General ethical and legal aspects of the use of genetically modified organisms (GMOs) for the biosensing of explosives

For the
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List of abbreviations

BCH	Biosafety Clearing-House
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Federal Office of Consumer Protection and Food Safety
D-BOX	Demining tool-BOX
DOW	Description of Work
EFSA	European Food Safety Authority
ERA	Environmental Risk Assessment
EU	European Union
FDA	Food and Drug Administration
GM	Genetically modified
GMO	Genetically modified organism
JRC	Joint Research Centre
LMO	Living modified organisms
NGO	Non-governmental organizations
P. putida	Pseudomonas putida
SNIF	Summary Notification Information Format
TNT	Trinitrotoluene

1. EXECUTIVE SUMMARY

The EU project D-BOX tackles the burning issue of anti-personal landmines and cluster munitions remaining from armed conflicts. This will be achieved through the development of innovative solutions that will be interfaced and integrated in a comprehensive toolbox that is going to provide demining stakeholders the best tools, methods and procedures.

Among other things D-BOX includes the development of highly-sensitive biosensors for the detection of explosives. The consortium pursues a new approach in which the common soil bacterium Pseudomonas putida is genetically modified to produce red fluorescent proteins upon recognition of TNT-signatures in liquids or soil.

The aim of this report is first to analyse the public acceptance and possible ethical objections to the use of a GM biosensor. We further recommend necessary technical and non-technical measurements to increase the public acceptance as well as to meet the ethical concerns.

We conducted a desktop research on the public acceptance and ethical aspects of the use of GMOs in general and it became evident that the public acceptance of GM technology varies considerably with its specific application. As our study only aims at analysing the public acceptance and ethical aspects of the use of the DBOX GM biosensor, we conducted interviews to learn about the public opinion of this specific case.

The interviews have shown that the public opinion is divided. In general there are two different attitudes:

- The first group generally disapproves of the use of a GM biosensor. They regard the possible risks as too high. They think that in the absence of a sound proof that the GM biosensor is harmless; the precautionary principle should be applied. Additionally this group has serious doubts whether this demining technique will work at all and whether it will be better than conventional methods.

- The second group sees the GM biosensor system as generally positive. They think that this technique is a promising way to complement and improve the already established demining technologies. They consider the European GM legislations as quite restrictive. Thus, they think if even the EU approves of the GM biosensor, they will have no further objections.

The most serious risk is seen in a possible antibiotic resistance marker gene. Several interview partners think that an approval process could fail due to the antibiotic resistance of the bacteria. Other mentioned risks are for example a negative impact on the ecosystem, gene transfers to other organisms and especially the non-reversibility of the release of the biosensor.

The experts also offered suggestions how the safety of the biosensor could be improved. For instance, it was suggested to use suicide genes, $RecA^-$ mutants, auxotrophic bacteria or transient gene expression.

Apart from these technical suggestions the interview partners considered an involvement of the local population as well as transparency as most important to the success of the project.

Our desktop research on the public acceptance of the GMOs in general has shown that non-food products like medical applications find more acceptance; they are seen as less risky and more ethically correct than food applications. As demining is generally seen as very beneficial to the people, we can expect that the risk-benefit balance of the GM biosensor is seen as similarly favourable as of medical applications.

It was also shown that regardless of considerations of risks and benefits, if someone has moral objections to GMOs it acts like a “veto”. If GMOs are perceived as unnatural or if GM technology is seen as “tinkering with life”, then this perception would seriously influence the acceptance of GM technology in general.

The correlation between GM knowledge and personal attitude has been the topic of many research studies. The results of these studies are diverse or even contradictory. Nevertheless, many researchers have serious doubts whether educating the public in gene technology would result in higher levels of acceptance.

An important factor is that people who express trust in public authorities tend to have a systematically more positive view on GM technology. However, the European people have stronger trust for consumer organisations, environmental groups, physicians and also scientists. Biotech industry and governments are less trusted.

Regarding the ethical aspects of the use of the GM biosensor two organizations have been identified, which have published a detailed analysis of bioethics including the specific case of GM technology: the Nuffield Council of Bioethics and the Australian Gene Technology Ethics Committee.

There are three important issues in this area. The first is the general welfare of the citizens. Thus, the precautionary principle has to be applied, so that harm to the people and the environment is avoided. The second is the maintenance of people's rights, for example their rights to freedom of choice. The third one is the principle of justice, which requires the burdens and benefits of this new technology to be fairly shared among those who are affected by them. An additional forth issue would be the ethical status of the natural world itself. It has to be decided if GM technology itself is unethical. Some people may perceive GMOs as unnatural or intrinsically wrong.

It further appears that mainstream theology in the three monotheistic religions accepts GM technology as long as environmental and health risks are taken seriously and human benefits are clearly visible.

For the notification of GMOs for the experimental release into the environment the national genetic engineering act in connection with Directive 2001/18/EC – part B applies. As the research work on the GMOs is done in Germany, the German genetic engineering act (GenTG) is relevant. Here the German Federal Office of Consumer Protection and Food Safety (BVL) is responsible as the leading authority for approving the release of GMOs.

If the results of the experimental release are positive, the GMOs can be made available to third parties either free of charge or for a fee ("placing on the market"). The placing on the market of a GMO is governed by the national genetic engineering act and the provisions of part C of Directive 2001/18/EC. The applicants must apply to the competent authority of the EU country, where the GMO is going to be marketed for the first time – i.e. in the case of the biosensor also in Germany. The national authority prepares an assessment report within 90 days. It sends the applications to the European Food Safety Authority (EFSA), if at least one other EU country reasonably objects to the assessment report. After receiving EFSA's opinion, the EU Commission grants or refuses the authorisation. The overall process usually takes 3 to 4 years. Up to know there have been only two product approvals of genetically modified microorganisms for the release to the environment (bacterial and yeast biomass).

If the biosensor is placed on the marked in a country outside the EU the national regulations of this country apply. The information platform of the Biosafety Clearing House contains further information about these non-EU countries. Apart from the placing on the market itself the applicants have to observe the export laws. Hereby regulation (EC) No 1946/2003 on transboundary movement of genetically modified organisms implements the provisions of the Cartagena Protocol on preventing biotechnological risks.

2. INTRODUCTION

The use of highly-sensitive biosensors for the detection of explosives is an emerging technology that exploits the ability of living cells to sense trace amounts of explosive chemicals like TNT and convert this input into visual output signals that can easily be measured.

This forms the basis for high-resolution stand-off detection: in principal one target molecule is sufficient for the production of optical marker proteins, e.g. fluorescent proteins that are produced thousand-folds in each cell and enable the amplification and therefore the detection of trace amounts of explosives.

Bacterial whole-cell biosensors offer the advantage of mapping suspicious areas within significantly shorter time frames of days instead of weeks, because microbial expression systems are faster in producing visual read-out signals than plants.

