ruminants. The case study compared two differing production zones; the rainfed, extensive livestock production system in the mountainous north of the province and the irrigated, intensive livestock system found in the flatter parts of the south of the province. Initial meetings occurred with a number of key Moroccan stakeholders, from the high profile Ministries of Agriculture and Health and the Governor of Sidi Kacem Province, to local veterinary and medical services and commune presidents. These meetings identified 29 communes suitable for the case study, with all commune presidents and households of the selected farms contacted for sensitisation. Information on knowledge, attitudes and practices regarding tuberculosis and brucellosis was collected from 257 farmers, shepherds and school children, along with 11 veterinarians and 7 medical doctors. Questionnaires to gather economic data were also administered.

Whilst waiting for Moroccan authorities to make an exception to existing legislation regarding compulsory slaughter for all animals testing positive to BTB skin test and/or brucellosis RBT, animal sera were collected for brucellosis testing via alternative assays. The final baseline included 62 randomly selected douars (villages) across the province (as per the agreed cluster sampling methodology), with 55 and 67 households sampled in the rainfed and irrigated zones respectively. The final results were bovine tuberculosis (n = 1187 cattle) herd prevalence of 75.4% (in 57 rain fed herds) and 76.1% (in 67 irrigated zone herds). Brucellosis (n=1200 animals) herd prevalence 3.3% (58 herds) in the rain fed and 10.4% (67 herds) in the irrigated zone. For sheep (432 and 991 for the Rain Fed and Irrigated Zones, respectively) and goats (36, and 48 for the Rain Fed and Irrigated Zones, respectively), all samples were serologically negative. These serological examinations were complemented with a bacteriological analysis of cow milk, with 2/21 milk samples from seropositive lactating cows yielding Brucella abortus, confirmed by PCR.

b) Nigeria

In Nigeria, the cattle and small ruminant populations of chosen settled and nomadic Fulani communities were surveyed for brucellosis, BTB and helminths. Initial sensitization meetings occurred with local heads of Kachia Grazing Reserve (KGR) and Vom Plateau area in north-central Nigeria. Diseases identified as important by the local communities were brucellosis, liver fluke and trypanosomiasis.

The first field survey was performed in KGR in March 2011, with 1700 cattle, 268 sheep and 79 goats belonging to 68 households tested for brucellosis, trypanosomiasis, and helminths. Questionnaires were also administered. Unexpectedly about 50% of cattle were on a dry season migration, leading to sample bias for older female animals, or females with suckling calves. A new census was obtained (June 2011) and a second survey (June/July) on cattle which had been away for migration determined the prevalence of brucellosis (Rose Bengal test), with simultaneous BTB testing via single intradermal comparative tuberculin test [SICCT]. A deworming intervention was implemented both as an incentive to cattle owners to participate and to assess the impact of this on the previously-detected heavy parasite infestations, including of zoonotic parasites. Follow up on this point was conducted in August. Studies in Vom Plateau started in July-2011.

For BTB (1945 cattle; 40 households) herd prevalence was low (2.5%). Concerning brucellosis, cattle in KGR (1972 animals; 40 households) showed individual apparent seroprevalence of 1.0% and 20.0% at
herd level, interpreted as indicative of a chronic state of the infection in cattle in extensive systems. In contrast, intensive farms had individual prevalence of 13-19%. Small ruminants in KGR (n 1500) had low or negative seroprevalence. Concerning human brucellosis in KGR (n 1126), there were only a few suspicious cases, none confirmed, despite consumption of raw milk, assisting in animal births, home slaughtering of animals and milk processing. Due to the rapid destabilization of this area of Nigeria in the latter half of the project, and intervention on KGR could not occur. Instead, conjunctival brucellosis vaccination was evaluated on a nearby commercial cattle herd, the results of which fed into the deliverable 5.4 and part of 5.6 documents.

c) Tanzania

The Tanzania case study concerned brucellosis and BTB in the villages and pastoralist populations of the Morogoro region of eastern Tanzania. Four administrative districts were chosen (Ulanga, Mvomero, Kilosa and Kilombero) given their interface with wildlife in the Mikumi - Selous ecosystem.

A two-phase data collection plan was designed to carry out data collection. For BTB, 46/109 villages were selected for sampling (5 households per village/6 cattle per household; 30 cattle from each study village). Tissue collection from slaughterhouses/slabs and sampling in Kilosa and Mvomero districts was also undertaken. The overall prevalence for BTB in cattle - determined by the intradermal cervical comparative method - revealed 3.7% (n=189) of 1288 cattle tested positive, with household prevalence of 20.6%. Concerning wildlife, 2/63 buffaloes (3.17%) were positive for BTB using gamma interferon test. Body tissues (lymph nodes, liver and lung) from 34 wildlife animals of different species were cultured for isolation of Mycobacterium tuberculosis complex. No Mycobacteria were isolated.

The determination of the overall prevalence of brucellosis in Ulanga, Kilombero, Mvomero and Kilosa districts for domestic livestock and Mikumi-Selous ecosystem, stratified by individual species, was 14.3% cattle, 0.5% goats and 0.6% sheep. The results indicated that Ulanga district had the lowest prevalence 10.4% and Kilosa had the highest 16.3% for cattle but the difference was not statistically significant (P=0.08). The study of brucellosis in wildlife was extended to a total number of 60 buffaloes and one impala sampled from Mikumi National Park, while 4 elephant, 6 buffaloes, 6 wildebeest, 2 hartebeest, 2 zebra, 4 bushbuck, 1 reedbuck, 2 impala and 1 sable were sampled from Selous Game Reserve. The overall prevalence of brucellosis in Mikumi-Selous ecosystem was 13.6% for buffaloes all other species were negative. It was also found that all positive buffaloes were from Mikumi National Park.

