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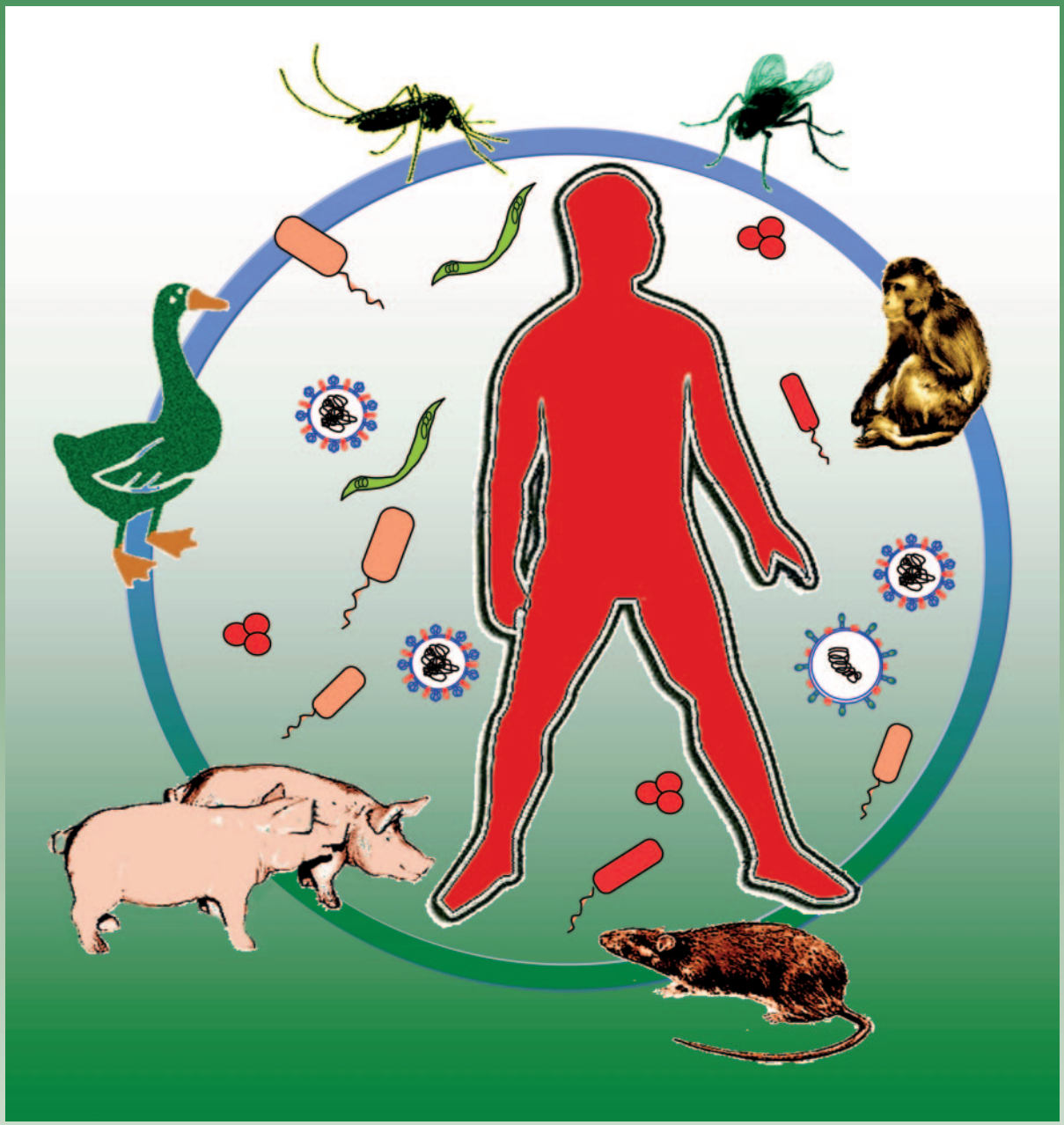
Combating the threat of zoonotic infections



EASAC policy report 08

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building science into policy at EU level

EASAC

EASAC – the European Academies Science Advisory Council – is formed by the national science academies of the EU Member States to enable them to collaborate with each other in providing advice to European policy-makers. It thus provides a means for the collective voice of European science to be heard.

Its mission reflects the view of academies that science is central to many aspects of modern life and that an appreciation of the scientific dimension is a pre-requisite to wise policy-making. This view already underpins the work of many academies at national level. With the growing importance of the European Union as an arena for policy, academies recognise that the scope of their advisory functions needs to extend beyond the national to cover also the European level. Here it is often the case that a trans-European grouping can be more effective than a body from a single country. The academies of Europe have therefore formed EASAC so that they can speak with a common voice with the goal of building science into policy at EU level.

Through EASAC, the academies work together to provide independent, expert, evidence-based advice about the scientific aspects of public policy to those who make or influence policy within the European institutions. Drawing on the memberships and networks of the academies, EASAC accesses the best of European science in carrying out its work. Its views are vigorously independent of commercial or political bias, and it is open and transparent in its processes. EASAC aims to deliver advice that is comprehensible, relevant and timely.

EASAC covers all scientific and technical disciplines, and its experts are drawn from all the countries of the European Union. It is funded by the member academies and by contracts with interested bodies. The expert members of project groups give their time free of charge. EASAC has no commercial or business sponsors.

EASAC's activities include substantive studies of the scientific aspects of policy issues, reviews and advice about policy documents, workshops aimed at identifying current scientific thinking about major policy issues or at briefing policy-makers, and short, timely statements on topical subjects.

The EASAC Council has 26 individual members – highly experienced scientists nominated one each by the national science academies of every EU Member State that has one, the Academia Europaea and ALLEA. It is supported by a professional secretariat based at the Royal Society in London. The Council agrees the initiation of projects, appoints members of project groups, reviews drafts and approves reports for publication.

To find out more about EASAC, visit the website – www.easac.eu – or contact EASAC Secretariat [e-mail: easac@royalsociety.org; tel +44 (0)20 7451 2697].

Cover illustration: Zoonotic infections are transmissible, directly or indirectly, between insects, vertebrate animals and humans. Done by Hilde Merkert (University of Würzburg, Germany)

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EASAC Secretariat
The Royal Society
6–9 Carlton House Terrace
London SW1Y 5AG
tel: +44 (0)20 7451 2697
fax: +44 (0)20 7925 2620
email: easac@royalsociety.org

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Foreword

Infectious disease knows no borders. Zoonoses – those infections transmissible between vertebrate animals and humans – account for much of the infectious disease burden in Europe, whether the impact is defined in public health or in socio-economic terms.

This report is the latest in a series published by the European Academies Science Advisory Council (EASAC) on strategic issues in tackling infectious disease. Our previous publications within this broad domain are:

(i) "Infectious diseases – importance of co-ordinated activity in Europe", Report, May 2005

(ii) "Vaccines: innovation and human health", Report, May 2006

(iii) "Tackling antibacterial resistance in Europe", Report, June 2007

(iv) "Impact of migration on infectious diseases in Europe", Statement, August 2007.

Throughout this work, we have examined the European priorities for public health and innovation associated with disease surveillance, preparedness, responsiveness and control. Our recommendations identify the current and future needs for infrastructure, skills, investment in fundamental science, and support for the development of novel healthcare products and services. We explore these pervasive themes in the current project, with specific reference to the cross-border threats posed by zoonoses.

We welcome the valuable progress that has already been made at the European level in recognising the problem of emerging zoonoses. However, there is concern about the increasing threats arising in consequence of a range of factors including climate change, the every-increasing pace of international travel, and the previous lack of attention to the study and control of disease vectors. We identify particular challenges and opportunities for building better collaboration between human and veterinary science in order to combat zoonoses and advance both human and animal health – in pursuit of the objective of "one health". Collectively, we need to do better in preparing for the unexpected and, in our report, we describe the opportunities for EU leadership in building both research and surveillance networks and in supporting global strategic activity. We urge further effort to study the impact of globalisation on infectious disease emergence and control; these broader efforts to clarify the ecology of zoonoses require the application of the social sciences as well as the biological sciences.

Our goal, as in previous EASAC reports, is to review the relevant science to stimulate, inform and catalyse further debate on the current situation and on future opportunities and threats, and to indicate where there are current gaps and uncertainties in the evidence base and where policy development is needed. It is vital to capitalise on what has already been achieved in co-operation between Member States. Our recommendations across a broad front of public health policy and innovation policy are addressed to those who are responsible for policy-making at the EU and Member State levels and to others involved, in particular in research-funding bodies, companies, professional and regulatory groups.

While this report was in preparation, I was honoured by my colleagues in EASAC in being elected Chairman of EASAC. I take this opportunity to pay tribute to my predecessor as Chairman, Professor David Spearman, for his considerable efforts in creating the EASAC capability to serve as a means for the science academies to work together on policy issues. For this report, I am also pleased to repeat his judgement on the previous report in this series, that it does much to continue the tradition to provide an independent and objective source of high-quality analysis and advice about the scientific aspects of public policy issues.

This report, prepared at EASAC's own expense, is a response to feedback received on EASAC's earlier work. We welcome further feedback on any of the points that we have raised in the present report and suggestions for how we in the scientific and policy-making communities can work together to take forward the recommendations.

The report was prepared by consultation with a group of experts acting in an individual capacity. It was independently reviewed and approved for publication following procedures established by the Council of EASAC. I thank all my colleagues for giving their time so generously to ensure that this report makes a comprehensive and timely contribution to a most important area for European policy-makers.

Volker ter Meulen
Chairman, EASAC

Summary

Zoonotic infections are defined as those transmissible, directly or indirectly, between vertebrate animals and humans. Zoonoses account for many of the recently emerging infectious diseases with high potential for public health and socio-economic impact (for example, influenza and severe acute respiratory syndrome (SARS)) and for the continuing, major burden associated with food-borne infection. There is an important European responsibility in public health to combat the cross-border threats from communicable diseases. Accordingly, it is essential for policy-makers to enhance the sharing of information, to co-ordinate control measures to reduce the fragmentation in preparedness and responsiveness, and to build critical mass in research and development capabilities.

