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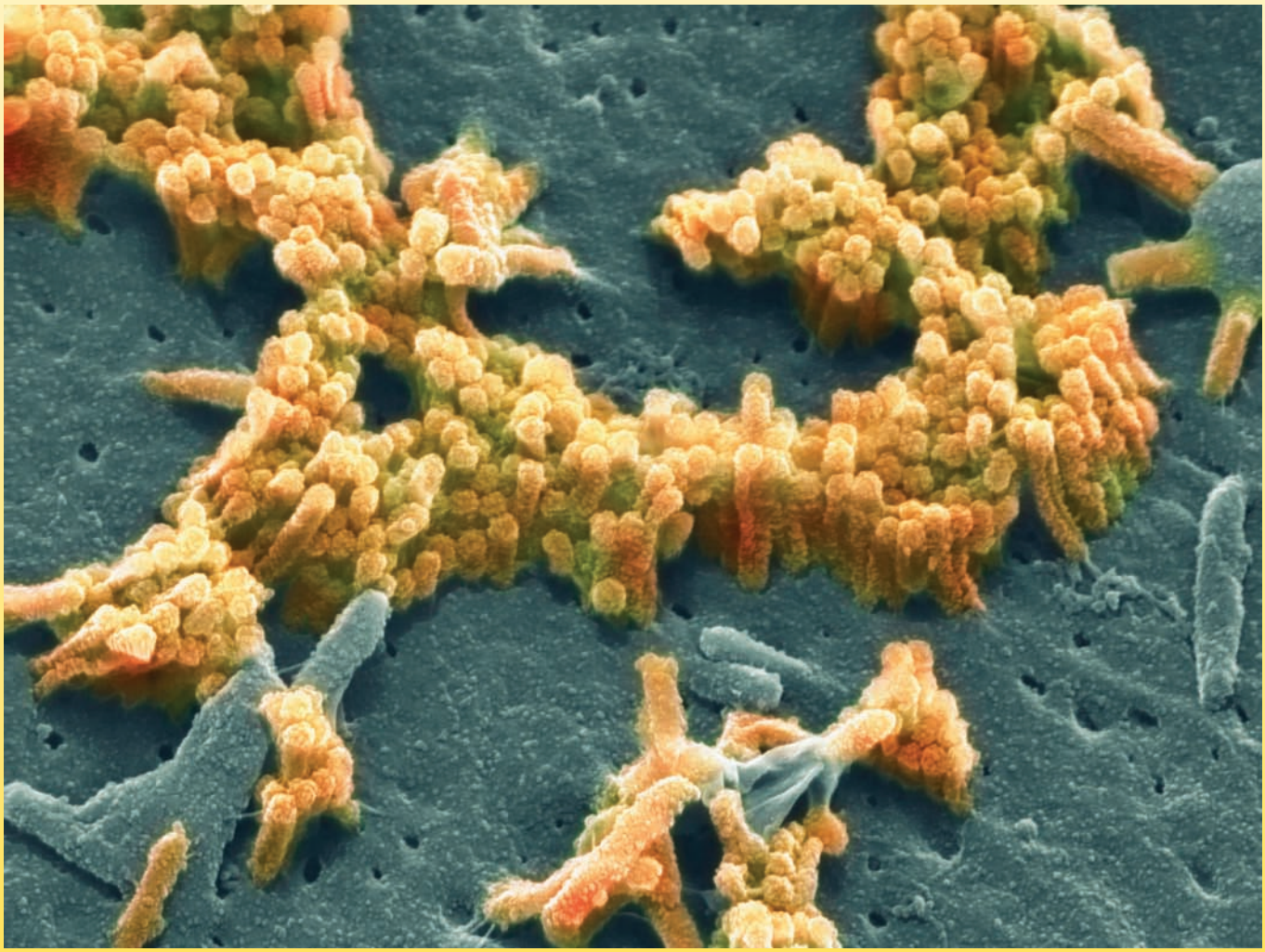
European public health and innovation policy for infectious disease: the view from EASAC



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building science into EU policy

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 giving 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 EASAC's working 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 specific 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 27 individual members – highly experienced scientists nominated one each by the national science academies of EU Member States, by the Academia Europaea and by ALLEA. The national science academies of Norway and Switzerland are also represented. The Council is supported by a professional Secretariat based at the Leopoldina, the German National Academy of Sciences, in Halle (Saale) and by a Brussels Office at the Royal Academies for Science and the Arts of Belgium. The Council agrees the initiation of projects, appoints members of working groups, reviews drafts and approves reports for publication.

To find out more about EASAC, visit the website – www.easac.eu – or contact the EASAC Secretariat at secretariat@easac.eu

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Cover image: H1N1 swine flu virus: coloured scanning electron micrograph of virus particles (virions, yellow). Credit: Science Photo Library.

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Contents

Foreword

Infectious disease continues to represent a major public health challenge for the European Union (EU). During the past six years, the European Academies Science Advisory Council (EASAC) has supported a series of studies on issues that public policy-makers need to consider within the domain of infectious disease. In the present report, we bring together key parts of our previous analyses, identifying where there are cross-cutting issues, reinforcing common themes and conclusions, and updating our recommendations to take account of recent scientific advances and policy developments. Adopting this overarching perspective confirms previously expressed EASAC views that it is critically important for the EU to be ambitious in addressing the following priorities:

- Strengthening disease surveillance capabilities.
- Creating the evidence base as a core part of public health infrastructure.
- Providing the research infrastructure to continue building excellence in basic, translational and clinical sciences and training the next generation of researchers.
- Encouraging private sector innovation for health and wealth creation.
- Ensuring coherent and co-ordinated action across different policy-making departmental functions, recognising that health issues are often very relevant to strategic decisions in other policy areas.
- Identifying opportunities for European involvement at the global level, for surveillance, research, innovation and strategy development.

EASAC acknowledges that much has already been achieved across a broad front by the European Institutions and at Member State level. However, the public health problems are urgent and there is significant scope to do more in drawing on the resources of the scientific community to translate research outputs to inform and improve health services and public health policy. This also requires the scientific community to do more to identify and fill the current gaps in knowledge while scanning the horizon for new opportunities and challenges in advising policy-making. During the six years of our work in this area, EASAC has consistently emphasised the importance of partnership – between academia, industry, health services, the charitable sector, government – and we continue to urge new models of collaboration, accompanied by new efforts to communicate about the issues to society-at-large.

In compiling this report, EASAC was helped considerably by some of the experts who had been involved in our previous Working Groups. I thank them for their continuing commitment to ensuring that EASAC delivers strong, evidence-based messages; these colleagues are cited in Appendix 2 of this report. I also take this opportunity to thank again all who have been involved in some capacity in the previous projects. So far, we have involved about 80 experts from across Europe in the infectious disease series of Working Groups and capitalised on the work of another 40 in academy-organised workshops. In addition, I thank my EASAC colleagues for their enthusiastic support for this work.`

We hope that our report will stimulate and sustain further debate. EASAC welcomes discussion on any of the points that we have raised, on key matters that might be studied in future work, and on how, collectively, we can take forward the mutual interests embedded in our recommendations.

Volker ter Meulen
Chairman Biosciences Steering Panel and
Past-President, EASAC

Summary

There have been major advances during the past century in research into and treatment of infectious disease. However, assumptions that most infectious disease had been conquered are now seen to have been misplaced, and European populations remain vulnerable. In addition to resurgent infections such as tuberculosis (TB) and the growing threat inherent in antimicrobial drug resistance, there are newly emerging microbes, especially those transmitted from animals (zoonoses) and new variants of influenza virus. The public health burden imposed by communicable diseases is exacerbated by the increasing mobility of humans, animals, vectors and pathogens, and by other effects of environmental change and globalisation.

During the past six years, EASAC has undertaken a series of analytical studies into infectious disease. These have provided evidence and stimulated further debate to inform policy-making for public health and innovation in EU institutions and Member States. The aim of the present EASAC report is to integrate and reinforce the cross-cutting themes and conclusions that have emanated from the previous work, while taking account of more recent developments in science and policy. During these six years, there have been significant changes both in the overall pattern of disease, for example the increasing problems of antimicrobial drug resistance and the appearance of H1N1 influenza, and in the EU infrastructure for dealing with infectious disease, most notably the introduction of the European Commission's Health Strategy (2008–2013) and the maturation of the European Centre for Disease Prevention and Control (ECDC). However, the broad scientific needs associated with setting the priorities for tackling infectious diseases have not changed substantially and there is much still to be accomplished.

What should be done? In EASAC's view, it is essential to continue to improve EU policies to sustain and augment the defences against infectious disease:

- To address the public health and economic impact of major threats, particularly antimicrobial drug resistance, a problem found both in healthcare settings (healthcare-acquired infections) and in the community.

- To improve surveillance procedures and the networks required to gather, analyse and disseminate data on the epidemiology of infectious diseases across the EU. This requires continuing efforts to standardise and co-ordinate present practices and develop new methodologies for patient care and research (for example the construction and curation of large databases; and new approaches to signal detection and syndromic surveillance).

- To support fundamental science and its translation, improve interdisciplinary linkages and revive neglected disciplines, conduct research on human behavioural determinants of infection spread and control, streamline the regulation of clinical research and develop new research funding and organisational models.

- To integrate the surveillance and research agendas on human and animal infectious disease in pursuit of 'one health', with shared commitment to implementation of new technologies.

- To facilitate the infrastructure for innovation, including new forms of public–private partnership and support for smaller companies. It is vital to reduce obstacles to the development of smart diagnostics, therapeutics and vaccines and to capitalise on the new opportunities resulting from advances in science. There is also need to share the lessons for public health and healthcare learned from previous experience, for example the recent H1N1 influenza pandemic, in order to secure an environment for innovation even in those circumstances where the balance of benefit and risk is still uncertain.

- To monitor and understand the global impact of environmental change on infectious disease.

- To ensure accurate and timely communication of information about infectious diseases and their management to the public.

For each of these policy priorities it is pertinent to develop capabilities both to respond to current diseases and to prepare for the future: we can be sure that there will be new threats even if we cannot define their precise nature. EASAC judges that although many of the issues to be faced are scientific, technical or regulatory, there are also political challenges: one of the pervasive problems has been a relative lack of political visibility at the EU level. Tackling these broader political challenges requires the following:

- Reassessing the balance of responsibilities for public health between the Member States and the European Commission and its agencies.

- Exploring the implications for increased public investment in health infrastructure and research and development (R&D), even during a period of economic weakness and uncertainty.

- Participating in global strategic discussions: recognising that infectious disease knows no borders

and that health policy must be part of other policy debates, particularly those concerned with the economy, environment and other societal priorities.