After obtaining ethical clearance, a total of 1225 people from 49 villages at 8 identified were tested for brucellosis using the RBT, and questionnaires assessing KAP and risk factors of disease transmission were undertaken. The overall seroprevalence of brucellosis in humans was found to be 20.53% (n = 371) from a total of 1807 cases of fever and non-febrile patients. Household survey and trace back was only feasible for 369 households. In addition to classical risk factors, close proximity to wildlife was identified as a brucellosis risk factor of difficult interpretation.

d) Mozambique

Farms in Zavala and Govuro districts of Mozambique were sampled for BTB and brucellosis. An initial visit
to the district of Zavala was done to undergo mobilization of the farmers to be involved in the study (objectives, methodologies, advantages) and for collection of data. In the pilot survey done in Zavala in 2010, 150 animals tested were negative for brucellosis (Rose Bengal Test) and 1.9% out of 156 tested were positive in the skin intradermal test for BTB. Taking into account that these results indicated very low prevalence, the study in Zavala was discontinued, and a new area (Guvuro) selected. The resulting cross sectional study carried out from 2011 to 2012 in Govuro district resulted in 1137 cattle from 290 households subjected to the BTB intradermal cervical comparative test, where 450 (39.6%) were found positive using a cut-off of >=4mm. The study demonstrates that according to field condition in Govuro, the BTB cervical comparative test is potentially more effective and practical than the BOVIGAM assay, as part of a diagnostic program aimed at detecting BTB in cattle. More importantly, the data show that the prevalence of BTB is extremely high in cattle in Govuro district. For brucellosis, on the other hand, 749 animals were tested and seroprevalence (based on use of the Rose Bengal Test) was 5.2%. In summary, whereas the individual seroprevalence of brucellosis is moderate, the incidence of BTB is very high. Therefore, in Govuro a test and slaughter approach obviously would not be possible.

Significant research conclusions have emerged from the Morocco, Nigeria and Mozambique case studies, suggesting two different pictures for brucellosis seemingly relate to management; extensive or semi-extensive (high herd, low individual prevalence) versus intensive (high herd, high individual prevalence). The human results from the Nigerian and Tanzanian case studies parallel the low and high individual seroprevalence in cattle in KGR and Morogoro respectively, which is also a significant finding. Small ruminants do not seem overly affected - or a source of - human brucellosis. The second significant conclusion is that BTB does not appear to overlap with brucellosis: seen by the serious problem in Guvuro and Sidi-Kacem, with its impact in KGR and Morogoro less important. Whereas an integrated strategy for diagnosis is clearly cost-effective, the different pictures obtained for these two diseases and the lack of effective immunoprophylactic BTB measures preclude a full integration of an integrated control. Of the three groups of control tools (sanitary education, test and slaughter and vaccination) only sanitary education can be focused on both diseases simultaneously.

The three main conclusions of the WP5 studies are therefore:
1. The results of Case Studies combined with the evaluation of the knowledge of the diseases show that intensification, while creating the conditions for better control, often results in increased brucellosis prevalence in developing countries because of imperfect or no knowledge of control measures.
2. Awareness and health education programs addressed to prevention and control of zoonotic diseases such as tuberculosis and brucellosis are fundamental. Therefore, integration of diagnosis and education (knowledge of the diseases, transmission, risk groups, general and food hygiene, etc.) are the simplest and most effective and realistic measures to control both diseases in the conditions of all case studies (considered in DL 5.4). As an added value, it can also contribute to development and modernization of livestock management and promote veterinary actions as well as human development.
3. Control of brucellosis by vaccination requires specific strategies depending upon presence of the human disease, prevalence and breeding systems and means (see deliverable 5.4). Conjunctival vaccination, where vaccination is feasible, is the method of choice.

WP6 Improve and Develop Control and Prevention Strategies for Dog / Small Ruminant-Associated NZDs
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail, France
Work Package 6 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To improve and develop control and prevention strategies for the dog / small ruminant-associated neglected zoonosis cluster (cystic echinococcosis, leishmaniasis and rabies) in endemic developing countries, taking into account economic, sociological and cultural aspects related to the diseases as well as traditional knowledge.
2. To develop cost-effective disease control strategies for cystic echinococcosis, leishmaniasis and rabies.
3. To develop integrated disease control packages for the dog / small ruminant-associated zoonosis cluster.
4. To provide information for incorporation under WP11 into materials to be used in training and capacity building activities.
5. To provide information for advocacy, and strategic options for control and prevention of neglected zoonoses to be disseminated under WP12 to governments, technical assistance agencies (e.g. FAO, WHO, etc) and donors.

Field activities to meet WP6 objectives were undertaken in Morocco and Mali, with a joint intervention to address cystic echinococcosis, rabies and leishmaniasis successfully undertaken in Sidi Kacem province (Morocco), and a rabies dog-vaccination coverage assessment in Bamako city (Mali). In Morocco, Sidi Kacem Province was chosen as it represents a large population of humans, dogs and livestock, with the known co-existence of both bacterial zoonoses and dog/small ruminant diseases allowing for a joint investigation with WP5. Moreover, the province was considered a “naïve” province in terms of disease control, given no official measures regarding the three diseases had been undertaken in this area prior to ICONZ activities. Canine blood-testing and micro-chipping activities also contributed to census figures for dog populations in this province, which were previously unknown. Extensive dissemination has also occurred in the Morocco WP6 case study, with ICONZ activities contributing significantly to the existing policy frameworks and national NZD activities such as World Rabies Day.

a) WP6 research outputs in Morocco

To investigate the potential risk of dog as vectors of rabies in Northern Africa, epidemiological studies consisted of blood sampling and microchip of dogs in the selected areas, in addition to echinococcus investigations in livestock. To determine the cost-effectiveness of the different interventions and evaluate their lasting impact and potential synergistic effects (in order to improve the design of future large-scale interventions), the ICONZ partners of the Institut Agronomique et Vétérinaire Hassan II conducted ongoing socioeconomic and sociocultural studies regarding these three zoonoses. Municipalities involved were randomly associated with a two-pronged cluster randomized protocol to evaluate the effectiveness of an integrated intervention taking into account several diseases at once:

Arm 1 - rabies and human health education, with dogs >6 weeks vaccinated against rabies
Arm 2 – all three canine diseases were addressed via delivery of the following veterinary services i) rabies vaccination, ii) deworming treatment against echinococcosis and iii) an insecticide collar against sand flies to prevent leishmaniasis. Human health education was also undertaken as per Arm 1.
Twelve month follow up of blood and stool samples were collected from dogs in the intervention communities, regardless of participation, in order to compare health status between the two. Knowledge, attitudes and practices of owners regarding these diseases were also assessed in order to highlight the benefits of integrated intervention and evaluate the benefits in terms of both finances and health. Over six publications have been produced, or are in progress, from this work in Morocco.

