Important Considerations for Sustainability, Social utility and Ethical Assessment of Late Blight Resistant GM Potato




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Important Considerations for Sustainability, Social utility and Ethical Assessment of Late Blight Resistant GM Potato

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GenØk – Centre for Biosafety (www.genok.no) is an independent research institute founded in 1998 and located in Tromsø, Norway. GenØk is engaged in the field of biosafety and gene ecology research on modern biotechnology, nanotechnology, synthetic biology and other technologies emerging from these. This institution also works on capacity building and advisory activities related to biosafety. GenØk focuses on a precautionary, holistic and interdisciplinary approach to biosafety. In 2007, GenØk was appointed national competence center on biosafety by Norwegian authorities.

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Summary

This Biosafety Report intends to contribute to ongoing efforts to translate the criteria concerning sustainability, ethical justifiability and social utility in the Norwegian Gene Technology Act into more concrete terms. It does so by presenting ten assessment questions that are important to consider when assessing whether late blight resistant (LBR) genetically modified (GM) potato contributes to sustainability, benefits society and is ethically justifiable in a Norwegian agricultural context. Late blight is the most devastating disease on potatoes globally. Current control measures in conventional potato production are largely based on chemical treatment with fungicides that is costly, both for potato producers and the environment. If successful, cultivating LBR GM potato may result in a reduction of fungicide applications to control the late blight disease in potato production. Hence, LBR GM potato is claimed to be one of the first GM plants that have the potential to solve a serious problem for Norwegian and European farmers.

The ten assessment questions relating to social utility, sustainability and ethical justifiability that are presented and discussed in this report are:

1. *Does the LBR GM potato contribute to solve an important problem for Norwegian potato producers?*
2. *Is there a demand for the LBR GM potato among Norwegian potato producers and consumers?*
3. *What are the alternative approaches to breed for LBR potato varieties?*
4. *Is the GM potato plant's LBR durable over time?*
5. *Does the LBR GM potato reduce the need for fungicides to control LB over time?*
6. *Is the LBR GM potato safe for human health and the environment over time?*
7. *Does the profitability of farmers who cultivate the LBR GM potato improve over time?*
8. *Does the LBR GM potato affect opportunities for co-existence between GM, conventional and organic potato production, and the diversity of commercial potato varieties available to farmers?*
9. *Does the LBR GM potato affect farmers', manufacturers' and consumers' freedom to choose different potato varieties cultivated under different production systems?*
10. *Is the LBR GM potato available for further breeding and research?*

The report highlights uncertainties associated with these assessment questions, suggests areas for further research and strategies for monitoring.

The report is written as part of a three-year research project (2013- 2016) funded by the ELSA program of the Norwegian Research Council (project number: 220621). The project intends to examine, through participatory and deliberative assessment methodologies, potential ethical, social and sustainability aspects from cultivating and marketing LBR GM potato in Norway. The report draws on insights generated during stakeholder discussions and public meetings on this topic, as well as review of relevant literature.

1. Introduction

This Biosafety Report outlines issues that are important to consider when assessing sustainability, social utility and ethical implications of cultivating late blight resistant (LBR) genetically modified (GM) potato in Norway. It intends to contribute to the operationalization of the criteria relating to sustainable development, ethical justifiability and benefit to society in the Norwegian Gene Technology Act (1993), and builds on the efforts made by the Norwegian Biotechnology Advisory Board in translating these criteria into more concrete terms (Norwegian Biotechnology Advisory Board 2009, 2011, 2014).

The report presents ten assessment questions that are particularly relevant to consider when assessing cultivation of LBR GM potato in a Norwegian agricultural context. The report points to knowledge gaps and uncertainties associated with these assessment questions, suggests areas for further research and strategies for monitoring.

1.1. Late blight resistant GM potato

This potato has been genetically modified to increase its resistance to potato late blight. Potato late blight, caused by a fungus-like organism called *Phytophthora infestans,* is the most devastating potato disease worldwide. Current control measures in conventional potato production are largely based on chemical treatment with fungicides that is costly, both for potato producers and the environment. Improving host plant resistance is considered the most sustainable way to control late blight (Rietman et al. 2012; White and Shaw 2010), but classical introgression breeding for late blight resistance is challenging for several reasons:

(i) The potato has a very complex genetics (highly heterozygous and polyploid), which creates crossing barriers and makes it difficult to transfer traits from wild *Solanum ssp*. to commercial potato varieties

(ii) Desirable traits, such as late blight resistance, are often associated with undesirable traits, which must be removed through several generations of backcrosses to the commercial potato variety (linkage drag)

(iii) The potato is propagated vegetatively and the reproductive fertility is often limited

(iv) *P. infestans* has a very high evolutionary potential and can therefore easily adapt and overcome host plant resistance. Experience from cultivating LBR potatoes has therefore shown that the potato plant's resistance is easily broken once the potatoes are put into large-scale commercial production.