In our view, the common elements required to inform policy development across a broad front are the generation and use of knowledge. Research is important in multiple ways: as the basis for improving health service practice, as the resource to support innovation and education, and in furnishing the evidence base for the policy-maker. The EU must be more ambitious in capitalising on its scientific capabilities and leadership and in building new linkages between academia, industry, health services and politics. Our recommendations are directed not only to policy-makers but also to researchers. EASAC and member Academies accept an ongoing responsibility to promote dialogue among the scientific, medical and policy communities and with the public. Collective activity is essential to communicate and use the available scientific evidence in pursuit of societal goals while establishing where there is uncertainty that can be reduced by filling gaps in knowledge.

1 Introduction

1.1 The impact of infectious disease

Infectious disease worldwide accounts for about one-quarter of all deaths. Estimates suggest that communicable diseases currently represent about 10% of the total burden of disease in Europe (Jakab 2007), although this is based on limited data for selected countries and diseases and comprehensive, more robust evidence should be collected (Van Lier et al. 2007). Although the evidence base is still imprecise, it is clear that the prevalence of infectious diseases and the impacts on mortality and morbidity in Europe remain a major problem for individuals, their families and for public health systems.

There have been major advances in research into and control of infectious disease. The impact of vaccination, for example, can be dramatic. Successful vaccination campaigns have led to the global eradication of smallpox and the elimination of poliomyelitis from most regions of the world. In Europe, there has been effective control of diphtheria, tetanus, *Haemophilus* influenzas type b and hepatitis B. More recently, there has been significant expansion in vaccination coverage by meningococcal C conjugate vaccine and human papilloma virus vaccine. However, challenges remain to ensure high vaccination coverage, perhaps particularly for measles.

Optimism that most infectious diseases had been conquered by improved public health measures is now seen to have been too complacent. In the EU, as elsewhere, we face newly emerging threats: new influenza virus variants; new pathogenic microbes, especially those transmitted from animals; resurgent infections such as TB; resistance to antimicrobial drugs; and the threat of bioterrorism. These challenges are compounded by increasing migration and other travel and effects of globalisation.

In particular, the growing problem of antibiotic resistance in both the community and in healthcare-acquired infections represents a major health and economic burden for the EU (Kaier et al. 2008). Recent data from the European Antimicrobial Resistance Surveillance Network and the ECDC indicate that resistance to antibiotics is increasing and that up to 400,000 patients annually are reported to suffer from infections due to bacteria resistant to multiple antibiotics[1].The consequences of this increase in resistance, for public health systems and for innovation priorities are considerable. It remains true that, despite many warnings, there is still 'substantial unpreparedness of European public health authorities to face this worrisome emergency' (Carmeli et al. 2010), exemplified by the emerging threat in Europe posed by acquired carbapenemases in Gram-negative bacteria[2]. Part of this current threat can be attributed to an impact of globalisation whereby increased medical tourism (travel for elective, often cosmetic, surgery) leads to rapid spread of resistant bacteria from Asia to Europe, most notably recently the Gram-negative bacteria carrying the New Delhi metallo-beta-lactamase-1 (NDM-1; Kumarasamy et al. 2010). The combination of resistance to multiple antibiotics and the ready transmission of the encoding gene between various bacterial species creates a potent new threat worldwide. An escalating threat linked to antibiotic resistance is also exemplified by recent changes in the public health impact of *Clostridium difficile,* characterised by increasing incidence of infection and higher case-fatality rates than previously described, coincident with the emergence of a hyper-virulent strain resistant to fluoroquinolones (Clements et al. 2010). However, other recent data (Bauer et al. 2011) find that the *C. difficile* virulent variant (PCR ribotype 027) is less prevalent in Europe than initially thought and further epidemiology is required. High rates of antibiotic-resistant *C. difficile* infections and attributable mortality are found even in EU Member States with relatively low national levels of antibiotic consumption.

The cost of treating infectious disease is much greater than the cost of prevention; and communicable diseases have major economic effects as well as health effects. Rapid expansion in trade, foreign investment and international travel means that infectious diseases have adverse effects not only on direct and indirect health costs but also, for example, on economic growth and security (OECD 2009 and Box 1).

1.2 EASAC objectives: what policy problems should be addressed?

In 2001, the national science Academies of the EU Member States formed EASAC to provide expert, independent science advice to those who make policy in the EU. Recognising the public health priority, EASAC started analysing the domain of infectious disease. We aimed to provide evidence to inform better cohesiveness in EU policy-making across a broad agenda for public health infrastructure, the development of more effective interventions and the support of research and training, with concerted co-operation between the human and veterinary sciences.

In collecting and analysing this evidence, we directed our messages to policy-makers and opinion-leaders in the European institutions (the Commission, Parliament and Councils of Ministers), at the Member State level, and in other relevant bodies (for example the World Health

[1] *Multidrug resistant bacteria remain a public health issue in Europe.* 16 November 2010, at www.ecdc.europa.eu.

[2] Carbapenems are often the last line of effective treatment available for infections with multi-resistant Enterobacteriaceae such as *Escherichia coli* and *Klebsiella pneumoniae*.

Box 1 Examples of economic impact of infectious diseases (EASAC 2005, 2007a, 2009a)

The annual healthcare costs of hospital-acquired infections in the EU were estimated at 7 billion euros (ECDC 2008) but this probably grossly underestimates direct costs. Recent US data indicate 1.7 million episodes of healthcare-associated infections annually, resulting in 99,000 excess deaths and costing the US healthcare systems more than $35 billion (Zilberberg and Shorr 2010). In Germany the cost of sepsis alone may reach 2 billion euros a year. There are also increasing costs for many healthcare systems arising from litigation associated with healthcare-acquired infections.

In England, the direct economic burden for all infectious disease, calculated from the costs of primary care, hospital admission and hospital-acquired infection, was estimated as more than 20 billion euros annually (Finch and Hunter 2006). Net impact will also be very much greater when other societal costs are included (Fonkwo 2008). For example, the global cost of the severe acute respiratory syndrome (SARS) epidemic in 2002–2003, including effects on travel, tourism and economic growth was, controversially, computed to be more than €100 billion.

A review of recent published cost-effectiveness studies reveals a relative paucity of work on the burden of antimicrobial resistance although, to some extent, this evidence gap is beginning to be addressed (Paul 2010).

Organization (WHO) and trade associations). Moreover, just as infectious disease knows no borders, so there are implications for EU policy beyond the EU: EASAC's work on infectious disease policy takes into account the priorities for wider international analysis, co-operation and action. We recognise that our input needs to be integrated with many other related EU activities: our objective is to provide the scientific evidence and expert perspectives to inform policy, stimulate further debate on the challenges and indicate some specific options for change.

There are, of course, many other related activities by other bodies. However, EASAC sees a continuing need for objective, impartial analysis to raise political and public awareness of the key issues. We believe that it is also necessary to continue to explore how advances in science are bringing new opportunities within range for innovative, improved healthcare and public health programmes. EASAC is well placed to provide an independent view on where science can inform policy development, by drawing on evidence from across a broad range of scientific disciplines in the EU and further afield. We acknowledge an important collective responsibility for Academies to explain to policy-makers what is known and must be taken account of, while communicating to the wider scientific community their role to elucidate what is not yet known but should be. Although some of the policy issues may be perceived as matters primarily for attention at the Member State level, there is also a considerable role and responsibility for the European Community. Among these are the following priorities:

- Understanding the demographics of disease patterns.
- Co-ordinating surveillance efforts.
- Supporting fundamental science.
- Training the next generation of scientists.
- Reducing barriers to innovation.

It is impossible to tackle infectious disease solely at the local level.

Although most of the EASAC messages have been addressed to policy-makers, we have become increasingly aware of the concomitant need to help inform the public about key issues for risks and their management. There are important areas where public opinion has significant influence on the degree to which scientific evidence can contribute to improved health: for example, in immunisation strategies; in the preparedness for climate change adaptation responses and health threats from emerging diseases; and in reducing the stigmatisation of high-risk groups (such as migrants with TB) that impairs their access to health services. The Academies, with the broader scientific and medical communities, have a role to provide accurate and relevant information and to advise others, for example the media, on how to communicate the issues in a responsible way.

Where are we now? The purpose of the present EASAC publication is to consolidate and reinforce themes and conclusions that have emerged from our previous work over a period of six years, identifying where there are commonalities for policy development across different infectious diseases. We are convinced that it is still essential to take account of many of our earlier recommendations if the EU is to sustain and improve its defences against infectious disease. Tackling drug resistance is an urgent task; and many of the other issues raised previously by EASAC – for data collection and use, innovation, integration across human and animal health, tackling the consequences of environmental change – remain highly important in defining broad policy objectives. We illustrate where changes have occurred in science and policy since our initial analyses, evaluating performance and prospects, and updating our recommendations where appropriate. We find that the importance of scientific underpinning of priorities for disease prevention and control in the EU has not diminished since our initial analyses. Generally, where we had identified growing public health hazards, these have continued to escalate in importance (ECDC 2010a).

The following chapters review the key emerging themes and conclusions from the previous EASAC work. In Appendix 1 we provide a brief synopsis of the individual EASAC reports and statements.

2 Collection, curation and use of disease surveillance data

Good scientific data are essential for establishing effective health services and informing health policy. One cross-cutting theme that has emerged from all of the EASAC projects is the imperative to improve the standardisation of methods for collection, quality control and interpretation of infectious disease data (pathogen characteristics and their resistance profiles). This knowledge is essential both to provide a robust basis for effective monitoring and responsiveness in public health systems and to set strategic priorities.

The early EASAC analyses identified scientific weaknesses inherent in the inconsistent use of modern molecular technologies in surveillance and relatively poor pan-European co-ordination in procedures for collating and reporting of national data. Inadequate capacity was reported, particularly in some of the newer Member States. EASAC advised that the development of a coherent strategy for surveillance required a staged approach to constructing the evidence base: agreeing guidelines on testing; identifying priorities for existing and newly emerging pathogen monitoring; and developing and managing databases that will facilitate the international sharing of data.

Since the initial expression of these concerns (EASAC 2005), EASAC has welcomed the considerable efforts, led by the ECDC and WHO, to form active communicable disease surveillance networks at the European level. What should be done next? There is still room to do much more, exemplified by the finding of problems in surveillance of hospital-acquired infections (EASAC 2009a) where there is a need to do more to quantify the burden, strengthen national surveillance systems and data collection (co-ordinated by ECDC) and consistently implement infection control standards across the EU. Such surveillance still often does not involve microbiological confirmation of case-finding and may reflect different operational priorities between countries, further confounded by the reluctance of some institutions to publicise their data. Improved cost-analysis of hospital-acquired infections is also a priority, in part to convince decision-makers to increase their efforts to fight the spread of microbes in hospital settings.