Vaccination against rabies

A total of 5526 dogs were vaccinated against rabies, with 4651 receiving a first vaccination and 875 a booster at 12 months. Baseline blood samples tested 320 sera with the ELISA antibody detection kit BioPro®, where 14 positives corresponded to a pre-intervention rabies vaccination coverage of 4.3%. During the three phases, the number of primary vaccinations rose to 96.7%, dropping to 48.5% in the second session and 40% in the third. This increase in immunization coverage in the douars, taking into account the end of the experiment the number of first vaccination, reminder and the number of dog 6 months of vaccination, have resulted in 2713 dogs properly vaccinated in the area, corresponding to a new coverage rate of 13%.

Screening of leishmaniasis Dogs and application of anti-sand fly collar

During the second phase dogs were also sampled for anti-leishmaniasis antibodies, with 469 and 501 canine sera analysed from Arm 1 and Arm 2 respectively (Kalhazar test). Positive cases were detected in 95 (16.8%) and 67 (11.8%) of cases in these areas prior to the seasonal risk period, with these positive dogs removed from the experimental cohort. All negative dogs were microchipped for identification with dogs in Arm 2 receiving an anti-sand fly collar (Scalibor®).

During Phase 3, 166 and 215 dogs were recovered from Arm 1 and Arm 2 respectively using the microchip, signifying return rates of 35.4% and 42.9%. The search for anti-Leishmaniasis antibodies was done to detect newly infected animals during the high-risk summer period from May to September. The results show that 25 (15.2%) and 56 (26.0%) dogs were positive in Arm 1 and 2 respectively. A difference between the two study areas was noted, dogs who still had their collar at the time of control demonstrating protection levels of 100%.

Dog worming and treatment evaluation

During the three phases of action, 1200, 928 and 280 dogs received antihelmintic treatment in Arm 2, while dogs of Arm 1 received no treatment. Post-intervention analysis revealed found 5 (3%) and 2 (1.6%) of dogs to be positive for E. granulosus in Arm 1 and 2 respectively. The low post-intervention prevalence prevented an assessment of the efficiency of the deworming intervention, despite prevalence being slightly lower in the treated area.

Table 1: Summary of the Moroccan WP6 research approach

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline data collection and intervention</td>
<td>Intervention: rabies vaccination minimum 300 dogs</td>
</tr>
<tr>
<td>Delivery mode: FPS</td>
<td>Questionnaire: dog and owner details</td>
</tr>
</tbody>
</table>
Tests: blood samples  
Intervention: rabies vaccination, deworming, minimum 300 dogs  
Delivery mode: FPS  
Questionnaire: dog and owner details  
Tests: blood samples

6 month follow up Intervention: 2nd rabies vaccination  
Following of 300 dogs negative for Leishmaniasis  
(these dogs received Microchip for identification)  
Delivery mode: FPS  
Tests: blood and stool samples from dogs, Intervention: 2nd rabies vaccination deworming  
Selection of 300 dogs negative for Leishmaniasis to put on insecticidal collar (these dog will receive Microchip for identification)  
Delivery mode: FPS  
Tests: blood and stool samples from dogs  
12 month follow up Intervention: 2nd rabies vaccination  
Faeces collect for echinococcosis  
Blood sampling in the 300 dogs negative follow for Leishmaniasis (dog identified by Microchip)  
Questionnaire: dog and owner details  
Delivery mode: FPS  
Tests: Canine blood and stool samples  
Intervention: 2nd rabies vaccination  
Faeces collect for echinococcosis  
Blood sampling in the 300 dogs negative follow for Leishmaniasis (dog identified by Microchip)  
Questionnaire: dog and owner details  
Delivery mode: FPS  
Tests: Canine blood and stool samples

Outcomes of health education activities undertaken in Morocco

A total of 2,885 people in Sidi Kacem province benefited from health education on the three zoonoses. The objectives of the education intervention focused on the transmission and dangers to humans associated with these diseases. The behavior and traditions were discussed vis-à-vis their contribution to the transmission of pathogens between dog, animal livestock and humans. Appropriate language was used, with good reliance on visual media to transmit the key messages. Evaluation of the health education activity was undertaken via a final questionnaire, with a total of 340 responses revealing the following outcomes:

i) Knowledge of cystic echinococcus

After health education sessions, 82.1% of respondents had knowledge of hydatid disease, compared to 50% before. Similarly, the role of the dog in the parasitic cycle was understood by 67% of respondents, as compared to 21% in the beginning. The survey also highlighted hygiene relevance was understood by 29% of people, and despite 57% of dog owners still giving offal to their dogs, some now bury (21.8%) or burns it (22%).
ii) Knowledge of visceral leishmaniasis
The survey showed 67.9% people gained knowledge of visceral leishmaniasis from the health education sessions. The transmission was understood by 46.8%, with the dog’s involvement obvious for 54.7% of respondents. Regarding prophylaxis against the sand-fly vector, insecticides (64.4%) were most common, with only 3.2% using nets at night. No means are made to fight against biting insects for 34.7% of people.

iii) Knowledge of rabies
The study found that 98.8% knew rabies ad its zoonotic nature, however only 71.5% knew the mode of transmission of the disease. For rabies, the main source of information remains ongoing health education sessions (90.0%). Regarding post-bite measures, 94.1% of people indicated they consult a doctor if bitten.

b) WP6 research outputs in Mali

In Mali, a rabies vaccination coverage investigation was undertaken in Bamako city according to the protocol established with WP3, with two small scale vaccination trials conducted (at no cost to dog owners) in 17 posts. The objective of this study was to estimate vaccination coverage of the mass vaccination campaign and determine the effectiveness parameters of the intervention.

Vaccination coverage and the proportion of ownerless dogs was estimated by mark-recapture transect study and a Bayesian model. The estimated pre-intervention vaccination coverage was 17% (95% CI 14.0 -21.7 %), significantly lower than the 70% recommended by WHO. Dog owners reported several reasons for not bringing their dogs to the vaccination posts, such as lack of confidence handling their dogs (16%) and lack of information (25%); however no clear reason was given for 37 % of respondents. Despite low coverage, the conclusion was that it is feasible to carry out vaccination campaigns in Bamako District, however stakeholders including communities and local authorities are to be central to the decision making process through identifying locally acceptable vaccination strategies. In summary, a better understanding of these “access” parameters will allow work towards effective elimination of dog rabies in Bamako to occur.

In conclusion, the work undertaken in Mali shows that rabies poses a significant human and animal health risk, with transmission levels appearing higher than other countries of the region. Despite the proportion of ownerless dogs being less than 10%, community participation in the vaccination process is lacking, resulting in insufficient coverage to prevent transmission of canine-mediated rabies. Ongoing work identifies the factors of access to mass vaccination in the communities of Bamako towards a plan for dog rabies elimination in the district of Bamako and later for other regions of Mali. A total of six publications and 2 postgraduate theses have been produced as a result of the ICONZ Mali case study.