This EASAC report discusses the contribution that scientific knowledge can make in informing evidence-based strategies to both monitor and manage current zoonotic infections and to prepare for the emergence of new disease, "to expect the unexpected". The report reviews developments since the Netherlands Presidency of the EU Council priority theme on zoonoses in 2004. Progress has been made in the EU in four main areas: in recognising that emerging zoonoses are a problem for Europe, in integrating activity between the human and veterinary sectors to foster "one health", in supporting global strategic activity, and in building research networks. However, there is still much more to do to tackle the opportunities and challenges associated with zoonotic infections.

Our recommendations cover key issues for public health, research and innovation policy. They require action at the level both of the European Institutions and Member States.

Epidemiology, surveillance and the monitoring of risk

We recognise that much has already been achieved by the European Commission in creating expert surveillance networks but we emphasise the continuing needs:

- Improving standardisation of data collection and procedures for data mining.
- Formulating methods to monitor zoonotic agents in wild animals and companion animals, as well as the monitoring of livestock, which is well established.
- Generating a consensus set of priority pathogens for surveillance.
- Improving the local surveillance of zoonoses, particularly at the farm level, and integrating regional reporting systems.
- Consolidating and progressing linkage between the European Centre for Disease Prevention and Control and the European Food Safety Authority as a core element in improving the co-ordination between the human medical and veterinary communities and ensuring rapid communication of information about food-borne zoonoses.
- Reassessing the degree of decision-making that might be allowed to the European agencies to support their growing responsibilities, and facilitating interaction between the agencies and the scientific community to clarify the priorities for action.
- Understanding that European harmonisation of strategy development and standardisation of procedures does not entail adopting the lowest common denominator but rather ensuring that the best scientific advice is used consistently to inform policy-making and, thereby, improve risk assessment, risk management and risk communication.

International co-operation

We urge the European Commission and Parliament to provide support for international initiatives such as the Global Early Warning System for zoonoses and the G8 Science Academies' recommendations on infectious disease. We also recommend:

- Taking a broader geographical view of proximal threats – infectious disease can move rapidly between continents and the threat to the EU is not confined to neighbouring countries.
- Considering the potential impact of climate change and the changing global pattern of infectious disease.
- Progressing new research partnerships with developing countries to learn more about the early stages in zoonotic disease transmission.
- Ensuring that the potential impact of zoonotic infections in human migration is given sufficient attention in the strategy development on migration and health begun during the Portuguese Presidency of the EU Council and continuing during the Slovenian Presidency.

Research and education

Although we appreciate that the European Commission funding for research is not unlimited and that policy-makers receive many requests for support, we

believe that there are, currently, significant deficits in the research coverage that should be funded at the European level. In particular, we recommend that areas for further consideration include:

- Capitalising on new research opportunities coming within range for the investigator-driven study of basic science, for example the mechanisms of interspecies transmission, host adaptation, pathogenicity and antimicrobial resistance.

- Addressing major gaps in research on vector-borne zoonoses (in particular, in vector biology, distribution and evolution) and zoonoses transmitted by contact with wildlife – identifying as a priority for Framework Programme 7.

- Assessing the socio-economic impact of zoonotic infections and the interventions to prevent or treat infection – requiring a close working relationship between DG Sanco and DG Research.

- Supporting better provision of information about infectious diseases throughout the education system to promote awareness in the community-at-large, to develop skilled healthcare professionals, and to provide for the next generation of researchers.

Innovation

To mobilise financial resources in support of research excellence, we recommend to EU policy-makers:

- Stimulating the environment to encourage investment in new diagnostic products, for example a diagnostic chip with broad virology coverage.

- Providing increasing support to the DG Research initiatives, the Global Animal Health Technology Platform and the Innovative Medicines Joint Technology Initiative to encourage participation by all stakeholder groups in focusing on disease priorities. Significant financial and intellectual commitment is required from the industry sectors, but to secure this commitment, the European Commission must streamline project-funding procedures.

- Identifying new incentives to support the private sector in human and animal vaccine and chemotherapy research and development.

1 Introduction

1.1 What are zoonoses?

A zoonosis is any infection that is naturally transmissible, directly or indirectly, between vertebrate animals and humans. Some agents cause disease both in the animal host and in humans; others are commensal in the animal host. An increase in the emergence and re-emergence of infectious diseases is evident in many parts of the world (Weiss and McMichael, 2004). Many of these emerging diseases are zoonoses.[1] An emerging zoonosis is one that is newly recognised or that has occurred previously but shows an increased expansion in geographic, host or vector range.

More than 1,400 species of infectious agents are known to be pathogenic for humans, and approximately 60% of these are zoonotic (although most are not highly transmissible between people). Most "new" human pathogens reported in the past 25 years have zoonotic origins, and the risk of zoonotic infection is predicted to continue to increase (Brownlie et al., 2006). A broad range of animal reservoirs and transmission routes have been identified and the infectious agent can be viral, bacterial, rickettsial, parasitic (protozoan or metazoan pathogens), fungal or prion-related. RNA viruses have often been judged best able to cross the species barrier. In classifying zoonoses according to their primary reservoir or mode of transmission (Van der Giessen et al., 2004), four main categories can be identified: (i) vector-borne zoonoses; (ii) zoonoses transmitted by direct or indirect contact with wildlife; (iii) zoonoses transmitted by direct or indirect contact with food or agricultural animals; and (iv) zoonoses transmitted by pets.

Although it is not possible to predict which zoonoses will emerge in the future, more can be done to use current scientific knowledge to inform policy development to prepare for future infections, in particular to understand the risk factors leading to emergence of new diseases and to develop more robust, standardised systems for surveillance and response. It is the purpose of the present EASAC report to review the issues for policy-makers and to indicate where science can contribute to strategy development. Our aim is to summarise the current situation, to clarify, particularly where there is uncertainty, gaps and fragmentation in the evidence base, and to identify priorities for concerted policy action.

1.2 Previous EASAC work on infectious disease

The introductory EASAC report on Infectious Diseases (2005) noted the importance of zoonoses, both in contributing to the current burden of disease in Europe and as the prime source for the threat of newly emerging disease. The policy issues for zoonoses and vaccine innovation were explored in greater detail in the subsequent EASAC report on Vaccines (2006) and issues for antibacterial resistance in the EASAC (2007) report.

Following feedback to the previous reports received from the European Commission, scientific societies and industry, the Council of EASAC agreed to initiate a further study, specifically on zoonoses, to review what progress has been achieved and what more needs to be done to implement roles and responsibilities previously identified for the EU and Member States. The scope of the inquiry and membership of the Zoonoses Working Group are described in Appendix 1.

[1] For example, SARS, avian influenza, bovine spongiform encephalopathy (BSE)/variant Creutzfeldt-Jakob disease (vCJD), Nipah virus encephalitis, viral haemorrhagic fevers, variant *E. coli* infections, *Salmonella enteritis*. A comprehensive listing of global zoonoses is provided in the Merck Veterinary Manual (Merck & Co. Inc., 2006).

2 European policy and research on zoonoses

2.1 What is needed in EU policy?

The proposal by DG Sanco for the EU health strategy adopted in 2007 (http://ec.europa.eu/health/ph_overview/strategy/reflection_process_en.htm) emphasises the importance of EU co-ordinated action on cross-border health threats from communicable disease, "*. . . where Member States cannot act alone effectively and where co-operative action at the EU level is indispensable*." Preparedness, surveillance and response mechanisms have become a responsibility shared between national health authorities and the European Commission and, as the DG Sanco strategy document reiterated, zoonoses account for much of the health threat posed by infectious disease in the EU. The recently adopted conclusion by the Employment, Social Policy, Health and Consumer affairs Council of the EU (EPSCO)[2] confirmed that it is necessary to enhance co-ordination of national measures and to improve information-sharing and communication at the European level for surveillance and control of communicable diseases and in supporting effective cross-sectoral collaboration.

In common with the other tasks for tackling infectious disease, discussed in previous EASAC reports, policy-making to address the uncertain challenges posed by zoonoses must be based on good science with expert, evidence-based risk assessment and horizon-scanning, a shared understanding of the likely priorities and using transparent decision-making processes, partnership with stakeholder groups and improved risk communication (Reynolds, 2005). Prioritisation requires identification of the unmet medical needs, evaluation of the scientific opportunity and assessment of the potential health economic impact. It is also crucial to ensure that the impact of public health intervention is thoroughly evaluated to inform future decision-making. Policy-makers are sometimes tempted to implement new policy before strategies previously introduced have been appropriately assessed.

2.2 What has already been achieved by the EU?

Decision 2119/98/EC of the European Parliament and Council[3] established the Community Network on Communicable Diseases. According to its operative criteria, zoonoses should be reported within the Early Warning and Response System. DG Sanco has done much to support the surveillance networks, but in the view of the Working Group there is still room for improvement in provision of data access and data mining, in sustainable funding of the networks, in training functions and in the principles and procedures for addressing emerging threats. The growing allocation of resources to the European Centre for Disease Prevention and Control (ECDC) provides both the opportunity to better understand the European burden of disease, and the means to co-ordinate definition of the minimum dataset and quality to be delivered by national systems. These points will be amplified in the following chapters. Directive 2003/99/EC[4] (Appendix 2) provides the basis to inform the work priorities of the ECDC and of the European Food Safety Authority (EFSA) in its remit to monitor zoonoses, zoonotic agents, antimicrobial resistance in zoonotic agents and food-borne outbreaks of disease. The new reporting system on food-borne outbreaks introduced by EFSA under the Zoonoses Directive and the ongoing work organised by EFSA to ensure harmonised reporting are important developments.

2.3 Support for research networks

Among major research initiatives supported by the European Commission are the Networks of Excellence funded by DG Research in Framework Programme 6:

(i) MedVetNet, on the prevention and control of zoonoses, integrating veterinary, medical and food sciences in the field of food safety (www.medvetnet.org). A wide range of interdisciplinary activities has developed from the initial focus on themes relating to epidemiology, detection and control, host-microbe interactions and risk assessment.