Some of the key points raised by EASAC previously, that we believe are still relevant, are as follows.

2.1 Collecting and using human data

2.1.1 Identifying priorities

We emphasised the importance of continuing efforts to develop flexible surveillance systems as an integral part of risk assessment and management of current disease priorities, but which also have the ability to anticipate new threats (examples are provided in EASAC 2005, 2007a, 2008). Monitoring at the national and regional levels can be further strengthened by extending the scope of scientific discussion beyond the public health authorities when refining the consensus list of infections (pathogens and their strains) that should be subject to routine surveillance.

Our previous work has noted the crucial importance of improving surveillance of antibiotic-resistant pathogens. It is also becoming increasingly important to characterise and address the increasing frequency of drug resistance in viruses (EASAC 2007a) and fungi (EASAC 2009a) in human infections. For example, an initial association of azole resistance in *Aspergillus fumigatus* with environmental fungicide use (EASAC 2009a) has been published in detail (Verweij et al. 2009) and raises issues for policy co-ordination across regulatory departments concerned with health, agriculture and manufacturing. As part of improved surveillance it is important to harmonise susceptibility testing, not just for bacteria, where the EUCAST process (European Committee on Antimicrobial Susceptibility Testing; www.eucast.org) has delivered significant achievements, but for all micro-organisms.

2.1.2 Standardising datasets

The generation of consistent and easily accessible data demands continuing commitment to quality assessment and the sustained funding of surveillance networks. Consistency requires standardisation of methodologies and practical implementation of those standardised techniques for phenotyping and genotyping across the EU, with clarification of the minimum dataset required for case definition. The needs are particularly acute in drug susceptibility testing and the collection of strain and molecular typing data. Although the European Commission has funded many typing studies, these have tended to be confined to the research setting and now need to be transposed to the routine health services and the information accrued thereby also used to inform health policy.

EASAC has previously discussed options for the organisation of Reference Laboratories and their networking across the EU, to draw on expertise in molecular epidemiology and to encourage the development of analytical standards and the exchange of data. Real-time data should be provided to the ECDC, who must be given the necessary resources to continue building their benchmarking, co-ordinating and training roles. The real-time communication of laboratory data raises issues for data management and for policy. That is, the strategic role of the ECDC to provide advice in managing infection to the Member States should be well defined (examples are provided in EASAC 2007a, 2008).

Through these efforts to standardise and network, the EU can take a lead to strengthen the surveillance infrastructures in those Member States (and accession states and other neighbouring countries) that have not yet been able to develop a modern system (examples are provided in EASAC 2008, 2009b). There have been particular concerns expressed about the quality of training in molecular microbiology at the local laboratory level, where the clinical samples may first be received, and about the consistency and efficiency in linking local laboratories into public health reporting systems. These concerns persist.

A related challenge, also relevant to the defence against bioterrorism, is the development of methods to improve detection of novel pathogen signals superimposed on a background of variable 'noise' level. The delay in identifying the recent outbreak of chikungunya in Europe (EASAC 2010) emphasizes the importance of doing better in detecting new signals, together with communicating new information and networking between international and Member State health authorities. Informatics-based approaches have much to contribute by drawing on the advances in interpretation of other large, multiple datasets. We have previously also advised that syndromic surveillance systems should be further evaluated (EASAC 2008), using health-related data (obtained at the bedside and in the laboratory) that precede diagnosis but which may signal disease sufficient to warrant further public health response. Syndromic surveillance has emerged as a mechanism to complement other, passive and active, surveillance systems. However, the automated extraction of relevant information from routine laboratory and clinical databases remains technologically challenging. The priorities in public health informatics to achieve syndromic surveillance include use of standard medical terminologies, definition of data requirements, appropriate data exchange protocols and consideration of data protection requirements. Research in biostatistics and modelling must also be encouraged to provide new tools for timely detection of outbreaks and understanding of the dynamics of epidemics. It may be that alternative datasets might also be useful to support syndromic surveillance and outbreak detection; for example, mining of 'social media' data sources might provide a surrogate monitor for infectious disease.

2.1.3 Using databases for patient care and research

The generation of interactive, user-oriented databases of pathogen genotypic and phenotypic information would be of great value in improving the understanding of the relationship between pathogen molecular variation and clinical consequences (for example, for TB; EASAC 2009b). For such databases to be successful it is essential to adopt diagnostic methods that are consistent, reproducible and comparable between laboratories. These databases will have extensive value in research as well as in the delivery of healthcare. And, if databases can be extended to include data on the corresponding human samples, then the interplay between pathogen and patient can also be explored.

This is an area of rapidly increasing research interest with implications for patient care. Recent results, for example, from a genome-wide association study for host susceptibility to meningococcal disease in Western/Southern European population cohorts (Devila et al. 2010) provide evidence of a role for host genetic variation in the innate immune system (complement activation) in human susceptibility to infectious disease, although much remains to be done to explore mechanisms involved. Research funding bodies are now likely to face a rapidly increasing volume of requests for support to conduct genome-wide association studies to assess host determinants of infectious disease. We note that it is important for researchers to include enough, well-phenotyped samples to ensure the appropriate statistical power to derive meaningful clinical associations. At the same time, it is highly desirable for funders and other policy-makers to consider how the rapidly increasing volume of data on gene–disease associations will be used to generate new approaches to clinical care.

Comprehensive databases of patient information serving as knowledge platforms could, variously, improve drug susceptibility testing, enhance the modelling of future drug-resistance patterns and act as a resource for developing new interventions. They will also become part of the new high-quality evidence base to support international policy-making. However, the difficulties to be faced in creating such a resource should not be underestimated. Global co-ordination to deliver an effective database combining EU and other effort presents a challenge for technical, institutional and ethical reasons (Fears et al. 2010b). EASAC recommends that the European Commission, together with other European funding bodies, should focus on the needs for data infrastructure as a priority for the support of research in the European Strategy Forum on Research Infrastructures roadmap. As an example of a first step, 'Virolab', the virtual laboratory funded by the seventh Framework Programme, provides an interesting pilot project for collating information from disparate databases as a decision-tool in targeting personalised medicine for human immunodeficiency virus (HIV) and other infectious diseases. More generally, useful lessons may also be learnt from initiatives such as the European-wide 'Elixir' effort to establish and maintain operational infrastructure for biological information, particularly focusing on genotyping databases.

Further integration with other types of database can also now be conceived. To prepare for new challenges, such as climate change, it is vital to modernise surveillance based on trans-European early warning systems that have the

capability to integrate epidemiological and environmental data (EASAC 2010). To this end, a start can be made by linking pre-existing databases rather than developing entirely new surveillance structures. The work of the European Environment and Epidemiology Network[3] on this is welcome.

2.1.4 High-risk cohorts

Currently, there are gaps in the monitoring of high-risk groups, for example migrants (EASAC 2007b), other ethnic minority groups and those with concurrent disease. It must be assumed that many cases of infectious disease are missed at both the early contact stage, when a migrant enters the EU, and subsequently for those migrants with vulnerable socio-economic status. Member States need to understand the collective importance of sharing good practice in screening and follow-up. The extent of the problem is unknown: evidence cannot be derived from case reports alone because of the lack of denominator information. Well-designed research studies should be initiated to define risk and track trends. To reiterate the previous point, such studies must use standardised protocols for collecting and analysin data. Since the earlier EASAC analysis, it has become clear that 'pendulum' migration can be a significant source of severe transmissible infections. This refers to the phenomenon whereby citizens of the former Soviet Union and other Eastern European countries work abroad periodically, travelling back and forth with risk, in particular for the spread of drug-resistant TB and TB–HIV co-infections. EASAC advises that medical surveillance must now be focused on this high-risk group.

It is, of course, not only the various migrant groups who are increasingly mobile. The potential risk posed by air travel more generally in spreading TB, for example, was discussed by EASAC (2009b). A recent analysis of global air traffic patterns (Centre for Research on Inner City Health 2009) found that the EU generates more than 19% of the world's international traffic and represents a high-risk destination for globally imported infectious diseases. In terms of their international interconnectedness and risk, the top 10 cities globally are all located within the EU.

2.2 Collecting and using animal data

Previous EASAC work has also consistently noted the need to improve co-ordination between the public health and veterinary health communities, to ensure rapid communication of information about zoonoses (EASAC 2008) including the development of antibiotic resistance (EASAC 2007a). Multidrug-resistant bacteria, both pathogenic and commensal[4], are very common in farm animals in parts of Europe. Communication between those working in the human health and veterinary sectors has improved for food-borne pathogens but some of the emerging zoonoses (particularly vector-borne) have been relatively neglected.

The concept of 'one health' requires very good collaboration between the ECDC, European Food Safety Authority (EFSA) and others to remove unnecessary barriers in integrating surveillance mechanisms for human and animal infections. It is also important to ensure collaboration between departments responsible for health and agriculture. In previous work, EASAC emphasised several priorities:

- More coherent, longer-term effort in surveillance that extends to vectors and hosts as well as pathogens. For example, there is a need for new methods in the monitoring of zoonoses in domestic, companion and wild animals.
- Recognition that surveillance is multidisciplinary and must extend beyond centralised expert systems. For example, there is scope for improved regional assessment with reporting systems for unexplained excess animal mortality encompassing integration of local monitoring, particularly at the farm level.
- The use of surveillance data to assess the threats from emerging zoonoses according to different climatic, developmental and policy models, taking account of all resources for early intelligence of new threats, for example from sentinel animal species.

Since our earlier analysis, there has been increasing consensus that a surveillance strategy to identify disease outbreaks in animals before they spread to humans should be accompanied by attempts to identify and prevent environmental disturbances that contribute to disease emergence and spread in animal populations (Kuehn 2010). The impact of climate change is likely to be significant in this (EASAC 2010).

Despite some progress in collaboration between the human and animal disease sectors, a case can still be made for an internationally unified, scientifically informed approach to zoonotic disease, perhaps building on the voluntary, internet-based programme for reporting disease outbreaks (Program for Monitoring Emerging Infectious Disease, www.promedmail.org; Himsworth 2010). EASAC suggests that the European Commission and its agencies should consider further how to work with WHO and the World Organization for Animal Health (OIE) to design global surveillance and management systems that can incorporate local networks and academic expertise.

[3] http://ecdc.europa.eu/en/healthtopics/climate_change/Pages/index.aspx

[4] It is relevant to note that components of the commensal microbiota could be involved in disease development of immunocompromised patients (Tlaskalova-Hogenova et al. 2004).