It is argued that the GM approach enables more efficient late blight resistance breeding than classical introgression breeding, as this approach enables researchers to introduce several resistance genes in elite potato varieties. Hence, this approach is expected to result in potatoes with more durable late blight resistance that also perform well for other desired qualities (Haverkort et al. 2016).

The genes introduced in LBR GM potato are called resistance (*R*) genes and are derived from wild potato species (*Solanum ssp*.) found in Central and South America. These *R* genes recognize *P. infestans* and prevent infection, thereby provide wild potato with natural resistance to potato late blight. More than 20 *R* genes have so far been identified and are available for transformation (Rodewald and Trognitz 2013).

It is possible to develop LBR GM potato that only harbor genes from naturally crossable relatives. These type of GM plants are called cisgenic plants. Several European research teams are currently developing late blight resistant GM potatoes that harbor up to three different *R* genes which are tested in field trials in different parts of Europe (European Commission 2016). The American company J.R. Simplot has also developed three varieties of LBR GM potato and approval for cultivation in the US is expected by the end of 2016 (Simplot 2016). Other US based research environments and the International Potato Centre in Peru (CIP) are also developing LBR GM potato (Halterman Lab 2015, Wisconsin University 2012, Cornell University 2013, International Potato Center 2014), and they do carry out field trials taking place in developing countries.

1.2. The regulatory context

The Norwegian Gene Technology Act (1993) regulates the production and use of genetically modified organisms (GMOs) (Gene Technology Act 1993). It stipulates that approvals can be granted in Norway if it is demonstrated that the production or use of the GMO does not have detrimental effects to the environment or human health, represents a benefit to society, contributes to sustainable development and is ethically justifiable.

The terms "sustainable development", "benefit to society" and "ethical justifiability" are complex and can be interpreted differently in the context of GMOs. The interpretations used for this Biosafety Report is inspired by the work of scholars (Rosendal and Myhr 2009, Catacora-Vargas 2014), that has specifically analyzed these criteria for GMO risk assessment in a Norwegian context, and do also draw on the Norwegian Biotechnology Advisory Board's contributions on how to operationalize the assessment criteria (Norwegian Biotechnology Advisory Board 2009, 2011, 2014).

Societal utility refers to public welfare considerations. Issues relevant for a GMO assessment include production-related issues (e.g. access to seeds, profitability for farmers and benefit sharing), social and justification considerations on a global level (e.g. equity between the Global North and South), and societal need and demand (e.g. public acceptability and demand, and whether the GMO contributes to solve an important problem).

Sustainable development is interpreted according to the World Commission on Environment and Development's (WCED) 1987 definition, which refers to the possibility of people to meet their needs without compromising the ability for future generations to meet their own needs (WCED 1987). It implies to consider environmental/ecological, societal and economic impacts of GMOs, taking a long term and global perspective (i.e. considering impacts in the producer country).

Ethical justifiability relates to whether the GMO contributes to the common good and is in line with the ethical values on which society is funded. Assessing ethical justifiability implies to consider whether the GMO respects or infringes eco-ethical values (e.g. the integrity and intrinsic value of nature and ecological balance) and commonly shared anthropocentric values (e.g. well-being, autonomy, solidarity, equity and justice). It involves a situational analysis in which alternatives to the GMO approach are identified, and a consideration for how the impacted parties will be affected by the different alternatives.

The Precautionary principle regulates actions associated with uncertainty and is an underlying principle for GMO regulations in Norway. It comes into play when there is scientific uncertainty and reasonable doubt concerning adverse effects with the adoption and use of a GMO. The principle is considered a key issue in a sustainability assessment, as this involves considering long-term perspectives, global, environmental and health impacts that are often associated with uncertainty.

1.3. Outline of the report

This report presents ten assessment questions that are consider particularly relevant to evaluate ethical, social and sustainability implications related to the specific case of LBR GM potato in a Norwegian agricultural context:

1. *Does the LBR GM potato contribute to solve an important problem for Norwegian potato producers?*
2. *Is there a demand for the LBR GM potato among Norwegian potato producers and consumers?*
3. *What are the alternative approaches to breed for LBR potato varieties?*
4. *Is the GM potato plant's LBR durable over time?*
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10. *Is the LBR GM potato available for further breeding and research?*

The potential impacts caused by the LBR GM potato plant itself (throughout the whole production chain) and its production system, should be taken into account in an assessment of these questions. This concerns potential impacts throughout the whole production chain and by the production system it is likely to be cultivated under. Furthermore, the LBR GM potato should be compared to its closest genetic relative, cultivated in the same agro-ecological system and taking the strategies used to control late blight in conventional potato production at the time of the evaluation into account as this is currently the dominating production form in Norway.

