

Miljødirektoratet Postboks 5672 Sluppen 7485 Trondheim Dato: 28.09.15

Vedlagt er innspill fra Gen $\emptyset$ k – Senter for Biosikkerhet på fornyelse av gjeldende godkjenning i EU under 1829/2003/EF av søknad **EFSA/GMO/RX-001**, mais event 1507, fra Pioneer Hi-Bred International, Inc. og Dow AgroSciences LLC som gjelder mat, fòr, import og prosessering av genmodifisert mais **1507**.

Vennligst ta kontakt hvis det er noen spørsmål.

Med vennlig hilsen,

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Vår ref:2015/H\_RX-001 Deres ref: 2015/9179

# Assessment of the renewal of the current approval in EU under 1829/2003/EF of EFSA/GMO/RX-001 1507 maize.

Sent to

Norwegian Environment Agency

by

GenØk- Centre for Biosafety September 2015



# **KONKLUSJON PÅ NORSK**

Vi trekker frem mangler i oppsummert søknad og data som ikke gir grunnlag for en konklusjon om sikker bruk, samfunnsnytte og bidrag til bærekraft av **1507 mais**. Søker har ikke inkludert noe av den informasjonen omkring samfunnsnytte og bærekraft av **1507 mais** som kreves i den norske genteknologiloven (Appendix 4) for godkjenning i Norge.

#### Hovedkonklusjon og anbefalinger:

Genøk–Senter for Biosikkerhet viser til brev fra Miljødirektoratet angående offentlig høring som omfatter fornyelse av gjeldende godkjenning i EU for **1507 mais** i bruksområdet import og prosessering og til bruk i för og mat eller inneholdende ingredienser produsert fra **1507 mais**.

Søker gir ikke opplysninger som adresserer vurderingskriteriene bærekraft, samfunnsnytte og etiske aspekter som forutsettes anvendt i den norske genteknologiloven. I denne sammenheng er det viktig å få dokumentert erfaringer med hensyn på effekter på miljø, helse og samfunnsaspekter. Denne type dokumentasjon er ikke tilstrekkelig i søknaden om omsetting av **1507 mais** til import og prosessering og til bruk i för og mat eller inneholdende ingredienser produsert fra **1507 mais**.

Vår konklusjon er at norske myndigheter ikke godkjenner bruk av **1507 mais** til import og prosessering og til bruk i för og mat som det søkes fornyet godkjenning av.



#### ASSESSMENT OF THE RENEWAL OF THE CURRENT APPROVAL IN EU UNDER 1829/2003/EF OF EFSA/GMO/RX-001 1507 MAIZE.

As a designated National Competence Center for Biosafety, our mission at GenØk in advice giving is to provide independent, holistic and useful analysis of technical and scientific information/reasoning in order to assist authorities in the safety evaluation of biotechnologies proposed for use in the public sphere.

The following information is respectfully submitted for consideration in the re-evaluation of product safety and corresponding impact assessment of event **1507 maize**, setting out the risk of adverse effects on the environment and health, including other consequences of proposed release under the pertinent Norwegian regulations.

We have previously commented on stacks containing maize event 1507 in:

- EFSA/GMO/NL/2009/65, MON89034 x 1507 x NK603 (January 2010)
- EFSA/GMO/NL/2011/92 for 1507x59122xMON810xNK603 (April 2012).
- EFSA/GMO/BE/2011/99 for Bt11x59122xMIR604x1507xGA21 (July 2012).
- EFSA/GMO/DE/2011/103 for Bt11xMIR162xMIR604x1507x5307xGA21 (October 2014)
- EFSA/GMO/BE/2013/118 for MON87427 x MON89034 x 1507 x MON88017 x 59122 (August 2015).



#### Specific recommendations

Based on our findings, we propose some specific recommendations, summarized here and detailed in the go-through below.