3 Priorities for strengthening the science base

Improved surveillance, improved awareness and the introduction of standardised infection-control measures are highly important short-term objectives for better public health preparedness and responsiveness. However, they are not sufficient. An equally important pervasive theme in all of the EASAC work has been the need for public policy-makers to commit to the longer-term, research, agenda. The priorities span a continuum from fundamental science, epidemiology, translational and clinical medicine to new product and service development, and operational research.

The starting point in the extensive EASAC analysis of research gaps and opportunities has been to acknowledge what the EU has already accomplished in successive Framework Programmes and other European Commission initiatives. It was not the purpose of the EASAC recommendations to provide a detailed account of research priorities although our publications have led to discussion on specific topics. We also appreciate that European funding is finite and can never match all of the requests from the scientific community: we perceived our role as indicating where there are gaps in the science evidence base and where there are new opportunities to generate knowledge. Our main points can be summarised as follows.

3.1 Supporting investigator-driven basic research

Europe has a tradition of excellence in infectious disease research but there is no room for complacency. The bibliometric evidence (EASAC 2007a) suggests that EU competitiveness will decline unless there are new efforts to reinforce research capacity in this area. We believe that the EU must retain a broad research competence to provide the resource for health services innovation and the flexibility to respond rapidly to new threats. Although the initial return on investment in functional genomics research may be slower than some had predicted, these efforts must be continued. Public funding is still needed to fill the gap between basic research (identification of promising targets) and demonstrating proof-of-concept. Animal models of disease are critically important as a tool in basic research to understand mechanisms of pathogenesis and their control.

The necessary research capability can be exemplified in two critical areas:

3.1.1 Reverse vaccinology (EASAC 2006, 2009b)

This involves searching for new molecular targets for vaccines (for example for TB) by studying genome sequence information. Funding agencies must realise that spectacular advances in DNA sequencing capabilities require the simultaneous pursuit of an ambitious and diverse research agenda of fundamental science, for example to characterise pathogen functionality and to understand the innate immune system, in part to enable the development of better defined adjuvants.

3.1.2 Tackling antibiotic resistance (EASAC 2007a, 2009a)

Public-sector research also has a major role to play in the identification and characterisation of pathogen targets to serve as the discovery resource with which to embark on a new era of antibiotic development. This must encompass knowledge of genomics coupled with basic research on the function of essential genes in pathogens, including the study of mechanisms of transfer and dissemination of resistance gene, the determinants of strain fitness and the study of host–pathogen relationships. Such knowledge will aid in tracing the epidemiology of resistance, finding susceptibility in already resistant pathogens and discovering new ways to prevent resistance arising. Previous EASAC analysis has provided a detailed account of the opportunities and challenges arising from genome sequencing and has described some of the novel options for countering infections, for example through inhibition of bacterial adherence and expression of virulence factors or targeting pathways that are implicated in the behaviour of microbial communities (such as quorum sensing) and in immunomodulation. Subsequent discussion has reaffirmed the importance of understanding bacterial self-protection mechanisms (in particular, biofilm formation) and, thereby, finding new approaches to making bacteria vulnerable to host defence mechanisms. If this can be achieved, it may be possible to improve the use of known antibiotics that currently do not work if a bacterial biofilm has developed; the 2011 Health Call of the seventh Framework Programme for research on tools to control microbial biofilm involvement in drug resistance is welcome.

3.2 Hosts, vectors and pathogens: integrating the human and veterinary research sectors

In addition to the value accruing from integrating epidemiology across the sectors, there are also common research priorities, especially in studying how pathogens cross the species barrier and extend their host range: progress is being made (see, for example, Streicker et al. 2010). Such research may also aid better targeted surveillance of those species most likely to be hosts

for emerging zoonoses. Feedback from companies to EASAC after the earlier work (EASAC 2008) supports the objective of better integration of the human and veterinary research agendas that might allow a more rational use of resources for developing novel products for human and animal health, provided a more ambitious scope does not lead to slower progress in either or both sectors.

Research in other disciplines such as entomology, vector biology and microbial ecology has been relatively neglected and yet is newly critical for translational medicine if we are to understand the increasing incidence and spread of infections in humans and in animals occurring as a result of climate change and other environmental pressures. For example, there is a broad research strategy to be adopted in characterising the biology of European tick species (the vector responsible for clinically significant disorders such as lyme borreliosis, ehrlichiosis and tick-borne encephalitis and the veterinary threat of African swine fever; EASAC, 2010), their current geographic distributions, potential for future expansion and propensity for one species to replace another.

Two recent findings reinforce the importance of better sectoral integration in research and surveillance. First, West Nile virus transmission has recently been reported in several EU countries, including Greece, Romania and Hungary (ECDC 2010b). Secondly, a small colony of a tropical species of mosquito *Aedes aegypti* has been identified in the Netherlands, possibly associated with the importation of tyres. This is an important vector elsewhere in the world for yellow fever, dengue and chikungunya. Although the mosquito is unlikely to survive the winter in Northern Europe, its presence implies there may be a problem for other Member States who monitor new vector invasions less rigorously (Enserink 2010).

Research is essential, not just for understanding the zoonotic origin of human disease, but also for characterising the diseases of animals that are economically important in Europe. Recent analysis showed, for example, that the expansion of blue tongue virus (BTV) in Western Europe is likely to be a direct consequence of climate change acting on species of the vector *Culicoides* such that BTV will be established as an endemic disease in the EU (EASAC 2010). Since the BTV outbreak, more money has become available for entomological research. However, this research would have been much more effective in steering policy, if started earlier (and sustained). Further progress in characterising BTV and other vector-borne diseases should now be possible by using molecular biological techniques to identify and monitor that proportion of vectors carrying the highest pathogen load, responsible for disease transmission. This research should be actively pursued.

3.3 Researching human behaviour

It is important to understand the behaviour of human as well as microbial and vector populations. Research in the social sciences (including economics, sociology, anthropology and psychology) can be expected to clarify some of the institutional and individual determinants of antibiotic resistance relating to antibiotic use and implementation of infection control procedures. Such research, on the human factor, can also be helpful in targeting behavioural modifications to improve rational prescribing, compliance with guidelines and promotion of hospital hygiene, particularly hand hygiene, and the implementation of hygiene measures in community settings. Work cited in previous EASAC publications (2007a, 2009a) has recently appeared in an updated form (Hulscher et al. 2010) analysing the human factors that underpin hospital practice and identifying opportunities for improvement strategies for intervention at the country, hospital and physician levels.

The study of human behaviour is equally important in preparing for other infectious disease threats, in understanding the human population responses to environmental change and the associated new leisure and land use patterns that may increase exposure to pathogens, vectors and animal hosts. Furthermore, social science research is critically important as a tool to measure the socio-economic impact of infections and public health interventions to control infection. The better economic assessment of the costs and benefits of infectious disease and its control will help to provide the impetus to raise political awareness about public health and inform development of the policy options (examples are provided in EASAC 2009a, b). This research discipline is advancing relatively rapidly. A UK study (Smith et al. 2009), modelling the economic impact of pandemic influenza, demonstrated the flexibility of assessing impacts on mortality and morbidity in various situations relating to vaccine efficacy and social distancing options (such as school closure and prophylactic absenteeism). Generally, there is further need to ensure that the management of disease outbreaks is well-informed by the available scientific evidence base (Timen et al. 2010).

EASAC has previously recommended the application of quantitative modelling to forecast future trends and the impact of new control strategies (for example for drug-resistant TB; EASAC 2009b). It is more difficult, of course, to use models to predict the emergence of new diseases in Europe, although we can be sure that they will emerge (EASAC 2010). What can and should be done is to use a systems approach to bring together all relevant surveillance and research data, from the social as well as the biological sciences, to provide the earliest intelligence on new threats, anticipate trends, test hypotheses and inform the policy debate. The Academies are well placed to help explore possibilities and collate the evidence

necessary to reduce uncertainty and inform options for action.

3.4 Increasing the momentum in clinical and translational research

3.4.1 Biomarkers

The EU public sector lacks adequate capacity in clinical and translational research. Previous EASAC publications document some particular weaknesses in this regard. For example, clinical trials on vaccines, if measuring the prevention of disease, must be large, lengthy and expensive (EASAC 2006, 2009b). It is a priority, therefore, for academic and industry researchers, with regulatory authorities, to identify, validate and use biomarkers (proxy indicators of clinical endpoints) to serve as the correlates of infection and protection. The advances in genomics, transcriptomics, proteomics and metabolomics introduce new opportunities for developing biomarkers of disease and the response to intervention. It can be expected that use of such markers will shorten the duration of clinical trials and make them more feasible for the public sector to undertake. An iterative approach, involving both basic and clinical research, is required to screen and validate sensitive and specific markers in infection research. It is often the clinical outcome that informs pre-clinical understanding, leading to introduction of more relevant animal models and indicators of efficacy and safety (Fears et al. 2010b).

3.4.2 Clinical Trials Directive

There are, however, more general continuing problems in the EU clinical research environment. The academic clinical-science community has voiced considerable concern about the unintended negative impact of the Clinical Trials Directive on public-sector clinical research. Detailed analysis of the problems and suggested recommendations for reform have been undertaken by Academies under the auspices of the Federation of European Academies of Medicine (FEAM 2010). EASAC endorses the FEAM analysis and recommendations, and we emphasise that DG Sanco must continue to consult with the academic research community during revision of the Directive. We also emphasise, more generally, that the European Commission must increase its efforts to consult widely within the scientific community earlier on in the policy development life cycle to prevent other unintended consequences of legislative initiatives.

3.5 Education and training

There is a lack of trained researchers in many key disciplines in basic and clinical microbiology. Furthermore, the erosion of the knowledge base in veterinary research has been even worse. Although these deficits require action by Member States, it is also desirable that research projects funded at EU level should provide additional support for skill development and researcher mobility, coupled with proactive encouragement for structured yet flexible career development pathways and agreement on how it may be possible to harmonise elements in the medical curriculum for specialists.

As noted previously, other key disciplines such as entomology, where skills have become scarce, must be revived if we are to retain EU capacity to document and differentiate pathogen vectors. Public health entomology and public health epidemiology should no longer be regarded as skills necessary only for those intending to work in developing countries. In this context, EASAC welcomes the recent announcement by ECDC to support a network of medical entomologists and public health experts in arthropod surveillance to improve preparedness towards vector-borne disease[5].

3.6 New forms of research infrastructure and funding

Progressing the various research priorities and improving the linkages between basic, clinical and translational research would be facilitated by the introduction of new forms of research support. We believe that our previous recommendations remain valid. These are as follows.

