A future task in good hands

Bundesamt für Naturschutz

Input on Mandate on Genome Editing

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- 11th GMO Network Meeting 03.07.2020 -





Draft Opinion on GE (SDN-1, SDN-2)

Welcome that the issue (hazards of SDN interventions) has been taken up, also with a view to the ECJ ruling.

Focus on insertion of foreign genes and intended (molecular) changes.

Not covered:

- Multiplexing and consecutive interventions
- On-target effects
- Broader comparison of conventional breeding and GE
- (Several steps involved in SDN interventions

Multiplexing

- Multiplexing and consecutive applications (sgRNA**s**)
- Allows for **deep genomic interventions**
- An issue in 2014, several examples in plants since then
- GE multiplexings are the **main SDN-1 applications**
- GE's **current and upcoming potential** has changed from 2012 (EFSA opinion on SDN-3) to 2020.
- **ECJ** (24) "….*the production of modifications of the genetic heritage to increase at a rate out of all proportion to the modifications likely to occur naturally or randomly…..*"
- **Relevant GE applications** excluded from opinion

On-Target Effects (OnTEs)

- Unintended changes at target region
- Various **terms** and **categories**: Bystander mutations, on target damage, genome rearrangements, large deletions
- **DNA**, but also **RNA** and **protein** level:
  exon skipping and alternative splicing
- With mammalian cells, but **also plant cells**
- **Often overlooked** due to short-ranged PCR and NGS
  (e.g. Mou et al. 2017, Hahn and Nekrasov 2019)

On-Target Effects ….*continued*

- Could occur at **off-target regions as** well due to unwanted genome editing at off-target sites
- What is the **extent** of OnTEs?
  (Kosicki et al. 2018, Thomas et al. 2019)
- What are the **causes** and **factors** for OnTEs?
  (Weisheit et al. 2020)
- Method development, calls for good practice/testing
- OnTE issue **esp. relevant with multiplexing** (sgRNA**s)**

Conventional breeding and genome editing

EFSA (2012) and the Draft Opinion on GE (2020) compare them by the number and type of mutations, but not

- the **overall approach** (based on phenotype or genotype)
- the applicability of the OTE-concept
- ***where* mutations occur** (halfway random vs patterned; genetic linkage; accessibility of the genome; more than one gene copy)
- the **specific characteristics** of both approaches.

Conclusion

- Draft opinion concentrates on **GE's specificity**, but does not look into its **power** and **potential**.
- Assessing the **entire GE-plant** (different levels) in place of focusing on the insertion of foreign genes and on intended molecular changes.

Thanks to Anke-Christiane Hein and Fritz Waßmann

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Thank you for your attention