QUESTIONNAIRE

Implementation and enforcement of the GMO legislation with regard to new genomic techniques:

1. Have you been consulted by companies/organisations/research institutes for regulatory advice or another issue on products developed or to be developed by NGTs ? *Yes/no*
    - o If yes, please provide details on the request.

Yes.

Details of requests for regulatory advice or other issues on products developed or to be developed by NGTs received:

- There has been some extra communication with establishments and need for clarification in "grey area cases", such as the question whether fish receiving DNA vaccine is to be regarded as GMO or not. In Norway research on DNA vaccines is regarded as contained use of GMO, but fish treated with approved DNA vaccine has in at least one case been regarded as non-GMO.
- There has also been more communication with establishments beginning to use CRISPR/Cas9 with the aim of creating GMO crops and other GMO plants as food and feed.
- Possible field trial of a CRISPR-edited crop plant, and whether an application for field trial under the deliberate release framework would be necessary if the trial was to be conducted in a greenhouse not approved for contained use.
- Request for financial support for development of NGT-plants. An application under the deliberate release framework would be needed if the greenhouse is not approved as a contained use facility. Frequent requests regarding requirements for approval of transport and import as deliberate release of NGT organisms pursuant to regulations of the Norwegian Gene Technology Act. In all cases until now, transport and import for research purposes, where the research lab is approved for contained use of GMOs, have not required approval, as long as labelling, packaging and transport document requirements according to regulations are followed[1].

2. Have you taken specific measures (other than inspection) related to the application of the GMO legislation to NGT-products? *Yes/no*
    - o If yes, please describe the measures and, if possible, their effectiveness.
    - o If yes, what best practices can you share?
    - o If no, please explain why not.
    - o If yes or no, have you encountered any challenges or limitations, including administrative burden or costs? *Yes/no*
        - If yes, please describe
        - If yes, how can these challenges or limitations be overcome?
        - If no, please explain why not.

[1] Regulations relating to the labelling, transport, import and export of genetically modified organisms

No.
NGT-organisms are regulated according to the Norwegian Gene Technology Act.

3. Have you adapted your inspection practices to cover all NGT-products and to ensure the enforcement of traceability requirements? *Yes/no*

o If yes, please describe these practices (e.g. adaptation of multiannual control plans) and, if possible, their effectiveness (including of physical checks).
o If yes, what best practices can you share?
o If yes, have the adapted inspection practices created additional requirements/burden for operators and/or public authorities? *Yes/no*

- If yes, please provide concrete examples/data.

o If no, please explain why not.
o If yes or no, have you encountered challenges or limitations, including administrative burden or costs? *Yes/no*
If yes, please describe.
If yes, how could these challenges or limitations be overcome?
If no, please explain why not.

Contained use: No. All NGT products are covered by the inspection practices for traditional GMO. No extra inspection practices have been adapted. Establishments are inspected every five years. The system with notifications on all contained use of GMO is effective in maintaining an overview of what is being conducted.

Food and feed: No. Although Norway has implemented directive 2001/18/EF in the EEA agreement, the regulations 1829/2003/EF, 1830/2003/EF and implementing acts are not yet implemented. Hence, we have partly national legislation regarding authorization and labelling of GMO food and feed (GMOs and processed GM products), but no specific legislation regarding traceability of GMO products besides ordinary traceability requirements. Traceability within the scope of regulation 1830/2003/EU is thus not relevant in Norway. No GMO food and feed are authorized in Norway, and thus our inspection practice is a question about controlling for illegal products and the withdrawal of them. For the time being, we consider that the possibility for unintended import of NGT products from third countries to Norway is very low compared to the possible import of illegal, more “conventional” GM food and feed products (cf. no GM food and feed products are authorized in Norway). In addition, detection of NGT products is insuperable by means of analytic tools.

All other uses: No. For inspection of genetically modified organisms for all other purposes than food and feed, inspection practices have not been adapted specifically to control NGTorganisms on the market. To our knowledge no known NGT-organisms are currently on the market for other purposes than food or feed. Considering the possible applications of NGT in other areas (outside food and feed), inspection practices would have to be adapted in the long run, if such products were to be controlled. Amongst others with regards to analysis and detection of NGT-organisms.

4. Do you have experience or information on traceability strategies, which could be used for tracing NGT-products? *Yes/no*

Yes.

o If yes, please describe the traceability strategy, including details on the required financial, human resources and technical expertise required.