The development of these assessment questions draws on discussion with key stakeholders in potato production in Norway (Gillund et al. 2014, 2015, 2016), and on a review of relevant literature. The questions are grouped according to the assessment criteria they are considered most relevant for. As these criteria are interlinked, many of the assessment questions are relevant for more than one criteria. Importantly, the list of assessment questions is not exhaustive and the report does not intend to answer the suggested assessment questions. Rather, the report intends to present information that that are of relevance for these questions, also areas characterized by uncertainties are highlight together with suggestions for topics that needs further research.

2. Important Considerations when Assessing Social Utility

Does the LBR GM potato contribute to solve an important problem for Norwegian potato producers?

Potato late blight is considered one of the most severe problems for Norwegian potato production (Sæthre et al. 2006, Gillund et al. 2016). The disease has become more aggressive during the last decade and might increase further with climate change, as more rainfall is predicted during growing seasons creating more favorable conditions for fungal diseases in general (Cooke et al. 2011). Additionally, *P. infestans* may remain in the soil in the form of oospores that are better preserved at cold temperatures. This may explain the fact that infections from oospores are common in Norway, and are resulting in outbreaks of the disease earlier in the growing season as well as longer time periods for prevalence of the disease in the soil (Cooke et al. 2011).

The most common sources for late blight in Norway are infected tubers (seed tubers or volunteers) and *P. infestans* oospores in the soil. The disease spreads quickly from potato plant to potato plant in the form of fungal spores carried by wind and rain. Infected potato plants that are not treated will eventually die. Moreover, infected tubers become brown, unattractive and the quality is to low that it can be consumed as food or feed. The most widely cultivated potato varieties in Norway are not very resistant to late blight. More resistant potato varieties are available, but these are not widely cultivated in Norway or Europe as they are generally not considered to perform sufficiently well for other product related qualities (Cooke et al. 2011).

Current control measures in conventional potato products largely rely on spraying with synthetic fungicides throughout the growing season. About half of the total fungicide applications in Norwegian agriculture are used to control potato late blight (Plantevernleksikonet 2011). The disease is the most important factor for reduced yield and quality in organic potato production (Agropub 2015). The annual losses associated with late blight in Norway are estimated to be around 55 – 65 million NOK. These estimations include costs associated with buying and applying fungicides (48,5 million NOK), yield loss (5 -14 million NOK depending on severity of late blight infections) and inspection, research and advisory service (3,3 million NOK) (Sæthre et al. 2006).

Knowledge gaps and research needs:

To describe the severity of the late blight problem in Norway, we recommend updated statistical data on:

- The prevalence of the late blight disease in different potato producing regions in Norway
- Economic losses caused by the disease (e.g. control measures, yield loss and monitoring strategies)
- Other important costs and losses associated with potato production (e.g. losses caused by other important potato diseases or other factors contributing to yield loss or reduced quality)

Is there a demand for the LBR GM potato among Norwegian potato producers and consumers?

Conventional LBR potato varieties are not widely adopted by Norwegian potato producers, partly because they are not considered to perform sufficiently well for other qualities. It is therefore reasonable to assume that there is a demand for LBR potato varieties, which also perform well for other properties appreciated by farmers, processing industries and consumers. Cultivating LBR potato varieties may also contribute to meet the goal of reduced dependency on chemical treatment of plant diseases in Norwegian agriculture (Norwegian Ministry of Agriculture and Food 2016), and satisfy consumer demands for food produced without chemicals. At present farmers also use considerable time during the growth season to monitor their potato crops for late blight infestations, hence LBR potato varieties may improve farmers' psychological well-being as they will be relieved from the concern that their crop will be severely damaged (Gillund et al. 2016).

Whether it is a demand for *genetically modified* LBR potato is, however, arguably dependent on public acceptance of GM food in general. Empirical research on consumer's acceptance of GM food in Norway is limited and out dated. Still, reluctance towards GM food tends to be the dominant attitude among Norwegian consumers (Hviid Nielsen 2012). For instance, the Network for GMO free Food and Feed in Norway works for a restrictive approach to GMOs in Norway and represents a broad range of interest organizations, including farmer unions and one of the largest food chains in Norway (Coop Norge) (http://gmofrimat.no/).