3.6.1 Medical microbiology and clinical infectious diseases

In recommending options for improving the infrastructure for basic and applied microbiology and infectious disease research in the EU, EASAC suggested rebuilding links between universities and associated hospital-based microbiology services (EASAC 2007a). Where such links had existed they have been much weakened by successive reorganisations in many Member States. EU-funded studentships, fellowships and research projects could be part of a credible approach to encourage new linkages between the functions for a broad remit covering infectious disease management at the bedside, mechanisms of disease, clinical and molecular epidemiology, target elucidation and improved screening assays.

3.6.2 Centres of Excellence

In satisfying additional objectives to integrate between disciplines there is considerable scope to develop multidisciplinary Centres of Excellence, as noted in several previous EASAC studies (for example, EASAC 2005, 2008, 2009b). Such Centres of Excellence in

[5] Start of VBORNET activities. December 2009. Further information available at www.ecdc.europa.eu.

infectious disease could be expected to span research competencies including epidemiology and field experience, social science, mathematical modelling, genomics, bioinformatics and, perhaps, drug discovery as well as microbiology and immunology. Centres must be networked to ensure research capacity is available to all the Member States and to provide access to the total patient population. Such Centres could also play a major role in training by offering master's and PhD programmes and specialisation in clinical microbiology and infectious disease.

3.6.3 New funding models

Long-term multidisciplinary research into infectious disease is costly and will only thrive at the EU level if supported by new types of funding model. EASAC has previously welcomed the proposal that the current Framework Programme system, based on competition between individual research groups and fragmented research priorities, should be reformed to incorporate the concept of Grand Challenges (EASAC 2009b). In this new model, which might also be expected to attract new sources of funding from Member States, it is proposed that policy-makers would agree the societal priorities and the scientific community would identify the specific goals for co-ordinated and sustained research inquiry. Although EASAC does not wish to pre-empt discussion on which Grand Challenges should be selected for the eighth Framework Programme, tackling Gram-negative bacteria (see section 4.2) can be seen as an example of an EU and global priority that fulfils the criteria for what should be considered in health research: an agreed societal need, feasible goals, excellent base of research and industrial capacity with viable prospects for implementation of research advances. We now recommend that the broad area of public health and infectious disease, with a particular focus on translational medicine, should be considered by the European Commission as a Grand Challenge.

4 Innovation for health and wealth creation

Innovation is vital, both for better patient care and for European economic competitiveness. Addressing the currently unmet medical needs in infectious disease requires better connectivity between research advances and the development of novel diagnostics, therapeutics and vaccines. There will also be opportunities to use the products in new ways, for example in diagnostic–therapeutic combinations in personalised medicine. However, innovation encompasses many complex, lengthy, expensive and uncertain processes.

Previous EASAC analysis (EASAC 2007a) substantiated the concern expressed by many other groups in the EU and USA about a declining pharmaceutical R&D therapeutic pipeline for certain infections, in particular those caused by Gram-negative bacteria. As we observed elsewhere (Fears et al. 2010b), if increasing antibiotic resistance threatens a return to the 'pre-antibiotic era', then it would be difficult to overestimate the net impact on the practice of modern medicine, highly dependent on the surgery and other intensive care that becomes impossible without effective infection treatment.

The nature of the impediments in innovation for companies large and small has been discussed extensively in previous EASAC work. Where are we now? Since the initial EASAC analysis in 2005, although the pharmaceutical sector has remained highly important for EU competitiveness, concerns about sector viability (total pharmaceutical R&D) have continued to grow (Box 2). The figures for investment and output in Box 2 relate to all therapeutic areas taken together but it is likely that the conclusions apply equally to infectious disease R&D.

There are many issues for policy-makers to consider in encouraging industry innovation. Not least, there are challenges to face in the regulation of marketing, pricing and reimbursement, to counter industry perceptions of declining return to investment in the infectious disease therapeutic area. Against this background, there is no certainty, but there can be some optimism, that new approaches to risk-sharing in public–private partnerships will help to drive R&D. The importance of stimulating public–private collaboration has been a consistent theme in EASAC recommendations. We welcome EU initiatives introduced since our previous analysis, but we also now suggest that policy-makers should consider the expansion of collaborations to include research taking place outside the EU. For example, research conducted by pharmaceutical companies globally could be included as part of the pharmaceutical partner's contribution to joint strategies developed by the European Commission within Framework Programmes and other innovation support mechanisms.

Box 2 The pharmaceutical sector in Europe 2010

- The pharmaceutical industry is one of the leading technology-based industries in Europe (including Switzerland), amounting to 17% of total European business R&D investment. The next highest is software and computer services, at 10% of the total. However, the top two European R&D companies are Swiss, albeit with much of their R&D located in the EU.
- By comparison with data collected up to 2005 (presented in Table 2 of EASAC 2007), the pharmaceutical market is undergoing a major shift to China and other emerging economies in Asia. Ultimately this is also likely to affect the location of company R&D.
- R&D expenditure in both Europe and the USA appears to have been declining since 2007, at a time of increasing costs.
- Over the period 2005–2009 in terms of the nationality of the parent company, Europe accounted for 52 new chemical or biological entities compared with 66 for the USA (17 for Japan, 11 for other countries), confirming the pattern of declining EU competitiveness recorded for the 5 years before 2005. However, Europe outperformed the USA according to this metric in 2009 (12 new compounds compared with 8).
- Approximately 20% of the new medicinal entities launched are now derived from biotechnology. In Europe the biotechnology small and medium enterprise (SME) sector is growing but still not as fast as in the USA.
- Vaccines continue to be a European strength. Sixty per cent of vaccine R&D projects in 2008 were based in Europe, although Europe accounts for only 30% of the global market.

Latest data from 'The Pharmaceutical Industry in Figures' (EFPIA 2010), available at www.efpia.org.

4.1 Diagnostics

Case studies were described in previous EASAC reports, for example for TB (EASAC 2009b), antibacterial resistance (EASAC 2007a, 2009a) and for zoonoses (EASAC 2008) where we presented the case for diagnostic biochips with broad applicability. Because many of the infections treated with antibiotics occur in community settings (and with a greater frequency in lower-income settings), there is need to develop cheap, rapid, reliable methods to diagnose common viral and bacterial pathogens to underpin decision-making algorithms in prescribing. Analysis of the case studies and other evidence reveals some general points.

4.1.1 The costs of inadequate diagnosis

Uncertainty in diagnosis is a major reason for the inappropriate use of antibiotics and, hence, contributes to the growth of resistance. Poor diagnosis carries multiple high costs: for the patient in terms of wrong treatment, continuing ill health and, at worst, premature death; for the clinician in terms of unnecessarily increasing patient load; for microbiology laboratory staff in terms of ineffective use of their resources; and for public health systems generally in terms of the increasing number of contagious patients and the waste of limited resources.

4.1.2 Current obstacles in developing novel diagnostics

There are weaknesses in setting and sharing standards between laboratories. These are compounded by weaknesses in translating from the research conducted in academia and the smaller companies to a commercial scale. Market pull for new diagnostics is weak because health budgets are fragmented and there is difficulty in demonstrating that increased spending on diagnosis will be cost-effective in reducing the costs of subsequent clinical care and improving clinical outcome.

These points are discussed in detail in the previous EASAC publications; the principle behind a recent initiative by the European Commission[6] jointly with the EU pharmaceutical industry is laudable. In 2011 the Innovative Medicines Initiative (IMI) will start to fund a pre-competitive project to identify and develop rapid, reliable, point-of-care microbiological diagnostic tests with the intention to facilitate both clinical practice and the conduct of research trials. This and future IMI consortia have an important role to play in providing the knowledge needed to drive innovation. It should be added, however, that given the objective to develop 'patient-friendly' diagnostic tests, it is vital to take account of patients' views in the IMI consortium to capitalise on the expertise of the core partners from academia and industry.

4.2 Therapeutics

Partnership between the public and private research sectors is also critically important for drug innovation. Individual academic groups can, of course, usefully collaborate with individual companies after the pre-competitive research phase as well as when part of pre-competitive consortia. However, EASAC analysis found that academic scientists often have only a limited understanding of what industry expects in validated drug targets and it is prudent not to overvalue what academic research can deliver unless industry commits to teaching what is necessary for drug discovery research. Examples for improving the flow of both information and researchers between industry and academia were described previously (EASAC 2007a), with a discussion of the critical success factors necessary for academia to attract industry interest in collaborative programmes. There are new forms of collaboration worldwide that may provide other examples of best practice for further consideration by EU policy-makers[7].

EASAC has also emphasised previously that policy-makers must find new ways to encourage the private sector to invest in innovation, by market-pull mechanisms and other incentives, and by simplifying regulatory hurdles without compromise to product quality, safety and efficacy (EASAC 2006, 2007a, 2009b). Subsequent feedback from companies to EASAC indicated that it would be helpful to simplify the clinical trial design initially required by regulatory authorities for drug registration. Rather than collecting efficacy data simultaneously for multiple clinical indications, one option might be to allow outline regulatory approval for proof-of-concept data demonstrating activity against a pathogen, providing that the company committed to collecting specific efficacy data in other indications subsequently. We suggest that this option warrants further attention.

4.2.1 Increasing political visibility of the problem

The issues for ensuring the next generation of antibiotics are not just scientific, technical and regulatory, but also political. There has been an increasing momentum in EU discussions calling for new antibiotics and exploring how to provide new incentives to encourage commercial R&D. A conference organised by the Swedish Presidency of the EU in 2009[8] discussed a joint report from the ECDC and European Medicines Agency that helped to clarify and quantify the gap between the burden of infection caused by multi-drug resistant bacteria, particularly the Gram-negatives, and the pipeline of new antibiotics (ECDC–EMEA 2009). The report and conference called urgently for a European and global strategy to address the gap. Since this initiative, a US–EU Transatlantic Task Force on Antimicrobial Resistance has been established to find ways to encourage R&D as part of an ambitious objective to develop 10 new licensed antibiotics within the next 10 years (Anon 2009).

Concomitantly, the Council of the EU (2009) recommended examination of the options 'to strengthen incentives to conduct research and development of new effective antibiotics within the academic as well as the pharmaceutical sectors as a whole, taking into account the situation of small and medium-sized enterprises'.

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6 Innovative Medicines Initiative Joint Undertaking, www.imi.europa.eu.

7 For example, the trans-national collaboration between a European pharmaceutical company, the Wellcome Trust-funded Seeding Drug Discovery initiative and the US Defense Threat Reduction Agency that has led to the identification of a new class of antibiotics that inhibit bacterial topoisomerases by a mechanism that circumvents fluoroquinolone resistance (Bax et al. 2010).