Within the D-BOX consortium a new approach is pursued in which the common soil bacterium Pseudomonas putida is genetically modified to produce red fluorescent proteins upon recognition of TNT-signatures in liquids or soil. The specific response is achieved by a genetic switch that is activated by TNT or its derivatives and induces the production of fluorescent proteins.

Experiments showed expressions of more than 100,000 fluorescent proteins per cell which leads to a strong optical signal. Laboratory results and field tests using sensor beads revealed a feasible detection range of 10 m for low aperture 20 mm optics and up to 300 m using a 300 mm high aperture LIDAR-system.

A possible drawback of this promising approach is the in many cases low public acceptance of gene technology applications and possible ethical objections as well as the long and complex approval process for the release of a genetically modified biosensor.

Despite the quite large number of research papers about GM applications (especially GM food), until now no research work about the public acceptance and ethical aspects of the use of GM biosensors for the detection of explosives is known.

Thus, the aim of this report is first to analyse the public acceptance and possible ethical objections to the use of a GM biosensor. We further recommend necessary technical and non-technical measurements to increase the public acceptance as well as to meet the ethical concerns. To achieve this aim the following issues are covered in this report

- A desktop research on the public acceptance as well as on ethical aspects of GMOs in general has been performed. The results have been used to draw conclusions for the specific case of the GM biosensor.
- A series of interviews have been performed to learn about the public acceptance and the ethical aspects of the DBOX biosensor. To get a meaningful picture of the public opinion three different groups were interviewed: Environmental and consumer protection NGOs, Governmental institutions and authorities as well as researcher in the area of bioethics.
- The legal aspects of the use of genetically modified biosensors as well as all relevant directives, decisions and regulations have been described. The relevant national and international organisations have also been specified.
- The approval procedure for the experimental release as well as for the placing on the market of the GM biosensor has been explained in detail.

3. INTERVIEWS – PUBLIC ACCEPTANCE OF THE USE OF GMOS FOR BIOSENSING OF EXPLOSIVES

In the literature there is a lot of information available about the public acceptance of GM food and also a little less about GM feed and other GM technologies like medical applications. But we couldn't find any publication about the ethical aspects or the public acceptance of GMOs for the detection of explosives.

In chapter 4, 5 and 6 the results of our desktop research regarding the public acceptance and the ethical aspects of GMOs in general are presented. As far as possible we used these results to draw our own conclusions regarding the public acceptance of the DBOX biosensor.

To complete these conclusions we performed interviews to be able to better assess the specific public acceptance of the DBOX biosensor.

To get a meaningful picture of the public opinion we intended to interview three different groups:

1. **Environmental & Consumer Protection NGOs:** First, it was shown that these organisations get a high level of trust from the population (see chapter 5.3). Additionally in many cases these organizations have been the ones to bring these issues to public attention in the first place.
2. **Governmental institutions and authorities:** These bodies have experience with GMO applications and the reactions of the public.
3. **Researcher in the area of bioethics:** They have a good overview of risks and ethical objections regarding new biotechnologies.

As there might be organizations which can't be clearly assigned into one of the three groups we developed more general conditions for possible interview partners (see chapter 3.1).

In a first step we performed a desktop research on the relevant legal GMO regulations as well as on ethical guidelines and on scientific papers regarding the public acceptance of GMO in general.

On the basis of this work we developed an interview guide to be able to specifically address the public acceptance and the ethical issues of the use of GMOs for the detection of explosives (see Annex 12.3).

3.1 Who was interviewed

As described in the DBOX DOW the interviews were limited to Germany due to budget constraints. This limitation makes sense, because the experimental release of the genetically modified biosensor will most conveniently take place in the home

country of the respective research organisation – i.e. in Germany (see chapter 10). Therefore the first assessment of the technology and the participation of the public will also take place in Germany.

In a first step we performed a desktop research to identify all possible institutions and organisations which might be suitable interview partner for DBOX. To do this we used the following conditions:

The interview partners should

- have a basic knowledge in gene technology (either as a natural scientist or due to his/her experience with ethical aspects in this area)
- be experts in the area of ethics AND/OR
- have a working knowledge in environmental protection & human rights in this area AND/OR
- have experience with the public acceptance of gene technology.

Therefore the number of suitable institutions or organisations was rather limited – overall 16 possible interview partners have been contacted.

It became apparent that it was quite hard to convince members from NGOs to be interviewed by us. There might be several reasons for this reluctance. One reason is that several environmental NGOs only deal with GM food and have no experience with other applications of gene technology. Thus, these organisations couldn't offer a suitable expert as an interview partner.

Another reason is that many environmental NGOs have bad experiences as interview partners with research organisations or industries. They said that they had the feeling that they were used as some sort of ethical stamp for GM projects and that there objections were not really included seriously in the assessment of the specific project.

They also complained that at the time of the interviews there was not much information available about DBOX. All of the already delivered reports got the security classification "restricted", so that we couldn't offer more detailed information to the possible interview partner. They told us that we would offer them "yet another fancy GMO project, which promises the moon" and that at this time of the project we were not able to answer detailed questions about the reliability, side effects and other factors which help to compare this technology with other demining technologies.

We acknowledge the fact that it is easier to speak about the risks and benefits of a new technology when there are already some experimental data available about the behaviour of the GMO in an environment similar to its target environment. On the

other hand we think that it makes more sense to include possible ethical objections to the technology right from the beginning, so that we are able to adapt our research work accordingly.

Many of the governmental institutions contacted were not willing to be interviewed by us. We can't offer an explanation for their refusals, because we simply didn't get an answer to our repeated requests. But we assume that there is no specific reason for this behaviour - a part from a high work load. However, most of the researchers contacted were very cooperative and agreed to be interviewed by us.

The organisations and institutions which we interviewed are listed in Table 1. We would like to thank all of our interview partners for openly sharing their experience with us and above all for the pleasant atmosphere they created.

Institute for Church and Society (Protestant Church)	Church	Interview
Office of Technology Assessment at the German Bundestag	Governmental	Interview
Greenpeace	NGO	Interview
University Hamburg (Islam studies)	Research	Interview
German Reference Centre for Ethics in the Life Sciences (DRZE)	Research	Interview
Ludwig Maximilian University Munich (Technology - Theology - Natural Sciences Institute)	Research	Interview
Julius Kühn-Institut (Federal Research Centre for Cultivated Plants)	Governmental/ Research	Interview
Federal Institute for Risk Assessment (BfR)	Governmental	Written statement

Table 1: List of interview partners.

Formally we proceeded as follows: We sent the possible interview partners an information sheet for volunteer participants as well as a consent form explaining our data protection measurements (see Annex 12.1 and 12.2). If they agreed to participate we asked them to sign the consent form and to send us the signed copy per mail or Email. Of course we also asked them if they needed any further clarification regarding our procedure or if they had any other questions about DBOX.

3.2 Results

First, we want to make it clear, that some of the statements of the interview partner are facts and others are personal opinions. These opinions sometimes differ between the interview partners and do not necessarily represent the opinion of the consortium.