(ii) Epizone, on epizootic diseases that constitute major risk factors for food production, including avian influenza (www.epizone-eu.net).

These Networks of Excellence have done much to establish good working relationships across the European research community, but Working Group members were concerned about their sustainability. It is now important to secure continuing European funding to maintain and further develop the networks, although their renewal must be on a competitive basis. There will be a continuing need for better co-ordination

[2] Press Release from 2786th Council meeting, 22 February 2007, 6226/07 (Presse 23).

[3] Commission Decision on the early warning and response system for the prevention and control of communicable diseases under Decision No. 2119/98/EC of the European Parliament and Council.

[4] Directive 2003/99/EC on the monitoring of zoonoses and zoonotic agents, November 2003.

in zoonoses research between different groups, to fill research gaps and avoid excessive duplication, while recognising the value of a degree of competition between research groups.

The Working Group also welcomed another initiative by DG Research, the European Technology Platforms:

(i) Technology Platform on Global Animal Health, initiated as a partnership to contribute to improving animal health and welfare, food safety and human health by focusing on research and development (R&D) for vaccines, therapeutics and diagnostics for major animal diseases. The published Strategic Research Agenda (www.ifaheurope.org/EUPlatform/SRA_May06.pdf) provides a comprehensive analysis of the opportunities and challenges relating to determination of priorities, gap analysis and the scope of basic research that is necessary to support innovation in animal health. One major issue in implementing the Strategic Research Agenda is who should fund it? There should be a plurality of funders, to include the Member States, and there may be potential for developing collaborative funding instruments using national funding streams – for example, an ERANet of funders. However, the Working Group advised that progress in addressing the important recommendations emerging from the gap analysis requires strong intellectual and financial support from industry.

(ii) The Technology Platform on Innovative Medicines Initiative has now been accepted by the European Commission for Joint Technology Initiative status. The goal is to overcome R&D bottlenecks in innovations in human medicines. It brings together large pharmaceutical companies, smaller biotechnology companies and academia in conducting the research and as part of broader discussions with regulatory agencies and patient groups. The Strategic Research Agenda (www.imi-europe.org) covers safety evaluation and efficacy evaluation, provision of education and training, and management of knowledge for infectious disease as well as other therapeutic areas. If companies and public-sector researchers are to remain committed to this novel consortium, it is important for the Joint Technology Initiative to deliver on its promise to reduce bureaucracy in project selection and support, and to resolve the current concerns raised by a relatively low provision of research cost overheads by comparison with what is available in other programmes funded by the European Commission.

2.4 Defining the strategic framework for zoonoses policy and research: follow-up to the Netherlands Presidency priority

A conference entitled "European Responses to Public Health Risks from Emerging Zoonotic Diseases" was held during the tenure of the Netherlands Presidency of the EU Council in 2004. As part of the preparation for this conference, RIVM (National Institute for Public Health and the Environment; Van der Giessen et al., 2004) published a report, "Zoonoses in Europe", and the Health Council of the Netherlands (2004) published its advice to the relevant Ministries in a report, "Emerging Zoonoses". Taken together, these reports provide a comprehensive review of the scientific knowledge on: the risk factors for the emergence of zoonoses; the impact of established zoonoses and the potential for future problems; public health issues for surveillance, prevention and control; opportunities for building collaboration between medical and veterinary sectors; and options for public communication of risk.

The Presidency conference concluded that there is, indeed, a need for a European strategy and programme in the field of zoonoses that encompasses:

1. More widespread recognition that emerging zoonoses are an important national, European and global problem.

2. Integration of inter-sectoral activity to develop responsiveness to emerging threats.[5]

3. Greater co-operation with international and intergovernmental organisations (World Health Organization (WHO), Food and Agriculture Organization (FAO), World Organization for Animal Health (OIE)) and more focus on capacity building in developing countries and the first circle of neighbouring countries to the EU (for example, Caucasia, Maghreb).

4. Support for research activities to address common challenges in prevention and management of zoonotic disease.

These four major elements, which can be conceived as constituting the strategic framework for informing policy on zoonoses, will be reviewed in detail in the remainder of this report, particularly for what has been achieved since 2004. In addition, the EASAC Working Group emphasised the importance of better education in communicating about infectious diseases – from elementary school through to medical school – a prerequisite for achieving progress in the four areas.

[5] The importance of collaboration between human and veterinary science is becoming increasingly recognised internationally. For example, in the USA current initiatives by the American Veterinary Medical Association and American Medical Association address the objective of "one medicine" to help fight zoonoses and advance both human and animal health (Enserink, 2007).

3 Recognising the importance of zoonoses

3.1 Surveillance, monitoring and risk-based approaches

In the view of the Working Group, since the Presidency conference in 2004 there has been increasingly widespread recognition of the importance of zoonoses in public health in the EU. This growing recognition has been stimulated by public concerns on visible threats, most recently avian influenza, and before that SARS, BSE and the fear of bioterrorism.

Animal health and food safety monitoring for specified agents and infections is now harmonised across the EU although the execution of the strategies requires continuing monitoring and national control plans are not fully harmonised.[6] In particular, there are clear reporting systems and strong networks for priority pathogens relating to food safety under the guidance of EU Reference Centres, and it is important for these Centres to be active in helping with the development of national control systems.[7] The avian and human influenza information systems also work consistently well across the EU (see subsequently for discussion of other EU influenza-preparedness planning). However, in the opinion of the Working Group, there are still technical problems in standardising methods of diagnosis using new, rapid technologies (based on polymerase chain reaction) for some pathogens for some countries. This has implications for the additional funding required for training. Financial pressures and continuing reduction of government services are a common theme for many Member States, threatening levels of equipment and staffing despite the improved general awareness of zoonoses in public health.

What is required to devise optimal surveillance systems? Primarily, a commitment to fund the capacity to provide ongoing data collection and real-time analysis, with procedures to use the information collected to inform policy and action, a feedback mechanism to foster continual improvement, and a remit to include all relevant human and animal infections (Hueston, 2006). Development and adoption of such systems in the EU necessitates further prioritisation of public-health goals and surveillance of pathogens that is complementary to host and environmental monitoring. As Hueston (2006) observes for the US, the successful performance of optimal surveillance systems can be monitored in terms of their ability to anticipate new threats, to operate flexibly, to involve public–private partnerships, to concentrate on risk management and to deliver incremental improvement in public health. These goals are equally applicable to the EU. Recent analysis by the European Society of Clinical Microbiology and Infectious Disease (ESCMID)[8] on the proposed DG Sanco public-health strategy highlights the desirability both of revising the list of communicable diseases (Appendix 2) with the objective of including additional pathogens and of harmonising diagnostic guidelines (a recommendation also made in the EASAC report on Antibacterial Resistance, 2007).

It must also be recognised that surveillance capacity is multi-disciplinary and encompasses a wide range of activities in addition to the centralised, expert surveillance systems. Most new disease patterns of public health importance will be detected locally by farmers, veterinary surgeons, nurses and primary care doctors. Therefore, it is also important to improve awareness and competence within this wider population to detect disease and to provide the funding (perhaps insurance-based) to encourage and facilitate farmers to report disease. It is vital that information from the local level is reported consistently through efficient communication channels and is heeded by the public health authorities. We welcome the recent announcement from DG Sanco[9] on a new Animal Health Strategy that includes the proposal to develop a harmonised EU framework of the criteria for responsibility and cost-sharing in the event of a disease outbreak. We ask that the forthcoming action plan for this Community Health Strategy includes a focus on zoonoses.

3.2 Socio-economic impact

Estimating the likely impact of zoonotic diseases in Europe with reference to health, social and economic costs is very difficult. There is considerable uncertainty on prevalence and significant underestimation of incidence because of the lack of standardised approaches to diagnosis and reporting of many diseases. Estimates (MedVetNet, 2005) suggest that there are nearly 400 million cases of food-borne infection in Europe annually with a potential cost to the EU of, perhaps, €40 billion annually. In detailed analysis of medical expenses and lost productivity, the Department of Agriculture estimated

[6] In some Member States, national control plans are not yet fully formulated: for example for *Salmonella* in poultry layers and broilers and for *Campylobacter*.

[7] EFSA Zoonosis Data Collection Reports on www.efsa.europa.eu/en/science/monitoring_zoonoses/reports.html.

[8] Response to DG Sanco consultation document "Health in Europe: A Strategic Approach", February 2007, on www.escmid.org.

[9] A new Animal Health Strategy for the European Union (2007–2013) where "Prevention is better than cure". DG Sanco, August 2007 on http://ec.europa.eu/food/animal/diseases/strategy/animal_health_strategy_en.pdf.

costs in the US as $7 billion annually for five food-borne diseases (*Campylobacter*, verotoxigenic *Escherichia coli* (*E. coli*) (0157:H7), Shiga toxin-producing strains of *E. coli*, *Listeria* monocytogenes, *Salmonella*). It was acknowledged that this cost estimate represented the "tip of the iceberg" as it does not account for the broad spectrum of food-borne illnesses or the wider-ranging repercussions for consumers, government and the food industry (Institute of Medicine, 2006).