Consumer surveys have, however, shown that the younger segment of the Norwegian population are more willing to accept GM food if they find that the product has clear benefits, particularly related to less use of synthetic chemicals for pest and disease protection (Magnus et al. 2009). Disease specificity (i.e. late blight resistance) was found to matter little for consumer support in a survey on attitudes to GM potato among US consumers (McComas et al. 2014). LBR GM potato may be developed as cisgenic potatoes (e.g. only harboring genes from crossable relatives or the same species), and it may be expected that consumers will be more positive to this approach (Haverkort et al. 2009). The 2010 Eurobarometer survey does support this hypothesis as it indicates consumers are more positive towards cisgenic GM plants (Gaskell et al. 2011). Similar attitudes are found in a study that compares consumer acceptance among US and European citizens, though this study shows there is a significant difference between the USA and countries in Europe, with a twice as high acceptance level of cisgenic plants in the USA (Lusk and Rozan 2006). Another consumer survey carried out in Europe finds that consumers consider cisgenic plants as GM and still favor for example labelling of such a technique (Kronberger et al. 2013).

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Knowledge gaps and research needs*:*
To describe the potential demand of LBR GM potato in Norway we recommend consumer surveys that particularly investigates:

- Attitudes to LBR GM potato among different segments of the Norwegian population and interested parties (e.g. consumers, farmers and potato retailers)
- Attitudes to cisgenic LBR potato in particular in the Norwegian population and among interested parties

What are the alternative approaches to breed for late LBR potato varieties?

Developing LBR potato varieties through classical introgression breeding is considered challenging and laborious (Vleeshouwers et al. 2011). Still, it also has advantages: While the GM approach currently can only exploit qualitative resistance mechanisms, both quantitative and qualitative LBR mechanisms can be exploited through classical breeding. Qualitative resistance is conferred by a single *R* gene and results in complete resistance to those strains of the pathogen that are recognised by the specific *R* gene. Quantitative resistance is mediated by multiple genes which each gives partial resistance to a broad range of *P. infestans* strains (Kou and Wang 2010). Qualitative resistance is considered to be more durable, but has been difficult to exploit in breeding programs as the genes underlying this resistance are still largely unknown, and because it is more complicated to breed for traits controlled by multiple genes (Du et al. 2013).

Despite the challenges associated with classical introgression breeding for LBR, ongoing potato breeding programs in Europe using such approaches, including marker assisted breeding, show promising results. One such example is Bioimpuls, a potato breeding program initiated by researchers at the Louis Bolk Institute and Wageningen UR who are working together with breeding companies and farmer-breeders to develop robust cultivars that are resistant to *P.infestans* (Almekinders et al. 2014). The cultivars Bionica and Toluca are well known examples of traditionally bred LBR resistant cultivars possessing *R* genes from different wild potato species (Lammerts van Bueren et al. 2008, Haverkort et al. 2009). Similarly, researchers at the French National Institute for Agricultural Research (INRA) aims to develop LBR potato cultivars exploiting both qualitative and quantitative resistance (Marhadour et al. 2013). The Sárvári research trust, based in Scotland, has been breeding for LBR potatoes since 2002 and has developed different Sarpo cultivars. Among them, Sarpo Mira is currently considered to be one of the most late blight resistant cultivar in Europe (White and Shaw 2010, Rietman et al. 2012). In Norway, researchers at Graminor carry out potato breeding. They have bred varieties such as Odinia and Troll that are quite resistant to late blight. Still, many of these late blight resistant potato varieties are not widely cultivated as they are not considered to perform sufficiently well for other qualities appreciated by farmers and consumers. Norwegian stakeholders have argued that breeding for late blight resistance is not prioritized in traditional potato breeding programs to the extent that it could have been. This is partly explained by the fact that fungicides currently control late blight effectively. The current fungicides that are used to control late blight are considered to be less harmful for human health than most herbicides and especially insecticides (Gillund et al. 2016).

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Knowledge gaps and research needs:
To map out possible alternative approaches to breed for late blight resistance. This effort needs to includes research that intends to identify:

- Current breeding efforts and approaches for LBR, particularly in Norway and Europe
- The priority given to LBR in potato breeding programs, particularly in Norway and Europe
- Possibly other potato breeding approaches for LBR that are under development

3. Important considerations when assessing contribution to sustainable development

Is the resistance of the GM potato durable over time?