In our first question we asked the interview partners about their general attitude towards a GM biosensor for the detection of explosives. They were asked to express their overall personal opinion without giving a detailed analysis of the pros and cons of the biosensor. Three of the interview partners see the DBOX biosensor as generally positive (subject to future findings); two see it as negative and three think that the actual data do not suffice to form an opinion.

Risks and drawbacks of the biosensor

In our second questions we asked for specific risks and drawbacks regarding the use of GMOs for the detection of explosives.

A first risk is seen in a possible negative impact on the ecosystem. Several interview partners see the release of the biosensor as a contamination of the local ecosystem. A mayor issue is seen in the non-reversibility of the release. At the moment it can't be predicted if the GM biosensor will colonise in the local ecosystem and how a possible damage scenario might look like.

Especially the risk of a possible gene transfer to other local organisms is seen as a critical factor. One interviewee said that the biosensor might transfer the property "fluorescence", but he doesn't think that this property will increase the fitness of the recipient. Particularly fatal might be a possible transfer of the genes responsible for the antibiotic resistance of the biosensor. It was mentioned that the antibiotic resistance of the biosensor might be the critical factor for the approval of the experimental release.

Another risk is seen in the properties of the original bacteria Pseudomonas putida. It was mentioned that P. putida has emerged as an occasional bacterial pathogen and that it also causes soft tissue infections in fish. Therefore it was suggested to use another harmless bacterium for the biosensor.

One interviewee is concerned about the sensitivity and/or the specificity of the biochemical reaction. If the biosensor would deliver false positive or negative results, this would be a serious issue, even a legal issue in the second case. Another open question is, if the biosensor system is sufficiently robust and suitable for the use in the field.

Another interviewee mentioned that in this area we also have to think of environmental ethics. We have to ask if it is morally acceptable to exploit the bacteria for our purposes, i.e. we have to see the "point of view" of the bacteria. On the other hand, the same argument would have to be applied for any form of agriculture or keeping of animals.

Other aspects which have to be taken into account are the principles of social and economic ethics. In this area we have to ask who is taking the decisions, who is affected and who will insure the possible damages.

In general the ethical assessment of this technology is viewed as difficult. On the one hand the precautionary principle applies. This principle implies that there is a social responsibility to protect the public and the environment from exposure to harm, when a scientific investigation has found a plausible risk. Thus the biosensor should be released only if further scientific findings emerge that provide evidence that no harm will result. On the other hand there are arguments, that we shouldn't deprive the population of new technologies and better demining processes.

It was mentioned that there is little the Islamic law would object in the area gene technology. In general gene technology is not seen as a problem. The interviewee doesn't believe that there might be arguments that the released GM bacteria could enter the food chain.

Nevertheless in Islamic countries there might be objections to the project. Not because of the genetic modifications of the bacteria, but because they wouldn't like to see western personnel with western technology to come into their country. It was suggested to involve the local religious leaders into the demining process that again would increase the acceptance of the local population. In general he sees transparency, public relations and the involvement of religious leaders as key to the success of the project.

An important issue for several interviewees is the comparison of the biosensor system with alternative demining technologies. They said that it would be important to know the specific characteristics of all the demining technologies (like reliability, safety, velocity, costs, etc.) before taking a decision pro or contra the biosensor system.

Possible technical measurements to reduce the risks of the biosensor

Some interview partners suggested using bacteria with suicide genes, to achieve that the bacteria - after they have fulfilled their purposes - die off rapidly. Other interview partners said that even with suicide genes the risk of a possible gene transfer to other organism persists.

It was also suggested to use $RecA^-$ mutants. Without the RecA protein the bacteria are not able to repair damages to their DNA after the exposure to UV light. Thus, in the open sunlight the $RecA^-$ mutants will die off faster.

A third suggestion was to use auxotrophic bacteria. If the biosensor is auxotrophic for a specific essential amino acid, then the biosensor will only be able to grow if this amino acid will be added to its growth medium. Otherwise the biosensor will die off.

Another way would be to use transient gene expression. Transient gene expression means a temporary expression of a gene by the non-permanent presence of a foreign gene. The interview partner said that in the US there are promising research projects with agrobacteria which use this technique.

Furthermore it was suggested to embed the modified gene into a sequence which usually isn't found in other bacteria. This way a gene transfer to other bacteria in the environment would be less likely.

In general it was said that an antibiotic resistance of the biosensor would be most problematic and that it is highly recommended to find a way around it.

Further ethical conditions for the use of GM biosensors

Several interviewees think that an involvement of the local people is very important. The local stakeholder should be informed about the advantages and risks of this method, so that the population is able to make an informed choice pro or contra the use of the GM biosensor.

In many cases the biosafety regulations in countries outside the EU will be less restrictive. The interviewees advised to apply in these countries the same level of biosafety standards and ethical norms like inside the EU.

Many interview partners believe that the application of the experimental release of the biosensor will be very difficult. This year there has been only one approval of release of a genetically modified microorganism – a live bacterial vaccine against an equine disease (in the stud farm of Paul Schockemöhle).

Although the EU law is very restrictive in this area, there are still voices who are not comfortable with the approvals. In general they are not opposed to the regulations themselves, but more to the implementation of the directives and decisions and to the organisations/persons involved in the assessments.

4. PUBLIC ACCEPTANCE OF GMOS IN GENERAL– STATISTICAL DATA

According to the latest Eurobarometer on biotechnology the Europeans do not see benefits of genetically modified food and consider genetically modified foods to be probably unsafe or even harmful. They also do not see the benefits of horizontal gene transfer[1], have strong reservations about its safety and do not feel that it should be encouraged. On the other side the Europeans accept the potential benefits of vertical gene transfer[2], although they have some reservations about safety and the potential impact on the environment. They approve of human gene therapy, but think that strict laws are needed to alleviate the concern about ethical issues.(TNS Opinion & Social, 2010)

In the following the statistical results regarding the public acceptance of gene technology are described in more detail.

4.1 GM food

A large majority of Europeans, 84% at EU27 level, have heard of genetically modified foods. In the Eurobarometer survey the attitude of respondents towards genetically modified (GM) foods was examined by asking respondents whether they agree or disagree with a series of statements. The survey reveals an overall suspicion of GM foods amongst the European public (see Figure 1).(TNS Opinion & Social, 2010)

[1] Horizontal gene transfer is a process in which an organism incorporates genetic material from another organism without being the offspring of that organism.
[2] Vertical gene transfer is a process in which an organism receives genetic material from its ancestor for example a parent or the species from which it was evolved.