- The regulator is encouraged to perform a re-evaluation of the maize event 1507, which includes glufosinate-herbicide applications.
- The regulator is encouraged to ask the applicant for assessment of potential adverse effects of glufosinate-ammonium and changes in weed management.
- The regulator is encouraged to ask the applicant to address the potential of non-target effects of Bt toxins.
- We find it ethically unacceptable to ban the use of glufosinate-ammonium based herbicides domestically due to health and environmental concerns, while supporting its use in other countries. This represents an unacceptable double standard for Norway, and we ask the regulators to reconsider the practice of separating health and environmental risk by national borders or regions.
- The applicant should include a full evaluation of the actual use of glufosinateammonium with maize event 1507 with a particular focus on the level of accumulation of herbicides in the plants, particularly the parts used in food and feed production, and whether or not these levels of exposure could cause acute and/or chronic health issues. This needs to be tested in animal and feeding studies, separating the effects of the plant and the herbicide(s) by using both sprayed and unsprayed plant samples.
- The applicant should include a section on the potential environmental implications for farm workers exposed to the herbicide and toxicity assessment for the farmers.
- The regulator is encouraged to ask the applicant to include a section on the potential environmental effects of the herbicide i.e. monitoring changes in use, potential drift into the surrounding area and ecosystems including water systems and wildlife.
- The regulator is encouraged to ask the applicant to further elaborate and investigate the increase and spread of resistance towards Cry1F and development of cross-resistance.
- The regulators are encouraged to ask the Applicant to provide a full ERA of the life cycle of maize event 1507, i.e. from being planted in the field and through the cultivation process, harvesting, transportation, processing, and as waste.
- The applicant should include proper analysis of chromosomal locations of the actual inserts and effect on endogenously expressed genes.



- We also encourage the Applicant to specify if they use microbial or plant derived proteins for their analysis of toxicology and allergenicity studies in the risk assessment of maize event 1507.
- We encourage the Applicant to perform and go through newer studies on toxicology and allergy with the relevant transgenic proteins.
- In order to meet the requirements for the NGTA, the regulator is encouraged to ask the Applicant to submit information relevant for the assessment of the social utility of the 1507 maize and its contribution to sustainable development. The information provided by the Applicant must be relevant for the agricultural context in the producing country/countries. The information should include issues such as: development of pest resistance in target populations, impacts on non-target organisms, co-existence consequences and possible impacts among poor and/or small-scale farmers in producing countries and share of the benefits among sectors of the society.

## **Overall recommendation**

From our analysis, we find that the information provided in the summary of the renewal of the current application has deficiencies that do not support claims of safe use, social utility and contribution to sustainable development of 1507 maize. **Critically, the Applicant has not included any of the required information to assess social utility and sustainability as required in Appendix 4 of the Norwegian Gene Technology Act, which would be necessary for consideration of approval in Norway.** A new application or reapplication should only be reconsidered with the delivery of the information requests recommended here, including any additional information deemed significant by the Norwegian authorities.

Therefore, in our assessment of **1507 maize**, we conclude that based on the available data, the Applicant has not provided the required information under Norwegian law to warrant approval in Norway at this time.



#### ASSESSMENT OF THE RENEWAL OF THE CURRENT APPROVAL IN EU UNDER 1829/2003/EF OF EFSA/GMO/RX-001 1507 MAIZE.

#### About the event

The maize event **1507** was made by particle bombardment of maize cells with a DNA fragment containing a part of a *Bacillus thuringiensis* (Bt) gene inserted encoding the insecticidal Cry1F protein and phospinothricin-N-acyltransferase (PAT) gene from *Streptomyces viridochromogenes* providing tolerance to the herbicidal active substance glufosinate-ammonium.

The re-application of maize event 1507 is for food, feed, import and processing and it has been cultivated since 2003 in U.S. It is also approved for cultivation in Argentina, Brazil, Canada, Colombia, Honduras, Japan, Paraguay, South-Africa and Uruguay.

Maize event 1507 is approved for feed and for other products than food in Norway under 2001/18/EC.

In EU, maize event 1507 is approved for food and feed according to 2001/18/EC and 1829/2003/EC in 2005 and 2006.

There is no cultivation of maize event 1507 in the EU. An application for cultivation is pending.