The costs of emerging zoonoses are particularly difficult to estimate but new diseases may be very disruptive on the global scale.[10] The net financial cost to the UK of BSE/vCJD was estimated by the UK government to be €6 billion (data up to 2002, Brownlie et al., 2006), and the UK government invested approximately €350 million on relevant research (up to 2002). The consequence of SARS to Asian countries as a whole was estimated at US$18 billion (in 2003). In 2006, the World Bank estimated that a severe human pandemic of H5N1 influenza could cost the global economy about 3.1% of gross domestic product – around US$1.3 trillion on a world gross domestic product of $40 trillion.[11]

3.3 Identifying zoonoses important for Europe

Following Directive 2003/99/EC, the European Commission listed those zoonoses that either must be included in monitoring programmes (list A, Appendix 2) or monitored according to the epidemiological situation (list B). Various scientific bodies have advised on which of these zoonoses represent the greatest priorities for Europe. Some of their conclusions are also presented in Appendix 2. Significant progress is being achieved in understanding priorities, but there is need for more work across a broad front to determine which of the current agents among all the routes of transmission should receive detailed attention and what should be looked for in the future. Subsequent sections in the present report further address these issues. Although specific emerging diseases cannot be predicted, it can be anticipated that something new will happen. Factors that are important in the emergence of infectious disease reflect the various changes in human ecology: increasing long distance mobility and trade, social disruption, changes in personal behaviour, human-induced global environmental changes (Weiss and McMichael, 2004).

3.4 Influenza

The zoonosis that has received most recent attention is avian influenza, in particular the H5N1 subtype. Initial EU actions to counter avian influenza and prepare for a human pandemic were described in a previous EASAC report (2006) in the context of the imperative to develop vaccines. We welcome the priority given by DG Research to funding influenza research projects.[12] At the public health level, the ECDC has provided a valuable resource in preparing and collecting risk assessments, guidance to public health authorities and advice to the general public (ECDC, 2006) and in reviewing pandemic influenza preparedness (ECDC, 2007). The latter ECDC report concludes that significant progress has been made by many Member States in conjunction with the European Commission and EU agencies, but that further work is needed to integrate planning across government departments at Member State level, to make plans operational at the local level, to ensure interoperability between countries and to do more to prevent seasonal influenza. The meeting of the European Health Forum in Gastein in October 2006 (www.ehfg.org) was rather more critical of what it perceived as weaknesses in pandemic influenza preparedness, in particular a lack of real action on international collaboration and vaguely formulated crisis plans. A joint report from academies in the UK (The Royal Society and The Academy of Medical Sciences, 2006) provides a detailed account of what is needed at the national level in linking science to policy[13] and adds to the criticism that there has been insufficient activity at the EU level to bring the planning of different Member States together (see also section 6.3 for further discussion of vaccination issues).

Swine influenza also poses important human public-health concerns. Pigs may act as host for adaptation of avian influenza viruses to mammals, and they may serve as mixing vessels for genetic reassortment between human and avian viruses.

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[10] Among the costs may be the multiple effects on tourism. For example, the impact of tick-borne zoonoses in forested areas may handicap traditional tourist sites in Europe.

[11] World Bank, "Avian flu: the economic costs", 29 June 2006 on http://web.worldbank.org.

[12] A recent publication from DG Research provides a detailed account of influenza research funded in Framework Programme 6 (http://ec.europa.eu/research/health/poverty-diseases/index_en.html). Framework Programme 7 establishes for the first time a dedicated activity "Emerging Infectious Epidemics" to include highly pathogenic influenza.

[13] Key issues covered include: procedures for control and eradication of avian influenza, better data collection for epidemiology and surveillance, development of novel diagnostics and vaccines and strategy for use of antivirals, generic forward planning at the global level, and developing better mechanisms for incorporating scientific advice in policy making. A recent update on these issues was provided in a symposium organised by The Royal Society and The Academy of Medical Sciences in November 2007 (summary available on http://royalsociety.org/document.asp?tip=0&id=7512).

4 Integration of activity between the human health and veterinary sectors

In reviewing the recommendations of the Presidency conference in 2004, it can be concluded that there has been increasingly widespread recognition of the importance both of zoonotic diseases and integrating inter-sectoral activity. There is now a good EU-wide system of reference laboratories for notifiable animal diseases. The mechanism to enable the addition of new notifiable diseases in EU surveillance networks (exemplified by avian influenza) is welcome. However, there is still more to be done at Member State and EU level to address the range of issues discussed in the following paragraphs.

Communication, co-operation and strategic coherence between human public health and veterinary systems are variable in Member States.[14] Communication is often good between the reference laboratories for human and animal disease, particularly in influenza, but there is more scope for sharing facilities. For the newer Member States in central Europe, historically good networks at the district level have been maintained and systems were generally improved to comply with EU entry requirements but relationships, and the efficiency of joint actions, are not always as good at the policy-making level. There is, again, the concern that financial restrictions are now degrading both the public health and veterinary systems.

In general, there is good integration of activity between the veterinary and human sectors for other major pathogens such as *Salmonella*, tuberculosis and rabies. In addition, some of the emerging zoonoses have been well recognised in Europe, for example BSE/transmissible spongiform encephalopathies (TSEs), trichinellosis, toxoplasmosis. However, in the opinion of Working Group members, there are other emerging zoonotic pathogens that have been relatively neglected or not effectively addressed in terms of an integrated, human–veterinary strategy, for example alveolar echinococcosis, human tick-borne babesiosis (EU1), neurocysticercosis, campylobacteriosis, cryptosporidiosis and verotoxigenic *E. coli*.

We conclude that research support for integrating the sectors has been strongest for food-borne pathogens whereas there are greater unmet needs for inter-sectoral research in vector-borne disease. One neglected area of research concerns arthropod vector populations and their changes in distribution and impact in Europe related to climate and ecological change or other causes (Box 1); this will be discussed further in chapter 6.

Box 1 Understanding the growing problem of tick-borne disease

Tick-borne diseases are increasing across the northern hemisphere, but the pattern of emergence is not uniform and cannot be attributed only to climate change.

Lyme borreliosis is the most prevalent arthropod-transmitted human infection in northern Europe. There are, currently, no plans to include this pathogen specifically in the listed diseases covered by European surveillance, and approaches to collecting data vary considerably. The problems with comparing data in Europe are discussed by Smith and Takkinen (2006).

Tick-borne encephalitis is also a common medical problem in parts of Europe and has demonstrated marked increases, for example in the Baltic States in the 1990s. Research using meteorological satellite imaging, to map temperature and moisture data over space and time, is helping to determine the impact of climate change on distribution. However, a strong case can also be made in attributing changes in incidence of tick-borne disease to local changes in human behaviour.[15]

There is a broad research agenda (see section 6.1) to characterise the populations of tick species in Europe, their current geographic distribution, future expansion and propensity for one species to replace another. Research in the social sciences is also required, to characterise those human population behavioural changes that may increase exposure to tick species – manifested, for example, in increased access to the countryside and pressure to conserve potential animal hosts.

In considering the range of zoonosis transmission routes, there is also need for more EU research to inform policy options on zoonoses associated with companion animals (pets).[16] A strong case can be made to increase the monitoring of companion animals, particularly cats and dogs, but also considering horses and exotic pets.

[14] In Switzerland, communication between human public health, veterinary health and the Swiss reference laboratories on reportable infectious diseases, including zoonoses, is considered to be excellent, and the Swiss network plays an active part in international organisations.

[15] Work of S. Randolph, 2003, Ticks and Politics on www.wellcome.ac.uk/print/WTD004548_print.html.

[16] For example, cat scratch disease (caused by *Bartonella henselae*) is not widely recognised in the EU, although in the USA the regional prevalence of infection in cats is estimated to be 6–30% (Brunt et al., 2006).

5 Greater co-operation at the global level

5.1 International partnership

Since the Presidency conference in 2004, the introduction of several new enabling initiatives will help to characterise and tackle more systematically the infectious disease burden at the global level. As noted previously, any EU strategy to combat zoonoses should involve non-EU neighbours, but it is also important to realise that infectious disease can rapidly move between continents as well as between neighbouring countries.

The WHO International Health Regulations adopted in 2007 provide a basis for the global management of infectious disease and encourage European countries to strengthen capacity, mobilise resources and provide support to developing countries. The joint WHO–FAO–OIE Global Early Warning System is welcome in providing a mechanism to share data on zoonotic outbreaks and epidemiological analysis, and to co-ordinate a response. European expertise and resources can make a major contribution to international partnerships. For example, the EU-financed networks (EnterNet, Pulse-Net-Europe, Campynet, Cryptnet) are supporting a wide range of relevant tools and skills, including provision of databases, training for uniform molecular methodologies, analysis of national data, web-based resources, repositories of reference materials and dissemination of knowledge. The G8 Joint Science Academies' statement on avian influenza and infectious diseases[17] emphasises the importance of supporting WHO, OIE and FAO initiatives, and the responsibility in assisting developing countries in capacity building. The G8 Science Academies recommended further study of the options for developing global surveillance capabilities, the mobilisation of resources to collect clinical and epidemiological data and to develop new vaccines and drugs. EASAC endorses these recommendations for further attention at the EU level.

We welcome the publication of the report from the meeting between WHO and the UK Department for International Development (DFID) Animal Health Programme on the control of neglected zoonotic diseases (WHO, 2006). The report describes examples of the dual benefits to be gained by the animal and human health sectors by investing in the integrated and co-ordinated control of zoonoses, especially endemic diseases, promoting the concept of "one health". We commend this report as one important source of information on the international research priorities meriting European Commission funding. In addition to the value of the assistance that Europe can provide in tackling developing country priorities, collaborative work is important to Europe, to acquire experience with some of these zoonoses so that European laboratories are prepared if the diseases reach Europe. As it is also important to develop coherence between the European Commission's R&D objectives and other policy objectives, we also welcome the focus on highly pathogenic agents that forms part of the Commission's foreign policy strategy for Asia.

Apart from the moral responsibility of the EU to help developing countries, it is clear that one essential element in controlling zoonoses such as rabies, echinococcosis, brucellosis and avian influenza is to focus on the animal reservoir, and that this focus requires partnership with developing countries. Although much of the EU response to zoonoses currently concentrates on the stage where geographically dispersed clusters of disease threaten to become pandemic, there is concomitant need for preventive effort earlier in the chain of transmission, at the stages where the microbe crosses species and when direct transmission first occurs person-to-person. This necessary preventive effort entails more research on how pathogens cross the species barrier as well as more global surveillance. As proposed in the recent paper by Wolfe et al. (2007), expanded research priorities might cover two major areas: (i) elucidating the origins of established disease, requiring systematic sampling and phylogeographic analysis of related pathogens in diverse animal species; and (ii) creating a global early warning system by selected monitoring of people with high-level exposure to animals.