WP7: Improve and Develop Control and Prevention Strategies for Neglected Pig-Associated Parasitic Zoonoses

Work Package 7 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:
1. To improve and develop prevention and control strategies for the neglected pig associated parasitic zoonosis cluster (porcine cysticercosis, human neurocysticercosis and taeniasis) in endemic developing countries of Africa, taking into account economic, sociological and cultural aspects of the disease as well as traditional knowledge

2. To develop cost-effective, disease control strategies for cysticercosis and taeniasis

3. To develop an integrated disease control package for the neglected pig associated parasitic zoonosis cluster

4. To provide information for incorporation under WP11 into materials to be used in training and capacity building activities

5. To provide information for advocacy, and strategic options for control and prevention of neglected zoonoses to be disseminated under WP12 to governments, technical assistance agencies (e.g. WHO, FAO) and donor bodies

The aim of WP 7 was to improve and develop prevention and control strategies for the neglected pig-associated parasitic zoonosis cluster (porcine cysticercosis, human neurocysticercosis and taeniasis) in endemic developing countries of Africa, taking into account economic, sociological and cultural aspects of the diseases as well as traditional knowledge. WP7 focused on case studies in two ICPCs; Mozambique and Tanzania. An early gap analysis on the current knowledge of porcine cysticercosis/human taeniasis (Afonso et al 2011) was used to guide the interventions against cysticercosis in Zambia and Mozambique, with particular focus on socio-cultural factors, as seen by the Community-Led Total Sanitation (CLTS) activities in Zambia and education intervention in Mozambique.

a) WP7 research outputs and results in Mozambique

The pilot disease burden assessment for porcine cysticercosis in the Mozambique study area of Morrumbala resulted in a total of 664 geo-referenced blood samples taken from 183 households in 8 livestock areas. The resulting antigen prevalence varied from 36.7% to 3.2% (mean 15.8%) between villages. A coprological survey, using Willis (qualitative) and McMaster (quantitative) methods, was performed on the same pigs showing an overall nematode prevalence of 67.5%. Eggs of Strongylida, Strongyloides, Metastrongylus, Ascaris and Trichuris and cysts of coccidian and Balantidium coli were found. From a total of 302 household samples, 179 questionnaires were collected in order to assess risk factors and economic losses related to porcine cysticercosis.

The intervention design considered the results from the pilot study in the context of the country needs, available human and financial resources and time; as a result, an educational intervention was agreed. A second ‘pre-intervention’ survey was undertaken to account for the long period between the pilot and intervention implementation, collecting over 350 pig blood and faecal samples and 400 questionnaires (200 from pig keeper’s and 200 from non pig keepers) in 8 livestock areas in Morrumbala district. Porcine cysticercosis analysis via antigen ELISA gave a prevalence of 6.8% (0-25%), whereas the prevalence of gastrointestinal parasites (73%) was comparable to the pilot results. Education materials were developed in pig health (zoonotic and transboundary diseases), pig production, hygiene/sanitation and meat inspection, with 10 villages from the pre-intervention baseline each assigned as either intervention or control villages. A seminar was organized to transfer education messages to local extension workers, who then delivered the information to the villages.
The case study in Mozambique was troubled by long term political instabilities in the study area, which largely complicated the study. As such, the educational intervention could not be fully evaluated, however valuable lessons were learned from the implementation, with several recommendations available for how to improve on the implementation of an educational intervention to ensure an optimal compliance and transfer/uptake of the messages. Despite significant mobilisation efforts, the turnout for these community meetings was very low. Part of the reason for this related to the aforementioned political tensions, however an anthropology student conducted follow-up research that discovered lack of time and lack of information regarding the trainings was a cause. As a result, important lessons have been learned regarding the implementation of educational interventions, especially in terms of what is required to improve compliance with disease control programmes in the event of greater priorities such as political instability.

b) WP7 research outputs and results in Zambia

The initial case study location for Zambia was Monze district, where implementation of a Community Lead Total Sanitation (CLTS) intervention was planned to assess the impact of this on a number of human gastrointestinal parasites. However, once baseline activities started, WP7 researchers realised that some of the selected villages were already CLTS triggered, leading to a change of site to Katete District in Eastern province which was known from previous studies to be endemic for T. solium. Baseline samples revealed a STH prevalence of 0-37.5%, with porcine cysticercosis ranging from 0-57.1%; study villages were allocated control/intervention based on these results.

The CLTS intervention was conducted via a partnership between the Ministry of Local Government and Housing and UNICEF, who organised the CLTS training workshop as a first step and undertook the intervention in 2012. The 4 month post-intervention follow in February 2013 visited all study villages, undertaking transect walks to observe latrine construction progress. Informal interviews were conducted at households with or without latrines, triangulated with interviews by the Sanitation Action Group (SAG) committee members and CLTS champions. Latrine construction in intervention villages was in general found to be progressing steadily.

Post-intervention analysis occurred 22 months post-triggering, covering all 20 villages in Katete, Eastern Province of Zambia. Despite sanitation coverage almost doubling from 26% to 48% during this time, over half of the households did still not own a latrine. Freedom from open defecation was not established, highlighting the challenges of human behaviour change, particularly in short periods of time (table 2).

The Zambian case study reached the important conclusion that the implementation of CLTS as an approach to control Taenia solium and soil transmitted helminths is not optimal and needs to be improved. The observations of increased latrine construction were highly variable between villages and in general even though the number of latrines doubled, the total coverage remained less than half of the households. No impact on disease occurrence is expected at this low level of latrine coverage. Special attention should go to poor, young and female headed households.

WP8: Improve and Develop Control and Prevention Strategies for Neglected Vector-borne Zoonoses
Work Package 8 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To improve and develop prevention and control strategies for zoonotic trypanosomiasis, tick-borne animal diseases and malaria (in some areas) in endemic developing countries of Africa, taking into account economic, sociological and cultural aspects related to the diseases as well as traditional knowledge.
2. To develop cost-effective disease control strategies for zoonotic trypanosomiasis, tick-borne animal diseases and malaria (in some areas).
3. To develop an integrated disease control package for zoonotic trypanosomiasis, tick-borne animal diseases and malaria (in some areas).
4. To provide information for incorporation under WP11 into materials to be used in training and capacity building activities.
5. To provide information for advocacy, and strategic options for control and prevention of neglected zoonoses to be disseminated under WP12 to governments, technical assistance agencies (e.g. WHO, FAO) and donor bodies.