## I. Assessment findings

The EFSA GMO Panel (references in EFSA Journal 2012) has evaluated the potential adverse effects of GM maize event 1507 on several occasions. Conclusions from the EFSA GMO Panel is that this GM maize is "unlikely to have any adverse effect on human and animal health".

GenØk has not assessed maize event 1507, previously. However, this event has been present in several multistacks assessed throughout the years.

Since this is a renewal, the original dossier used for approval of this event has not been made available. In its absence, we have consulted the Opinion of the Panel on Genetically Modified Organisms of the Norwegian Scientific Committee for Food Safety (VKM 13/327) which reports on the evaluation of maize event 1507, with special attention to issues relating to Norway.

Based on this report, and literature published since the commercialization of maize event 1507 (marketed as Herculex<sup>®</sup> I Insect Protection), we have the following comments:

• In the VKM report (13/327), it is stated that the *pat* gene included in the insert of this event is solely for the purpose of acting as a selective marker, and is not intended for use with herbicide in the field: "The PAT protein expressed in maize 1507 has been used as a selectable marker during the transformation process. The scope of the application for maize 1507 cultivation does not cover the use of glufosinate-ammonium-containing herbicides on maize 1507. Therefore, potential environmental adverse effects due to the applications of glufosinate-ammonium-containing herbicides in weed management are not considered by the VKM GMO Panel in this Scientific Opinion."

However, on the applicants' websites, the opposite is stated: "All HERCULEX hybrids contain LibertyLink® technology, making them tolerant to over-the-top applications of LIBERTY® herbicide." (Dow AgroSciences. 2015, Pioneer. 2015). Liberty® is the tradename of the glufosinate-ammonium herbicide marketed to be used with glufosinate-tolerant crops (LibertyLink® technology).

Clearly, there is a discrepancy between the manner in which this event was assessed, and the manner in which is used. The implications of this should include a re-evaluation of the event which includes glufosinate-herbicide applications, because the assumptions which the previous evaluation was based on are false. Potential adverse effects of glufosinate-ammonium use and changes in weed management have not been included in the VKM GMO Panel's evaluation.



This is particularly pertinent because glufosinate-ammonium belongs to a class of herbicides that are **banned in Norway and in EU** (except a limited use on apples) due to both acute and chronic effects on mammals including humans. Studies have shown that glufosinate-ammonium is harmful by inhalation, swallowing and by skin contact and serious health risks may result from exposure over time. Effects on humans and mammals include potential damage to brain, reproduction including effects on embryos, and negative effects on biodiversity in environments where glufosinate ammonium is used (Hung 2007, Matsumura et al. 2001; Schulte-Hermann et al. 2006).

It would be ethically incongruous and a double standard of safety for Norway (and European Union countries) to ban the use of glufosinate-ammonium herbicides domestically as a health concern, but support its use in other countries.

- Glufosinate was used during the field trials discussed in document 13/327, but a number of questions remain:
  - How well do the glufosinate-ammonium concentrations used during the field trials correlate with actual use on farms? Is this representative of real-world situations?
  - What are the environmental implications of using glufosinate-ammonium herbicides?
  - What are the health implications for farm workers using glufosinate-ammonium herbicides?
  - In the field trial section, it is stated that the *pat* protein was not detectable during all developmental stages (present at V9, absent at R1 and R4 see table 7 of the VKM report), yet glufosinate can be used with Herculex® crops as a post-emergence ("over-the-top") weed control. This appears to be inconsistent, since there is no information in the Herculex® product guide warning farmers that applications of the Liberty® herbicide after the V9 stage could lead to crop losses (the guide is very clear about which herbicides can be used without yield loss).
- Resistance to Cry1F by fall army worm (*Spodoptera frugiperda*) has increased since the VKM report, which stated "...resistant populations have not spread to any measurable extent from Puerto Rico to mainland USA, and that local selection from Cry1F-expressing maize in the southern USA has caused no measurable change in population susceptibility." At the time, resistant populations had only been reported in Puerto Rico (Storer et al. 2010) and was the fastest development of resistance ever documented to transgenic proteins, occuring 4 years after commercialisation (Tabashnik et al 2009). However, recent publications indicate that spread of resistant populations has taken place, and that resistant *S. frugiperda* populations have been found in Florida and North Carolina (Huang et al. 2014). Outside of the USA and Puerto Rico, Cry1F-resistant *S. frugiperda* have also been reported in Brazil (Farias et al.