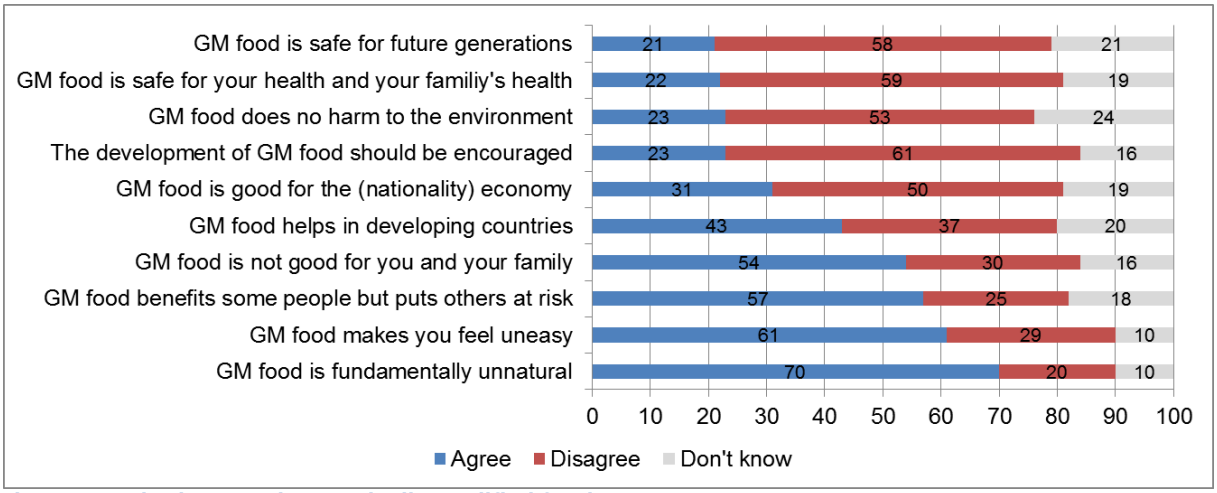

Figure 1: Attitude towards genetically modified foods. (TNS Opinion & Social, 2010)

4.2 Horizontal gene transfer

When an organism receives genetic material from another, this is called gene transfer. This gene transfer can be divided into two types. Firstly, there is horizontal gene transfer a process in which an organism incorporates genetic material from another, unrelated organism. In the second form - vertical gene transfer - an organism receives genetic material from a related organism, or ancestor.(TNS Opinion & Social, 2010)

In the Eurobarometer survey respondents' awareness and attitude towards horizontal gene transfer is examined by using the example of the artificial introduction of a resistance gene from another species, such as a bacterium or animal, into an apple tree to make it resistant to mildew and scab. Respondents were asked if they agreed or disagreed with a number of statements (see Figure 2).(TNS Opinion & Social, 2010)

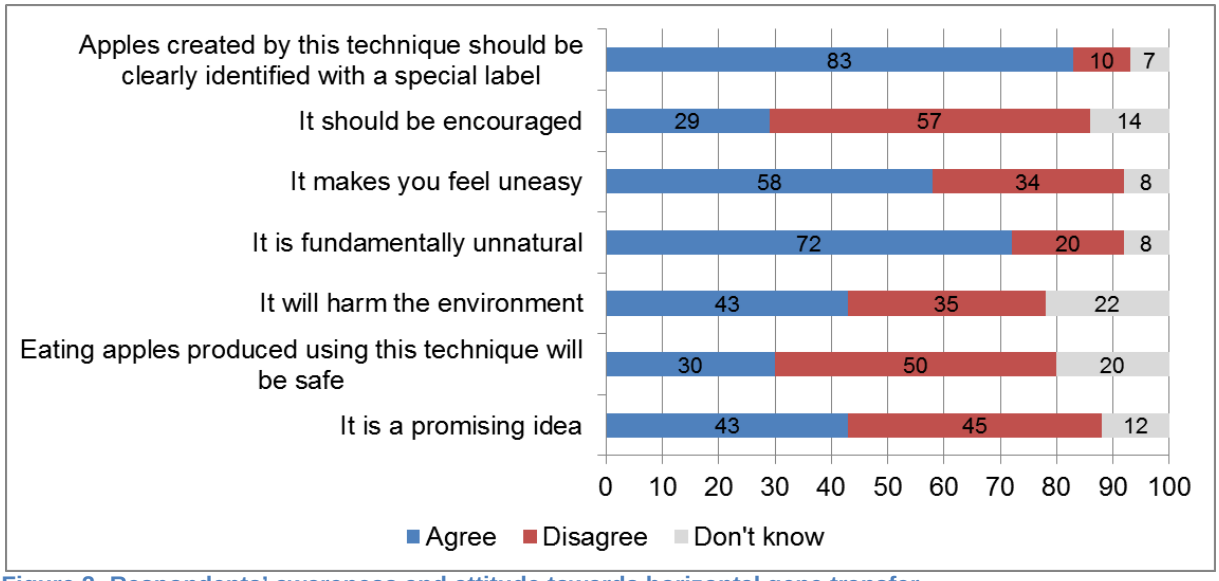

Figure 2: Respondents' awareness and attitude towards horizontal gene transfer. (TNS Opinion & Social, 2010)

4.3 Vertical gene transfer

To examine the awareness and attitudes towards vertical gene transfer the Eurobarometer survey used the example of artificially introducing a gene that exists naturally in wild / crab apples which provides resistance to mildew and scab. Respondents were asked if they agree or disagree with a number of statements (see Figure 3).(TNS Opinion & Social, 2010)

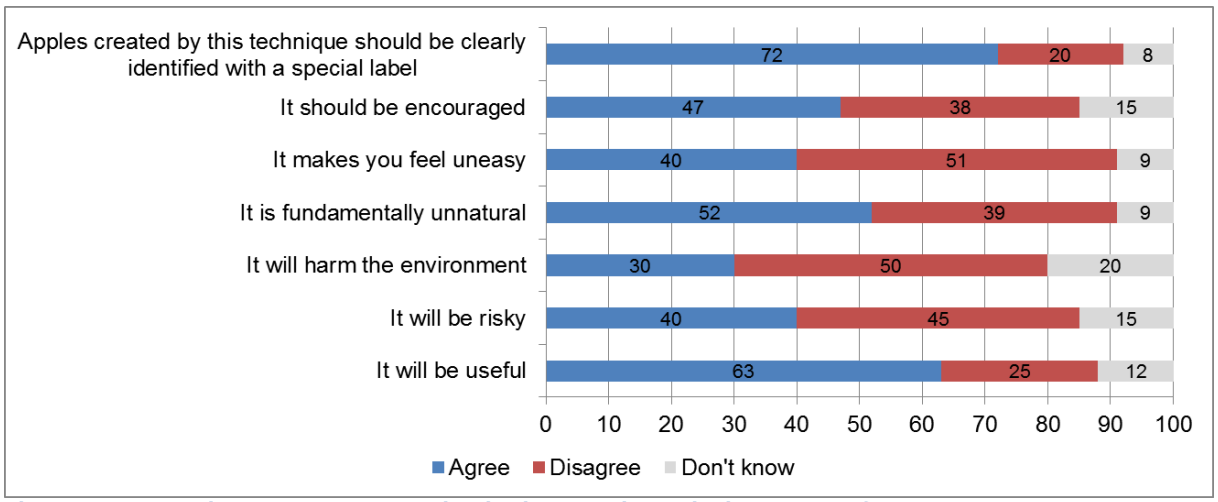

Figure 3: Respondents' awareness and attitude towards vertical gene transfer. (TNS Opinion & Social, 2010)

