

## **Keynote 1**

### **Health Technology Assessment of Human Germline Gene Editing**

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Health technological assessment (HTA) of the intervention into human DNA is not new but it has received a new twist with the announcement that first germline gene edited babies were born in China in November last year. For decades geneticists have followed generally accepted rule “do not interfere with germline genes in humans.” Because it would be fundamentally unsafe and extremely irresponsible trying to change the human germline with available genetic engineering technologies of recombinant DNA used for the creation of genetically modified organisms. In many countries a germline gene modification in humans has become prohibited by national laws or by guidelines. In Europe also by the Oviedo Convention of 1997, which is so far the only international legally binding treaty (for those member states of the Council of Europe which signed and ratified it) which forbids any inheritable interventions in human genome (Article 13). However, with the recent emergence of highly effective, targeted, cheap and easy to use CRISPR gene editing technology which have already been applied on human embryos the whole HTA landscape of the intervention into human germline changed. All previously already discussed issues like safety, moral, ethical, and social implications of human germline intervention have to be re-evaluated in a new context of the possible use of genome editing.

In my presentation I will focus at first on a classical divisions between interventions into somatic vs germline genes and between therapy vs. enhancement. Then I will discuss the safety issue from the perspective of off-target vs. on-target side effects. Until recently, off-target changes in the genome caused by gene transfer technologies were seen as a major safety obstacle for using them for human germ-line modifications. However, recent very rapid improvements in accuracy of existing genome editing technologies or developing a new generation of gene editing technologies like “base editing” and “prime editing” seem to lead to the stage when off-target changes in genome will be practically eliminated. The safety issue then will turn to a question of how safe are be well-intended, on-target genome interventions. It would not be the question of the accuracy of genome editing, the question of technology itself, but rather a question of our limits in understanding of human genome. In present time we are at the beginning to understand the whole complexity of human genome at work. Human genome is not a collection of independent genes, but rather a complex network of genes, regulatory elements and other types of DNA sequences interacting in overlapping ways. Therefore even well-intended on-targeted interventions into human germline could lead to unpredicted, unwanted harmful effects which will endanger health of subsequent generations.