ENSSER Statement
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New genetic modification techniques and their products pose risks that need to be assessed

Gene editing and RNA interference are powerful new genetic engineering techniques with no history of safe use. We believe that when these techniques are applied to living organisms, they should be regulated in the same way as other genetic modification (GM) techniques - including any null segregant products. There is no guarantee that the use of these techniques will result in predictable outcomes - or that any resulting products will be safe. Furthermore, we are deeply concerned that deregulation of some processes will result in the use of these techniques on living organisms in the open environment - a practice without precedent or a history of safe use.[1]

On 13th November, the Australian Senate will vote on whether to disallow amendments to the Gene Technology Regulations that deregulate a number of gene editing and RNA interference techniques. We strongly encourage Senators to support the disallowance motion, on the basis that it accurately reflects the current state of the science behind gene editing and gene silencing.

On 8th October, amendments to Australia's Gene Technology Regulations deregulated the creation and release into the environment and our food chain of modified organisms whose genes are altered using 'Site Directed Nucleases 1' (SDN-1). GM animals, plants and microbes produced using these techniques will hence no longer be subject to safety assessment or traceability requirements. The decision is based on advice from the Office of the Gene Technology Regulator that "SDN-1 organisms present no different risk than organisms carrying naturally occurring genetic changes."[2] A growing body of new peer-reviewed research now renders this conclusion untenable.

The deregulated technologies can be used to produce genetic changes that could never occur in nature. They can be used to make a series of different alterations to the same genes, or changes to many genes simultaneously or one after the other - either in a laboratory or in the open environment - with unknown ecological consequences. The techniques can also target areas of the genome that are normally highly resistant to mutation.[3] Furthermore, recent research has found that gene editing can result in numerous unexpected, unpredictable and undesirable outcomes, even at the intended gene editing site. This includes large deletions and complex rearrangements of DNA,[4] and the creation of new proteins.[5] It is important to note that these unpredictable and undesirable genetic mutations result after the gene editing tool has completed its task (e.g. of creating a break in the DNA) and will occur regardless of the precision of the initial edit.

The recent discovery that cattle that had been gene-edited to be hornless unexpectedly contained antibiotic resistance genes from bacteria illustrates why all gene editing techniques should be regulated.[6] The company which gene-edited the cattle using SDN-3, had claimed "we have all the scientific data that proves that there are no off-target effects."[7] After the discovery by others that genes from bacteria had been inserted into the cattle during the procedure, the company admitted "we did not look for [these bacterial genes]" and acknowledged a more thorough examination of the work "should have been done".

We cannot leave public and environmental safety to the expectations or assumptions of those who alter the genetics of living things and whatever potential hazards they chose to look for. Instead, we need impartial regulators empowered by strong legislation to protect public health and the environment.

Unexpected integrations of foreign DNA through the gene editing process have been observed in many species including mice, fruit flies, medaka fish, yeast, *Aspergillus* (a fungus*)*, the nematode *C. elegans,* the small crustacean *Daphnia magna*, and various plants.[8] Very recently, studies have shown that gene editing can result in the unintended integration in organisms' genomes of DNA from common reagents used in the tissue culture media or other contaminants.[9] Furthermore, applications of the SDN-1 technique can lead to modifications to genes as different or even more pronounced than introducing genes from other species. This is due to the ability to apply SDN-1 rapidly and repeatedly to the same genes or to simultaneously or serially alter many genes at once.

The regulatory changes will also deregulate the direct application of RNAs to alter gene expression. RNA interference (RNAi) through, for example, the use of "spray on" or other topical products may be hazardous to non-target organisms - including humans. It may also alter the DNA of ecologically critical non-target organisms such as protozoa. It is therefore of paramount importance that these products are thoroughly assessed for safety on a case by case basis.[10]

Under the regulatory changes, so-called "null segregant" organisms will also be regarded as non-GM if (1) they have gone through a genetic modification process but "no longer have the genetic modification or any traits that occurred because of gene technology" or (2) have not inherited a transgenic gene from a parent.[11] Both these examples assume that the genetic modification process has caused no unintended or unexpected changes or effects. Such organisms should not be deregulated until thorough checking standards are established.

Current genetic modification techniques - including gene editing and gene silencing - are not sufficiently specific to introduce only the intended molecular changes. Unexpected molecular changes could result in the production of novel toxins and allergens or unpredictable impacts on other organisms and ecosystems. Even intended molecular changes can result in unexpected effects, due to the incomplete understanding of the role (often multiple roles) of the gene sequences or gene product(s) in regulatory or metabolic processes[12]. For these reasons, it is vital that a case-specific risk assessment be conducted for all organisms modified by gene editing or RNAi.[13]

Regulation does not prevent responsible industries from bringing forward safe products that are sought by the public. However, it is essential to provide a series of checks and balances to stop potentially dangerous products from being released into our environment and food chain.

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