EUROPEAN SOCIETY for VIROLOGY

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President

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Padova, October 16th, 2013

TO:
Mr José Manuel Barroso
President of the European Commission
Berlaymont Building
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1049 Brussels, Belgium

CC:
Mrs Viviane Reding
Vice President of the European Commission
Commissioner for Justice, Fundamental Rights and Citizenship
Berlaymont Building
200 Rue de la Loi
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Mrs Máire Geoghegan-Quinn
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Dear Mr. President Barroso,

I am writing you on behalf of the European Society for Virology (ESV), which represents all National Societies for Virology active within Europe and is a forum for scientists active in all aspects of Virology from the European Union and beyond. The stated aim of the ESV is to advance the art and science of Virology and to foster the discipline of Virology in all its different areas of interest (basic, medical, veterinary, plant, environmental), from fundamental to translational science, and clinical and technological applications.

The ESV has been mandated also by the European Society for Clinical Virology to act at the appropriate institutional level to open a frank and clear discussion on the case involving the research performed by virologist Ron Fouchier of the Erasmus Medical Center at Erasmus University Rotterdam, the Netherlands, and, in more general terms, the freedom of research, the ethics in science, the importance of free dissemination of results, and the handling of security-sensitive data.

As you know, Ron Fouchier's research on the H5N1 influenza virus that was published in Science in June 2012 was and still is hotly debated. In this study, Fouchier's group shows that a few mutations can render H5N1, an avian virus, transmissible by aerosol between ferrets, which are used as the mammalian model to study the potential of pandemic spread of strains of influenza. Fouchier's work, along with a similar study performed by Yoshihiro Kawaoka of the University of Wisconsin and the University of Tokyo, was already under discussion worldwide in late 2011. The U.S. National Science Advisory Board for Biosecurity (NSABB) initially advised that these studies should not be published because their results could be used to transform H5N1 into a bioweapon. However, in March 2012, the NSABB reversed its decision and advised in favor of publication of the papers, in line with the advice one month earlier from international influenza experts that assembled upon invitation by the WHO.

The Dutch government has considered the publication of these results in Science as a form of "export". Based on Council regulation EC 428/2009 - that was issued in 2009 to prevent the spread of nuclear, chemical, and biological weapons - Fouchier was requested to ask for official permission (an export permit) before submitting his work for publication abroad. It remains unclear if a publication in a European international journal would have been allowed. As a consequence, while the paper of the Kawaoka group was published in Nature on May 2 of 2012, Fouchier's study was published only on June 22, after Fouchier obtained an export license (under protest) at the end of April.

Erasmus MC Rotterdam filed an appeal against the government's opinion that an export permit was required for this scientific publication and when this was rejected, it brought the case to the district court. The appeal was

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based on the fact that the Annex to Council regulation EC 428/2009 contained an exclusion clause for "basic scientific research" and information already "in the public domain". Since the ferret studies were designed to increase basic insights into the mammalian transmissibility of an influenza strain and the methods used in the study to generate mutants had been already described, Erasmus MC argued that both exclusion clauses applied to his study.

At the end of September 2013, the Dutch district court rejected Erasmus MC's appeal by stating that: (i) it is not up to the researchers to define their studies as basic or applied studies; (ii) transforming an H5N1 virus into an airborne pathogen could not be considered basic research and; (iii) even though the methods have been previously reported in the literature, the researchers had "taken steps and made choices that have led to entirely new outcomes."

In practical terms, this verdict means that – according to the Dutch district court - future scientific manuscripts dealing with all of the around 90 viruses and microorganisms that can cause disease in humans, animals, and plants that are listed in the Annex to Council regulation EC 428/2009 would require an export permit before they can be published in international scientific journals. Given that the EU acts as a single trade zone and that EC 428/2009 applies to all Member States, this Dutch ruling may have far-stretching implications for research and public and animal health within all EU Member States.

One implication of the Dutch ruling could be that national export authorities in the EU will need to screen 100s of scientific manuscripts annually, a tedious process for individuals who may not be fully knowledgeable about the common discourse of scientific publishing (it has been estimated that Dutch scientists alone publish ~100 manuscripts annually that deal with the agents listed in the Annex of EC 428/2009). It will almost certainly result in serious delays of scientific publications about pathogens that cause major natural outbreaks in humans, animals, and plants frequently, and that often demand rapid international dissemination of scientific data (the Dutch export process supposedly takes around 8 weeks for easy cases). More importantly, the Dutch interpretation of EC 428/2009 touches on sensitive issues such as academic freedom and freedom of publication, and may be hard to align with international agreements, such as the International Health Regulations of the WHO. Although the exclusion clauses in the Annex of EC 428/2009 probably were included to maintain the free exchange of scientific information in the interest of animal and public health, the strict interpretation of the Council Regulation by the Dutch Government and the Dutch District Court will put strong limits on such free exchange internationally.