2014). In order to prevent resistance development, the use of stacked/pyramided events utilizing multiple Bt proteins has been advocated (Niu et al. 2014), but considerations of this approach are outside of the scope of this evaluation, since 1507 expresses only one Bt toxin (Cry1F). It is however mentioned as development of cross resistance is an issue that might play a role as the use of Bt maize producing Cry1Ab in the same area as Cry1F might have caused a higher pressure on the selection of resistance (Velez et al. 2013).

- Knowledge gaps mentioned in the VKM report which have not been addressed but is elaborated in this risk assessment:
  - Aquatic organisms
  - Soil organisms
  - Fate of the protein

The lack of studies addressing these issues seem not to have been improved upon according to the summary of the application for renewal of approval.

• Presence of an additional copy of the Cry1F gene was detected using Southern blotting, but has not been located or characterized: "HindIII digestion and hybridisation with the cry1F probe resulted in two bands: one of 3890 bp size and a second, representing an additional copy that is larger and estimated at ~ 4000 bp in size. Hybridisation of the HindIII digest with the ubi probe resulted in one band of 3890 bp size and failed to reveal the ~4000 bp fragment. According to the applicant, this indicates that the promoter region is either absent in this additional copy or it is not intact."

It is not acceptable that a 4000 bp additional copy of this gene has been detected, but that no further comment is made other than noting its presence, and that it lacks the ubiquitin promoter. No information is given regarding its location, nor its possible disruption of expression of endogenous genes.

• Section 3.2.2.4 of the report calls for information regarding the chromosomal location(s) of the insert(s) (nucleus, chloroplasts, mitochondria or maintained in a non-integrated form) and methods for determination. This section has not been appropriately addressed. No information is given regarding which chromosome(s) the insert(s) are located on, nor how this was determined.

## **Recommendations:**

- The applicant is encouraged to perform a re-evaluation of the event which includes glufosinate-herbicide applications.
- The applicant is encouraged to include analysis of adverse effects of glufosinateammonium use and changes in weed management.
- The applicant is encouraged to include a full evaluation of glufosinate-ammonium use and health effects on farmers.
- The applicant is also encouraged to perform analysis showing chromosomal location of actual inserts and if they affect expression levels of endogenously expressed genes.



• Resistance development towards Cry1F and potential of cross-resistance development due to presence of other Bt-toxins is important and the applicant should evaluate this further.

## I.a Safety of Cry genes

Maize event **1507** contains a Bt protein, a Cry toxin, namely Cry1F. Cry toxins are claimed to be safe, however the potential of non-target effects of Bt toxins, including alternative modes of action have been addressed previously (Bøhn, et al 2008, Gilliand et al 2002, Crickmore 2005, Hilbeck and Schmidt 2006).

Negative effects of Bt- protein producing transgenic plants on non-target organisms are documented. A meta-analysis of published studies on non-target effects of Bt-proteins in natural enemies, (Lövei and Arpaia 2005) documented that 30% of studies on predators and 57% of studies on parasitoids display negative effects to Cry1Ab transgenic insecticidal proteins. Further, Cry toxins and proteinase inhibitors have often non-neutral effects on natural enemies, and more often negative than positive effects (Lövei et al 2009). A review by Hilbeck and Schmidt (2006) on Bt-plants, found 50% of the studies documenting negative effects on tested invertebrates.

Another issue is that many Cry proteins only have been tested with a very limited number of organisms: thus, activity outside of the target organisms of many Cry proteins may lack documentation simply because testing has not included sensitive organisms (van Frankenhuyzen, 2013). It can therefore not be excluded that sensitive species have been overlooked. The issue is complicated further by the number of variables which can affect toxicity testing, e.g. toxin preparation and purification, life stage of the test organism, differences in toxin expression hosts, as well as solubilization (or lack thereof) of the toxin, among other factors (van Frankenhuyzen 2009).

