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Summary of EASAC launch event on Gain of Function

Brussels 21 October 2015

Introducing the programme and objectives of the launch event for the EASAC report "Gain of function: experimental applications relating to potentially pandemic pathogens", Volker ter Meulen (Chair of the EASAC Working Group and of Biosciences Steering Panel) described how EASAC was formed by the national science academies of the EU Member States to enable them to collaborate in giving advice to policy makers[1].

The results from Gain of Function (GoF) research may help in understanding pandemic potential of the influenza virus. However, experiments to modify the transmission potential of avian influenza of subtype H5N1 and, thereby, elucidate factors affecting virus spread by the aerosol route, have been controversial. In the USA there is a *de facto* moratorium and in Europe members of the scientific community have expressed differing views about the value and risks of such research to policy makers in the European Commission. EASAC is now publishing a report[2] from a project drawing on previous work by academy members and bringing together scientists with a broad range of expertise and views, to explore where there is consensus, to clarify which issues are still unresolved, and to advise on what additional analysis is needed to assess future options for the research area. In the report, EASAC also emphasises which current EU regulations govern this research and what good practice already exists at a national level. EASAC messages are directed to academies of science worldwide, policy makers in the European institutions and in the Member States, research funding bodies, regulatory authorities, professional societies and others in the scientific community and, thorough the member academies, to the lay public.

Sir John Skehel (Francis Crick Institute, Vice President Royal Society and member of the EASAC Working Group) noted that researchers had initially been encouraged by funding bodies to propose research to study the determinants of the transmission potential of influenza viruses. However, experiments are of concern if their products or processes have potential to cause serious disease; issues are raised for biorisk management, encompassing biosafety (accidental release of a pathogen from containment), biosecurity (intentional misuse) and bioethics. GoF studies are already subject to stringent EU and national regulations and the generation of novel pathogens has previously been assessed in detail in the US National Academies Fink report.

The current work of EASAC on GoF research is relevant to all EU Member States and for collaborative EU research, as well as an input to support global decision making. The EASAC

[1] Further information on EASAC is on www.easac.eu and in a recent publication www.cam.ac.uk/projects/future-directions-scientific-advice-europe.

[2] http://www.easac.eu/fileadmin/PDF_s/reports_statements/Gain_of_Function/EASAC_GOF_Web_complete_centred.pdf

recommendations emphasise a layered approach with integration of responsibilities and action at researcher, research institution, research funder, national and international levels. Some issues remain controversial but EASAC outputs represent consensus in the Working Group and consensus among EASAC member academies. Among the critical issues addressed and reviewed in detail in the report are:

- Self-governance and scientific responsibility, at all levels in research – academies of science have a continuing role in promoting biosafety and biosecurity norms and in supporting audit of research practices.
- Benefit-risk assessment – raises multiple issues and it should be acknowledged that benefits are sometimes overstated by researchers but also that benefits may not be obvious until later. Benefit-risk assessment cannot be a "once and for all" calculation and it requires continuing, collective commitment to understand and communicate the issues.
- Research review and management systems – for example, researchers need to be sure that they can gain the information they need by doing GoF experiments only in this way rather than in a potentially less dangerous way.
- Biosafety and biosecurity issues and advisory mechanisms – EASAC recommends that no new EU-level body is required but Member States should have a clear national advisory approach and governance mechanism with statutory powers.
- Publication of sensitive information and options for management – EASAC advises that the European Commission's Export Control Regulation is an inappropriate and ineffective vehicle to block publication but that researchers and their institutions all have responsibility to make decisions about publishing sensitive information.
- Public engagement – trust and openness are crucial for researchers and their institutions. Academies and others in the scientific community should actively participate in public dialogue, articulating the objectives for research, the potential for benefit and risk, and the biorisk management practices adopted.
- Global context – how to inform discussion and decision worldwide? Countries vary in their standards, national guidelines, legal framework and in their attitudes to benefit-risk balance. Collectively, there is much to do to understand, share and implement good practice.

Ruxandra Draghia-Akli (Head of Health Directorate, DG Research and Innovation, European Commission) provided the perspective from the European Commission on GoF research and the EASAC recommendations. Three recent Framework Programme 7 projects can be identified with GoF components[3]. Currently, DG Research and Innovation is not aware of any GoF research being conducted in Horizon 2020 but ethical screening of project

[3] EMPERIE (European Management Platform for Emerging and Re-emerging Infectious Disease Entities, www.emperie.eu); PREMEDICS (Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses with Pandemic Potential using multidisciplinary approaches, http://premedics.biomedtrain.eu); ANTIGONE (Identifying key factors that contribute to the emergence of pathogens with human pandemic potential from pathogens with a zoonotic background, http://antigonefp7.eu). Other projects are relevant to a consideration of biosecurity issues (e.g. AntiBotABE, Neutralising antibodies against botulinum toxins A,B,E, www.antibotabe.com).

proposals assesses whether research has "exclusive civilian focus", requires export licence or whether there are potentially other concerns. If issues are identified during ethical screening of a project proposal, then such a proposal undergoes full ethical assessment and, if needed, additional security scrutiny.