A main challenge with breeding for late blight resistance is to develop cultivars that are resistant to late blight over time. This is because *P. infestans* has a remarkable capacity to rapidly adapt to and overcome resistant host plants (Fry 2008). Single *R* genes that have been introduced to commercial potato varieties through traditional introgression breeding has consequently been defeated shortly after the potato varieties have been put in commercial production (Vleeshouwers et al. 2011). Researchers developing LBR GM potato try to overcome this challenge by adding up several single *R* genes (e.g. gene stacking) in the GM potato. They expect that this approach will make the resistance more durable (Zhu et al. 2012, Jones et al. 2014, Kwang-Ryong et al. 2014, Haverkort et al. 2016). Field trials with stacked LBR GM potato events show promising results (Haverkort et al. 2016), still it is difficult to predict how long the resistance actually will last and this answer can only be given after the potato is put in large-scale production and cultivated over time.

To strengthen the durability of LBR GM potato, it is recommended that the *P. infestans* population is monitored in the area where the GM potato is cultivated to detect if any of the *R* genes of a certain GM potato variety are broken by the pathogen. Furthermore, strategies to halt virulence development in the *P. infestans* population need to be established prior to large scale cultivation (Haesaert et al. 2015). The genetic diversity of the Nordic *P. infestans* population is particularly high and this strengthens the adaptive potential of the pathogen (Brurberg et al. 2011). Hence, resistance management and monitoring is particularly important in a Norwegian context. When developing monitoring and resistance management strategies it is also important to clarify responsibilities as well as the distribution of the costs for carrying out these tasks.

One proposed strategy for resistance management is to apply reduced dose rates of fungicides to prevent breakthrough of the entire *R* gene stack, if monitoring shows presence of virulence to individual *R* genes as components of *R* gene stacks (Haesaert et al. 2015). Another proposed strategy to prolong the potato plants resistance is to develop "dynamic GM potato cultivars" that consists of LBR GM potato plants where the composition of the set of *R* genes differs while all other properties are exactly the same. The idea is to change the set of *R* genes expressed by the GM potato event between the growing seasons or in different parts of the same potato field (Haverkort et al. 2016).

Knowledge gaps and research needs:
To further advance breeding programs for durable LBR potato varieties it is important to carry out basic research on:

- The molecular mechanisms underlying the observed LBR
- The mechanisms and evolution of the virulence development in the *P. infestans* population

To develop a plan for integrated LB control, monitoring and resistance management. This can for example be carried out by:

- Workshop to evaluate risk for virulence development in the Nordic *P. infestans* populations and suggest a resistance management program. The participants in this workshop should include experts on evolutionary genetics, quantitative population genetics, resistance evolution and fungal diseases, as well as potato producers, and agricultural advisors.

Does the LBR GM potato reduce the need for fungicides to control LB over time?

It is calculated that growing the LBR GM potato can reduce the need for fungicides by 80% when included as part of a crop-specific integrated pest management (IPM) strategy (Collier and Mullins 2010, Haverkort et al. 2016). Some spraying may be needed towards the end of the growing season to prevent LB attacks on senescing GM potato plants since they do not confer the same level of LBR (Jones et al. 2014), and some spraying is also proposed as a strategy to halt virulence development within the pathogen population (Haesaert et al. 2015). The extent to which cultivation of LBR GM reduces fungicide depends on whether and to what degree the GM plant possesses resistance in the foliage, the tubers or both. There are studies indicate that the LBR GM potato may confer both foliar and tuber resistance, while other studies indicate the contrary (Halterman et al. 2008, Kirk et al. 2001, Park et al. 2005, Platt and Tai 1998). Importantly, the potential of LBR GM potato to reduce fungicide use in the long run depends on the durability of the resistance of the LBR GM potato. Knowledge about the expected durability of the LBR GM potato together with strategies to strengthen the durability is therefore highly relevant for the assessment of the fungicide requirement over time.

Knowledge gaps and research needs:
To evaluate the extent to which cultivation of LBR GM potato reduces fungicide use (in concentrations or numbers of applications), it is important to carry out field trials to identify:

- Fungicide requirements for cultivating LBR GM potato under different climatic conditions and during all phases of the growing season.

- Tissue-specific expression of *R* genes and to what extent they confer LBR in different parts of the potato plant
- How secondary pests responds to a) reduced spraying against *P. infestans*, and b) less prevalence of *P. infestans*.

Is the LBR GM potato safe for human health and the environment over time?