Acute T.b. rhodesiense HAT occurs in areas endemic for vector-borne diseases that affect human livelihoods either directly (public health) or indirectly. Tick-borne diseases (TBDs) are endemic in areas of HAT and AAT and compromise livestock production. Integrating tsetse and tick-borne disease control methods would help livestock keepers control HAT and result in increased use of draught power and cattle manure (controlling HAT and improve livestock health and productivity).

A review of existing information on tsetse and zoonotic trypanosomiasis was undertaken to assess the different HAT control approaches currently being implemented in Uganda; use of RAP in the live bait technology (SOS), traps (local government) and SIT targeting tsetse eradication (PATTEC) were reviewed and considered when selecting the potential case study areas, resulting in the development of an integrated vector-borne (tsetse and ticks) disease control protocol [http://www.iconzafrica.org/Document.mvc/Group/21].

WP8 activities centred on identifying an optimal control strategy for the rhodesiense HAT cattle reservoirs in the southeast of the country, with a major intervention undertaken in Tororo district to assess the percentage of cattle required to be treated in order for this to occur. The eighteen-month longitudinal RAP randomised controlled trial demonstrated the following major outcomes:
1) Spraying only 25% of a village cattle herd is sufficient for the control of T. brucei s.l. in low tsetse challenge settings. The coverage would need to be increased to 50–75% in high tsetse challenge areas and where T.vivax and T.congolense are problematic.
2) Treating all cattle with a prophylactic or curative trypanocide at the beginning of the control program and once per year for 2 more years would offer control in high transmission areas.
3) The project RAP cost US$6.81 per animal per year; comparable to the 4 curative doses of trypanocide/animal/year normally required to keep animals under high tsetse challenge, but without the risk of build-up of trypanocide resistance.
4) The cost to the farmer to participate in the RAP intervention was US$0.31 per animal per year
5) The observed reduction in infection with T.parva indicated RAP is unlikely to disrupt endemic stability to
tick-borne diseases (TBDs); an epidemiological equilibrium that is known to maintain a large population of cattle protected against TBDs.

Issues relating to farmer based application of RAP for uptake and adoption have been explored and policy makers appraised of solutions. It has been a requirement by the Coordinating Office for the Control of Tsetse and Trypanosomiasis in Uganda (COCTU) for the Leader of WP8 to appear at every Technical Committee meeting of the Uganda Trypanosomiasis Control Council (UTCC) to provide verbal information that can guide ongoing activities to improve control and advocacy T&T control in Uganda.

WP9: Socio-Economic and Institutional Aspects
AVIA-GIS, Belgium

Work Package 9 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To collect existing information and data on the cost-effectiveness of various control strategies for each of the neglected zoonoses under consideration by ICONZ.
2. To set up activities with ICPC participants in ICONZ to fill knowledge gaps on cost-effectiveness of control strategies for neglected zoonoses.
3. To analyse the cost-effectiveness of integrated intervention packages being tested and validated under WPs 5-8 for each of the neglected zoonoses clusters.
4. To formulate recommendations as to appropriate medical/veterinary structures, liaison and cost-sharing for the effective control of NZs.
5. To provide overarching support to other WPs, especially WPs5-8 & WP10, in socio-economic and institutional matters.
6. To harmonise with WPs 3 & 5-10 in providing training materials be taken up by WP11 and to provide information for advocacy to be disseminated by WP12.

The core work and major research outputs of WP9 has been to analyse the cost-effectiveness of the integrated interventions undertaken by WP5-8, described as follows:

i) WP5 – brucellosis and bovine TB:
ICONZ socioeconomic data was collected on livestock bovine TB and brucellosis, and human brucellosis in some cases. The Nigeria intervention used a conjunctival S19 vaccine in cattle, utilising data on the impact of brucellosis on cattle fertility in Nigeria to estimate the cost-effectiveness. In Tanzania, a study was undertaken of brucellosis patients presenting at hospitals, to evaluate the costs incurred by the disease. Together with information about the brucellosis sero-positivity of at-risk groups such as butchers and febrile illness, an analysis of the cost-effectiveness of screening high risk groups with the Rose Bengal Plate test was achieved. For BTB, an initiative led by WP3 added a stochastic element to an existing herd model in order to model the losses due to BTB in extensive and intensive cattle production systems in Ethiopia (Tschopp et al 2012).

ii) WP6 – echinococcus, leishmaniasis and rabies:
An intervention in Morocco aimed to simultaneously control rabies, leishmaniasis and cystic
echinococcosis, of which the costings were analysed in Morocco. For leishmaniasis, it was concluded that the insecticide-impregnated collars - while effective - were not retained by a sufficiently high proportion of dogs, and they were priced towards a European tourist taking their pet into leishmaniasis-endemic zones. Surprisingly, the cost of rabies vaccine was significantly higher than the cost price in Europe, and echinococcosis dewormer was similarly expensive. In liaison with WP3, data on the costs of dog-keeping and willingness to pay for rabies vaccination in an urban situation was collected in Mali. The results of this, in terms of people’s knowledge of the disease are being analysed and papers are in preparation.

iii) WP7 – Taenia solium
WP7 interventions consisted of Community Led Total Sanitation (CLTS) in Zambia and community education in Mozambique. The costs of the Mozambique initiative were calculated. However, this proved difficult for CLTS in Zambia as it was undertaken by UNICEF and did not quantify villager inputs. However, both case studies provided evidence from pig keeping communities to demonstrate that whilst pig keeping was profitable, farmers invested almost no cash in the enterprise, apart from purchase of pigs for breeding or fattening. Thus it appears that current options for controlling cysticercosis, which require extra expenditure from pig farmers, are likely to meet limited success.

iv) WP8 – zoonotic HAT
Interview data collected by WP10 provided an estimate of the costs faced by HAT patients. A detailed cost analysis of the 22 village intervention was also undertaken, with a cohort of 660 cattle keeping households interviewed at 6-monthly intervals with respect to cattle productivity and animal health expenditures.