8 Innovative Incentives for Effective Antibacterials, Stockholm, September 2009.

The Council asked the European Commission to develop a comprehensive action plan within two years with firm proposals for incentives and other policy mechanisms of support. Similar points relating to unmet needs have been emphasised in the European Medicines Agency's (EMA's) draft strategic objectives for the period to 2015 (EMA 2009a). A joint Opinion published by the Agency with ECDC and EFSA (EMA 2009b) noted the problem of increasing antimicrobial resistance in humans (particularly with infections of *Salmonella* and *Campylobacter*) that is a consequence of transmission from animals and food[9].

In further follow-up, the Swedish Government co-organised another conference in September 2010 to review the options for agreeing priorities in R&D for new therapeutics and diagnostics, for enhancing knowledge-sharing in drug discovery and for evaluating the impact of different combinations of incentives[10]. This accelerating momentum in discussion, with the increasing political visibility, is important and we believe that the EASAC analyses made previously (2007a, 2009a) remain highly relevant. However, it is important to move on from discussion to concrete action. It is also noteworthy that TB was not included among the pathogens discussed during the Swedish Presidency conference, which we consider to be a worrying omission.

4.2.2 Tuberculosis

The EU shares the worldwide problem where a growing number of TB strains are resistant to the commonly used agents, necessitating the use of more complicated, expensive and less well-tolerated treatment schedules (EASAC 2009b). Moreover, extensively drug-resistant TB (which is resistant to the most powerful first- and second-line drugs) has been documented in more than half the EU Member States and threatens the progress made previously in the control of TB (EASAC 2009b; Fears et al. 2010a). There are some urgent issues to resolve in current TB regimens – to remove inconsistencies in the management of drug supply across the EU and to address problems of drug interaction in HIV–TB combination therapies – but it is also essential to design effective new drugs and implement them rapidly into clinical practice, to shorten and simplify the treatment regimens and to counter the development of resistance.

Although resurgence in the TB drug pipeline is promising (Koul et al. 2011), EASAC advised that the magnitude of the challenge should not be underestimated and that there is merit in new global forms of public–private partnership to communicate and capitalise on the newer research findings. The announcement in March 2010 that the Gates Foundation, the TB Alliance and the Critical Path Institute are supporting collaboration between several pharmaceutical companies and non-governmental organisations (NGOs) to expedite the testing and delivery of TB drug regimens to the market (Burki 2010) is very encouraging. However, in the view of EASAC, it is equally important to involve academics in this collaboration to help clarify biological uncertainties, such as the interaction between the TB pathogen and the patient's immune system. And, as the topic of infrastructure for TB medicine will be included within the next round of IMI funding in 2011, it is important to ensure complementarity and co-ordination between the EU and other international initiatives. It will also be important to assess whether the principle embodied in the model of collaboration funded by the Gates Foundation could be applied to other anti-infective R&D.

4.3 Vaccines

As noted in the EASAC (2006) report, the vaccine industry in Europe has a strong legacy (see also Box 2). However, vaccine innovation is susceptible to many of the same general impediments as therapeutic drug innovation. If EU competitiveness is to be maintained, policy-makers must find new ways to encourage company investment and to promote vaccine uptake. There is continuing EU need to develop vaccines: for new influenza strains together with DNA influenza vaccines and other novel vaccines that induce broad-based immunity; for tackling established diseases such as TB, HIV and respiratory syncytial virus and other respiratory pathogens; for emerging diseases such as West Nile virus infection and tick-borne encephalitis virus; and for antibiotic-resistant pathogens and nosocomial infections. Innovative thinking is also required to develop public health strategies that maximise vaccine impact (for example for tackling measles and rubella). The issues and the scientific opportunities are discussed in detail in previous EASAC reports (2006, 2008, 2009b); the brief update presented here will be exemplified by some of the innovation policy issues associated with the acquisition of EU preparedness for pandemic influenza.

We have previously described the extensive EU actions to prepare for the potential of H5N1 avian virus to generate an influenza pandemic. Our analysis (EASAC 2008) was prescient in also calling attention to the important public health concerns posed by swine influenza. Most experts conclude that H1N1 (A(H1N1)2009) was pandemic with only mild impact compared with previous pandemics, so far[11], but warn that there is danger of creating a false

[9] There is growing evidence for the transmission of antimicrobial resistance to humans through the food chain (Sheldon 2010), exemplified by a rise in the number of bacteria producing extended spectrum beta-lactamases. There is still need to reduce the use of antibiotics in farming: analysis by the EMA shows that the wide variation in use between countries (with the Netherlands highest) cannot be explained by differences in the demographics of animal species alone (Grave et al. 2010).

[10] Conclusions from this conference, 'Turning a new page on antibiotics', are at www.reactgroup.org/dyn/,125.html.

[11] Mild, at least, by comparison with some predictions. World Bank experts in 2009 estimated that an H1N1 pandemic could wipe out 3.5% of global GDP (Shetty 2009).

sense of security: the next emerging infectious disease may be much more of a threat and there is continuing reason to reinforce and adapt pandemic preparedness for a wide range of scenarios.

Some media and political commentators have asserted that the actual impact of H1N1 was disproportionate to the extensive measures taken to combat it. In EASAC's view, this criticism is misplaced: Europe has been fortunate so far. Some conclude that this good fortune was greatly helped by the speed of reporting of surveillance data, the public health response, social distancing precautions and vaccine availability (ESCMID/The Lancet 2010). Other commentators suggest, however, that surveillance systems were not that good at answering the most relevant questions or sharing national results. In some countries, there appeared to be loss of professional confidence in the vaccine, such that its use was variable.

Furthermore, the response by WHO and the global health community has been attacked by some for creating a 'false pandemic', and vaccine manufacturers were accused of subverting the decision-making processes. This scepticism about the H1N1 pandemic has become conflated with the anti-vaccine lobbying that acts to undermine other immunisation strategies in Europe. Parliamentarians in the Council of Europe were particularly vocal in calling for re-examination of the public health strategy and expressing distrust about industry motives (Council of Europe 2010), but members of the European Parliament also raised concerns (Euractiv 2010). It is very unfortunate that so much political alarm can be manifested in the absence of independently verified scientific evidence (Anon 2010a).

What lessons can be learned from the global experience (Box 3)?

Box 3 Lessons learned from the H1N1 influenza pandemic—the view from EASAC

- Data collection. —The virus was probably circulating in pigs for many years; the public health and animal health communities should increase surveillance for emerging diseases, particularly in sentinel animal populations known to pose a risk for man. Better human seroprevalence data, the 'gold standard' in surveillance, are also necessary as the basis for predicting trends. There has been too much reliance on weak, proxy indicators such as the number of people hospitalised or reporting influenza-like illnesses. There must also be careful assessment of reports of side-effects
- Virus characterisation. More attention to detailed virology would have been helpful, for example to clarify the observation that the over-65s, normally the most vulnerable group for seasonal influenza, appeared less likely to contract the H1N1 strain. This may be attributable to pre-existing partial immunity, although the effects were more severe in those who did contract the strain.
- Comparing the experience of different Member States. Vaccine uptake rates showed great variation (for example, they were high in some Scandinavian countries, low in some Mediterranean countries). It would be valuable to conduct research to understand these differences in public attitudes and in the attitudes of those working in the primary healthcare sector.
- Support for vaccination. It is essential that the scientific and medical communities articulate the value of vaccines to counter extremist, anti-vaccination lobbying and to build public trust (Anon 2010c). However, although there must be standardised analysis of issues across the EU, it may well be that mechanisms to provide better information to the public should be customised according to needs of Member States. That is, although policy development requires EU-level involvement, targeting of that policy may need to be refined at the local level. The Academies have a key role to play in communicating balanced information, based on scientific evidence, at the country level to counter scepticism (Anon 2010b). As it would be very complacent to assume that the threat of future pandemics can be discounted, new vaccines will be required, in part to take account of antigenic drift and the potential for virus reassortment. The threat of pandemics will be compounded if unfair criticisms discourage vaccine manufacturers from committing to a future rapid response.
- Handling risk and uncertainty. The Royal Society in the UK organised a meeting to discuss how to handle uncertainty in science, including health science[12]. There would be merit in the Academies stimulating further discussion on the issues appertaining to pandemics. Such discussion should involve industry and governments across the EU as well as the scientific community, to address the risks and uncertainties associated with pandemic preparedness and responsiveness. There is also need for further discussion on developing a new reality in the roles of the public health agencies at EU and national level, building on the public trust in them, and this requires new resource.

[12] Handling Uncertainty in Science. The Royal Society, March 2010. Abstracts available on www.royalsociety.org.

4.4 The role for SMEs

Previous EASAC work has examined some of the challenges for SMEs as innovators in tackling infectious disease, a function that was also highlighted by the EU Council conclusions on antimicrobial resistance (2009). The EU Competitiveness Council in July 2010 emphasised that a shorter path must be created between research and market through SME innovation if the objectives of the Europe 2020 strategy are to be realised.

SMEs have contributed evidence to EASAC projects about the problems they face in accessing finance and skills and in participating in Framework Programmes (EASAC 2007a, 2008). More recent data show that these general problems persist:

- In the seventh Framework Programme Cooperative Health Theme, only 10% of the budget has been currently assigned to SMEs, despite a target of 15%. A proposal for increasing participation by biotechnology-based SMEs was recently published by the trade association EuropaBio (2010), consistent with the points emerging from the previous EASAC analysis, recommending improvements in information provision, better specification of the content of project calls, and more attention to consortium development and the procedures for project approval and funding.

- The EASAC conclusion that SMEs require new sustained sources of funding has been reinforced by analysis (Huggett et al. 2009) showing that the follow-on financing for biotechnology-based SMEs remains weak in the EU compared with the USA.

We reiterate our previous recommendation that it is important to sustain and strengthen the biotechnology sector in the EU.

5 Building EU roles in public health

Policy-makers have a broad agenda to cover in developing a strategy for tackling infectious disease that takes account of the issues for research, professional education and innovation as well as for surveillance, disease prevention and healthcare delivery. The economic downturn may both exacerbate the challenges posed by infectious disease and reduce the opportunity to respond. New research (Acinaminpathy and Dye 2010), using a statistical model to analyse data on economics and TB rates in Central and Eastern European countries, finds that the link between economic recession and infectious disease is stronger than previously assumed. However, as the authors conclude, 'while financial crises may be inevitable, or indeed unforeseeable, their adverse effects on health need not be.'