Although we don't have experience with specific traceability strategies for tracing NGT-products, we suggest building on the same control system as for "conventional" GM products. That is, if food and feed products imported are not labelled as GM, one must assume that they are of non-GMO origin. Then the importers must prove that such products are of non-GM origin (including non-NGT), and during inspection present adequate documentation from the producer of the product as part of the importers in-house control system. The documentation must be specific for the lot or batch and trace back to the raw materials used in the products. General statements or guarantees claiming that the product is non-GMO, is not acceptable.

o If yes, what best practices can you share?
o If yes or no, have you encountered challenges or limitations, including administrative burden or costs? *Yes/no*
If yes, please describe.

Even with this kind of comprehensive documentation control, it is not completely possible to trace a NGT-product when there are limited, or no, analytic tools available. Nevertheless, today this kind of control probably is the only system that can be used for tracing the origin of food and feed products that are not analysable, e.g. NGT-products or conventional GM-products without DNA such as oils, sugar etc. No GMO food and feed are authorized in Norway today, and thus our inspection practice is a question about controlling for illegal products and the withdrawal of them.

5. What other experience can you share on the application of the GMO legislation, including experimental releases (such as field trials and clinical trials), concerning NGT-products in
o agri-food sector;
o industrial sector;
o medicinal sector.

No experimental releases (field trials nor clinical trials) have been applied for so far in Norway. There has, however, been a small increase in the number of notifications of NGT-related research within contained use facilities.

Agri-food sector:
A small increase in the number of applications for projects with the aim of establishing CRISPR/Cas9 as a method in plant- and fish production. The projects are still in the research phase and in contained use only. (In 2019/2020 four applications for plant/GMM + plant research with the aim of establishing the method for production of potato, salad, strawberry and raspberry. Four applications/notifications for fish with the aim of establishing the method for food production.)

Medicinal sector:
A small increase in the number of notifications about the use of CRISPR/Cas9, mainly in mouse models and laboratory cell lines in contained use facilities (five notifications about mouse models in medical research, one notification about zebra fish in medical research, two notifications about cell lines in medical research in 2019/2020).

6. Have plant varieties obtained by NGTs been registered in national catalogues? *Yes/**no***
    - o If yes, please specify.

No.

7. Do you require specific information in national catalogue when registering plant varieties obtained by NGTs? *Yes/no*
    - o If yes, please specify.

No.

Information on research and innovation:

8. Have you supported with national funding programmes NGT-related research projects/programs (ongoing or finalised in the last 5 years), including on identification or traceability? *Yes/**no***
    - o If yes, please provide an overview of the project/program including title of project, a brief summary with scope and objectives, the amount of national funding received and possibly specify if the receiving entity is public or private.
    - o If yes or no, please highlight the potential challenges encountered when supporting/funding NGT-related research and any consequences from these challenges.

Yes, national funding programmes are available through The Research Council of Norway (RCN). There has been an increase of applications the past 5 years for funding of research projects with NGT-related research in crop plants, fish (aquaculture), and in medicinal applications. A number of large projects have been granted funding over a longer time period.

Table: Overview projects granted funding for NGT-related research through The Research Council of Norway (RCN)

Year	***Title of project***	***Total funding***	***Recieving entity***

2020–2024	FOODPRINT: Traceability and labelling of gene-edited products in the food chain	NOK 11 887 996,00	Public
2020–2026	Virulence motifs of piscine myocarditis virus causing CMS in Atlantic salmon	NOK 11 974 998,00	Public
2019–2023	Preparing for disease control by gene editing for a more sustainable livestock production	NOK 5 925 998,00	Private
2019–2023	Genome-wide CRISPR screen to identify the defining elements of antigen-presenting cells	NOK 3 463 000,00	Public
2019–2021	CRISPRized Immortality– Novel approaches to immortalize fish cell lines - 3Rs	NOK 3 980 997,00	Public
2019–2022	Fighting antimicrobial resistant infections by high-throughput discovery of biofilm-disrupting agents and mechanisms	NOK 4 520 000,00	Public
2019–2023	Genome editing - a game-changer in aquaculture: Conditions for social and moral acceptance	NOK 9 432 996,00	Public
2019–2022	Towards a sustainable control of wheat dwarf virus disease in China and Norway by application of CRISPR and Next Generation Sequencing	NOK 4 399 991,00	Public