WP9 also investigated options for intersectoral cost-sharing and policy initiatives for One Health. An in-depth study of policy and institutions in relation to the control of NZDs was undertaken in Nigeria, Tanzania and Uganda (Okello et al 2014). The study of policy issues undertaken under WP9 highlights the fact that the neglected zoonoses are still almost completely overlooked in international priority setting and that the decline in sub-Saharan Africa’s veterinary services has particularly impacted on those routine activities which previously ensured that zoonoses were controlled (meat inspections, rabies vaccination, etc.).

The cost-effectiveness of ICONZ and other documented interventions to control NZDs were also analysed, with two key conclusions:

i) A prescriptive approach to intersectoral cost-sharing has been deemed not practical. Although the separable cost method advocated by Roth et al (2003) provides a useful basis, there are a number of factors making this difficult to implement in practice. In only a few cases (probably brucellosis, trypanosomiasis and anthrax) are the benefits to the livestock sector sufficiently high to justify the veterinary sector supporting a high proportion of the control costs.

ii) Funding NZD control comes from a number of sources, ranging from patients and livestock keepers to international donors, hence it is clear the options go beyond simple allocation between veterinary and medical services. The conclusion from the ICONZ case studies was that countries need to determine their own route to ensuring that adequate budget lines for NZD control are available.
WP10 Cultural Aspects, Gender Issues, Traditional Knowledge and Messaging in the Control of NZDs
Sokoine University of Agriculture, Tanzania

Work Package 10 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To establish current knowledge, attitudes and practices with regards to the presence, transmission factors, impact, and control of neglected zoonoses in the case-study area.
2. To characterise and facilitate the role of women in relation to the control of neglected zoonoses, not just as direct beneficiaries from improved livestock and human health, but also in terms of their key role in the success of local control programmes.
3. To review existing messaging tools in all media that are used to support disease control activities for the neglected disease clusters addressed by ICONZ.
4. To identify appropriate tools and channels to reach target communities and affect health behaviour and environmental factors.
5. To create health messaging tool kits for strategic scenario-diagnosis, planning and targeting and monitoring of public health interventions, including a central repository for field-tested messaging material.
6. To provide overarching support to other WPs, especially WPs 5–8 & WP9, on gender issues, use of appropriate messaging and adaptation of control strategies to local cultural contexts.

Work undertaken within WP10 aimed to understand not only the risk factors for transmission and maintenance of NZDs, but also to ascertain why people behave the way they do, thus bringing in the cultural element to the ICPC studies. WP10 provided overarching support to all the ICPC case studies through training, monitoring and analysis of results, resulting in the following outputs:

Morocco: KAP studies were conducted for leishmaniasis, rabies, BTB, brucellosis and echinococcosis, with a slaughterhouse assessment for echinococcosis published and other work on brucellosis in progress.

Mozambique: A questionnaire survey combining KAP study and disease burden analysis was undertaken as part of a PhD thesis. The research assessed the role of women in pig production and control of Taenia solium transmission.

Nigeria: A series of focus group discussions, interviews and questionnaires exploring KAP of Fulani herders in the Kachia Grazing reserve formed part of three separate PhD theses. Results demonstrated that the Fulani, who live well below the poverty line in Nigeria, are marginalized from both veterinarian and medical services, with generally low knowledge on NZD transmission and risk. A specific focus was given to gender dynamics, examining the role of women in the household and their potential contribution to the control of zoonoses.

Tanzania: KAP studies for human brucellosis and bovine tuberculosis have occurred and formed part of four MSc theses. A KAP study on the social dynamics of mass dog vaccination in Tanzania also formed a PhD thesis chapter and has been published, along with a study on the role of women in Maasai pastoralist communities and the potential avenues for involving them in the control of brucellosis, specifically centred...
on boiling milk.

Uganda: Baseline questionnaire data and FGDs explored community KAP for zoonoses more generally, whilst HAT patients were interviewed on the impact of the disease, forming part of two PhD theses and several publications.

Zambia: Questionnaires were developed with a strong gender component, investigating the inner working of the households with reference to water, hygiene and sanitation practices, work division and pig management practices and aim to understand any gendered dimensions to the CLTS intervention.

Mali: A KAP study was conducted for echinococcus, leishmaniasis and rabies.

WP10 outputs have resulted in 6 postgraduate theses and over 13 publications, as well as two courses for ICONZ associated students on Qualitative Research Methodologies.

WP11: Capacity Building Through Technology Transfer and Training

Work Package 11 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To build diagnostic, prevention and control capacity for neglected zoonoses in targeted African countries.
2. To train individual scientists, medics, veterinarians and other appropriate personnel within the human health and livestock production sectors in diagnosis, epidemiology, prevention and control of neglected zoonoses.
3. To provide training packages on prevention and control of neglected zoonoses at community level to medical, veterinary and agricultural personnel as well as community leaders, livestock keepers and householders, with particular regard to the importance of the role of women.

A questionnaire survey addressing the needs for capacity building and available training options within the ICONZ partners drove the initial training planning process that resulted in the delivery of the following 9 capacity building courses over the ICONZ project period [http://www.iconzafrica.org/Document.mvc/Download/11/790]:

1. GIS and Spatial Epidemiology, Distance learning course 2010.
2. Diagnosis of Zoonotic Brucellosis, Cysticercosis and Tuberculosis, Mozambique, 2010
3. Research methodology course, UNZA, Tanzania, 2011
4. Data management, Rabat, Morocco, 2011
5. Qualitative Research Methods, Lusaka, Zambia, 2011
6. Socio-economics short course, Rabat, 2011
8. Research methodology course, Bamako, Mali, 2012 (cancelled)
9. Multivariable statistics using STATA, Nairobi, Kenya (offered through DBL, UCPH)

In April 2014, the University of Copenhagen launched the electronic learning tool on T. solium
cysticercosis. The Vicious Worm (TVW) [http://www.theviciousworm.org] that included a new policy brief and information sheet on cysticercosis. TVW has been widely distributed at a number of international meetings and conferences, including CYSTINET, the WHO experts committee on cysticercosis in Genève, ICOPA in Mexico and the WHO NZD4 meeting in Geneva. TVW was also tested among mid-level professionals from a cysticercosis endemic area in Tanzania in April 2014. A pre-post questionnaire exercise investigated their knowledge and understanding on T. solium before and after having tried TVW, both immediately after having tried the tool and two weeks later, the results of which have been incorporated into a publication (Vang Johansen et al 2014).