4.4 Gene therapy

The Eurobarometer survey reveals that 63% of the Europeans approve of research involving human gene therapy. The respondents were asked if they approve of gene therapy which involves treating inherited diseases by intervening directly in the human genes themselves (see Figure 4).(TNS Opinion & Social, 2010)

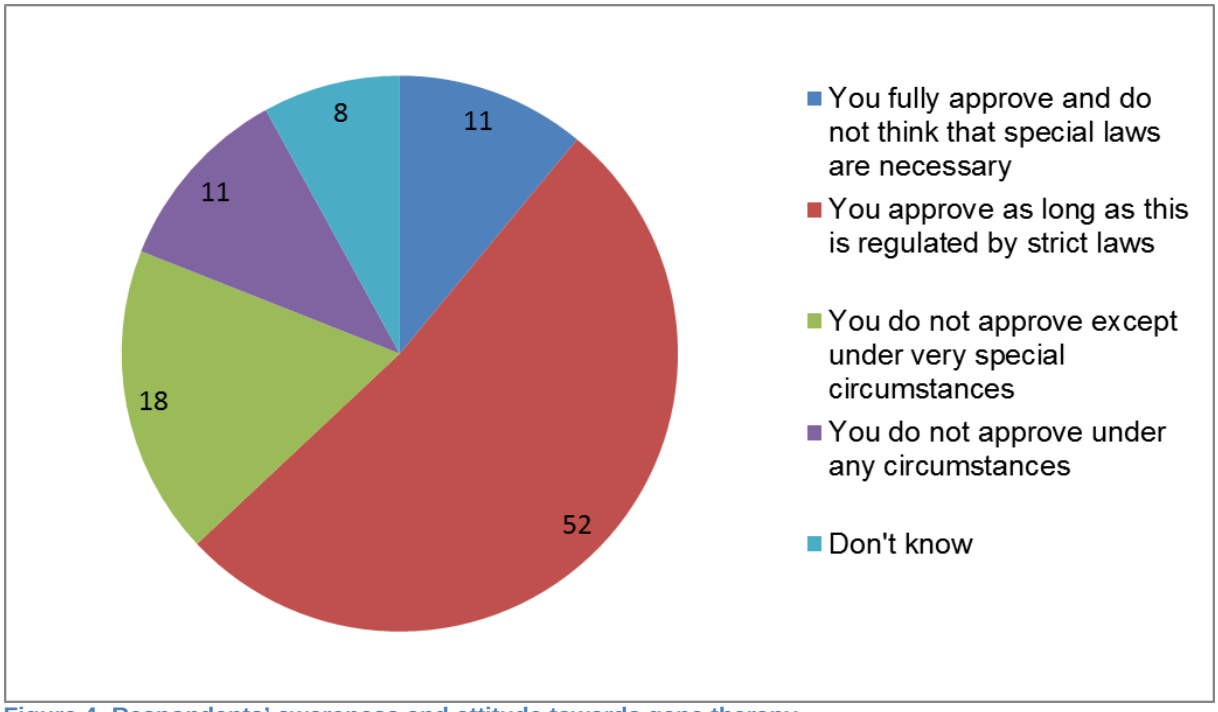

Figure 4: Respondents' awareness and attitude towards gene therapy. (TNS Opinion & Social, 2010)

5. PUBLIC ACCEPTANCE OF GMOS IN GENERAL - EXPLANATIONS

Public attitudes are considered an important factor influencing both the use of GM technology and its development. A survey of the European Parliamentary Technology Assessment with 71 experts showed that a majority of experts expect public attitudes concerning future GM non-food products to become more positive over the next 10–15 years, while the level of acceptance of GM food products will remain unchanged (see Figure 5). (European Parliamentary Technology Assessment, 2009)

Non-food products may find more acceptance, as health issues are less sensitive, and new products may be associated with clear advantages. In particular, GM plants for medicines received support because of the importance of the product, in contrast to ornamental flowers.(European Parliamentary Technology Assessment, 2009)

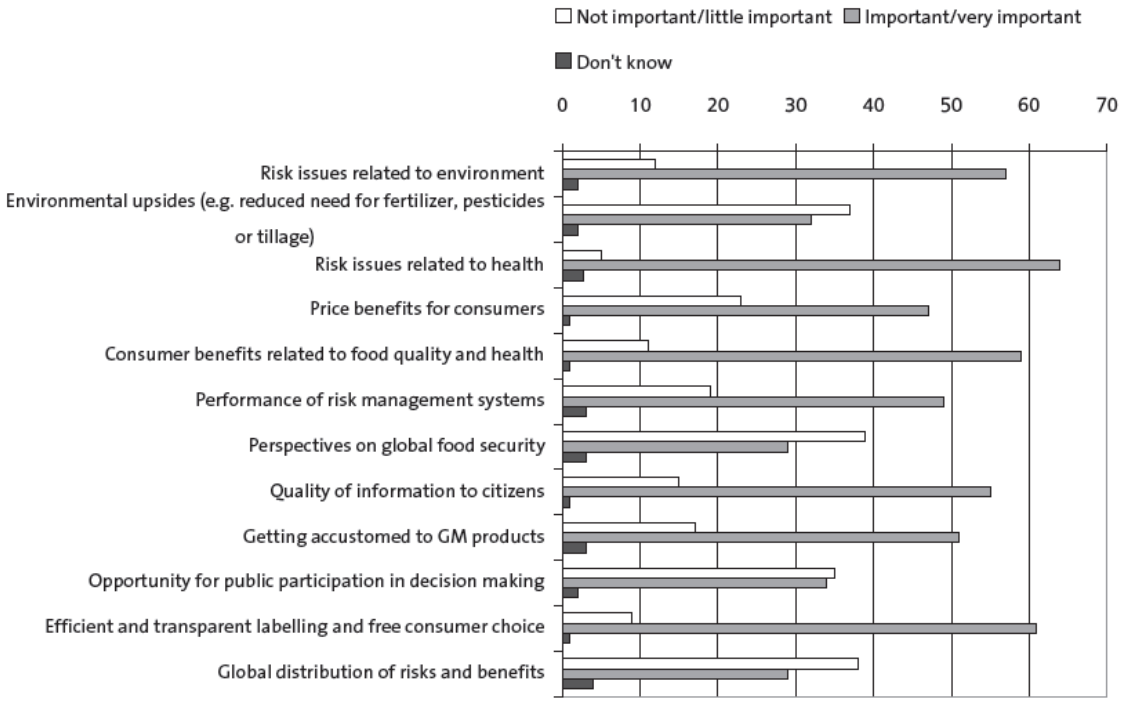

Figure 5: Factors influencing public attitude concerning GM plants and food (Survey of the European Parliamentary Technology Assessment with 71 experts, European Parliamentary Technology Assessment, 2009).