It is possible to develop cisgenic LBR GM potato, and these GM plants may be more safe than transgenic potatoes. The GMO panel of the European Food and Safety Authority (EFSA) concluded in 2012 that the risks associated with cisgenic and traditionally bred plants are the same, while transgenic plants may result in novel risks (EFSA 2012). This conclusion was gene-based, meaning that because the genes are known to be safe, the cisgenic approach was also considered safe. Other researchers, do, however, emphasize that even if the inserted gene is known, this does not mean that uncertainties associated with the transformation process are known. Hence, in contrast to the conclusion of the EFSA, it is argued that, in terms of food and environmental safety, cisgenic cannot be regarded as equivalent to conventional breeding, nor that the safety of the products resulting from traditionally breeding and cisgenic technologies are similar, based on the unknown behavior and effects of the genes in the transformation process and their functioning within the mechanisms of the host plant (e.g. random integration of genes in the host genome) (Schubert and Williams 2006, Wilson and Latham 2007, Austrian Agency for Health and Food Safety 2012). It is also documented that chromosomal position can play an important role in the expression of the *R* gene (Kramer et al. 2009). This exemplifies some of the difficulties of predicting the function of a genetic construct when moved into a new host, even when the host is a closely related species.

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As already discussed, it is expected that cultivating LBR GM potato will reduce the need for fungicides to control late blight. This means that consumers and producers may be less exposed to fungicides, which is also important to take into consideration when assessing the safety of this type of GM potato.

***Knowledge gaps and research needs**:*

To evaluate the safety of cisgenic GM potato on human health it is important to carry out research on:

- The protein being produced by the cisgene, as well as checking for its allergenic potential or any unexpected alterations in protein structure and quantity
- Metabolic disturbances caused by the introduction of the novel trait or by the expression of cisgene. This can be achieved by untargeted molecular approaches such as multi-omics analyses

Does the profitability of farmers who cultivate LBR GM potato improve over time?

Whether farmers benefit economically from cultivating LBR GM potato depends on how it influences the use of input factors (e.g. seed potato, herbicides, fertilizers, fuel, labor, capital etc.) per production unit. Norwegian potato producers spend most money on buying seed potato (approximately 40% of the total variable costs), while fungicides only accounts for 6% of the total costs. Other important cost are fertilizers (28%), herbicides (3%), synthetic chemicals to kill haulm (5%), and transport of the potato crop (18%) (Pettersen et al. 2014).

Cultivating LBR GM potato is expected to reduce the money and time farmers spend on spraying with synthetic fungicides to control late blight. It is estimated that Norwegian potato producers spend 48,5 million NOK on buying and applying fungicides to control late blight ever year (Sæthre et al. 2006). Field trials with LBR GM potato indicate an 80% reduction in the need for fungicides to control late blight (Haverkort et al. 2016), which means that close to 40 million NOK, can potentially be saved when cultivating LBR GM potato in Norway. Moreover, additional costs associated with the labor and energy required to apply fungicides may also be reduced.

Approximately 25% of the potatoes planted every year in Norway are currently certified seed potatoes, the remaining 75% are seed potatoes that farmers reuse from their own harvest (*personal communication* Muath Alsheik 10.10.2016). Still, buying seed potatoes represent the most important cost for Norwegian potato producers. The extent to which farmers will profit from cultivating LBR GM potato will therefore also depend on the price of seed potatoes, farmer opportunity to use GM potatoes from their own crop as seed potatoes, and how frequently farmers must buy new seed potatoes.

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Measurements to ensure segregation of GM and non-GM potato production lines, and avoid unintentional spread of GM potato must be in place if GM potatoes are to be cultivated in Norway. Therefore, farmers cultivating LBR GM potato will most likely have some additional costs to comply with co-existence, segregation and labelling requirements.

***Knowledge gaps and research needs**:*

To assess whether farmers benefit economically from cultivating GM LBR potato, it is important to conduct research to estimate:

- How farmers will be impacted economically from the expected reduction in fungicide use when cultivating GM LBR potato, taking also into account the cost of seed potato and opportunity to reuse potatoes as seed potato
- Costs to comply with requirements for co-existence and segregation between GM-potato and non-GM potato in the production chain

Does the cultivation of LBR GM potato affect opportunities for co-existence between GM, conventional and organic potato production, and the diversity of commercial potato varieties available to farmers?

The potato plant's biological characteristics (i.e. vegetative propagation, limited seed production and no wild relatives in Norway) reduce the potential for accidental spread of GM potato to neighboring farmland and in the surrounding environment in Norway. Risks of unintentional spread of GM potato is therefore mainly related to handling of GM seed potatoes and GM potatoes during cultivation, storage, processing and transport (Finne 2005).