2018–2022	Bioøkfelles: Assessment of econ. and bio. implications, prospects and risks by implementation of new gene tools in modern bio-production	NOK 9 997 992,00	Public
2018–2021	The case for Regulation of Synthetic Biology and the Need for a New Category of Risk An Interdisciplinary analysis between the EU and the US	NOK 3 149 000,00	Public
2018–2022	ReWrite: New knowledge to navigate the rewriting of human/nature relations through genome editing in the search for sustainable food	NOK 8 993 988,00	Public
2018–2019	Avox - Automatisert verktøy for akselerert, presis og trygg genredigering innen planteforedling.	NOK 252 645,00	Private
2018–2022	Gene Editing to Innovate Norwegian Breeding Industries	NOK 8 959 983,00	Private
2018–2022	TRANSPOSE: Transposable elements as agents of genome evolution and adaptation following a recent whole genome duplication	NOK 12 500 000,00	Public
2018–2022	The role of whole genome duplication in vertebrate adaptation	NOK 9 662 250,00	Public
2018–2021	ERA-NET: Microbial conversion of C1 to value-added products by integrated systems and synthetic biology	NOK 4 997 992,00	Public

2018–2021	Clathrin-mediated regulation of T cell activation and intercellular communication	NOK 3 113 000,00	Public
2018–2022	How to build a glass house: Revealing fundamental components of diatom cell wall biomineralization	NOK 9 694 000,00	Public
2017–2027	Centre for Cancer Cell Reprogramming (CanCell)	NOK 167 000 000,00	Public
2017–2020	Evolution of umami taste receptor (T1R1-T1R3) system in vertebrates and its role in gut-brain axis communication	NOK 3 116 000,00	Public
2017–2020	Exploring N-terminal acetyltransferases with functional genomics	NOK 3 133 000,00	Public
2017–2020	Precision Genome Editing: Bench to Business	NOK 4 989 896,00	Private
2017–2020	Optimization of the CRISPR/Cas9 knock-in technology and application in salmon and trout	NOK 4 439 995,00	Public
2016–2020	ERA-NET: STREPTOMYCES-BASED CELL FACTORIES FOR THE PRODUCTION OF TACROLOGUES DRUGS	NOK 5 087 989,00	Public

2016–2021	ACCELERATED EVOLUTION IN CHORDATES AND THE ORIGIN OF LARVACEANS	NOK 7 737 000,00	Public
2016–2022	Multi-scale brain plasticity - from molecules to behaviour in life-long learning	NOK 9 359 000,00	Public
2016–2019	Identification of novel cell cycle proteins in Staphylococcus aureus	NOK 6 414 000,00	Public
2016–2019	Mechanosensing by Cardiac Fibroblasts Regulates Myocardial Fibrosis	NOK 3 200 250,00	Public
2015–2023	DL: DigiBrain - From genes to brain function in health and disease	NOK 39 769 939,00	Public
2015–2020	Understanding postsmolt maturation in Atlantic salmon in the context of new, closed production systems	NOK 9 599 990,00	Public
2015–2018	Cytotoxic lymphocyte function in regulation of human autoimmunity	NOK 7 000 000,00	Public
2015–2020	Follicular regulatory T cells. Probing their mode of suppression by a novel technique	NOK 3 082 500,00	Public

2015–2019	Aggregation and pooling of patent portfolios, the effect on industry and entrepreneurial activity in the Nordic region.	NOK 1 534 998,00	Private
2015–2017	FunBiotics: Efficient production of antibiotics from fungi	NOK 9 899 993,00	Private
2014–2018	Systems biology of bacterial methylotrophy for biotechnological products from methanol	NOK 4 999 206,00	Public
2014–2019	MIcrobially produced Raw materials for Aquafeed	NOK 13 299 971,00	Public
2014–2019	Food-grade bacterial vectors as novel tuberculosis vaccines	NOK 10 163 989,00	Public
2014–2017	Unraveling the chromatome of specific loci	NOK 7 056 998,00	Public
2013–2018	New Principles of mycobacterial killing in host macrophages	NOK 9 128 998,00	Public
2013–2017	Role of interleukin-33 in vascular stability and viral immune defence	NOK 7 973 996,00	Public

2012–2022	Sars International Centre for Marine Molecular Biology Research, 2013-2022	NOK 194 999 961,00	Public
2012–2018	Sterile salmon by targeting factors involved in germ cell survival: novel vaccination strategies for sustainable fish farming (Sketch 40)	NOK 38 449 919,00	Public
2012–2018	Pathogens in the food chain - persistence, elimination and risk management	NOK 25 000 000,00	Public

9. How do you see NGT-related research evolving?

Based on an increasing trend reported by The Research Council of Norway (RCN) regarding applications for funding of NGT-related research, and the increase in notifications of NGT-related research in contained use facilities to the Norwegian Health Directorate, there is a relatively high activity level of NGT-related research in Norway with projects mostly falling within the agricultural, aquaculture and medicinal applications. Taken together with the knowledge we have from public consultation processes conducted by the Norwegian Biotechnology Advisory Board, there seems to be a broad range of stakeholders within private and public research institutes and companies that are undertaking research with the aim of developing NGT-products relevant for the Norwegian market.