The European Commission welcomes the EASAC report and its recommendations will be considered for further practical guidance for research applicants and evaluators in Horizon 2020. In particular, the following EASAC recommendations were welcomed:

- Self-regulation and harmonisation
- Benefit-risk assessment
- Public engagement
- Publication of sensitive information
- Global dimensions

The European Commission also agrees that no new EU-level bodies are required to manage GoF research issues. Other conclusions from the EASAC report were agreed in principle, with some caveats:

- Collecting information already in place in the Member States – any new role for the Health Security Committee would have to be supported by the Member States, who manage the Committee's agenda.
- Revising the Export Control Regulation – the scientific community has so far not used the opportunity (announced in the Working Group and on the EASAC website) to make concrete contributions to the revision of export control legislation. Work on the revision is now far advanced and it would not be easy to accommodate changes at this point.
- As a research funder, because of the principle of subsidiarity DG Research and Innovation is not in a position to ascertain what effective regulatory frameworks are in place in all Member States/institutions – this again requires due attention at the country and authority level where such research is conducted.

In conclusion, the European Commission finds the EASAC report thorough, clear, balanced and helpful, and encourages EASAC to continue to engage widely in pursuing resolution of the issues. The European Commission also suggested to EASAC to tackle the issue of the definition of basic research in the context of dual use and GoF studies.

Ronald Atlas ((University of Louisville, USA and member of National Academies advisory committee on GoF research), in contributing a perspective from the USA, observed that their initial focus had been on biosecurity, with biosafety concerns developing subsequently. The initial actions by the NIH, NSABB and National Academies and the current pause in GoF research funding, are discussed in the EASAC report. The first National Academies workshop in December 2014[4] identified several important emerging themes for continuing US discussion, and these themes resonate with the EASAC conclusions for the EU:

[4] http://dels.nas.edu/Workshop-Summary/Potential-Risks-Benefits-Gain/21666?bname=bls

- The scope of the review of policy of GoF research should not be defined too broadly.
- There may be experiments that should not be performed: concerns are legitimate but what is much less clear is how to inform, evaluate, quantify and weigh the concerns.
- Risk-benefit calculation is not simple (and there are differing views on benefit, with the US government focus being on "near term practical benefits").
- It is an international challenge.
- Accepting personal and institutional responsibility is essential.
- There is need to educate policy makers and the public.

In the USA, a quantitative risk-benefit analysis is being conducted[5] with results expected in January 2016. The National Academies will convene a second workshop in March 2016 as a public platform to generate broad discussion and the NSABB has the mandate to provide advice to the US government by that date. A recent NSABB meeting (September 2015) developed some interim conclusions[6]:

- As with all life sciences research involving pathogens, GoF research involves risks.
- The US already has a robust policy framework.
- There are several points throughout the research life cycle where risks can be managed.
- The adoption of an "adaptive policy approach" is likely to be preferred – building on current frameworks with oversight and mitigation measures commensurate with risk.

The EASAC report is seen to be a very important input to the continuing US debate: EASAC is invited to engage further with the National Academies' activities and to help ensure congruence between EU and US decisions on policy.

Panellists were invited to give short contributions and then help lead general discussion. The panellists were Simon Wain-Hobson (Institut Pasteur Virology, France and Working Group member), Andre Knottnerus (Maastricht University, Royal Netherlands Academy of Sciences and Working Group member), Mike Skinner (Imperial College London and Chair of the UK Health and Safety Executive's Scientific Advisory Group on Genetic Modification, Contained Use) and Mike Catchpole (Chief Scientist, European Centre for Disease Prevention and Control, Sweden). Among the key points, building on issues raised by the earlier speakers, were:

- Importance of influenza research In the UK, for example, the potential for a pandemic is identified as the first priority in the UK Cabinet Office Risk Register for

[5] Gryphon Scientific Progress update http://osp.od.nih.gov/sites/default/files/2%20Gryphon%20Scientific%20-%20Risk-Benefit%20Analysis%20of%20GOF%20Progress%20Update.pdf

[6] NSABB Working Group Progress Report http://osp.od.nih.gov/sites/default/files1%20Kanabrocki%20-%20NSABB%20WG%20Progress%20Report.pdf

2015[7]. While it is difficult to know where the next breakthrough in scientific understanding will come from, it is vital that research continues to inform the resources for preparing for and controlling infectious disease.

- Publication of sensitive information The role of journals and their editors needs further consideration to take account of the growth of online publishing. But it is also important to appreciate that the researcher/funder/ethics committee and others must consider publication issues at the beginning, and throughout, the project. The scientific community is becoming more experienced in how to handle these issues and conform to agreed standards but there are still challenges in sharing and applying good practice globally.
- Public engagement The conduct of science is dependent on public trust but scientists have often not been effective in their explanations to the lay public. There is need to learn how to do better and this brings implications for education and training.
- Responsibilities of Member States The layered approach to exercising responsibilities, recommended by EASAC, requires that there are checks and balances in place at the national level – and these too act to generate public confidence. Member States should examine what more they can do in developing advisory body capacity. Options for involving security experts merit further discussion and the InterAcademy Partnership project[8] provides one opportunity to explore global solutions.
- Wider public health context Risk assessment and management have implications beyond the institutional level necessitating, in addition, better pandemic preparedness and responsiveness frameworks at the national level. These frameworks must encompass diagnostic capacity, surveillance systems, antiviral and vaccine health delivery services, and international coordination.
- Wider international context There are good opportunities to develop the momentum for dialogue and policy harmonisation between the US and EU.

[7] https://www.gov.uk/government/publications/national-risk-register-for-civil-emergencies-2015-edition
[8] IAP Biosecurity Working Group, http://www.interacademies.net/ProjectsAndActivities/10880/27693.aspx