Regulations to assure co-existence between GM, conventional and organic potato production are not yet in place in Norway, but the Norwegian Scientific Committee for Food Safety has provided recommendations for co-existence management strategies (Norwegian Scientific Comittee for Food Safety 2006). This report concludes that it is very unlikely that cultivation of GM potato in Norway will result in unintentional presence of GM potato in organic and conventional potato batches above a threshold of 0,9 %. Suggested strategies to ensure co-existence includes; (i) an isolation distance of 20 m between fields with GM potato and non-GM potato, (ii) careful cleaning of machinery for potato seeding, harvest, transport and storage if this is to be used for different production forms, (iii) careful monitoring of GM potato fields to remove GM potato tubers and volunteer potato plants after harvest, and (iv) specific requirements for cultivation intervals if non-GM potato is to be cultivated in fields where GM potatoes have grown (Norwegian Scientific Comittee for Food Safety 2006).

One issue that could be relevant to consider in relation to potential unintentional spread of GM potato, is the common practice of cultivating potatoes in private gardens in Norway, where many households reuse and share seed potatoes. Such practices may interfere with intellectual property protection of GM potato and pose challenges for co-existence management.

70 different potato varieties are approved for cultivation in Norway (Plantesortsnemnda 2016). Among these, approximately 40 varieties are grown to some degree, which includes 12 varieties that are most commonly cultivated in Norway. Most of these varieties are quite susceptible to late blight (Møllerhagen 2015). Factors that may influence whether cultivation of LBR GM potato will influence the diversity of commercial potato varieties available to farmers include: the intended use of the GM potato (direct consumption/ processing), whether the GM potato is suitable for the agronomic conditions specific to Norway, and if it satisfies specific consumer preferences.

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Knowledge gaps and research needs:

To evaluate how cultivation of GM LBR potato may influence the diversity of commercial potato varieties that are available to Norwegian farmers and consumers it is important to:

- Conduct field trials to test whether the LBR GM potato is suitable for the agronomic conditions specific to Norway
- Conduct an expert workshop to develop guidelines for co-existence between GM, conventional and organic potato production and segregation in the production chain (i.e. storage, transportation and processing line)

4. Important considerations for an assessment of ethical justifiability

Does cultivation of LBR GM potato affect farmers', manufacturers' and consumers' freedom to choose different potato varieties cultivated under different production systems?

Democratic rights, such as the freedom to choose what you want to grow as a farmer and eat as a consumer is important in our society. The mandatory labelling of GM food in Norway is one example of recognition of this right. To what extent cultivation of LBR GM potato will influence farmers', manufacturers' and consumers' freedom to choose which potato they want to grow and eat, will depend on a wide range of factors that are difficult to predict prior to commercial release. Several questions were raised when Norwegian stakeholders discussed this issue (Gillund et al. 2015), such as (i) may LBR GM potato dominate future potato markets and thereby reduce the diversity of other potato varieties available to farmers and consumers? (ii) can potato producers reuse GM potato from their own harvest as seed potato? (iii) could cultivating LBR cisgenic GM potato that express several *R* genes increase the selection pressure within the pathogen population and possibly speed up the development of multi-resistant *P. infestans* strains? If so, will future potato producers be faced with a more aggressive pathogen? How will a potential approval of LBR cisgenic GM potato in Norway influence potato producers who choose not to cultivate GM potato? Will it be difficult for a farmer who has started to grow LBR GM potato to return to conventional or organic potato production in the future?

Importantly, a potato farmer is allowed to save a part of its potato harvest to reuse the next year as seed potato, under the Plant Breeders Rights (PBR) that secures breeders ownership and control over potato varieties currently cultivated in Norway. This opportunity to reuse seed potato is important for the Norwegian potato industry, as farmers take around 70-75% of their seed potatoes from their own crop. LBR GM potato is patented which implies that the farmers must obtain a license from the patent holder to cultivate and implies that farmers are typically not allowed to reuse seeds.

Knowledge gaps and research needs:

To evaluate how cultivation of LBR GM potato may affect farmers', manufacturers' and consumers' freedom to choose different potato varieties cultivated under different productions systems it is important to conduct research on:

- How the introduction of patented seed potato may affect farmers' rights and control over their crop?

- Potential changes in the Norwegian potato market posed by the introduction of LBR GM potato
- How cultivation of LBR GM potato influences the P. infestans population in the receiving system, and possibility to practice other potato production forms and late blight control strategies today and in the future

Is the LBR GM potato available for further breeding and research?