10. Have you identified any NGT-related research needs from private or public entities? *Yes/no*

Yes.

o If yes, please specify which needs and how they could be addressed.

As described earlier, most activities are on a research level in approved contained use facilities. The needs described below have been identified in applications under the contained use framework.

Needs as expressed by the establishments and researchers in applications received under the contained use framework:

- To be part of the scientific development in their fields of expertice.
- International competitiveness; several of the establishments are distributing their products internationally.
- Some of the establishments are cooperating in a joint research project supported by The Research Council of Norway (RCN). They wish to establish CRISPR/Cas9 as a method for food organisms (potatoes, berries, fish).

Possible ways to address the needs – contained use framework:
1. To have a hazard level-based notification/application system for the end products of NGT, with notification only for variants proven to already exist in the population of an organism, and small requirements for products with a low hazard level. For contained use: In the case of option 1: Keep the hazard level based notification/application system until documentation of the characteristics of the end product.

2. To exclude certain defined forms of NGT from the scope of the directives.

11. Could NGT-related research bring opportunities/benefits to science, to society and to the agri-food, medicinal or industrial sector? *Yes/no*
Yes.

- o If yes, please provide concrete examples/data.

NGT related research would be expected to give rise to opportunities/benefits depending on the nature and outcome of the research, as holds true for all types of research activities.

In Norway ethical considerations, societal benefits and sustainability is assessed on a case by case basis for each GMO under the deliberate release framework pursuant to the Norwegian Gene Technology Act. NGT-organisms would be subject to these assessments. No such application under the deliberate release framework has been received at this point, and a general statement of benefits to society of NGT-related research cannot be given at this point.

Within the agri-food sector no general statements of opportunities/benefits can be given at this point.

With regards to NGT-related research in the medicinal sector the competent authority for contained use the Norwegian Health Directorate, points out that the CRISPR/Cas9 technology can offer more precise and less expensive methods for manipulating genes in model animals or cell culture to study gene function or develop therapy for different diseases.

- o If no, please explain why not.

12. Could NGT-related research bring challenges/concerns to science, to society and to the agri-food, medicinal or industrial sector? *Yes/no*

Yes and no.

- o If yes, please provide concrete examples/data.

NGT related could also give rise to challenges/concerns depending on the nature and outcome of the research, as holds true for all types of research activities. These challenges/concerns could for example be if there were any risks to the environment or human/animal/plant health from NGT-organisms produced from NGT-related research activities, if NGT-releated research was considered ethically unjustifiable and at odds with public moral, or pulls an area into a direction that would decrease its sustainability.

The area of NGT-related research is also expanding and evolving at a fast pace. New application areas and new tools are constantly foreseen and developed both for applications and research. This happens within all areas of biological sciences from human health to food/feed production, industrial applications and environmental monitoring. At the same time little is known of effects in the environment and on health due to the novelty of these methods. There might be a lack of data when conducting risk assessments etc.

There are positive opportunities for the use of new genomic techniques in gene therapy. Research in this field can can suffer from setbacks if unregulated use of NGT leads to public scandals, and regulations could help prevent such setbacks.

- o If no, please explain why not.

More research provides more knowledge about both positive potential and possible hazards. Strong regulation on the other hand can send false signals about hazard, which can lead to less public acceptance, further leading to less research funding and less gained knowledge.

Information on public dialogues and national surveys:

13. Have you or other institutions/bodies/entities organised national dialogues concerning NGTs? *Yes/no*

Yes.

- o If yes, please describe briefly the content, methodology and conclusions.

The Norwegian Biotechnology Advisory Board (NBAB), is an independent body consisting of 15 members appointed by the Norwegian government. The main task of the Norwegian Biotechnology Advisory Board is to evaluate the social and ethical consequences of modern biotechnology and to discuss usage which promotes sustainable development. NBAB has on their own initiative, prepared a statement on a possible level-based regulation of deliberate release of GMOs, including products developed by NGTs. Included in the process was an invitation from NBAB to engage in a public debate with arranged open meetings and a public consultation to get comments and thoughts from all relevant stakeholders.

14. Have you or other institutions/bodies/entities organised national surveys, which assessed public opinion on NGTs? *Yes/no*

Yes.

- o If yes, please describe briefly the content, methodology and conclusions.

