The importance of being the change

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Abstract A conference entitled "Stop Vivisection Counter-Conference" and focusing on the European Citizen Initiative (ECI) "Stop Vivisection" discussed the state of the art of non-animal alternatives, in terms of funding, legal aspects and official response of the EU Commission to the ECI, on December 6th 2016 at the EU Parliament in Brussels. The ECI by Stop Vivisection reached over a million certified signatures and stated: "Considering clear ethical objections to animal experiments and solid scientific principles that invalidate the "animal model" for predicting human response, we urge the European Commission to abrogate directive 2010/63/EU on the protection of animals used for scientific purposes and to present a new proposal that does away with animal experimentation and instead makes compulsory the use - in biomedical and toxicological research - of data directly relevant for the human species". A call for change demanding a clear and specific response by the European Commission to move to human-based research, as more specific and predictive for the human species. The results of the ECI and the response by the EC are discussed here, with particular focus to what prompts future changes and what it expected by the Commission in response to the EU citizens.

Keywords Replacement; Alternatives; non-animal methods; non-animal approaches; Stop Vivisection; European Citizen Initiative; European Commission; ECI

On December 6th 2016 the "Stop Vivisection Counter-Conference" expressed its view at the EU Parliament in Brussels, in a conference focusing on non-animal alternatives, the state of funding and the legal aspects of the official response of the EU Commission to the European Citizen Initiative (ECI) by Stop Vivisection. An ECI is an invitation to the European Commission to propose legislation of EU competence and needs to be supported by at least one million EU citizens, coming from at least 7 out of the 28 member states, this allows citizens to participate directly to changes to the EU law affecting all members states. Stop Vivisection is one of the three ECI to have been successfully completed to date, raising 1,173,130 certified signatures. As stated in the EU website this ECI had as main objectives: "Considering clear ethical objections to animal experiments and solid scientific principles that invalidate the "animal model" for predicting human response, we urge the European Commission to abrogate directive 2010/63/EU on the protection of animals used for scientific purposes and to present a new proposal that does away with animal experimentation and instead makes compulsory the use - in biomedical and toxicological research - of data directly relevant for the human species". A call for change urging a clear and specific response by the Commission to move to human-based research, as more specific and predictive for the human species.

Amongst its requests, the ECI asked the Commission to prompt an analysis of the state of the art of animal experiments, in terms of its putative effective value as predictor of human responses. In reply to the ECI the Commission organized a Conference aimed to connect and exchange information on animals’ use and alternatives entitled "Scientific Conference: Non-Animal Approaches - The Way Forward" the 6-7th December 2016. At the same time, the "Stop Vivisection Counter-Conference"
was occurring at the European Parliament, arguing that the Commission response was not sufficient, the time allocated to discuss on the actual usefulness of the animal model, at the Commission's Conference, was too limited and could not provide a constructive evaluation of the animal model, as requested by Stop Vivisection. Moreover, the time proposed to the Stop Vivisection promoters, in their opinion, was insufficient to illustrate their arguments and prompt real change. Above all, it was argued at the Counter Conference, that the Commission did not answer the specific questions and requests from the EU citizens via the ECI, but was avoiding answering in details to the scientific arguments and detailed evidence against the use of animals in science and research, reported by Stop Vivisection in the attached document, as a dossier provided to the Commission as supporting evidence. The ECI also asked the Commission to stop animal experiments and revise the 63/2010/EU, at least until properly evaluated using retrospective data analysis, both in toxicology and regulatory testing, as well as basic and applied research, as the animal model and animal experiments, they argued, have never been "validated" against their effective usefulness for humans. Using advanced human-based methods and technologies needs to be promoted, financed and pushed by legislation, financial commitment and exchanged knowledge. The "Stop Vivisection Counter-Conference" proposed, as well as confirming the urgent need to stop and take stock on animal experiments to date, to launch their "phasing out", as a social and institutional objective. The request to stop and take stock springs from the need to obtain a more efficient and safer research for humans and protect the human species, relying on human data and not extrapolating irrelevant data from animal models.

Amongst the speakers were Gianni Tamino, Andre Menache, Ray Greek, Michèle Rivasi, Elisabet Berggren and Candida Nastrucci. The main topics of the Counter-Conference, were concerning the lack of scientific validity of the animal model and animal experiments to predict a response in humans to drugs, therapies or human diseases, and the failure of the animal model in all areas of research. Personally, I concentrated my talk on the need to end the concept of 3Rs, to focus on the 1R of Replacement, that is the final goal of full replacement of the Directive 62/2010/EU. Furthermore, I reported the lack of funding for Replacement Alternatives and the difficulty in finding funds to create Courses on Replacement Alternatives and non-animal methods and the need for education and exchanging information on non-animal methods amongst scientists. Also, I have suggested to give priority to improve on the scientific culture to use and develop non-animal models and experiments, in all areas of research, particularly in basic and applied research. All the speakers agreed on the great need for increased funding for Replacement Alternatives, non-animal methods and for education on these methods and strategies in research, in order to prompt the change to a non-animal paradigm for research. Furthermore, the urgent need to make concrete changes to the legislative, cultural and financial framework, in order to move efficiently towards a research using advanced models based on the study of human beings, and the use of these non-animal methods, was agreed by the speakers. The need for better and specific human-based research is impellent, also by regulatory authorities, using a more efficient scientific validation procedure, as well as, using all the available replacement alternatives methods and strategies and the non-animal methods for research. Research, both basic and applied, and research & development, are the areas where the use of animals accounts for around 65% of all animals used in EU, although not compulsory by law.