A quantitative review analysis based on 42 field experiments showed that unsprayed fields of Bt-transgenic maize plants have significantly higher abundance of terrestrial non-target invertebrates than sprayed conventional fields (Marvier et al. 2007). Thus, Bt-plants with a single Bt-gene inserted may represent an improvement for non-target organisms in the environment. However, an indication of some negative effects of the Cry1Ab toxin itself, or the Cry1Ab maize plant, on non-target abundance was shown in the same meta-analysis: when conventional (non-GM) fields were not sprayed, the non-target abundance was significantly higher than in the Bt-fields (Marvier et al. 2007).

Research on aquatic environments has sparked intense interest in the impact of Bt-crops on aquatic invertebrates including *Daphnia magna* (Bøhn et al 2008) and caddisflies (Rosi-Marshall et al 2007). Given the potential load of Cry toxins (also in combination with herbicides) that may end up in aquatic environments, further studies are warranted. Douville et al. (2007) presented evidence of the persistence of the *cry1Ab* transgene in aquatic environments: more than 21 days in surface waters, and 40 days in sediments. A follow-up on this study in 2009 indicated possible horizontal gene transfer of transgenic DNA fragments to aquatic bacteria (Douville et al 2009).



Impacts on soil microflora and fauna, including earthworms (Zwahlen et al. 2003), mychorizzal fungi (Castaldini et al. 2005) and microarthropods in response to Cry endotoxins have also been reported (Wandeler et al. 2002; Griffiths et al. 2006; Cortet et al. 2007). The significance of tri-trophic effects of accumulation, particularly of insecticidal Cry toxins (Harwood et al. 2006, O`brist et al. 2006) is not clear. It has been demonstrated that sub-chronic dosages of Cry proteins may affect both foraging behavior and learning ability in non-target bees (Ramirez-Romero et al. 2008), with potential indirect effects on recipient populations. Given the important role of bees as pollinators, such effects may have consequences for both primary production and on entire food-webs.

In relation to health impacts, a publication by (Dona and Arvanitoyannis 2009) reviewed the potential health implications of GM foods for humans and animals, including incidences and effects of increased immunogenicity, amounts of anti-nutrients, possible pleiotropic and epigenetic effects, including possible reproductive and developmental toxicity. They conclude that while there is strong evidence for health concerns, testing and exposure duration may have not been long enough to uncover important effects.

A recent study in mice showed that exposure to purified Cry1Ab resulted in specific anti-Cry1Ab IgG1 and IgE production, indicating inherent immunogenicity and allergenicity. Further, mice exposed to leaf extracts from both MON810 and unmodified maize demonstrated influx of lymphocytes and eosinophils in the broncho-alveolar lavage, and increased cytokine release in mediastinal lymph node cells (Andreassen et al. 2015). Further studies should also include animals with immunodeficiencies and/or animals exposed to other stress agents simultaneously.

The potential adjuvancy of Cry proteins has previously been addressed by the GMO Panel of the Norwegian Scientific Committee for Food Safety and EFSA (VKM 13/327 and EFSA references therein) where they also state that the adjuvance effect not has been analysed for all Cry proteins that are used in GM plants. This is not discussed and should be followed up further.

## **Recommendations:**

- The regulator is encouraged to ask the applicant to address the potential of non-target effects of Bt toxins.
- The regulator is further encouraged to investigate the potential role of Cry1F as a protein having adjuvance effects.
- The regulator is encouraged to also ask the applicant to consider the evolution of cross-resistance towards Bt-proteins in target organisms.

## I.b. Herbicide tolerance traits

The GM maize event 1507 is glufosinate-tolerant and although this trait is used as a selection marker during transformation of plant cells, it also opens up the possibility for using glufosinate-ammonium as a herbicide, if needed.