The Norwegian Biotechnology Advisory Board (NBAB) has recently carried out a survey on public perceptions of gene edited food, with more than 2000 respondents,

as part of a collaborative research project on gene-editing in plant and livestock in Norway. The results showed that the attitudes towards gene edited food is more nuanced than what has been found in previous studies concerning genetically modified food. The purpose of the genetic change and the characteristics of the product were decisive for the opinions of the respondents. For example, the majority of the respondents were positive towards the use of gene editing in plants if the aim was to reduce the use of pesticides and crop losses. The majority of the respondents were also positive towards the use of gene editing in animals if the purpose was to improve animal welfare, e.g. improve resistance towards infectious diseases. A majority of the respondents were however negative towards the use of gene editing for more trivial purposes, such as changing the product appearance, e.g. color of salmon filèt, and towards increasing the production yield of farm animals.

In addition to the survey carried out by the Norwegian Biotechnology Advisory Board, GMO-Nettverket (in English; the GMO Network) has an ongoing survey regarding the public opinion on GMOs in general, however, the survey also includes two questions on NGT-products and gene drives. The results from the survey is not yet published.

Information on ethical aspects:

15. Have any national bodies or expert groups discussed or issued opinion on the ethical aspects of NGTs? *Yes/no*

Yes.

- o If yes, please describe briefly the content, methodology and conclusions.

Following a request from the Ministry of climate and Environment the Norwegian Environment Agency (NEA) commissioned a study on ethical aspects of genetically modified organisms in 2019. The study was carried out by an expert group of ethicists. The study forms part of the request from the Ministry regarding operationalization of the assessment of ethical considerations of a GMO, an important socio-economic criterion to be evaluated in every case of a deliberate release of a GMO pursuant to the Norwegian Gene Technology Act. Included in the study, was a case study of GMOs developed by NGTs. The Norwegian Gene Technology Act emphasizes considerations of public moral, and the study concluded that some of these NGT-products could be considered ethically justifiable given support from the public. The study is now under review by the Norwegian Biotechnology Advisory Board. Based on the study and the statement from the NBAB, NEA will give a recommendation regarding the operationalisation of ethical considerations according to the Norwegian Gene Technology Act to the Ministry.

Information on potential opportunities and benefits from the use of NGTs and NGT-products:

16. Could the use of NGTs and NGT-products bring opportunities/benefits to the agri-food, medicinal or industrial sector? *Yes/no*

- o If yes, please provide concrete examples/data.

o If no, please explain why not.

In the context of human health, the Political platform for the Norwegian Government acknowledges that genetic and biotechnological knowledge, and its practical application in the health services, have been an important part of the innovations in modern medicine for the benefit of humans. The Norwegian Government will:

- Facilitate increased research and further develop specialized competence in gene- and biotechnology.
- Encourage further development of personalized medicine.
- Facilitate the transfer of results from both clinical research and basic medical research to diagnostics and patient care.

17. Could the use of NGTs and NGT-products bring opportunities/benefits to society in general, such as for the environment, human, animal and plant health, as well as social and economic benefits, in the short, medium and long term? *Yes/no*

o If yes, please provide concrete examples/data.
o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

18. Do you see particular opportunities for SMEs on the market access to NGTs? *Yes/no*

o If yes, please explain under which conditions
o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

19. Do you see benefits/opportunities in patenting or accessing patented NGTs or NGT-products? *Yes/no*

o If yes, please describe and provide concrete examples/data.
o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

Information on potential challenges and concerns of NGT products:

20. Could the use of NGTs and NGT-products raise challenges/concerns for the agri-food, medicinal or industrial sector? *Yes/no*

o If yes, please provide concrete examples/data.
o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

21. Could the use of NGTs and NGT-products raise challenges/concerns for society in general, such as for the environment, human, animal and plant health, as well as social and economic challenges, in the short, medium and long term? *Yes/no*

- o If yes, please provide concrete examples/data.
- o If yes, under which conditions do you consider this would be the case?
- o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

22. Do you see particular challenges for SMEs on market access to NGTs? *Yes/no*

- o If yes, please explain under which conditions.
- o If no, please explain why not.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

23. Do you see challenges/concerns in patenting or accessing patented NGTs or NGT-products? *Yes/no*

- o If yes, please describe and provide concrete examples/data.
- o If no, please explain why.

Norway refrains from answering at this point. This question is regarded as partly political and would require further national coordination.

Final question

24. Do you have other comments you would like to make? *Yes/no*

- o If yes, please provide your comments here.

From a regulatory standpoint, in particular, detection and traceability of non-authorized NGT-products is currently a challenge. Some changes introduced in a genome by NGT may also occur naturally**.**