WP12: Communication and Dissemination

Work Package 12 had the following specified objectives which resulted in the following outputs over the ICONZ project lifetime:

1. To secure the commitment of governments and donor bodies to control neglected zoonoses.
2. To ensure effective communication among all stakeholders within and outwith ICONZ, through publications, reports, meetings and workshops.
3. To promote the establishment and acceptance and support the activities of the Advisory Committee for Neglected Zoonoses.
4. To maximise the impact of the research investment by improving the availability of information on all aspects of neglected zoonoses covered by this project and by disseminating the project results by means of guidelines, tools, workshops, learning materials, policy briefings and research publications.

Appraisal of policy makers as to the importance of NZD is a cornerstone to the activities and outputs of WP12. Both international and national policy makers have been alerted to ICONZ activities and outputs via countless advocacy opportunities at meetings and conferences, the ICONZ website, open-access publications and the high level NZD3 and NZD4 International meetings hosted by the WHO in Geneva in 2010 and 2014. WP12 took a major lead in the organisation of the 4th International meeting on the control of Neglected Zoonotic Diseases (NZD4) in conjunction with EC FP7 project ADVANZ and the WHO, OIE, FAO Tripartite. This took place on the 19–20th November 2014, WHO HQ, Geneva, where over 150 policymakers discussed how they can turn ‘Advocacy into action’. A major conclusion of this meeting was that ‘whilst challenges undoubtedly remain regarding refinement of control tools and their application in low-income settings, these should not prevent large-scale implementation of control programmes. There is now the opportunity to capitalize on the existing knowledge, experience and political will to move ‘From Advocacy to Action’”. Individual ICPCs have also continued to undertake stakeholder meetings and workshops with policy makers in their respective countries, as evident by the large number of dissemination meetings ranging from school children to veterinary/medical staff and policymakers at all levels. ICONZ has also mentored over 50 PhD and Masters students from across Europe and Africa, creating a generation of researchers who are knowledgeable about One Health and who possess the network of contacts to continue in this field.

The ICONZ website [www.iconzafrica.org] was launched in period one (May 2009) and maintained and developed throughout the project lifetime. An interactive members’ area remains an essential platform for sharing internal documents between partners. Additionally, eight ICONZ newsletters with e-updates in
between as necessary have been produced and disseminate widely amongst stakeholders at various international health and policy meetings. The magazines have been warmly received by partners and stakeholders and have proven to be a useful advocacy tool.

Close cooperation and coordination has taken place between ICONZ and European donors, WHO TDR (Zoom in), WHO, DFID Research into Use, the European Technology Platform for Global Animal Health (ETPGAH), FP7 DISCONTOOLS and the Animal Health ERA-Net EMIDA to generate synergies. Relationships were also built with other EC FP7 projects OH-NEXTGEN and ADVANZ, and ICONZ was represented at the 1st, 2nd and 3rd International One Health Congresses in Melbourne, Bangkok and Amsterdam respectively.

WP12 has collaborated with WPLs to produce a series of disease-specific guidelines and recommendations for the control of each of the 8 NZDs, and also country-specific recommendations from the 7 ICPCs. These guidelines will be published in a special issue of Acta Tropica, and also have the potential to be developed into policy briefs by the ICPC leaders for further dissemination at national level zoonoses meetings. The outputs and learning from ICONZ will be made publically accessible via both journal publications and presentation on One Health websites. In this way, the legacy of ICONZ will continue.

Potential Impact:
ICONZ has contributed a substantial and impressive amount of evidence to confirm that intervening to control NZDs is possible, beneficial and cost-effective when considered from a societal point of view. ICONZ has clearly demonstrated that the control of these diseases in animal reservoirs represents an opportunity to address the constraints they pose to both human health and animal productivity, thereby contributing to poverty reduction and other broader health and development priorities outlined by the Millennium (MDGs) and Sustainable Development Goals (SDGs). Valuable lessons learned from ICONZ have contributed to over 100 peer reviewed publications, 9 book sections, over 50 postgraduate MSc/PhD student theses (& many more undergraduate and veterinary projects) and countless meeting and conference reports and presentations to policy makers, donors and researchers both internationally and in the ICPC countries.

ICONZ activities were undertaken in seven countries across Africa, given this is the only continent affected by all eight of the zoonoses targeted by the FP7 call. However disease control tools and disease control and prevention strategies developed and improved by the proposed project will be applicable to the wider developing world, particularly south Asia and Latin America; there is already evidence that this is happening in Southeast Asia (Lao PDR and Vietnam) as a result of the ICONZ student diaspora.

The ongoing impact of key ICONZ research outputs, findings, lessons and dissemination activities is summarised in the following section:

1. Neglected Zoonoses Research (NZR) Database: www.zoonosis.ac.uk/iconz

The methods used to gather information for all three components of the NZR Database are available in such a manner that the process can be continued with regular updating of the components, or repeated for
other diseases. Full details are on the website with the provision of a downloadable PDF detailing the standard operating procedures. This should allow a wide range of beneficiaries from the scientific community, industry, civil society, policy and media sectors to continue to use the database. An automated system was developed to identify publications and to categorise the relevant papers into the seven research categories. In the case of funders the information was obtained from the funders own web sites and information. In addition to the automated population system, efforts have been made to identify further funding to enable the database to be maintained and developed further with options currently under consideration with the BBSRC and the EU STAR-IDAZ project. Discussion will continue to take place re the possible transfer of the database to other organisations such as DISCONTOOLS.

2. Standardised methods for quantifying the costs and burden of NZDs:

A major reason for ‘neglect’ of the NZDs in various health and development agendas has been attributed to underreporting. A standardised methodology for quantifying the cost and burdens of NZDs was therefore a key component of ICONZ; if burdens and control costs are known, the political visibility of the NZDs will improve which in turn will drive advocacy and funding for their long term control.

The cross-sectional surveys conducted in the ICONZ case countries provided estimates on disease frequencies and risk factors in various settings, which was previously lacking or of questionable quality in many countries. ICONZ activities have now produced and tested standardised methods for quantifying the burdens and costs of NZDs, which are available in the public domain via a number of open-access journal publications, book chapters and online courses (e.g Narrod et al 2012, Tschopp et al 2012, . A livestock census tool enabling the automated generation of livestock maps to help address productivity losses from disease has also been developed along with methods for optimizing geospatial analysis of zoonotic diseases.

