

# What are we gaining from gain of function research?

There is controversy surrounding gain of function research, with contrasting views on its value. [EASAC published a report](#) discussing the risks and benefits of this type of research. Expounding on this work, Director of the Council's Biosciences Programme **Dr Robin Fears** discusses the importance of openness, public engagement and the harmonisation of good research practice across Europe

## **First off, what was the purpose of publishing a report on gain of function (GoF) studies and why is this such an important topic?**

The European Academies Science Advisory Council (EASAC) and its member academies have longstanding interests in the issues associated with research, innovation and health services delivery to tackle infectious diseases. For example, EASAC has previously published reports on zoonoses and on vaccines, both highly relevant generally in virology and also, in particular, in advising on ways to improve European preparedness and responsiveness for influenza outbreaks.

GoF experimental studies, linking genetic and functional information, have a long history of providing very useful information in virology. For example, in the study of virus characteristics, the development of relevant animal models of infectious disease, and in antiviral drug design and vaccine development.

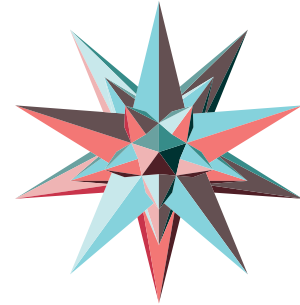
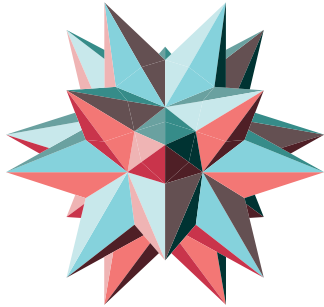
But, recently, some GoF research, particularly on the experimental modification of avian influenza strains such as H5N1 with the objective to study their transmissibility, has attracted controversy. Differing views about the value of such research were communicated from the scientific community to the EC which, if not clarified, were likely to lead to confusion about research priorities.

Following feedback from the EC to EASAC, we agreed to initiate a project on GoF research, to publish a report that would explore where there is consensus on key questions, to identify where further assessment of the issues is required and to clarify options for public policy development at the EU and national levels.

## **Can you tell us about the controversy surrounding recent GoF studies? Where has this stemmed from and what it can be attributed to?**

The controversy related primarily to research studies attempting to understand how viruses might acquire transmissibility between people. Such experiments may have the potential to generate pandemic pathogens: dangerous experiments require robust assessment with special consideration and precautions before they can be carried out.

Concerns include the potential impact with regard to biosafety (that is, the need to implement containment measures to avoid accidental release of virus into the environment and protection measures to avoid exposure of personnel) with the objective to safeguard researchers, the general public and the environment at large. Concerns are also raised about biosecurity (that is, the need to implement protection measures against intentional



### GAIN OF FUNCTION

In GoF research, pathogens are modified to alter their capabilities. It has had important uses in supporting therapeutic drug and vaccine selection and development. However, in 2014 the US Government paused this type of research on influenza, SARS and MERS viruses in order to allow time to investigate concerns about potential biosafety and biosecurity risks. In the EU, meanwhile, the scientific community had expressed a range of views about the potential benefits and risks associated with GoF work.

misuse), with particular regard to the potential dual use of modified pathogens.

The controversy stems from the various communication efforts of members of the scientific community who may have differing perspectives on the relative potential risks and benefits of this GoF research, reflecting their different backgrounds in science, value systems or expectations about the practical procedures for assessing and managing risk.

#### **On the other side of the coin, what are some of the notable benefits of the kind of research?**

GoF work may help to provide insight on the fundamental biology of the influenza virus, including virulence, immunogenicity, host range and transmissibility. Advances in fundamental knowledge will help to

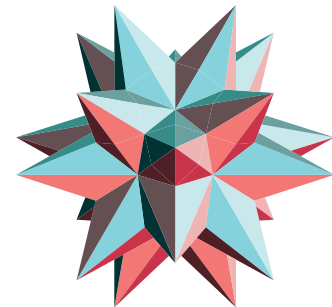
drive health benefits including the prioritisation and development of pre-pandemic vaccines.

However, there are many uncertainties in the data available for evaluating both benefit and risk of GoF studies on potentially pandemic pathogens. It is also the case that differing value systems have been applied in evaluating the data: incommensurable parameters measured in risk and benefit do not allow a value-free determination of the balance of risks and benefits to be made.

#### **Would you say that the EU's biosafety regulations are adhered to by research institutions in Member States?**

A main message in our EASAC report is that there are already stringent rules governing such research in the EU. Established EC legislation is implemented at the Member State level and is also underpinned by codes of conduct developed within the scientific community together with guidance on biosafety by international bodies such as OECD and the WHO. Our first EASAC recommendation is that it is vitally important that EU Member States and their research institutions and researchers follow the regulations and guidance that are already in place.

As discussed in the report, it is also essential that Member States share their experience to ensure harmonisation of good research practice across Europe. We describe roles for the EC in helping to collate and compare the experience of good practice across Member States and also in incorporating appropriate guidance for those research studies that are funded by the EC. The EASAC report provides detailed discussion of the research management frameworks in place at the EU level and exemplified by Member State case study analysis.



### THE REPORT

Sparked by controversy among virologists in Europe and US, EASAC established a group of leading European scientists to analyse the current situation of GoF research and explore future options. The resulting report, entitled 'Gain of function: experimental applications relating to potentially pandemic pathogens', highlights a number of critical issues and stresses the importance of public dialogue.