Studies on influenza virus transmissibility based on the "gain of function" technique used by Fouchier and in general research using this approach may as well require an official approval with delay in the dissemination of

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results and with discrimination of scientists working in specific European Member States compared to the ones based elsewhere. However, it has to be mentioned that, in this specific case, the "gain of function" was used to re-produce what nature already selected (as demonstrated by sequencing of field mutants) with the variation that the aim of the study was to predict/anticipate biological evolution and to provide us with critical information to specify preventive and therapeutic measures, e.g. the improved surveillance and proper evaluation of candidate vaccines and drugs. A bioterrorist organization (provided It has the facilities) could make a more powerful biological weapon (smallpox or botulin toxin) purely by a synthetic biology approach that exploits data already in the public domain without resorting to generate fancy virus mutants.

As European Society for Virology we clearly understand the legal and ethical aspects about research on potentially dangerous pathogens. But we also believe that this case clearly shows that it is time to initiate a debate within Europe, with the involvement of all relevant institutional bodies and stakeholders, to elaborate common and agreed lines to take on issues related to freedom in science, dissemination of results, and protection of sensitive data in the research area.

Many advances in science can be misused and thus research can be seen as "dual use research", with potentially positive and negative applications. In the field of life sciences, some research can even fall into the "dual use research of concern" (DURC) category, meaning that results could potentially be misused with serious consequences for Public and Animal Health and national security in general. But in our opinion, which is shared by the US NSABB, this does not mean that we have to prohibit research leading to these results or block publications. It means that we need to carefully consider the potential benefits of such research and to take into consideration the risks linked to it, as in the case of this specific study on the H5N1 virus. We urgently need an European consensus on these aspects to avoid negative consequences for individual European scientists and to avoid the risk that European research, as a whole, loses its competitive edge. Although influenza virus has been the sole topic of discussion thus far, the issue relates to research on many pathogenic viruses, fungi and bacteria that are on the dangerous pathogen list.

Viruses are widespread in the biosphere, being able to infect humans, animals, plants, bacteria and viruses themselves. They are obligate intracellular parasites and by definition they are potentially pathogenic, especially when they acquire the possibility to jump from their natural host to a new one and become able to efficiently spread in the new species (as is the case for pandemic influenza virus). Thus, studies aimed to understand how a virus can acquire these features should not be judged only on the base of its hypothetical future use in the generation of a bio-terrorist weapon, because these studies are principally conducted to provide critical

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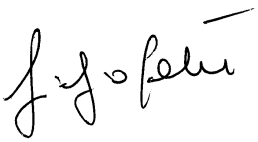
information to direct the development of efficient preventive and therapeutic approaches and to alert scientists and health officers in the fight against suddenly emerging natural health threats.

In the USA, an independent scientific advisory body (NSABB) is in place to advice the Government on issues related to Biosecurity, including "Dual Use" research. Moreover, on 29 March 2012 the US government has announced a policy for the "Dual Use " research it wishes to fund. In our view, it would be important to discuss the potential need for the establishment of an advisory committee at the European level, and to develop workable common policies for scientific research and publications.

Once again, it is not our intention to criticize or to disregard the work of jurisprudence experts and the rights upon which they found their evaluation in the superior interest of justice and people safety. What we would like to underline here, as a scientific organization, in the meantime that Europe considers adopting a body similar to the US NSABB, is the willingness to provide law officers with a proper scientific advice making available the expertise of our many European scientists. This advice could help magistrates/judges to take balanced and harmonized decisions throughout Europe for the sake of human and animal health.

Dear Mr. President Barroso, we know that "preparedness" against communicable health threats has a very high priority on the Commission's political agenda, with Directorate Generals and Units dealing specifically with this issue. For this reason and since the Commission represents not only the highest Institutional body in Europe but also the main funding body at the European level, both in the Research and in the Public Health area, we are addressing this letter directly to you. And we are confident of your consideration and your willingness to act in person or through your appropriate Services in order to deal with a serious gap concerning the implications of science with potential dual use in the European Union that this case has clearly brought to light.



Giorgio Palù, M.D., Professor