3. Improved diagnostic and control tools for NZDs

ICONZ activities and research outputs resulted in significant advances towards the improvement of diagnostic tests and control tools, which – like point (2) above – will ultimately lead to improved levels of reporting as a result of decreased misdiagnosis. Key highlights in this regard include:

Brucellosis - a new protocol for conjunctival application of the S19 vaccine will greatly improve compliance of farmers with vaccination standards, whilst the validation of the Rose Bengal Test for use on human sera has been deemed a significant contribution to the rapid diagnosis – and resulting effective treatment - of humans suffering from brucellosis.

Bovine tuberculosis – the successful validation of the tuberculin test under African conditions will ultimately result in much greater confidence of practitioners that BTB tests are being correctly interpreted. The success of potential future policy initiatives to control BTB, such as test and slaughter, greatly depends on the ability to confidently call a positive animal ‘positive’, which will improve community compliance with control initiatives.

Rabies – a quick, reliable and safe fluorescent immunohistological technique developed for rapid diagnosis on brain samples will improve both compliance and efficacy of PEP and response to rabies outbreaks

Taenia solium - The demonstration that a single oxendazole treatment of 30 mg/Kg is both effective and
safe is a significant contribution to the control of this neglected parasite.

4. Extensive public domain contributions to ICONZ, NZDs and One Health advocacy

It is widely acknowledged that apart from the aforementioned issues of misdiagnosis and underreporting addressed by ICONZ, another reason for the ‘neglect’ of NZDs is their lack of political power to attract substantial commitment from national governments and donors for control. Epidemiological and economic information regarding the burden and cost of NZDs will only be useful if decision makers and communities actually know what the NZDs are, and a critical mass is generated to improve their political profile, as we have recently seen with the NTDs. For this reason, the significant number of press releases, publications and presentations on NZDs, ICONZ and One Health more generally into the public domain will have a long term advocacy impact, ultimately resulting in more people ‘talking’ about NZDs and promoting their control.

Full details of media coverage and dissemination of ICONZ outputs is available in deliverable 12.8 and also section 4.2 and 4.3 of the ICONZ final report. Examples of significant press releases and publications that have promoted the NZDs and ICONZ to key policy makers and the general public include:

i) The following publication received significant media attention:

Mableson HE, Okello AL, Picozzi K, Welburn SC. Neglected Zoonotic Diseases: The Long and Winding Road to Advocacy. PLOS Neglected Tropical Diseases
http://www.plosntds.org/article/info:doi/10.1371/journal.pntd.0002800

Links to some of the media reports can be found here:
- http://www.sciencedaily.com/releases/2014/06/140606091753.htm

ii) This recently published article in PlosNTD policy platform describing the EU commitment to the NZDs, urging others to follow suite, had almost 600 views in the first week:

http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003505
iii) The Vicious Worm Tool, led by WP11, has had a press release announcing the launch of the tool:

http://news.ku.dk/all_news/2014/04/e-learning-contributes-to-fight-vicious-worm/

Followed by an article published in the high profile Guardian newspaper: ‘Could a video game stop the vicious worm?’ [Guardian newspaper, Wed 13th August 2014]


iv) ICONZ has had the following media coverage for World Health Day 2014


And has also featured in the University of Edinburgh 2014 annual review, with the following key quotation from Professor James Smith:

“What’s unique about (ICONZ), apart from its inter-disciplinary aspect, is that it’s happening now, at a point when we’re trying to decide what will follow on from the Millennium Development Goals. A large part of that has been to say ‘yes, there’s been big investment in HIV, Malaria, and Tuberculosis, all of which has been very important, but what next?’ ICONZ will help make these neglected zoonotic diseases a key focal point from 2015 onwards.”

http://www.ed.ac.uk/about/annual-review/publication

v) Advocacy at the ICPC level; rabies in Morocco

Countless activities have occurred to increase the profile of the NZDs at various levels, including policy makers and local communities. An example is the World Rabies Days celebrations that have received media coverage in Morocco from 2009-2013, with coverage on national television of the health education of Sidi Kacem school children, available at the following youtube clips:

https://www.youtube.com/watch?v=FHOpcItqiPo https://www.youtube.com/watch?v=ENf2OYUG04

vi) Advocacy at the international level; the third and fourth international meetings on Neglected Zoonotic Diseases and ICONZ Magazines

The third and fourth International Meeting on the Control of Neglected Zoonotic Diseases, hosted by the WHO Geneva headquarters in 2010 and 2014 respectively, each gathered over 100 policy makers and key decision makers each time to discuss NZD control and advocacy. ICONZ partners played a key role in each of these meetings, represented by a significant proportion of students, researchers and policy makers from the ICPCs and European work packages.

The development and dissemination of the eight ICONZ magazines over the project lifetime, including online links, as well as the document outputs from NZD1-4, will serve a valuable and long-standing repository of evidence and policy tools for NZD control in the future.

5. Innovative funding mechanisms for long term scale up for NZD control
A key acknowledgement at the recent 4th International Meeting for the Control of Neglected Zoonoses, with significant inputs from ICONZ partners and ICPC policy makers, was the requirement to develop innovative funding models for NZD control that moved away from traditional public sources. Development Impact Bonds are gaining traction in the international development sector as a means to generate the high requirements for up-front funding – known as front-end ‘loading’ – from private investors, who take on the risk of reward or loss as they would with any investment. The funds are directed to implement the control interventions on a large scale that is usually out of the remit of a public funding body. Outcomes are then assessed by an independent authority, which if met, results in the re-payment of investors with interest by a public funding body; such as national governments or multilateral donors. If the outcomes are not met, the investors absorb the loss. It is thought that with time, DIB models can be adapted and applied to a large number of NZDs, particularly those with proven control tools such as HAT, rabies and Taenia solium.

ICONZ research in Uganda, supported by WP3, WP4, WP8, WP10 and WP12 has contributed to the development of a unique new funding model for zoonotic HAT, based upon the DIB framework and supported by the WHO. In a unique partnership with UK organisation Social Finance Ltd and the Coordinating Office for the Control of Trypanosomiasis in Uganda (COCTU) – which recently appointed ICONZ WP8 Leader Professor Charles Waiswa as new Director - plans are underway to investigate how private investment could help tackle sleeping sickness on a large scale in the country. This proposal was presented at the 1st WHO Meeting for T.b.rhodesiense (rHAT) in October 2014, and the 4th Neglected Zoonoses Meeting – Advocacy for the Neglected Zoonoses at WHO in November 2014.

A press release announcing the launch of the Development Impact Bond initiative between DFID, University of Edinburgh, Social Finance Ltd and COCTU (Co-ordinating Office for Control of Trypanosomiasis in Uganda) can be found here:

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