Taking the global perspective also requires inter-sectoral assessment of impact. In case studies from the literature discussed by the Working Group (Zinsstag et al., 2005) it was found, for example, that control of human brucellosis in WHO programmes was not cost-effective when evaluated in terms of the human health sector perspective alone, but was cost-effective when including the impact on the agricultural sector. This inter-sectoral assessment has to be broadened further – to ecological system assessment – in those cases where wildlife has a role as maintenance host, for example bovine tuberculosis (TB) in badgers in the UK.

The wider role of ecosystems in communicable disease emergence merits further study. Other EASAC work in progress[18] is concerned with the broad assessment of ecosystem services in Europe and the influence of biodiversity on zoonotic infections. The complexity of ecosystem communities may play a significant part in resisting invasion by novel pathogens and may mediate the effects of climate and socio-economic change on

[17] Accessed through The Royal Society on www.royalsociety.org/document.asp?tip=0&id=4823.

[18] EASAC Working Group on Ecosystems Services, on www.easac.eu/page.asp?id=28.

human behaviour, vector and wildlife distribution and disease risk, as described elsewhere in this report. One important new initiative is the Framework Programme 6 Integrated Project, EDEN[19], which is evaluating and cataloguing European ecosystems and environmental conditions linked to global change that can influence the spatial and temporal distribution of human pathogenic agents.

5.2 Bioterrorism

The EASAC report on Vaccines (2006) reviewed some of the policy needs to combat bioterrorism. These may require developing preparedness to tackle novel zoonoses. Prospects of intentional harm associated with food-borne threats have been discussed extensively in the Institute of Medicine report (2006).

Previous exploration of the science and technology issues relevant to the operation of the Biological and Toxin Weapons Convention covered issues for diagnosis and surveillance of infectious disease, with particular reference to dual use issues (The Royal Society, 2006), and recommended further development and application of scientific discoveries for the detection, prevention and countering of disease. Specific issues for zoonoses as biological weapons will not be considered further in the present report, but we reiterate our previous recommendations that biodefence planning must be better integrated into public health infection surveillance and control systems at the EU level (see also section 6.5, about biosecurity). Every serious disease outbreak should be properly investigated, irrespective of whether bioterrorism is suspected, and we support the mandate of the ECDC to investigate outbreaks of unknown origin.

5.3 Movement of people and animals across Member State borders

As noted previously, the effects of globalisation exacerbate the risk of spreading infectious diseases not only through the movement of people but also through the increased movement of disease vectors, livestock, wildlife, companion animals and food products.

In horizon-scanning analysis by the Working Group, identification of potentially threatening pathogens for Europe, relating to animal migration or transportation, includes leishmaniasis and babesiosis. There is also concern about the possible introduction of new arthropod vectors. It is increasingly important for animal imports to be tested and quarantined to avoid bringing in novel infectious diseases. The movement of bushmeat (Parliamentary Office of Science and Technology, 2005) continues to be a problem for the EU although it is now illegal to import meat and dairy products in personal baggage from a non-EU country.

Identification of potentially threatening emerging pathogens related to human transcontinental mobility include *Taenia solium* neurocysticercosis (now occurring in the USA), *Entamoeba histolytica* ameobiasis (potentially reaching the threshold for cycles of transmission in European countries) and Crimean-Congo haemorrhagic fever (currently in Turkey). The Working Group proposed extension of the Epidemiological Task Force initiative with scope to tackle the issues for all exotic trans-boundary diseases and immediate attention to the haemorrhagic disorders.

In addition to consideration of future threats associated with human mobility, the impact of established infectious diseases must be given greater prominence in current policy development. The Portuguese Presidency of the European Council priority theme of "Migration and Health" provided an overview of migratory flows in the EU, analysing associated health challenges and reviewing Member State health policies and their impact (conclusions and recommendations from the Presidency conference are on www.hmelisbon2007.com/site. asp?ID = 6&IDIOMA = 2). Zoonoses contribute to the infectious disease burden associated with migration. EASAC has published a short statement on the impact of migration on infectious disease in the EU.[20] The EASAC statement proposes a number of actions needed to tackle R&D priorities and to fill information gaps, to share good practice on screening, surveillance and access to healthcare and "to expect the unexpected". The Working Group agreed that screening programmes for migrants must be accompanied by the same access to Member State healthcare systems as available for the rest of the population, and noted that zoonotic infections might become increasingly important in the assessment of the public health issues relating to migration.

[19] EDEN, Emerging diseases in a changing European environment, on *www.eden-fp6project.net*. Among the indicator human diseases that are being studied as especially sensitive to environmental change are tick- and rodent-borne zoonoses and West Nile fever.

[20] Impact of migration on infectious diseases in Europe, August 2007, on www.easac.eu.

6 Support for research and innovation activities

6.1 Defining the research agenda

It is vitally important to improve surveillance and the associated activities that are customarily included within the public health remit. However, these actions are not enough – particularly for the threat of emerging zoonoses. There is also need for sustained EU commitment to the basic and translational research that will help to build understanding of the challenges, and support application through novel diagnostics, therapeutics and vaccines. Some of the recent developments have been mentioned in section 2.3. We urge DG Research to continue funding work on infectious diseases as a priority area, and we urge Member States to support this prioritisation of effort when advising on Framework Programme 7 work plans.

The Framework Programme 7 Health theme provides relevant support expressed, for example, in the recent Calls for projects "Definition of research needs and priorities in Europe in the area of Emerging Infectious Epidemics" and "Strengthening research on prediction, identification, modelling and surveillance of newly emerging infectious disease in humans". With the latter, the Working Group noted that effective modelling requires good knowledge of the natural history of disease. We therefore welcome DG Research funding for validating modelling and economic evaluation of interventions for the control of infectious disease (for example, the Polymod project) and the use of these models in work funded by DG Sanco (for example, http://venice.cineca.org/polymod.html). Other scientific groups (notably the Framework Programme 6-funded Networks of Excellence and the Technology Platforms/ Joint Technology Initiative) have devoted considerable effort to identifying specific research priorities, and a systematic account will not be attempted here.

The Working Group noted, however, that there are challenges for Framework Programme 7 associated with establishing a critical mass of funding, selection of research priorities and with the need for better retrospective evaluation of the science funded, to assess its fitness for purpose and the added value derived. Although we appreciate that the European Commission hears many concerns from across the research community about lack of funding, there does appear to be a real insufficiency of investment in investigator-led basic research in infectious diseases (with the important exception of influenza). There is an opportunity to do better in understanding mechanisms of interspecies transmission, host adaptation and pathogenicity, including the molecular determinants of host specificity. For the four main categories of zoonoses (section 1.1), the Working Group advised the need for more research funding to be targeted preferentially on vector-borne zoonoses and those transmitted by wildlife. The Working Group emphasised the general need to support new ecology research in order to understand the determinants for the host range and populations of different vectors, the likely impact of climate and other environmental change, and the interaction between wildlife reservoir, vector and infectious agent. Scientific disciplines such as entomology where skills have become scarce need to be revived to document and differentiate vector species. Some specific examples are provided in Box 2 to build on the surveillance points made earlier.

Box 2 Identification of research priorities in relatively neglected areas in ecology and vector biology

- Changes in the biology and European distribution of arthropod vector populations by monitoring according to a standard European protocol. To include key insect species of the genera: *Culicoides, Anopheles, Aedes, Simulium*; and key tick species of the genera: *Ixodes, Dermacentor, Rhipicephalus, Haemophysalis, Amblyomma*.
- Changes in zoonoses related to changes in the European distribution of arthropod vector populations, for example leishmaniosis, human babesiosis (EU1) and ehrlichiosis/anaplasmosis.
- Changes in vector competence – pathogen movement into new vectors.
- Changes in the European distribution or population density of wildlife animal species which serve as important reservoir for the transmission of pathogens to humans. Key species include racoon-dogs and foxes (for *Echinococcus multilocularis*), racoons (for *Baylisascaris procyonis*), various rodent species (for various viruses, bacteria and parasites), birds and bats.
- Evolutionary adaptation of emerging zoonotic pathogens, to include the study of genetic diversity of key organisms and their evolutionary development to adapt to the changing European ecology.

6.2 Scientific opportunities for detection of infectious disease

Previous EASAC reports have emphasised the value of developing new rapid diagnostic tests, based on common technology platforms, sensitive, simple and cheap to use at the point of care. For avian influenza diagnosis, the Royal Society and Academy of Medical

Sciences report (2006) recommended that the European Commission should consider ways to stimulate an environment which would encourage investment in new diagnostic products. We agree and suggest, furthermore, that efforts to create this supportive environment would also be highly relevant to tackling other zoonoses.

A recent UK Foresight project (Office of Science and Innovation, 2006) ranged widely in exploring the scientific opportunities on which to build longer-term advances in the detection, identification and monitoring of zoonoses (Box 3). In reviewing these scientific opportunities, the Working Group confirmed the importance of additional priorities relating to the monitoring of animal reservoirs and vectors (Box 2) as well as pathogens. As was observed in the report of the Health Council of the Netherlands (2004), although it is virtually impossible to predict the pathogen nature or location of the next zoonotic outbreak, transmission by vectors may constitute an exception to this rule – if the monitoring of vector spread is improved.

Box 3 Selected scientific opportunities for future detection, identification and monitoring of zoonoses

Adapted from UK Foresight project:

- Data mining and fusion from disparate sources to detect emergence and track spread of new diseases and to generate meaningful information for decision-making.
- Non-invasive scanning and screening, based on thermography or novel imaging techniques and biosensors for fast throughput evaluation at ports and airports.
- Genomics and other -omics for faster, cheaper sequencing of pathogen genomes and microarray expression systems to identify pathogens and their characteristics (particularly drug resistance).
- Interrogation of signals and biomarkers, including immunosignatures, for early detection of host response to disease; possible application in syndromic surveillance methods.
- Predictive and real-time epidemiological modelling and simulation to help plan for future epidemics, predict impact and measure effects of control procedures.
- Engineering animal host genome to resist infection or to produce sentinel animals particularly susceptible to infection, for early detection of disease.