Herbicide tolerant (HT) plants are specifically designed to be used in combination with herbicides, and will be sprayed with the intended herbicide. Without spraying the introduction of HT plants would be useless. Surprisingly, these herbicides are often not tested as part of the assessment and risk evaluation of HT plants. In feeding studies with HT GM plants for quality assessment the herbicide is systematically overlooked, which represents a serious flaw in the testing and risk evaluation. Viljoen et al. (2013) found that in 13 out of 16 published feeding studies with HT GM crops the plant material used had not been sprayed with the intended cotechnology herbicide. There is also a gap in knowledge regarding herbicide accumulation and residues, including metabolic pathways and metabolites thereof. Bøhn et al. (2014) documented high levels of glyphosate residues in HT GM soybeans grown in the USA, and the same research group have published papers showing that such residues negatively affect the feed quality of HT GM soybeans (Cuhra et al. 2014; Cuhra et al. 2015). Moreover, safety testing (in relation to health and environmental issues) has been focused on the active ingredient in the cotechnology herbicides, and not the commercial formulations actually used, providing unrealistic and possibly misleading results (Mesnage et al. 2014; Surgan et al. 2010). Stacked HT GM plants are tolerant to one or more agrochemicals, allowing for combinatory and alternating use of several herbicides. Tolerance to multiple herbicides is also often combined with multiple Cry proteins that could have additive or even synergistic effects on non-target species and the environment. The maize event 1507 is an event that often is present in multistacks where these factor are of importance.

The application in question does not encompass the cultivation of 1507, however, it must be mentioned that we are of the opinion that the environmental effects of the herbicide, as an important co-technology and a potentially essential part of the cultivation of this event, should be discussed in the environmental risk assessment.

The main purpose of the expressed *pat* gene (infers glufosinate-ammonium tolerance) is to select for transformed maize cells when using glufosinate-ammonium. The presence of this gene also opens up the possibility of using glufosinate ammonium based herbicides later on, as during cultivation. We find it disconcerting that the presence of the herbicide has not been considered in the comparative assessment nor the toxicological assessment. In the toxicology assessment the applicant only focuses on the resulting proteins from the inserted genes, and do not discuss the potential of herbicide exposure through consumption of herbicide treated maize. A recent study found that glyphosate and AMPA accumulated in soybeans (Bøhn et al. 2014), highlighting the importance of including the herbicides in the comparative and toxicological assessment of GM crops with herbicidal co-technology.

#### Glufosinate-ammonium

Glufosinate-ammonium belongs to a class of herbicides that is banned in Norway and in EU (except for a limited use on apples) due to both acute and chronic effects on mammals including humans. Studies have shown that glufosinate-ammonium is harmful by inhalation, ingestion and skin contact. Serious health risks may result from exposure over time. Observations of patients poisoned by glufosinate-ammonium have found that acute exposure causes convulsions, circulatory and respiratory problems, amnesia and damages to the central nervous system (CNS) (Watanabe 1998). Chronic exposure in mice has been shown to cause spatial memory loss, changes to certain brain regions, and autism-like traits in offspring (Calas et al. 2008; Laugeray et al. 2014).



#### **Recommendations:**

- We find it ethically unacceptable to ban the use of glufosinate-ammonium based herbicides domestically due to health and environmental concerns, while supporting its potential use in other countries. This represents an unacceptable double standard for Norway, and we ask the regulators to reconsider the practice of separating health and environmental risk by national borders or regions.
- The applicant should include a full evaluation of the co-technology intended to be used with 1507 maize, namely the herbicide glufosinate-ammonium. Particular focus should be given to the level of accumulation of herbicides in the plants, particularly the parts used in food and feed production, and whether or not these levels of exposure could cause acute and/or chronic health issues. This needs to be tested in animal and feeding studies, separating the effects of the plant and the herbicide(s) by using both sprayed and unsprayed plant samples.

## **Toxicology and allergenicity**

In VKM report 13/327, the Norwegian Scientific Committee for Food Safety published an opinion on the food/feed and environmental risk assessment of maize event 1507. No homologies to known toxins or allergens was found and no IgE mediated allergic reactions was reported due to maize event 1507. However, as maize 1507 produces Cry1F and some Cry toxins have the potential to function as adjuvants, there issue on allergenic reactions must be considered.