Research is fundamentally important for health, environment protection and the maintenance of an healthy ecosystem. Therefore, science and institutions regulating research, should ensure that the best possible methods for research would be used and should evaluate all the results obtained and published to date, and attributed to animal experiments, before deciding if continuing to use animals, as the animal model was never "validated" against the scientific and predictive value for humans.

The "Scientific Conference: Non-Animal Approaches - The Way Forward", organised by the Commission, reported some relevant non-animal research and projects, and included academia, industry and animal welfare societies. Amongst the speakers the most relevant talks concerning alternatives and non-animal methods were the presentation by Reyk Horland with the progress with the human organ-on-a-chip, and its possible use in the future to completely replace animals using only cells from human tissues to obtain specific answers, quantifiable and accurate. The talk by Jarrod Bailey related on an analysis of the use of animal models to predict human toxicity and drug safety. Thomas Korff spoke on the role of scientific journals to influence the implementation and use of alternatives for replacement in the scientific fields, in biology and medicine, and how they can be used to define how animal experiments are performed and how they can be evaluated. However, in my opinion, the most interesting and original part of the conference was the conclusion of the final presentation summarized the combined updated comments, for every session of the conference, with the contribution by participants and external observers via the web. The combined comments helped to define the main bullet points concerning the "change" process, having as objective to "phase out" animal experiments. Amongst these points the most interesting to non-animal science were: "Citizens concerns should be considered"; "Funders, researchers and journals to come
together and create the right incentive". "There is significant concerns over how animal research is designed and how data is analysed"; "Some analysis show that experimental animals have no or very low predictive power for drug effect in humans". Some recommendations from Session 1 were: "Conduct a gap analysis of alternatives that are still lacking"; "Improve study design and data analysis (also for non-animal studies)"; "Invest higher proportion of funding in non-animal alternatives"; "Scientific peer review before starting the project"; "Need to publish negative results systematically - start with all publicly funded studies using animals"; "More "human" testing using cell based system or human on a chip"; "Funding should be dependent on quality of process, not just results". Session 2 stated amongst its conclusions: "Human cell based models and organs on a chip and its great potential, but still need an in vivo test to confirm if 3D - cell simulation reflects in vivo"; "Safety studies to investigate severe adverse effects could be replaced by in vitro models". Amongst the recommendations for session 2: "We need a coordinated research strategy/agenda"; "Short term use more in silico productions and in vitro cell systems"; "Long term human on a chip model of choice". "Development of patient DNA databases for research purposes". Session 3 conclusions added: "Need a paradigm change, moving away from 1:1 replacement of animal test with a non-animal one to integration of information and prediction of human effects". "International acceptance of alternatives is paramount"; "Need for political will". Session 3 recommendations included: "Need to carefully map uncertainties with animal tests"; "Need a new baseline and classification system to "validate" new methodologies"; Session 4 stated also: "New info not reaching approvers, funders company owners fast enough". "There is enough money to share knowledge, just needs to coordinate its use. Could the Commission help"? Some statements reported at the Conference, reflected the obsolete idea that the use of animals to model humans is still acceptable, as permitted, thereby the will to keep animals as models is reflected by comments, such as: "Human genomics helps to use animal models wisely and reduce use of larger species. Targeted gene editing of animals helps to exactly model a human disease". "Or Metabolism info and computer modelling can help bridge differences between species"; these statements demonstrated that the focus is still "adjusting" an animal to model a human being, and avoiding the real problem, that is that scientists using animals for experimental work are not studying the real human model, but they rely on animals as models for humans. However, animal models had never been scientifically validated as such, and they were never rigorously reviewed or retrospectively analysed, as requested instead by the validation process for replacement alternatives needing to be unreasonably compared to an animal model, although related to a real human cell/tissue/being. Amongst the concluding remarks is significant: "Attitude is important in education and training, with the right attitude you will find the right alternative" admitting that much of the effort to implement the #change# must be a responsibility of each individual scientist. Conclusions from even more sessions followed. Some of the suggestions and conclusions were innovative and useful, but considering the slow progress of Replacement and non-animal use in basic and applied science, in research projects and publications, in regulatory testing, and considering that the 3Rs is a 1959 concept, the progress is far too slow and in actual fact is not prompting an end to animal experiments and a "phasing out". In Europe the number of animals used for animal experiments, as reported by the EC in the Seventh Report, is around 11.5 million animals per year, and the numbers are believed to be higher now and to increase every year, with more genetically modified animals that are not even included in the statistics. 

In the initial few lines of its response to the ECI the EC states: "The EU shares the Citizens' Initiative's conviction that animal testing should be phased out. This is the ultimate goal of EU legislation". This is also the view of many scientists, which ever too often feel obliged to perform animal experiments for basic science to be able to publish their non-animal research, although often based on human cells or tissues. To words and intents towards real change, proper actions must follow: more funding, more advanced legislations, more controls on implementations and sanctions, more training on non-animal research and alternatives to replace animals, in all areas of science and research. A change of paradigm must occur, which seeks moving towards and reaching a better and more specific human-based research, which will never again need to use animals to compare and conclude for humans, as a human will never be the same as another animal.

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