It was also shown that medical applications were perceived to be more beneficial, less risky, and more ethically correct than food applications.(Frewer et al., 1995)

5.1 Risks

When talking about GM technology most opponents tend to mention risks – risks to the health of the population, to the environment and on a more general level the negative social and economic effects of the application of this technology. In the following the risks are described in more detail.

5.1.1 HEALTH

When releasing GM material, there is always a risk of contaminating non-GM plants and organisms. This is seen as a “loss of control”; because once GM material is released there may be no turning back. This contamination may lead to the development of new microbial strains that might be pathogenic. (Rastogi Verma, 2013; Lyndhurst, 2009)

A serious risk is the possible transfer of the antibiotic resistance marker genes[3] of the biosensor to pathogens in the environment transforming them into strains that are resistant to antibiotic therapy.(Rastogi Verma, 2013; Food and agriculture organization of the United Nations, 2003)

Another distressing problems with non-traditional proteins in GMOs is the risk of introducing allergens (usually glycoproteins) into the food supply of humans and animals.(Rastogi Verma, 2013; Kaeppler, 2000) In the case of DBOX this risk should be quite small. Allergens might pose a problem in GM food, but the fluorescent proteins of the biosensor could only enter the food chain via animals. The enrichment of these proteins in local animals should be quite small.

Another finding of research is that, although the public is concerned with the outcomes of technical risk assessments, they are also concerned about the uncertainty related to these outcomes, suspecting that risk assessments are based on an insufficient level of scientific knowledge.(Lassen et al., 2002; Gaskell et al., 2001) Consequently, the risk assessments currently conducted may especially not

[3] **Antibiotic resistance marker gene:** The techniques used for transferring a new gene into a plant are rather inefficient. Very few cells actually take up the gene of interest. In order to find the cells that have been successfully transformed, some kind of marker is needed.

To do this, the gene that will give the plant its new trait (gene of interest) is coupled with a marker gene. Plant cells are then transformed with both genes simultaneously. The vast majority of these marker genes work by giving genetically modified cells the ability to break down a poisonous substance.

Plant cells expressing an antibiotic resistance marker gene (ABR gene) are thus not harmed by that antibiotic. Treating the cells after the gene transfer with an antibiotic allows only the successfully transformed cells to survive. These cells also possess the gene of interest.

Although the marker gene serves no purpose after this procedure, it remains part of the genetically modified plant. Removing a marker gene from an existing transgenic plant is virtually impossible.GMO Compass, 2006

be able to address long term effects of genetically modified foods. (Frewer et al., 2004) and cited herein

Developing countries face additional difficulties in assessing the risks of these technologies because the technological knowledge related to them often forms part of the exclusive intellectual property of corporations in developed countries.(Food and agriculture organization of the United Nations, 2001b)

5.1.2 ENVIRONMENTAL

The unicellular nature and relative simplicity of microorganisms in general means that they are able to multiply very rapidly. Furthermore, bacteria demonstrate an extreme genetic adaptability due to the fact that they are haploid[4] and to the fact that they may acquire genes from other microorganisms (horizontal transfers[1]).(Gautier, 2008)

The danger posed by these genetically modified organisms is therefore related to their potential for adaptation to a new environment. In so doing their development may alter the animal and plant microbial ecological balance.(Gautier, 2008; Food and agriculture organization of the United Nations, 2001a)

Microorganisms are capable of acquiring new genes from other living microorganisms or microbial corpses in the natural environment. There are three main types of mechanism for gene transfer between microorganisms:(Gautier, 2008)

- **Conjugation** is a form of gene transfer between two bacterial cells.
- **Transformation** is a mechanism which allows some bacteria to acquire exogenous DNA[5] and to integrate it into its genome.
- **Transduction** is the transfer of bacterial DNA to other bacteria by a bacteriophage, a virus specific to bacteria.

These gene transfer mechanisms may allow microorganisms to acquire new properties. This means that a genetically modified microorganism has the potential to transfer, whether dead or alive, genes which have been modified in laboratories. Gene transfers between microorganisms and so-called “superior” organisms are less well-known, but nonetheless probably take place.(Gautier, 2008)

On the other hand we have to take into account, that there are various bacterial mechanisms which are capable of damaging foreign DNA which enters into the bacteria, making the bacteria unable to incorporate the foreign DNA. (Gautier, 2008)

[4] they only contain one chromosome, meaning that any mutation is clearly expressed.
[5] DNA from dead and lysated cells which circulates freely in the natural environment.

Furthermore, the process of gene transfer between microorganisms as described above does not allow gene flow between all species: some transfers may be limited to certain strains within a species, others take place between closely-related species or, more rarely, between phylogenetically distant species, and a small number occur between different bacterial genera.(Gautier, 2008)

However, the public is worried about the risk that GMOs can spread through nature and interbreed with natural organisms, thereby contaminating “non-GM” environments. In the end this could in turn affect future generations in an unforeseeable and uncontrollable way.(Rastogi Verma, 2013; James et al., 1998)

It is also speculated that random gene insertion, transgene instability and genomic disruption due to gene transfer may result in unpredictable gene expressions.(Rastogi Verma, 2013)

It is not yet known whether artificial insertion of genes could destabilize an organism, encouraging mutations, or whether the inserted gene itself will keep stable over generations.(Food and agriculture organization of the United Nations, 2003)

"Sleeper" genes could be accidentally switched on and active genes could become "silent": Organisms contain genes that are activated under certain conditions -- for example, under attack from pathogens or severe weather. When a new gene is inserted, a "promoter" gene is also inserted to switch it on. This could activate a "sleeper" gene in inappropriate circumstances. Sometimes the expression of genes is even "silenced" as a result of unknown interactions with the inserted gene. However, this is especially relevant in long-lived organisms (such as trees) and might not be relevant for microorganisms used for DBOX. (Food and agriculture organization of the United Nations, 2003)

To put it in perspective, it should be added that “laboratory creatures” have a tendency to lose their capacity to colonise an environment or even to survive in their natural habitat. Several experiments have demonstrated that once the model strains which are used in laboratories are removed from their test tubes, they have very little chance of surviving in their natural habitat. Nevertheless, these microorganisms, even if unable to survive in their natural habitat, are able, on their death and subsequent cellular lysis, to release DNA which may be captured by other microorganisms.(Gautier, 2008)

In DBOX we are using the bacteria Pseudomonas putida (P. putida) for the development of the biosensor. Apart from the health and environmental risks due to the genetic manipulation we also have to consider the risks related to the original organism.