The VKM report refers to toxicology studies where the origin of the Pat and Cry1F- proteins used in acute toxicology and repeated dose testing is unclear. In one of the cases, Pat is said to have a microbial origin.

Since we do not have access to the dossier, only the summary, we can not comment further on the toxicology and allergy part.

Also, all data presented in the go-through were older than 10 years.

## **Recommendation:**

- We suggest that the Applicant perform toxicity studies with plant derived proteins from the stack the Applicant applies authorization for here.
- We also suggest that the applicant perform and go through newer studies on toxicology and allergy with the relevant transgenic proteins.

## Environmental risk assessment (ERA) and monitoring plan

We emphasize the crucial role of the agricultural context in which these crops will be grown. There are several risks connected to the cultivation of genetically modified crops, among them gene flow (both to non-modified crops and wild relatives of the crop) and potential impacts on the surrounding ecosystems through affecting insect and plant life, small mammals and birds and aquatic life (i.e. non-target organisms) (Warwick et al. 2009).



Gene flow could have implications for insect life if cry-genes spread to wild maize relatives, or for herbicide resistance in wild maize relatives if genes such as *pat* are outcrossed. High doses and continuous use of herbicides promotes development of resistance in weed species, creating a snowball effect where doses used accelerate in response to weed resistance evolution. The herbicide will never be confined to the field but will also affect surrounding areas/ecosystems such as forests, meadows and aquatic run-off systems.

## The Norwegian Gene Technology Act §1 specifically states that

"The purpose of this Act is to ensure that the production and use of genetically modified organisms and the production of cloned animals take place in an ethically justifiable and socially acceptable manner, in accordance with the principle of sustainable development and without adverse effects on health and the environment".

We argue that it would be double standard and poor ethical judgment to condone the import and use of crops, without knowing the agricultural context in which these crops are produced, and what steps that are being taken by producers to minimize risk and ensure a sustainable production with minimal impact on the environment and health of workers and consumers. Information on what measures are being taken to minimize the risk of gene flow to wild relatives, and on the herbicide application regime is essential for evaluating the sustainability and environmental impact of this crop. Thus, we would like the ERA to consider the risks connected also to the cultivation of the crop.

## **Recommendation:**

• The regulators are encouraged to ask the Applicant to provide a full ERA of the life cycle of maize event 1507, i.e. from being planted in the field and through the cultivation process, harvesting, transportation, processing, and as waste. Specifically, more information on herbicide regime and residues should be included.

## Social utility and sustainability aspects

In addition to the EU regulatory framework for GMO assessment, an impact assessment in Norway follows the Norwegian Gene Technology Act (NGTA). In accordance with the aim of the NGTA, production and use of the GMO shall take place in an ethically and socially justifiable way, under the principle of sustainable development. This is further elaborated in section 10 of the Act (approval), where it is stated that: "*significant emphasis shall also be placed on whether the deliberate release represent a benefit to the community and a contribution to sustainable development*". These issues are further elaborated in the regulations relating to impact assessment pursuant to the NGTA, section 17 and its annex 4. In the following we identify issues that are relevant to consider in order to assess social utility and sustainability aspects, and highlight the need for further information to properly assess these issues.

#### Impacts in producer countries

The NGTA, with its clauses on societal utility and sustainable development, comes into play with a view also to health, environmental and socio-economic effects in other countries, such as where the GMOs are grown.