If coherence is to be achieved, public policy-makers must also address many other societal issues usually assumed to be outside of the remit of health and research departments, including issues associated with the economy, security, social inequity, school education, urban and rural development and land use. For the most part, these issues have fallen outside previous EASAC studies. But it has been a pervasive theme in the EASAC work that issues for health must be taken into consideration when developing other policies for addressing societal priorities. For example, we have observed that health issues have been relatively neglected in the debates on societal impacts of migration (EASAC 2007b) and climate change (EASAC 2010). This omission should be rectified; the scientific community has a responsibility to help policy-makers understand the relevance of health to other societal issues.

5.1 The balance between EU and Member State responsibilities

Public health is a relatively recent policy area for the EU[13]. Previous European Commission actions to develop the ECDC and to define a public health strategy are highly valuable, but a good case can still be made for an enhanced EU-level role for improved disease surveillance and for acting on the information collected (EASAC 2005). An expanded role would probably require further modification to the Treaty to allow DG Sanco and the agencies more executive powers to act in support of EU priority-setting for public health preparedness and responsiveness including, where appropriate, crisis management. EASAC also suggested (EASAC 2006) a central role for agreeing EU vaccination strategies. In time, using harmonised criteria, it may become possible to provide a single EU-wide recommendation for the use of a vaccine so that manufacturers can benefit from the centralised procedure for product approval. A single, evidence-based schedule for each immunisation would also be expected to accelerate clinical development and reduce costs.

EASAC has recommended collective discussion between the European Commission, European Parliament and Member States to re-assess the degree of decision-making that can be allowed to the EU agencies. The scientific community should also be an active participant in informing these strategic deliberations. We support stronger involvement by the specialised organisations ESCMID (European Society of Clinical Microbiology and Infectious Diseases) and FEMS (Federation of European Microbiological Societies) in informing policy development. Although it would perhaps be unrealistic to expect rapidly increasing European Commission powers in public health, we begin to detect a greater sense of co-ordination within the policy-making machinery as indicated by the transfer of responsibility for pharmaceutical policy from DG Enterprise and Industry to DG Sanco in 2010.

Much has already been achieved at the operational level since EASAC first made its recommendations. ECDC growth has matched EASAC expectations in various ways: growing its core analytical and advisory functions; increasing collaboration with WHO; developing a leading role in training European epidemiologists; and proving willing to seek advice from the wider community of professional and expert groups. We also welcome the increasing ECDC co-ordination with EFSA but reiterate that there is still much to be done to link the human and animal health agendas.

5.2 EU strategy in a global context

In the same way that health policy should not be considered in isolation from other policy issues, so EU priorities should not be considered in isolation from the rest of the world. Europe is not immune from the global spread of infectious disease. The EU has a moral responsibility to help tackle disease on the global scale. However, even if viewed solely in terms of EU parochial interests, infectious disease anywhere is a threat to the EU, as exemplified by antimicrobial resistance, TB and zoonoses.

Previous EASAC work led to various recommendations relating to international co-operation; since then we see that further progress is possible:

[13] Responsibility was introduced in Article 152 of the Maastricht Treaty in 1992 and exemplified in further detail in the Amsterdam Treaty in 1997.

- There is evidence of greater co-operation between the EU and international intergovernmental organisations although, of course, more can be attempted. A recent 'Tripartite Concept Note' from the Food and Agriculture Organization (FAO)–OIE–WHO (2010) describes an approach to sharing responsibilities and co-ordinating global activities to address health risks at the animal–human–ecosystem interfaces. This collaboration to develop complementary agendas and capture synergies across the sectors creates a new strategic context for European Commission involvement in global action.

- EASAC recommended previously that the EU should take a broader geographical view of proximal threats; microbes can move rapidly between continents and the threat is not confined to neighbouring countries. A global virus forecasting initiative[14] is now monitoring the interface between animals and humans in high-risk communities and sentinel populations to identify viruses while it is still possible to contain their spread. It may be valuable for the European Commission to support this initiative.

- There is considerable potential for the EU to help with capacity building to develop research and diagnostic laboratory services in neighbouring countries, both to the east and south, and developing countries. The announcement of a European Reference Laboratory Network for TB[15] that includes EU accession countries as well as Member States is a useful initiative but one that could be expanded.

- Health issues must be seen as a key part of the EU regional strategies introduced to tackle societal priorities, for example by the European Neighbourhood Policy and the European Mediterranean Union. The recent creation of the European External Action Service[16] incorporating DG External Relations may bring greater coherence to the European Neighbourhood Policy. We advise that health should be considered within the scope of the European External Action Service, because of its international importance and particular relevance to security. We regret that the programme and projects of the Union of the Mediterranean still do not include health as a primary focus, especially as antimicrobial resistance is such a prominent problem in that region. We recommend that this omission is rectified.

- Some good progress has been made in other joint research initiatives. For example, in the seventh Framework Programme there are collaborative health and environment interdisciplinary projects covering vector-borne diseases in Europe and Africa. And there is growing momentum in the work of the European and Developing Countries Clinical Trial Partnership (EDCTP) which invests in research trials while also promoting human and institutional capacity-building in Africa (EDCTP 2009). For the future, it is desirable that more Member States become part of EDCTP and that the expansion of collaboration beyond Africa is contemplated.

A recent Communication from the European Commission (2010) is timely in proposing an EU vision on global health that identifies a major role for research and may lead to new policy initiatives. However, this Communication does not mention disease surveillance and says little about innovation or priority-setting and, in our view, these also are essential elements for a global health strategy. Moreover, there is already a multiplicity of international organisations providing funds and building internal capabilities in developing countries but there is no mechanism that enables effective co-ordination among partners. Moreover, sometimes, there is poor alignment with recipient country needs for countering infectious disease (Leki 2010). We suggest that the European Commission, through the European External Action Service and other routes, helps to create a co-ordination mechanism.

There is much to be done. EASAC recognises its role to help build the critical mass of knowledge that will support a growing global influence of the EU. EASAC has recently become a regional network within the InterAcademy Panel and is building its contribution to InterAcademy Panel activities worldwide. We believe that there will be many new opportunities for Academies to work together globally to inform policy development.

[14] Including laboratory partners from Germany, UK and France. Further information is available at www.gfvi.org.
[15] First European Reference Laboratory network for tuberculosis launched, January 2010. Further information available at www.ecdc.europa.eu.
[16] Announced by the Council of the European Union, July 2010 11665/1/10REV1, Council Decision establishing the organisation and functioning of the European External Action Service. This function supports the Vice-President of the European Commission in their capacity as High Representative of the Union for Foreign Affairs and Security Policy.

6 Preparing for the future: continuing opportunities and challenges for shaping knowledge

The European Commission's Health Strategy (2008–2013) represented an important initiative that helps to bring coherence in European health policy. EASAC supports the focus in that Strategy on the threat of communicable diseases as a priority for European attention together with the appreciation that new technologies can play a major role in countering the threat. Nonetheless, the continuing development of EU policy to tackle infectious diseases requires yet more co-operation and flexibility to (1) identify and monitor the threats, by actions to improve epidemiology-based intelligence and data use, and (2) tackle the problems identified, through innovation of smart diagnostics, therapeutics and vaccines and the implementation of health policy conducive to better control and containment strategies. Although there have been some significant changes since EASAC started its work, there are further opportunities across the EU for co-ordination and consistency in objectives, best practices and plans. And the task is urgent if we are to tackle current threats, perhaps most particularly antimicrobial resistance and vector-borne diseases.

Table Summary of key areas identified for policy with examples for action

Policy area	Specific objectives
Public health: collection and use of data from human and animal surveillance (Chapter 2)	• Understanding demographics, disease impact and effects of environmental change. • Developing shared priorities and standards. • Defining and strengthening national systems, their networking and co-ordination. • Building ECDC resources and roles. • Monitoring high-risk population cohorts. • Introducing new methodologies for signal detection and syndromic surveillance. • Improving construction, curation and use of databases for patient care and research. • Achieving the 'one health' concept by co-ordination between public health and veterinary health (local–global monitoring) and between departments of health and agriculture.
Research and its infrastructure: prioritising and supporting the science base (Chapter 3)	• Capitalising on new opportunities in fundamental research and the connection to translational medicine. • Improving interdisciplinary linkages and reviving training in relatively neglected disciplines (e.g. microbiology, clinical infectious diseases, entomology, vector biology and ecology). • Characterising determinants of human behaviour in infection spread and control. • Streamlining clinical research regulation. • Progressing new models of research and training (e.g. multidisciplinary Centres of Excellence) and funding (e.g. 'Grand Challenges').
Innovation and competitiveness: reducing barriers and encouraging applications (Chapter 4)	• Progressing models of best practice for risk-sharing in public–private partnerships. • Diagnostics – develop quick, cheap, reliable methods to distinguish pathogens and inform rational prescribing. • Therapeutics: improve information flow between academia and industry, accompanied by simplification of regulatory hurdles and incentives for companies to develop novel drugs. • Vaccines: share lessons learned from H1N1 influenza pandemic so that investment in new vaccines is secured and vaccine value is well articulated.
Coherence across policy-making: building EU competencies and global partnerships (Chapter 5)	• According health issues greater prominence in other policy debates, e.g. on migration, climate change. • Increasing EU responsibilities for health, e.g. acting on surveillance information, harmonising criteria for immunisation strategies. • Initiating EU–international strategic discussion on human–animal–ecosystem interfaces. • Supporting capacity-building in neighbouring and developing countries and assigning health issues greater priority in the EU's external actions.

The common elements in informing future policy development are the generation and use of knowledge: this requires both surveillance and research. The major areas where we have brought forward recommendations in the present report, updating our previous analysis, are exemplified in Table 1. We believe that these conclusions are relevant for policy-makers at both the EU and Member State levels. The actions necessary to accomplish these objectives are discussed in detail in the preceding chapters and previous reports. Success in achieving the objectives depends also, in part, on building public awareness of infectious disease, its consequences and control: we reiterate our view that the scientific community has an important collective role to provide accurate, relevant and timely information to the public as well as to policy-makers.

New knowledge is critical, both for hypothesis generation and hypothesis testing, to improve the quality and reliability of the evidence base. As discussed in this and our previous work, research into infection should not be unnecessarily constrained by disease, discipline or sector boundaries. Medical practice and research depend on each other, and EASAC advises that the EU must be more ambitious in capitalising on its scientific capabilities and leadership. In our view, there is still a lack of awareness in some of Europe that research must be part of the general mission for health services. Research is crucially important in multiple ways: as the basis for improving health service practice; as the resource for medical industry innovation; as a driver for medical education; and in furnishing the evidence base to inform policy development.