Added in EASAC Working Group discussion:

- Monitoring and surveillance strategies based upon wildlife animal reservoirs[21] (natural sentinel animals) and investigations on arthropod vector populations.
- Studying host species' susceptibility and resistance to infection (research has been conducted for avian influenza but not other pathogens).
- Studying the potential of evolution of key pathogens, allowing their rapid adaptation to new ecological niches.

We support the Foresight approach in taking a broad view of what may be relevant R&D. For example, the genetic engineering of vectors[22] as well as animal hosts might be contemplated. Although such R&D objectives may be long-term, there is an associated short-term need for basic research in genomics to ascertain what might become feasible. However, Working Group experience with the current European sheep scrapie plan indicates the desirability of taking a cautious approach to genotype selection for pathogen resistance. In this context, there is also a need for EU research into the impact of the emergence of atypical scrapie and its possible transmission across the species barrier to humans.

In addition to reviewing scientific opportunities, the Foresight outputs delineated the strategic choices to be made by policy-makers. Thus, to what extent should the approaches for identifying disease be more proactive? Should the programmes for managing individual diseases be more co-ordinated? What options need to be considered in setting the framework for governance and regulation, in setting standards, defining criteria for interoperability and providing the necessary skills and infrastructure? In considering these questions, the EASAC Working Group emphasised the need to be more proactive, perhaps particularly in wildlife surveillance; satisfying this need could drive new technology development in diagnostics. For example, production of a single diagnostic chip to detect a broad range of viruses would greatly facilitate exploration of the spectrum of

[21] For example, evidence contributed from Slovakia to the Working Group discussion described the monitoring of *Trichinella* and *Echinococcus multilocularis* in the red fox to identify areas with a high risk of human infection. Extension of such monitoring requires improved performance of veterinary services and environmental organisations for the capacity to capture sufficient animals to be representative or, alternatively, the development of diagnostic methods for animal faeces *in situ*.

[22] By analogy with recent work on transgenic malaria-resistant mosquitoes (Marrelli et al., 2007).

disease in rodents, bats and other key hosts. We recommend that the European Commission provides additional funding in Framework Programme 7 to meet this diagnostic objective.

It is, of course, particularly difficult to plan to detect novel pathogens; syndromic surveillance of early indicators (Box 3) may facilitate such detection. However, there is a high degree of uncertainty about how to create systems of syndromic surveillance, defined by the US CDC as "*the collection and analysis of health-related data that precede diagnosis or laboratory confirmation and signal with sufficient probability a case or an outbreak to warrant further public health response*." Syndromic surveillance has probably been used most frequently in US military applications although there is potential value in the public health elucidation of emerging zoonoses. If successful, this would allow earlier detection of clinical patterns, thereby introducing an earlier public health response, enabling the rapid targeting of limited public health resources and, perhaps, also providing a basis for informed risk communication to allay public disquiet (Kelley, 2006).

6.3 Vaccines

The policy issues for human vaccine innovation in Europe were discussed in detail in a previous EASAC report (2006). Those recommendations are applicable to animal and human vaccines in proposing mechanisms to provide incentives for manufacturers, improving the research capabilities of the regulatory authorities, strengthening public-sector support for vaccine R&D and promoting vaccine uptake.

There is a lot happening in animal vaccination initiatives, funded by both public and private sectors, although there is room to do more. Global turnover on animal vaccines is estimated at €2.6 billion, with the EU share at about 50%, and a significant proportion of products are biotechnology based (Zika et al., 2007). The EU vaccine market for notifiable diseases in farm animals is highly dependent on official vaccination programmes and once eradication has been achieved, the vaccination programme is discontinued. Thus, there is a particular issue for diseases that can be eradicated in the EU where neighbouring countries remain a reservoir (for example, rabies). It is important that the relevant vaccines continue to be manufactured and stockpiled, that expertise and training programmes are maintained, and that pathogen stocks are securely retained for future research. Further discussion is recommended on the extent to which DNA banks can replace pathogen banks (with the potential advantage of necessitating less security).

The avian influenza vaccination strategies have received much attention. However, the Working Group noted that vaccination campaigns in endemic countries are not necessarily well monitored and are using different vaccine preparations, so variable success may be expected. Much more research is needed to find and monitor appropriate control measures (culling as well as vaccination strategies). Current regulations, guidelines, methods and experience in avian influenza vaccination were recently reviewed with the objective of supporting the OIE–FAO strategy in implementing vaccination programmes (www.avianfluvaccine2007.org/introduction.htm).

Compared with human vaccine R&D, the level of regulation to allow animal vaccine field trials and litigation pressures have, historically, been relatively light. This is no longer the case for genetically modified products. Biotechnology approaches are increasingly used in attempts to develop "marker" vaccines, which allow the distinction to be made between vaccinated and infected animals (and, thereby, enable disease monitoring). There are many R&D challenges in producing new veterinary vaccines even when it can be decided which are the target pathogens. For example, many infections are caused by multiple serotypes (as in avian influenza); there are major immunological differences between host species; there is often lack of public acceptance for vaccination of food producing species; there may be environmental constraints. Tackling these challenges requires more research on basic and applied immunology of the target animal species; completion of the genome sequencing of chicken, pig, dog and other target species now provides a valuable scientific basis for developing better vaccines. The work of the US–EC Task Force on Biotechnology Research relating to advances in immunology and vaccine discovery is welcome as an indication of the growing importance of this area to policy-makers.

There is a continuing problem in the relatively weak return on investment in vaccines for manufacturers, compounded by the problem of providing incentives to manufacturers to prepare for emerging zoonoses in the absence of a current market. We agree with the points contributed in evidence to the Working Group by the Academy of Medical Sciences in the UK that the European community must identify mechanisms to provide appropriate incentives for industry. Detailed discussion of the scientific opportunities underlying vaccine innovation and the necessary conditions to support technology transfer, facilitate animal vaccine development and regulation is provided in the outputs of the Technology Platform on Global Animal Health (see section 2.3).

The high-profile example of influenza vaccine R&D (section 3.4) illustrates the general importance of ensuring the sharing of virus samples, genetic sequences and data within the broader context of benefit-sharing. The WHO Resolution WHA 60.28

("Pandemic Influenza Preparedness: sharing of influenza viruses and access to vaccines and other benefits") requested the Director-general of WHO to identify and propose frameworks and mechanisms that aim to ensure the fair and equitable sharing of benefits.[23] One of the most important benefits derived from virus sharing is the continuing ability of WHO to assess the global risk of the emergence of a strain of influenza virus with pandemic potential, as required under the International Health Regulations. The information derived from risk assessment enables the updating of vaccines and diagnostics to contribute to global preparedness and responsiveness. It is vital for WHO to continue to co-ordinate provision of the global public health benefit and this role must continue to draw on European expertise and resources, requiring continuing commitment to surveillance and the development of countermeasures in public health as described throughout the present report.

6.4 Opportunities and challenges in chemotherapy

A previous EASAC report (EASAC, 2007) emphasised the priority need to develop novel anti-infective agents as a consequence of the growing problem of antibacterial resistance. The problem of antiviral resistance is also becoming more pronounced, for example the rapid development of resistance by H5N1 influenza to amantadine. Recent publications from one of the members of the Working Group (De Clercq, 2006; De Clercq and Neyts, 2007) reviewed the drugs currently available that could be used alone, or in combination, for prophylaxis and therapy of influenza A viruses and discussed the need to design and develop new antiviral agents. Novel agents for human medicine might emerge from research on known molecular targets such as neuraminidase or the viral uncoating process, but there is also merit in pursuing new strategies directed at relatively unexplored targets such as the viral proteins haemagglutinin, the viral RNA polymerase (and endonuclease) and the non-structural protein NS1. Furthermore, as has been shown for other viral infections, RNA interference could be a powerful means with which to suppress the replication of avian H5N1. Consideration of whether antiviral chemotherapy should be extended to animal use in view of the danger of accelerating development and transfer of drug resistance requires a case-by-case assessment of the opportunities to control animal disease.

An additional challenge – and opportunity – for chemotherapy resides in the problem of anthelminthic resistance, markedly increasing in veterinary medicine in Europe with gastro-intestinal nematodes of ruminants. Thus, for example, more than 80% of sheep farms harbour gastro-intestinal nematodes resistant to benzimidazoles; and many goat farms experience problems of multiple resistance to benzimidazoles and macrocyclic lactones.

We encourage the European Commission to continue to find ways to support public-sector scientists in chemotherapy discovery research and to build collaboration with the private sector.

6.5 Providing the infrastructure for research and its applications

Three other issues are of continuing importance. We discuss these below.

Biological containment facilities

Concern was expressed in an earlier EASAC report (2005) about the availability of facilities for handling pathogens. Informal discussion suggests that there has now been some significant improvement in infrastructure for biosafety laboratories and animal facilities. Although it is difficult to specify how many Level 3 and 4 laboratories are required in Europe, it is still important to ensure that they be operated cost-effectively: that is, their use is maximised and provides for the shared needs of other Member States lacking similar infrastructure and in support of research as well as diagnostic objectives. Furthermore, in seeking to determine future requirements, the Working Group observed that once a pathogen is eradicated, it becomes potentially more dangerous and requires a higher level of containment. The EU Biosafety Consortium, funded in the field of Security Research, is undertaking an inventory of BSL 3 and BSL 4 laboratories across Europe. A recent update on this project[24] indicated difficulty in identifying all relevant laboratory contacts across Europe and early responses to the survey showed significant variation in definition of what is covered by biosafety procedures. It is important to wait until the full results of this important project are available but it seems likely that there is need for further harmonisation and standardisation in the facilities for biosafety across Europe. Moreover, the Working Group highlighted one current deficiency in the absence of highest-level containment facility for the study of large animals (for example, cattle) for zoonoses with severe potential for human disease.[25]

[23] On www.who.int/gb/pip/pdf_files/PIP_IGM_2Rev1-en.pdf.