#### Social impact relevant for sustainability

Published reviews on sustainability-relevant aspects of social impacts from cultivating GM crops (e.g. impacts among poor and/or small-scale farmers in developing countries, share of the benefits among sectors of the society) indicate that these effects have been very complex, mixed and dependent on the agronomic, socio-economic and institutional settings where the technology has been introduced (Glover, 2010). Fisher et al. (2015) performed a literature review on empirical studies concerning social implications from cultivating GM crops, and found that between 2004 – 2015 there has only been 15 studies corning social implications of cultivating Bt-maize. They show that published literature is dominated by studies of economic impact and conclude that very few studies that take a comprehensive view of social impacts associated with GM crops in agriculture. Importantly, it is difficult to extrapolate on hazards or risks taken from data generated under different ecological, biological, genetic and socioeconomic contexts as regional growing environments, scales of farm fields, crop management practices, genetic background, interactions between cultivated crops, and surrounding biodiversity are all likely to affect the outcomes. Hence, it can not be expected that the same effects will apply between different environments and across continents. In order to meet the requirements in the NGTA, further investigations of social implications (e.g. economic, distribution of benefits, access to seeds and wellbeing) in the 11 countries where maize 1507 has been approved for cultivation is needed.

#### Co-existence management

The cultivation of GM plants in general is causing problems with regard to co-existence. For instance, Binimelis (2008) have investigated consequences on co-existence of Bt maize in Spain among small-scale farmer and has found that co-existence is very difficult and that farmers in some areas has given up growing non-GM maize. Information about the strategies adopted to ensure co-existence with conventional and organic maize production and information about consequences on co-existence in the producer countries of Maize 1507 is required

#### Impacts of the Bt-toxin on target and non-target organisms in the producer country

The 1507 maize confers resistance to certain lepidopteran and coleopteran pests. A growing number of studies and reviews indicate potential harm to a range of non-target organisms (Holderbaum et al. 2015; Marvier et al. 2007; Rosi-Marshall et al. 2007; Bøhn et al. 2008). Both impacts on non-target organisms and resistance development among target pests of Bt maize has been documented (Van den Berg et al. 2013; Van den Berg, 2013). Evaluation of resistance development within the target pest population and strategies suggested to halt this development, as impacts on non-target organisms is crucial in a sustainability assessment.

#### Impacts of and ethical considerations in relation to the use of glufosinate-ammonium

The 1507 maize confers tolerance to herbicides containing glufosinate-ammonium. According to the Applicant, this trait is intended to be used solely as a selectable marker during transformation. Still, as transfer of this trait may imply that glufosinate-ammonium can be used during cultivation of maize 1507, evaluation of impacts from applying this herbicide in the field is also warranted. Glufosinate-ammonium is a class of herbicides that are banned in Norway and in the EU (except a limited use on apples) due to both acute and chronic effects on mammals including humans (see section on Herbicide tolerance for references and further elaboration on this issue). Moreover, as cultivation of maize 1507 may involve the use of a herbicide that is banned in Norway, acceptance of this product would violate basic ethical criteria as laid out in the NGTA. Hence,



approval of Maize 1507 for food and feed uses could imply to support a double standard of safety for Norway on one hand, and safety for countries from which Norway may import its food and feed on the other.

#### Assessment of alternatives

It is also important to evaluate whether alternative options (e.g. the parental non-GM version of the 1507 maize) may achieve the same outcomes in a safer and ethically justified way. Furthermore, in order to evaluate whether the 1507 maize contributes to social utility, it is important to consider current and future demand for this GM maize product for food, feed and processing purposes in Norway and to what extent this demand is/can be satisfied by existing sources. GM maize accounts for approximately 30% of the current global maize production (www.GMO-compass.org). Non-GM maize is therefore abundant for importation to the Norwegian market and maize 1507 can therefore not be considered to meet a societal need or demand.

#### Recommendation:

In order to meet the requirements for the NGTA, the regulator is encouraged to ask the Applicant to submit information relevant for the assessment of the social utility of the 1507 maize and its contribution to sustainable development. The information provided by the Applicant must be relevant for the agricultural context in the producing country/countries. The information should include issues such as: development of pest resistance in target populations, impacts on non-target organisms, co-existence consequences and possible impacts among poor and/or small-scale farmers in producing countries and share of the benefits among sectors of the society.

#### Conclusion

The applicant does not attempt to identify socio-economic implications, nor demonstrate a benefit to the community and a contribution to sustainable development from the use of the 1507 maize and does therefore not provide sufficient information as required by the NGTA.



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