P. putida is a common inhabitant of soil, water and plants, but is also frequently isolated from the hospital environment. There P. putida has emerged as an

occasional bacterial pathogen in immunocompromised patients.(Anaissie et al., 1987) But there were also some reports of diseases due to P. putida in immunocompetent patients (like e.g. meningitis (Toru et al., 2008), bacteremia (Chen et al., 2005) and wound infection (Carpenter et al., 2008)). Additionally it was reported that P. putida causes soft tissue infections in fish.(Altinok et al., 2006).

The German Central Committee on Biological Safety (ZKBS) therefore classifies P. putida as a donor and recipient organisms for genetic engineering operations in risk group 2.[6] (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL), 2012)

5.1.3 SOCIOECONOMIC

The Food and Agriculture Organization of the United Nations stated in their ethics series that one of the important human rights principles that could bear upon GMOs, (although not included in the Universal Declaration of Human Rights) are the rights to informed choice and to democratic participation.(Food and agriculture organization of the United Nations, 2001a)

The right to democratic participation addresses the need for justice and equity, which are of major concern in the context of GMO-related decisions. Many young people, particularly the poor and powerless, have little education and no social entry point to influence decisions about GMOs.(Food and agriculture organization of the United Nations, 2001a)

This implies that before the DBOX biosensor is used for a local demining process, the local population has to be informed about the benefits and risks of the GM biosensor, so that they are able to take an informed decision about the future of their arable land.

5.2 Benefits

The public acceptance of GMOs is not only based on perceived risks and concerns, but also on the perception of the benefits of the technology. One of the clearest illustrations of the interaction of risk/benefit perceptions are the public's attitudes to different applications of GM technology. For example, the Eurobarometer (Gaskell et al., 2006) shows that EU consumers have an overall positive view of medical applications of GM technology: despite viewing it as risky, they are strongly aware of the potential benefits, which leads to an overall evaluation that medical applications are morally acceptable and should be encouraged. In comparison, uncertainty about

[6] There are 4 risk groups – from 1 (lowest risk) to 4 (highest risk).Bundesministerium der Justiz, 1990 P. putida mt-2 KT2440 with the vectors pKT262, pKT263 und pKT264 belongs to risk group 1.

the benefits and usefulness of food applications mean that, for the majority, the risks outweigh the benefits.(Lyndhurst, 2009; Gaskell et al., 2006; Blaine et al., 2002)

Instead of rejecting gene technology as such, it appears that most people base their assessment on judgements about the means and the end of each specific application.(Pardo et al., 2002) What matters here are not just the risks and benefits viewed in isolation, but the risk–benefit balance. Benefits that are seen as crucial will often offset risk perceptions.(Frewer et al., 1997; Gaskell et al., 2000)

The perceived risk-benefit balance not only varies with the specific application of gene technology, but also with the country in which the survey has been carried out. Taking GM food as an example: in most European countries, and specifically in Nordic countries, Britain, and Germany, consumers find benefits associated to GM food as insufficient to overcome their associated (perceived) risk. On the other hand, in the US and also in some European countries, such as Spain and Italy, consumers mainly reveal perceptions of risks and benefits associated with GM food, where benefits can potentially outweigh risks.(Costa-Font et al., 2008)

When talking about DBOX, the advantage of this technology is quite obvious: to provide the operators and end-users with a cheap and “easy to use” tool for the demining process.

One advantage of this technology is the low cost. Bacteria can be grown easily and without great expense: They need only a solution of sugar and some inexpensive chemicals. The cost of the technique can be considered very affordable—even for developing nations.(Burlage, 2003)

Another advantage is the tolerance of vegetation. Many techniques for mine clearance are adversely affected by the presence of vegetation. The biosensor system is actually improved by the presence of vegetation, which appears to conduct the explosives and magnify the signal. The biosensor system may be a good system for many areas of the world where removal of vegetation would have adverse environmental consequences.(Burlage, 2003)

Furthermore, the biosensor system will not be affected by stray bits of metal, because the technique only detects the presence of the explosive chemicals and not the ordnance package. According to (Burlage, 2003) this system will also find a raw explosive that is buried or find discarded ammunition that has been forgotten.

Burlage also stated that there will be little clean-up afterward, as the bacteria die off rather quickly and actually serve as a fertilizer for the soil.(Burlage, 2003)

When we add up all the benefits of the biosensor, it could be expected that the public acceptance of the GM biosensor might be similarly high as the public acceptance of medical applications.

5.1 Moral concerns

Analyses of surveys have shown that, regardless of considerations of risk or personal benefit, if someone has moral objections to genetic modification this acts as a "veto".(Gaskell et al., 2006)

This finding that risk is less significant than moral acceptability in shaping public perceptions of biotechnology holds true in each EU country and across all six specific applications of biotechnology in the survey[7].(Gaskell, et.al., 1997)

Such objections can be directed, for example, towards the perceived role of GMOs as "tinkering with life", which would collide with a certain understanding of nature.(European Parliamentary Technology Assessment, 2009)

Other people think that the human species has no right to use GM technology to dominate and alter the course of nature and make irreversible changes in the world environment for future generations.(Lyndhurst, 2009)

This perceived unnaturalness could be an important factor influencing the acceptance of gene technology. (Mielby et al., 2013; Siegrist, 2008) People may perceive genetic modification as unnatural, and consequently, they may have moral and ethical concerns that influence their perception of gene technology.(Bredahl, 1999; Miles et al., 2005)

Additionally to this perceived unnaturalness ethical concerns based in religious faith are (especially in the USA) a common barrier to acceptability of biotechnology. (Lyndhurst, 2009) and cited herein

5.2 Level of education

General attitudes to science and technology are found by several studies to be the strongest predictor of attitudes to GM technology.(Traill et al., 2004; Lyndhurst, 2009) and cited herein

[7] 1 - Genetic testing, using genetic tests to detect inheritable diseases such as cystic fibrosis. 2 - Medicines, introducing human genes into bacteria to produce medicines or vaccines, for example to produce insulin for diabetics. 3 - Crop plants,transferring genes from plant species into crop plants to increase resistance to insect pests. 4 – Food production, using modern biotechnology in the production of foods, for example to make them higher in protein, keep longer or change in taste. 5 - Research animals, developing genetically modified animals for laboratory research studies, such as a mouse with genes that cause it to develop cancer. 6 - Xenotransplants, introducing human genes into animals to produce organs for human transplants, such as into pigs for heart transplants into humans.Gaskell, et.al., 1997

For most adults, a sense of technological optimism or a general belief in the promise of biotechnology will precede attitudes toward a specific application of biotechnology and may become a filter for the reception and processing of new information on the subject. This model suggests that new information from a newspaper or a television broadcast is unlikely to change or reverse prior attitudes, but new information is added to the existing schema of information and experiences related to the subject. Over time, a flow of new information may either reinforce or erode a previously held position, but it is unlikely to do so quickly.(Pardo et al., 2002)

(Traill et al., 2004) reported that a high level of education is positively associated with benefit perceptions and negatively associated with moral concerns.