### ALL EYES ON THE EXPERT: DR ROBIN FEARS

#### Director, EASAC's Biosciences Programme

Dr Robin Fears began his professional life in biochemistry and spent three decades working in R&D in the UK pharmaceutical industry, initially in the cardiovascular and neuroscience areas. For the latter part of his time in industry he set up a R&D policy group in Europe to provide an interface between the company and the broader scientific and policy communities.

In 2002, he decided to become self-employed and initiated various working relationships in science policy with academic groups, national and local government and parliamentary bodies, industry and, increasingly, with academies of science. EASAC had already come into existence in 2001, formed by the national science academies of the EU Member States to enable them to collaborate in giving advice to European policy makers. Accordingly, among his consultancy activities, Fears developed the role to provide support on the biosciences to the work of EASAC.

### What are some of the potential costs of pandemics? How can these be abated?

WHO has estimated that [annual influenza epidemics](#) account for 3-5 million cases of severe illness and 250,000-500,000 deaths worldwide. The public health burden can increase dramatically during a pandemic and there may also be significant economic losses. One UK modelling study suggested that, depending on the severity, an [influenza pandemic could result in losses](#) of 0.5-4.3 per cent GDP.

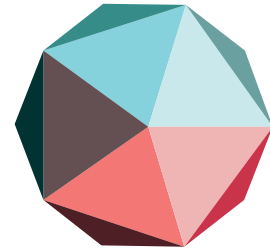
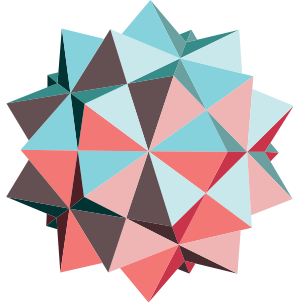
Over the past decades there has been an increase in detection and reporting of avian influenza viruses crossing the species barrier to infect humans that may result in severe disease. Preparedness against the threat of communicable disease has a high priority in the political agenda of the EU and its Member States. However, the current inability to predict which specific subtypes will cause the next influenza pandemic demonstrates the need to address gaps in the knowledge required to manage future pandemics more effectively. GoF research may play a part in helping to fill these knowledge gaps.

### What is your advice, to both society and the scientific community, regarding the threat of pandemics?

In our previous publications on infectious diseases, EASAC has made various recommendations to support better preparedness for future epidemics and pandemics. These recommendations include attending to issues for improving disease surveillance and monitoring, data collection, curation and use, vaccine development, clarification of environmental and societal determinants of disease, and research on basic biology.

In our present report, EASAC focuses on the issues for conducting and managing research on potential pandemic pathogens to provide the resource for healthcare innovation.

Our recommendations are targeted variously to the research community, including academies of science, research funders, regulators and policy makers and we also explore how to build better public engagement about the important issues in GoF studies. We see considerable need for



scientists to articulate the objectives for their research, the potential for benefits and the biosafety management practices adopted.

### **Can you give an insight into the GoF report's key findings and what the implications of these are?**

Our key findings, representing EASAC Working Group and member academy consensus, cover a wide area. Recommendations on GoF research include issues for research review and management on a case-by-case basis, actions for self-regulation and harmonisation of good practice, elucidation of bioethical considerations, benefit-risk assessment challenges and opportunities, biosafety advisory options and the publication of sensitive information. We emphasise that attention to key biosafety issues is imperative at all stages of the research endeavour, from first formulating the research idea through to intended publication of the results.

Our main messages concentrate on biosafety but we recognise that there are also implications for biosecurity and we highlight the responsibility for researchers, research institutions and publishers to seek appropriate advice about biosecurity. We emphasise throughout that there must be layered approach to integration of biosafety responsibilities at the researcher, research institution, research funder, national and EU levels. These responsibilities must include conforming to the stringent rules and guidance already existing. We note the relevant place of self-regulation but this means that there are checks and balances on research within the scientific community, not that each researcher is free to decide for themselves what procedures to follow.

We also recommend that further commitment is essential to extend the debate on GoF issues worldwide. Clearly, there are implications for many in the scientific and policy-making communities in the EU and worldwide, not least for academies of science themselves. We recommend that academies of science have a continuing role to play especially in promoting and increasing understanding of biosafety and biosecurity norms and in encouraging informed discussion of the qualitative and quantitative assessment of risks and benefits.

### **SPREADING THE WORD**

EASAC held a public discussion event last October to launch the report and stimulate debate on key messages. In addition to contributions from the Council's experts in the Working Group, other leading scientists were invited to contribute views from the Member State level, and perspectives from the US and the EC. The summary from this meeting is published on:

[www.easac.eu/home/easac-news/detail-view/article/summary-of-t.html](http://www.easac.eu/home/easac-news/detail-view/article/summary-of-t.html)

Since then, EASAC has continued to be very active in disseminating its main messages through its academies, to the wider scientific community by publishing commentaries in peer-reviewed scientific journals, and in debate with biosecurity experts worldwide in preparation for the next review of the Biological and Toxins Weapons Convention. Public discussion is continuing, for example a major meeting was hosted by the US national academies in March, where EASAC again contributed its findings. "Our goals are to continue to catalyse and support discussion and action based on our report's main messages," Fears concludes.

**[www.easac.eu](http://www.easac.eu)**