The effectiveness of innovation to tackle infectious disease depends not only on the strength of the individual functions – the quality to be found in universities, companies and health services – but also on the strength of the linkages between them. Europe requires better sharing of those skills traditionally compartmentalised within the separate domains of academia, industry, the charitable sector and government. If we are to be successful in achieving the agreed societal objectives, there must be new models of collaboration to generate and use knowledge to inform policy development and implementation: between the public and private sector scientific communities, between Member States and between the human and animal health communities. Much of EASAC's work during the past six years has been directed at analysing these opportunities and communicating this message of partnership. EASAC and member Academies acknowledge a continuing responsibility to catalyse dialogue among the research and policy communities – together with patients and the public – both on the nature of the scientific evidence and the scope of the policy agenda.

Appendix 1 EASAC publications

EASAC publications draw on discussion within Working Groups composed of experts, acting in an individual capacity, nominated by member Academies and on the outputs from international meetings organised by member Academies. Projects are usually accompanied by an open call for evidence. All draft publications are peer-reviewed by independent experts nominated by EASAC.

Infectious diseases – importance of co-ordinated activity in Europe (report: EASAC 2005)

In this introductory publication, based on discussion at a scientific meeting co-organised by the German Academy of Sciences Leopoldina and the Academie des Sciences, France, EASAC previewed some of the topics that would be investigated in more detail by a series of projects to clarify key issues for public health and innovation. These topics included disease surveillance, public health system infrastructure, the basic research and skills agenda, industry innovation and EU competitiveness, public engagement, and the particular needs of the newer Member States. In addressing this policy agenda, EASAC focused on those matters primarily agreed to fall within the remit of the EU but emphasised the importance of ensuring that the provision of scientific advice at the European level is complemented by parallel activity in the Member States.

In developing the framework to be used in all subsequent work, EASAC began by analysing EU policy and R&D support already in place, within a global context of emerging issues, actions and needs for both the public and private sectors.

Vaccines: innovation and human health (report: EASAC 2006)

Noting that Europe had been historically successful in both the relevant basic science and vaccine development, EASAC evaluation took as its starting point (1) the very great value of vaccination in both public health and economic terms and (2) the spectrum of current infectious disease problems that could be resolved by improving current vaccine preparations and developing new vaccines. These opportunities were considered against the background of obstacles: scientific, technical, economic and legal, exacerbated by public misperceptions.

The EASAC report discussed case studies for future preparedness for H5N1 influenza and for facing bioterrorism and the prospects for vaccination in disease eradication. Taking account of evidence collected from vaccine manufacturers and member Academies, key recommendations covered the importance of capitalising on scientific advances (for example reverse vaccinology and the synergy between human and veterinary research), technical developments (for example, the availability of novel adjuvants), new approaches to safety assessment (for example, the use of integrated databases) and new mechanisms in regulatory approval (for example, designation of fast-track vaccine candidates). It was also judged to be of the greatest importance, collectively, to do more to demonstrate and communicate vaccine value and thereby promote public uptake.

Tackling antibacterial resistance in Europe (report: EASAC 2007a)

After feedback on the earlier reports, including discussion at the European Commission and European Parliament, EASAC now focused on the challenges presented by the emerging global pandemic of antibacterial resistance, highlighting the core importance of new science in mounting a coherent effort to tackle resistance. Although there has been no shortage of other reports and policy initiatives concentrating on short-term actions to contain resistance in hospitals and the community, EASAC presented the evidence-based case for longer-term investment in basic science and innovation to deliver novel therapeutic agents.

The EASAC report documented the current resistance problems for major pathogens, noting also the relative decline in EU scientific activity and the weaknesses in the anti-infective drug pipeline. Collecting evidence from the academic community, large and small companies, EASAC reviewed both the promising new scientific approaches, which might be expected to lead to new pathogen target selection, and the selection criteria for such targets to serve in the development of broad-spectrum antibiotics. In supporting points made in the previous reports, it was concluded that significant progress in innovation could be expected if the public and private research sectors committed to new forms of partnership and if EU policy-makers identified new approaches to funding and incentives that would encourage additional external investment.

Healthcare-associated infections: the view from EASAC (statement: EASAC 2009)

The 2007 report on antibiotic resistance was followed by discussion at the national level, organised by member Academies and by an inter-academy scientific meeting on healthcare-associated infections, many

of which demonstrate antimicrobial resistance. The EASAC Statement in 2009 focused on those infections occurring after admission to hospital or exposure to other healthcare interventions and provided input to discussions organised by successive Czech and Swedish presidencies of the EU Council.

In addition to reiterating points made previously about the importance of the basic biomedical research and diagnostic/therapeutic innovation agendas, this statement identified some of the critical research priorities in the social sciences that may help to elucidate the behaviour of human as well as microbial populations. EASAC also noted the growing importance of considering the inter-sectorality of policy development, exemplified by connections between the human and veterinary health sectors and by the need to connect policy-makers in regulatory departments concerned with health, agriculture and manufacturing.

Impact of migration on infectious diseases in Europe (statement: EASAC 2007b)

As part of an input to the Portuguese presidency of the EU Council priority on migration and public health, EASAC evaluated some of the issues for infectious disease in the high-risk migrant groups. According to data from the United Nations, migration accounts for 75% of population growth in developed countries but health issues have received comparatively little attention by EU policy-makers. The EASAC analysis was based on the experience of Member States across the EU as it is important not to generalise about migration or infectious disease: for example, the approach to screening and management may differ for those diseases that spread relatively slowly (TB, HIV) from those that pose a more acute threat.

Various challenges for healthcare systems were identified: how to achieve consensus on those infections most relevant to migration; how to evaluate and share information on current screening practices and alternative approaches; how to improve migrant awareness of the healthcare system and facilitate access and follow-up; how to determine the burden of disease, the nature of the health inequalities and the net public health risk attributable to migration. EASAC recommended that there is a need to collect more data proactively so that public health policies for high-risk groups can be informed by a sound evidence base rather than dominated by political agendas.

Combating the threat of zoonotic infections (report: EASAC 2008)

After feedback was received in response to the previous projects, EASAC initiated specific work on zoonoses, those infections naturally transmissible, directly or indirectly, between vertebrate animals and humans. Assessment of the current situation enabled EASAC to review progress made since this policy priority was established by the Netherlands presidency of the EU Council in 2004.

Most new human pathogens reported in the past 25 years have zoonotic origins. The EASAC project assessed four priorities within the policy framework: the need for increasing awareness that zoonoses are an important EU problem; the importance of collaboration between human and veterinary medicine to develop 'one health' responsiveness to emerging threats; the global environment for the EU; and research tasks to prepare for the unexpected. Key issues were illustrated by case studies.

This report appeared at a time when the ECDC was beginning to demonstrate real progress in addressing EU weaknesses in surveillance and capacity-building that had been identified in previous EASAC work. EASAC recommended further support of ECDC and other EU initiatives that show promise in encouraging participation by stakeholder groups to tackle disease priorities, for example the Innovative Medicines Initiative and the Global Animal Health Technology Platform.

Drug-resistant tuberculosis: challenges, consequences and strategies for control (report: EASAC 2009)

TB had been considered conquered in many European countries but has re-emerged as a significant problem, and a growing number of TB strains are increasingly resistant to the standard anti-TB regimens. Against a background of detailed statistics documenting TB public health and economic impact, and projecting future trends in disease incidence, the EASAC report reviewed weaknesses associated with the use of the current generation of diagnostics, therapeutics and vaccines. Acknowledging the wider interest in better strategies against TB, EASAC created working links with WHO and the Foundation for Innovative New Diagnostics to collect evidence and develop recommendations. The EASAC analysis brought together evidence for scientific opportunities and market failure, helping to understand what is now rate-limiting for mounting an effective response against TB. EASAC concluded that a strategic framework to control TB requires action to strengthen data collection, raise medical professional vigilance and public awareness, increase investment in basic research and support innovation. This can best be achieved by collaboration at the global level to build partnerships for research, healthcare delivery and policy development, if accompanied by new commitment within the EU.

Climate change and infectious diseases in Europe (statement: EASAC 2010)

Climate change, like infectious disease, does not stop at borders. However, its impact on infection has, hitherto, received little attention in policy-making. This EASAC work was based on the output from a meeting co-organised by the German Academy of Sciences Leopoldina and the Indian Academy of Sciences (individual presentations have now also been published: see Friedrich et al. (2010)). There are still many uncertainties to resolve in the evidence base in order to clarify, quantify and forecast the impact of climate change on the incidence of human and animal infections and on the mechanisms of transmission and geographic distribution. The EASAC publication takes a case study approach to analyse the aetiology of human infections that pose a current or future threat to Europe: rodent-borne viruses (for example, hantavirus); arboviral diseases (for example, chikungunya, West Nile virus fever); and parasitic disease (for example, dirofilariasis, leishmaniasis). There are also growing and re-emerging threats of animal disease for Europe: for example blue tongue virus, Rift Valley fever virus and African swine fever virus.

The analysis reinforces recommendations made in previous EASAC work about the importance of establishing modern surveillance and early warning systems. EASAC concluded that although it is vital to strengthen the evidence base at the local, national and European levels, it is also important to appreciate that much of the adaptation that may be required to respond to the impact of climate change is basic preventive public health. Raising the visibility of these issues does not apply only to the policy-making community: the scientific and medical communities must also do more to inform and educate themselves about the health consequences of climate change.

Appendix 2 Process for preparing this report

After discussion by Council members of EASAC in June 2010, a draft was prepared by Volker ter Meulen (President of EASAC until December 2010 and Chairman of the Biosciences Programme) and Robin Fears (Secretary of EASAC Biosciences Programme) and reviewed with Jos WM van der Meer (Vice-President of EASAC) and Jorg Hacker (President of the German Academy of Sciences Leopoldina). The draft report was then circulated for further discussion with a group of experts selected from the previous EASAC Working Groups. We thank the following colleagues for their comments on the draft:

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List of abbreviations

BTV	Blue Tongue Virus
DG Research	European Commission Directorate-General for Research
DG Sanco	European Commission Directorate-General for Health and Consumer Protection
EASAC	European Academies Science Advisory Council
ECDC	European Centre for Disease Prevention and Control
EDCTP	European and Developing Countries Clinical Trial Partnership
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFSA	European Food Safety Authority
EMA/EMEA	European Medicines Agency
ESCMID	European Society of Clinical Microbiology and Infectious Disease
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization
FEAM	Federation of European Academies of Medicine
HIV	Human Immunodeficiency Virus
IMI	Innovative Medicines Initiative
NGOs	Non-Governmental Organisations
OIE	World Organization for Animal Health
R&D	Research and Development
SARS	Severe Acute Respiratory Syndrome
SME	Small and Medium-sized Enterprise
TB	Tuberculosis
WHO	World Health Organization

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