[24] Personal communication from project co-ordinator to Mettenleiter in the Working Group.

[25] Building a BSL 4 laboratory and animal facility, adequate for housing large animals, is due to begin in 2008 at the Friedrich-Loeffler-Institut, to be completed in 2011.

The provision of biological containment facilities also needs to take account of the developing strategy in biosecurity. In July 2007, the European Commission adopted a Green Paper on biopeparedness[26]: the aim is to stimulate debate at the European level on how to reduce biological risks and to enhance both preparedness and response capabilities through a biological all-hazards approach. Such an approach takes into consideration potential risks from a terrorist attack or other intentional release (see section 5.2) and naturally occurring disease. Appropriate security practices cannot be built without a strong safety culture. The Green Paper provides a stimulus to improving security while building on safety rules and best practice, but we express caution: it is important to avoid over-regulation and the introduction of new bureaucratic measures in addition to those already in place.

Human resources in infection surveillance, management, prevention and risk assessment

Previous EASAC reports (2005, 2006 and 2007) have recommended increasing EU commitment to developing skills and continuing education and training programmes in microbiology and infection control in both human and veterinary science. These issues remain important.

Animal research

Medical advances, for both human and animal benefit, have depended on animal research and are likely to continue to do so. Animals should only be used in research when the research cannot be done in other ways (for example, *in vitro* or by computer simulation), and then only with care.

Many in the scientific community have expressed concern that current revision of Directive 86/609/EC on the protection of animals used for experimental and other scientific procedures may inadvertently constrain the opportunities to make new discoveries in fundamental science and to apply new knowledge in the development of needed diagnostics, therapeutics and vaccines. One particular area of concern for researchers is the recent declaration from Members of the European Parliament requiring the adoption of a timetable for replacing the use of non-human primates in research. There is a significant body of evidence demonstrating the value of non-human primates in medical research, and a major area of inquiry is infectious diseases (Weatherall, 2006). EASAC endorses the findings of the Weatherall Report and urges the European Commission and European Parliament to give full consideration to the scientific evidence demonstrating the need for regulated research using animals for carefully selected research questions.

[26] European Commission Green Paper on bio-preparedness, on www.eubusiness.com/Living_in_EU/biopreparedness.

7 Assessing the challenges and finding solutions: from policy development to action

7.1 Taking forward the strategy to combat zoonoses and foster "one health"

The broad agenda for policy on zoonoses, discussed in the previous chapters, covers science-based surveillance and control, R&D investment and prioritisation, human–veterinary strategy co-ordination, all within the overarching framework for delivering improved procedures for risk assessment, risk management and risk communication. Education is needed to support better recognition and understanding of zoonoses at all levels of society, including professional bodies. Although, traditionally, many education issues – particularly in primary and secondary schools – are considered a responsibility of Member States, the recent Rocard report on Science Education[27] proposes ways to improve science education at local, national and European levels. In higher education, the EASAC Working Group suggested that there may be opportunities for provision of common courses on infectious disease to veterinary and medical students, so helping to provide the training basis for "one health"

Within this broad agenda, some cross-cutting themes can be discerned as the basis to inform the public health policy making priorities (Box 4).

Box 4 Cross-cutting themes for the zoonoses health-policy agenda

1. Identifying potential for improvement in current systems: developing collaborative approaches to integrating policy and action, involving all stakeholders:

- Co-ordinating multiple EU surveillance networks, data access and synthesis, training, interventions; addressing deficits in science.
- Meeting public communication and information needs.
- Horizon-scanning and creating expert systems to assess threats from emerging zoonoses with capability for independent, evidence-based risk assessment.

2. Optimising responsiveness:

- Implementing a coherent strategy for supporting innovation for vaccines, diagnostics and therapeutics (human and veterinary).
- Identifying and implementing other prevention and control measures.
- Contingency planning based on modelling and simulation studies.

3. Preparedness for societal and environmental change:

- Quantifying the impact of human and animal movement across borders.
- Addressing the consequences of climate change.
- Seeking consensus on other globalisation issues.

4. Education and training:

- Promoting awareness in the general population.
- Developing and maintaining a skilled healthcare workforce.
- Providing for the next generation of researchers.

We emphasise that the ECDC has a central analytical and advisory role in many of these areas. ECDC and EFSA resources represent critical parts of the co-ordinated system for risk assessment and communication. We believe that the case has been made for doing more to progress from co-operation to harmonisation in human health, for providing better links with the European veterinary strategy, and for doing more to understand possible scenarios for zoonoses in determining the risk of initial transfer and risk of spread. ECDC should also take a lead in building interaction between epidemiologists in Europe and elsewhere; we welcome the activities of ECDC in 2007 in organising the first European Scientific Conference on Applied Infectious Disease Epidemiology and in co-ordinating The European Programme for Intervention Epidemiology Training.

We also welcome the recent commitment shown by ECDC to seek advice from a wide range of professional and scientific expert groups, including EASAC, and we support ECDC objectives to increase their resources. However, because of the limited resources available to the European Commission we advise that it is not the highest priority for ECDC itself to have its own reference laboratory facilities. It is higher priority for ECDC to continue to build a good network with laboratories in the

[27] "Science Education Now: A renewed pedagogy for the future of Europe", High Level Group on Science Education, DG Research 2007, EUR 22845.

Member States and to second ECDC staff to these centres of excellence.

We support the objectives of ECDC to increase links with EFSA with clear agreement on how information is exchanged, avoiding inappropriate duplication and, where possible, standardising data collection for all zoonotic diseases irrespective of whether the disease is "listed" (Appendix 2). The activity of EFSA and ECDC in publishing an annual "Zoonosis report" and the establishment of one European centralised technical framework for all surveillance data (The European Surveillance System, TESSy) are important initiatives. Under subsidiarity, the statutory powers for managing infection currently remain at the Member State level. However, it is crucial that further discussion between Member States and the European Commission explores the extent to which European agencies might acquire new decision-making roles with which to support the co-ordinated control of communicable diseases at the Community level. Furthermore, the scientific community has an important collective responsibility to formulate guidelines for testing and disease management. If this responsibility is exercised, then there is an opportunity for the European Commission, Parliament and Council jointly to consider the policy options to take forward implementation of scientific guidance in a manner that the Member States can accept. Guideline formulation and implementation must also be accompanied by commitment to compile the evidence base to measure impact.

7.2 EASAC recommendations

Epidemiology and surveillance

We recognise that much has been done to create surveillance networks at the European level but there are still major challenges to be faced:

(i) There must be continuing effort to refine the consensus list of diseases subject to routine surveillance, based on public health needs. There is ongoing need to improve co-ordination between the medical and veterinary communities and ensure rapid communication of information about zoonoses.

(ii) More attention is required to generate consistent quality datasets, to support optimal data access and data mining, and to ensure sustainable funding for the surveillance networks. We encourage ECDC to continue developing The European Surveillance System, to validate reported data and to progress the long-term surveillance strategy, which includes the continuing evaluation of the quality of the surveillance systems.

(iii) There is a need for new methods to monitor the occurrence of zoonotic agents in wild animals.

(iv) The ECDC has a central role in surveillance, in providing the key linkage with the EFSA, in helping to understand and prepare for future scenarios to assess the threats from emerging zoonoses, and in leading collaboration with epidemiologists internationally. There is value in initiating collective discussion between the European Commission, Parliament and Member States to re-assess the degree of decision-making that may be allowed to the European agencies to support their increasing roles and responsibilities in the area of infectious diseases. The scientific community also needs to do more to provide expert advice to inform this discussion and to work with the agencies – we urge the scientific community to use the opportunities for collaboration provided by ECDC, to identify scientific priorities on zoonoses and to complement the current work of the Technology Platforms and Networks of Excellence.

(v) Policy-makers must recognise that surveillance is multidisciplinary and encompasses a wide range of activities in addition to the centralised expert surveillance systems. There is a need for improved local monitoring, particularly at the farm level, and reporting systems for unexplained, excess animal mortality together with a need to integrate the regional activities.

International co-operation

The EU could do better in bringing together the planning of different Member States, with international partners, to prepare for the challenges faced by health systems in responding to acute threats such as pandemic influenza. We also recommend that the European Commission continues to develop its efforts to support joint thinking on issues of mutual interest and build support for international initiatives, in particular the Global Early Warning System for zoonoses and the G8 Science Academies' recommendations on infectious disease. In addition:

(i) EU policy-makers need to look beyond an immediate focus on countries neighbouring the EU and to appreciate that infectious disease can move rapidly between continents.

(ii) The European Commission should fund new research partnerships with developing countries to understand the early stages in zoonotic disease transmission: for example by systematic analysis of related pathogens in diverse animal species and the selected monitoring of humans with high level exposure to animals.

(iii) It is highly important to address the potential impact of climate change and the changing global pattern of infectious diseases.

(iv) Zoonoses contribute to the infection burden associated with human migration. EASAC

welcomes the recent initiative of the Portuguese Presidency of the EU Council on migration and health to analyse the principal health challenges and review health policy impacts. We urge the forthcoming Presidencies in Slovenia, France and the Czech Republic to provide continuity in policy attention to this important area.

Research and education

We appreciate that European funding for research is finite and can never match all the requests from the research community, but we judge that there are current gaps in the area relating to zoonotic infections. Although better co-ordination between research groups must continue to be encouraged to avoid unnecessary duplication, there are now significant opportunities to fund critical areas:

(i) It is important to support investigator-driven fundamental science, even in those disease areas previously deemed relatively unimportant in public-health terms. The EU must maintain a broad range of scientific expertise to ensure the flexibility to respond rapidly to new threats. Opportunities for basic research coming into range include the study of mechanisms of interspecies transmission of infection and host adaptation and pathogenicity.