The answer to this question will depend on how the breeder's ownership of an LBR GM potato is protected. GMOs are often patented, which means that other persons must have a license from the patent holder to do research or ta carry out further breeding on the material. Some patents prevent anyone other than the seed company from conducting research or further breeding on GM crops. The ownership of conventionally bred plant varieties are currently protected under Plant Breeder Rights (PBR), which gives the breeder an exclusive control over the breeding of a particular variety. However, in contrast to patents, PBR implies 'breeder's exemption' that allows breeders to use each other's varieties in breeding programs without necessarily obtaining a license or agreeing on financial compensation.

All the *R* genes introduced into LBR GM potato varieties that are currently under development by European research institutes are patented. Interestingly however, the *R* genes isolated within the Durph project is patented by the Wageningen University under a "humanitarian use licensing". This implies that poor countries may, under certain conditions, get available *R* genes that can be introduced by genetic engineering into local potato cultivars. Information about the requirements specified in the license is important in order to evaluate how poor countries and farmers may benefit from the technology.

Knowledge gaps and research needs:

To consider the availability of the LBR GM potato for further breeding and research it is important to know:

- The requirements given by the patent holder on further breeding and research on the LBR GM potato variety, and how these requirements differ from breeders rights on conventionally bred potato cultivars currently cultivated in Norway

5. Conclusions and recommendations for further research

This Biosafety Report presents ten assessment questions that are consider particularly relevant to evaluate ethical, social and sustainability implications of cultivating LBR GM potato in a Norwegian agricultural context. The report does not provide a full assessment of these questions and do not make any conclusions about the ethical justifiability, social utility or sustainability of the potential cultivation of LBR GM potato in Norway. Rather, it summarizes some of the information that is available to assess these questions and points to further research needs. The ten assessment questions discussed in this report and research needs identified are presented in the table.

Assessment question	*Recommended areas for further research:*
Does the LBR GM potato contribute to solve an important problem for Norwegian potato producers?	Updated statistical data on: • The prevalence of the late blight disease in different potato producing regions in Norway • Economic losses caused by the disease • Other important costs and losses associated with potato production
Is there a demand for the LBR GM potato in Norway?	• Consumer surveys (including population and among interested parties) on: • Attitudes to LBR GM potato • Attitudes to cisgenic LBR potato
What are the alternative approaches to breed for LBR potato varieties?	Research that identifies: • Current breeding efforts and approaches for LBR potatoes, particularly in Norway and Europe • The priority given to LBR in potato breeding programs, particularly in Norway and Europe • Other potato breeding approaches for LBR
Is the GM potato plant's LBR durable over time?	Basic research on: • The molecular mechanisms underlying the observed LBR • The mechanisms and evolution of virulence development in the *P. infestans* population Conduct an expert workshop to: • Evaluate risk for virulence development in the Nordic *P. infestans* populations and suggest a resistance management program
Does the LBR GM potato reduce the need for fungicides to control LB over time?	Field trials to examine: • Fungicide requirements for cultivating LBR GM potato under different climatic conditions and during all phases of the growing season • Tissue-specific expression of *R* genes and to what extent they confer LBR in different parts of the potato plant • How secondary pests responds to reduced spraying against or less prevalence of *P. infestans*
Is the LBR GM potato safe for human health and the environment over time?	Research on: • The protein being produced by the cisgene, as well as checking for its allergenic potential or any unexpected alterations in protein structure and quantity • Metabolic disturbances caused by the introduction of the novel trait or by the expression of cisgene. This can be achieved by untargeted molecular approaches such as multi-omics analyses
Does the profitability of farmers who cultivate the LBR GM potato improve over time?	Research to estimate: • How farmers will be impacted economically from the expected reduction in fungicide use, taking also into account the cost of GM seed potato and opportunity to reuse potatoes • Cost to comply with requirements for co-existence and segregation between GM-potato and non-GM potato in the production chain
Does the LBR GM potato affect opportunities for co-existence, and the diversity of commercial potato varieties available to farmers?	Expert workshop to: • Develop guidelines for co-existence between GM, conventional and organic potato production and segregation in the production chain Field trials to: • Test whether the LBR GM potato is suitable for the agronomic conditions specific to Norway
Does the LBR GM potato affect farmers', manufacturers' and consumers' freedom to choose different potato varieties cultivated under different production systems?	Research on: • How the introduction of patented seed potato may affect farmers' rights and control over their crop? • Potential changes in the Norwegian potato market posed by the introduction of LBR GM potato • How cultivation of LBR GM potato influences the *P. infestans* population in the receiving system, and possibility to practice other potato production forms and late blight control strategies today and in the future
Is the LBR GM potato available for further breeding and research?	Information about: • The requirements given by the patent holder on further breeding and research on the LBR GM potato variety, and how these requirements differ from breeders rights over conventionally bred potato cultivars currently cultivated in Norway

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