(ii) Previous research support for integrating the human and veterinary sectors has been strongest for food-borne pathogens. There are unmet needs for inter-sectoral research in vector-borne diseases and on zoonoses associated with wildlife and companion animals (including exotic pets) to understand the risk factors involved in the emergence of zoonoses. There is a broad agenda of research possible in these hitherto neglected areas, ranging from ecological study of vector biology, distribution and evolution to the social-science study of human behavioural change.

(iii) Assessing the socio-economic impact of zoonotic infections and public-health interventions.

(iv) Supporting better provision of information about infectious disease throughout the education system to promote awareness in the community-at-large, to develop skilled healthcare professionals and to develop the next generation of research scientists. This requires action starting in elementary schools and continuing through to higher education, especially teaching about zoonoses in medical, veterinary and food-science facilities.

Innovation

It is important for the European Commission and Parliament to stimulate an environment that will encourage new investment in diagnostic, therapeutic and vaccine products. In particular:

(i) The European Commission must find new ways to provide incentives to European vaccine manufacturers to support their engagement in R&D, to improve the research capabilities of the Regulatory Authorities, to strengthen public-sector support for vaccine R&D and to promote vaccine uptake. These recommendations are equally applicable to human and animal vaccines.

(ii) There is a need to develop new strategies directed at unexplored targets for antiviral chemotherapy, and there is concomitant need for further expert discussion on whether such approaches should be extended to cover animal use.

(iii) The recent UK Foresight project on the detection, identification and monitoring of infectious disease is a starting point for further consideration of the opportunities for new diagnostic applications in Europe. For example, we believe that there is particular potential for developing a broad virology chip for monitoring the spectrum of pathogen in wildlife species. We recommend that Europe is more proactive in the monitoring of animal reservoirs and vectors as well as pathogens.

(iv) There is a growing need to bring together industry, public research and higher education capabilities to support research on zoonoses and the development of novel diagnostics, therapeutics and vaccines. We welcome the initial progress made in the Global Animal Health Technology Platform and the Innovative Medicines Joint Technology Initiative. We urge the industry sectors to support these initiatives, both intellectually and financially, and to continue to work with DG Research to identify how bureaucracy in project selection and management can be minimised.

List of abbreviations

BSE	Bovine spongiform encephalopathy
CDC	Centers for Disease Control and Prevention (USA)
DFID	Department for International Development (UK)
DG Sanco	Directorate-General for Health and Consumer Protection
EASAC	European Academies Science Advisory Council
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
EPSCO	Employment, Social Policy, Health and Consumer affairs Council of the EU
ESCMID	European Society of Clinical Microbiology and Infectious Disease
EU	European Union
FAO	Food and Agriculture Organization
HIV	Human immunodeficiency virus
OIE	World Organization for Animal Health
R&D	Research and development
SARS	Severe acute respiratory syndrome
SIV	Simian immunodeficiency virus
TB	Tuberculosis
TSEs	Transmissible spongiform encephalopathies
vCJD	Variant Creutzfeldt-Jakob disease
WHO	World Health Organization

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Appendix 1: Working Group remit and composition

This Appendix covers key questions posed in the Call for Evidence, and covered by the Working Group.

1. What has happened since the Netherlands Presidency conference in 2004 ("European Responses to Public Health Risks for Emerging Zoonotic Diseases"), in particular with recommendations made on the need for more widespread recognition that zoonotic diseases are a problem, the need for better inter-sectoral activity and international engagement and for support of research activities?
2. What is the current situation in each Member State for co-ordination between human public health and veterinary systems? Which disease areas have not yet been integrated in EU planning but should be?
3. What further resources and action are needed at EU level for: (i) diagnosis and surveillance; (ii) prioritisation of research agendas, skills and career development, infrastructure; (iii) improving preparedness in hitherto neglected areas; (iv) vaccine innovation?
4. What are the issues for EU public health arising from animal and human mobility?

This report was prepared by consultation with a group of experts acting in an individual capacity and was reviewed and approved by EASAC Council. A Call for Evidence was published on the website (www.easac.eu), and the Working Group met twice to consider issues, completing the draft report in December 2007.

Members of the Working Group

Volker ter Meulen (Chairman)	President of the German Academy of Sciences, Leopoldina
Erik De Clercq	Rega Institute for Medical Research, University of Leuven, Belgium
Pavol Dubinsky	Parasitological Institute SAS, Kosice, Slovak Republic
Malcolm Ferguson-Smith	Department of Veterinary Medicine, University of Cambridge, UK
Bruno Gottstein	Institute of Parasitology, Vetsuisse Faculty and Faculty of Medicine, University of Berne, Switzerland
Hans Dieter Klenk	Institute for Virology, Philipps University, Marburg, Germany
Alenka Kraigher	Communicable Diseases Center, Institute for Public Health, Ljubljana, Slovenia
Bohumir Kriz	Centre of Epidemiology and Microbiology, National Institute of Public Health, Prague, Czech Republic
Thomas Mettenleiter	Friedrich-Loeffler Institute, Greifswald-Insel Riems, Germany
Bela Nagy	Hungarian Academy of Sciences, Veterinary Medical Research Institute, Budapest, Hungary
Charles Pilet	French Academy of Sciences; National Academy of Medicine; Veterinary Academy; Alfort Veterinary School, France
George Saroglou	Department of Internal Medicine, University of Athens, Greece
Eystein Skjerve	Norwegian School of Veterinary Science, Oslo, Norway
Robin Weiss	Division of Infection and Immunity, University College London, UK
Tadeusz Wijaszka	National Veterinary Institute, Pulawy, Poland
Robin Fears (secretariat)	EASAC, UK

A late draft of the Working Group output was discussed with Cornelius Schmaltz and Isabel Minguez-Tudela (DG Research), Masja Straetemans (ECDC), Franz Karcher (DG Sanco), Declan O'Brien (Technology Platform on Global Animal Health) and Franz Allerberger (ESCMID). We are grateful for their comments.

Appendix 2: EU priorities for policy and research on zoonoses

1. Zoonoses specified in association with Directive 2003/99/EC

List A: zoonoses and zoonotic agents to be included in monitoring:

Brucellosis and agents thereof

Campylobacteriosis and agents thereof

Echinococcosis and agents thereof

Listeriosis and agents thereof

Salmonellosis and agents thereof

Trichinellosis and agents thereof

Tuberculosis (due to *Mycobacterium bovis*)

Verotoxigenic *Escherichia coli*

List B: zoonoses and zoonotic agents to be monitored according to the epidemiological situation

1. *Viral zoonoses*

Calicivirus

Hepatitis E virus

Influenza virus

Rabies

Viruses transmitted by arthropods

2. *Bacterial zoonoses*

Borreliosis and agents thereof

Botulism and agents thereof

Leptospirosis and agents thereof

Psittacosis and agents thereof

Tuberculosis other than in list A

Vibriosis and agents thereof

Yersiniosis and agents thereof

3. *Parasitic zoonoses*

Anisakiasis and agents thereof

Cryptosporidiosis and agents thereof

Cysticercosis and agents thereof

Toxoplasmosis and agents thereof

4. *Other zoonoses and zoonotic agents*

2. Identifying priorities: other scientific investigation

The total number of zoonoses in Europe is greater than those specified in lists A and B. A description of the current indigenous and imported zoonotic diseases in one Member State (UK) is provided by the Health Protection Agency (www.hpa.org.uk/infections/topics_az/zoonoses/table.asp). The material compiled preparatory to the Netherlands Presidency conference in 2004 (Appendix IV, Van der Giessen et al., 2004) provides a comprehensive list of zoonotic diseases with etiological agent, most likely animal reservoir, mode of transmission and geographical distribution. Additional expert analysis used to inform the Presidency conference (Health Council of the Netherlands, 2004) identifies the major emerging zoonotic diseases for Europe as avian influenza and food-borne bacteria (becoming increasingly virulent and acquiring increasing antimicrobial resistance), with potential increasing threats from Hanta viruses, orthopox viruses, Lyme borreliosis, Rift Valley fever, West Nile virus and monkeypox.

In bibliometric study, in a search of the Medline database 2000–2006 (Vorou et al., 2007) for all zoonotic agents, emerging pathogens were identified as: *Rickettsia* species, *Anaplasma phagocytophilium*, *Borrelia burgdorferi*, *Bartonella* species, *Francisella tularensis*, Crimean-Congo haemorrhagic fever virus, Hanta virus, Toscana virus, West Nile virus, tick-borne encephalitis virus, Sindbis virus, highly pathogenic avian influenza, variant Creutzfeldt-Jakob disease, *Trichinella* species and *Echinococcus multilocularis*. A detailed review of viral zoonoses in Europe has been made by Kallio-Kokko et al. (2005).

The OIE in 2004 also identified the main global threats for emerging zoonotic diseases:

- Vector-borne diseases: West Nile fever, Rift Valley fever, Japanese encephalitis, Crimean-Congo haemorrhagic fever, leishmaniasis.
- Bacterial zoonotic diseases: bartonellosis, leptospirosis, Lyme borreliosis, plague.
- Animal coronaviruses: SARS.
- Emerging viral pathogens: Hanta viruses.
- Tuberculosis: *Mycobacterium bovis*.

One goal of the Technology Platform on Global Animal Health is to prioritise the risk of animal disease to assist in the allocation of research funding and implementation of control measures. Prioritisation would take into account the quantification of public health and socio-economic impact, and horizon-scanning to identify pathogens that are not yet considered important (but where there is risk of introduction to the EU). The initial ranking of those major diseases that are zoonoses included avian influenza, rabies, neglected parasitic diseases, food-borne zoonoses (including *Salmonella*, *Campylobacter*, *Escherichia coli*, *Cryptosporidium*), TSEs and tick-borne diseases.

For further information:

EASAC Secretariat
The Royal Society
6–9 Carlton House Terrace
London SWIY 5AG
tel +44 (0)20 7451 2697
fax +44 (0)20 7925 2620
email easac@royalsociety.org

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