Others also have shown that people with a higher level of educational achievement hold more positive attitudes toward genetic modification than people with a lower level of education.(Gaskell, 1998; Hoban, 1998) Higher educational achievement is often seen to be related to better knowledge about a certain issue, and owing to this, more highly knowledgeable people are more likely to accept gene technology than people with a lower level of education and corresponding lower level of knowledge.

On the other hand (Verdurme et al., 2003) did not find a relationship between educational achievement and attitudes toward genetically modified foods.(Connor et al., 2011)

5.3 Knowledge of gene technology

The correlation between knowledge and attitudes has been the source of controversy in research on the public understanding of science. Although many studies, both quantitative and qualitative, have examined this issue, the results are at best diverse and at worst contradictory. (Allum et al., 2008) found a small positive correlation between general attitudes towards science and general knowledge of scientific facts. However, this general relationship varies substantially between different domains of science and technology; e.g. he reported that the correlation between general knowledge and attitudes to GM food is practically zero.

The Eurobarometer (Gaskell et al., 2006) also found no difference in levels of support between those claiming to be familiar with GM and those who were unfamiliar, although those with better understanding were slightly more likely to judge GM to be morally acceptable. Similarly, (Traill et al., 2004) found that perceived knowledge is consistently insignificant as a driver of attitudes.

An analysis of an earlier version of the Eurobarometer also showed that knowledge is poorly correlated with support for all the applications of biotechnology. They concluded that more knowledge does not necessarily lead to greater public acceptance (which was already discovered by other industries trying to introduce

controversial technologies such as the nuclear industry). But the situation with respect to biotechnology is more complex. The survey suggests that people with greater knowledge are more likely to express a definite opinion about biotechnology; but this opinion can be positive or negative. (Gaskell, et.al., 1997)

Other researchers found a positive relationship between scientific knowledge and a positive attitude towards GM technology. For example, (Ceccoli et al., 2012) showed that support for GM foods is positively associated with scientific literacy. They also found that media exposure matters; specifically, frequent reading about science and the importance of the Internet as a source of information about science are positively associated with support for GM foods.

(Costa-Font et al., 2008) even concluded that knowledge has been categorized as a singular human attribute that noticeably enhances the likelihood of GM food acceptance, especially when objective rather than perceived knowledge is examined. They therefore recommended that policy makers should guarantee the dissemination of GM scientific knowledge in order to assure a high level of objective knowledge among their base population.

Other researchers found an U-shaped relationship between knowledge and attitudes Hereby both supporters as well as opponents have been shown to possess higher levels of knowledge compared with people having neutral attitudes.(Christoph et al., 2008; Connor et al., 2011)

(Connor et al., 2011) showed that on the one hand basic biological knowledge has a significant but very small impact on people's risk and benefit perception of gene technology. On the other hand, specific knowledge about gene technology has a small negative impact on people's risk perception of nonmedical applications. Based on their results, they had serious doubts as to whether educating the public about gene technology or gene technology modules in biology teaching would result in higher levels of acceptance of this technology.

Similarly (Mielby et al., 2013) found that people who achieved a higher knowledge score were more likely to condition their acceptance of a GM application on its purpose. One interpretation of this is that with differences in the perceived balance of risk and benefit, scientific literacy plays a greater role, whereas perceived differences in naturalness are more important in the absence of a basic knowledge of biology and genetics.

5.4 Trust and confidence

One factor that has emerged as being of great importance in understanding public acceptance of genetically modified foods has been that of trust, whether in regulatory institutions and the motives of scientists, or in information about the risks

and benefits of particular technological applications of science and technology.(Frewer et al., 2004)

When people have limited knowledge about a certain technology, they have to rely on social trust to assess the risks and benefits of that technology.(Siegrist et al., 2000) It was observed that those who trust government and the food industry tend to think GM technology is less risky, whereas those who trust activists believe the opposite.(Traill et al., 2004)

Based on Eurobarometer data it was also concluded that for all three groups of biotechnologies discussed (medical, agricultural/food, and animal experiments), people who express trust in public authorities tend also to have a systematically more positive view: they are more likely to say that biotechnology should be encouraged; to regard it as morally acceptable; and to view it as less risky.(Gaskell, et.al., 1997)

In fact, worldwide consumers have stronger trust for sources of information that are supposed to be driven towards the protection of individuals' wellbeing and environmental rights. This is the case of consumer organisations, environmental groups, physicians and also scientists. In contrast, biotech industry and governments are less trusted.(Costa-Font et al., 2008)

Individuals seem to more strongly accept the risks reported by environmentalists than the benefits reported by industry and government. As (Traill et al., 2004) stated, the majority of respondents see GM in food production as having a 'middle risk level' since 'government and industry trust implies counterbalancing perceptions of GM benefits, and trust in environmental groups more risk perception'.

On average, more Europeans preferred international organizations such as the United Nations and the World Health Organisation to either their own national or pan-European public bodies. Self-regulation by scientific organizations also rated highly.(Gaskell, et.al., 1997) According to the most recent Eurobarometer the Europeans think that medical professionals and university academics are the best advisers for issues concerning biotechnology.(TNS Opinion & Social, 2010)

One potential reason for the lack of trust in institutions and institutional activities is that the public perceive that institutions have failed to take account of the actual concerns of the public as part of their risk management activities.(Frewer et al., 2004)

There are links to voices criticising the way food scandals (like the BSE scandal) have been dealt with and how expert committees and regulatory bodies have failed to provide and act upon expertise, independent of special interests. Accordingly, the perceived lack of accountability has contributed to a reluctance to accept

reassurance from experts that there is no risk.(Marris et al., 2001; European Parliamentary Technology Assessment, 2009)

It was also reported that there is an important trust divergence among Europeans and Americans, since the last ones reveal more reliance on the FDA than Europeans on either the EU or the worldwide biotech technology.(Costa-Font et al., 2008)

In another survey the importance of understandable, down-to-earth communication about GM plants was identified, although it was emphasised that the social acceptability of GM plants does not only depend on the level of information. In other words, more information does not necessarily mean more people will accept the technology.(European Parliamentary Technology Assessment, 2009; Flemish Institute for Science and Technology Assessment, 2003; Biosafety Interdisciplinary Network et al., 2003)

In a large experimental study involving consumer samples from Denmark, Germany, Italy, and the UK, (Scholderer et al., 2003) tested the effects of different information strategies on consumers' attitudes to genetically modified foods. None of the information strategies resulted in attitude change. This was true of ''balanced'' information about food biotechnology in general, information about the risks and benefits of specific products, and different advertising formats promoting a ''hard sell'' approach. In all cases, consumer attitudes proved remarkably resistant to change.(Frewer et al., 2004)

(Frewer et al., 2004) concluded that institutional transparency, coupled with the integration of public concerns into policy development and implementation, should facilitate the introduction of emerging technologies and their applications.

6. ETHICAL ASPECTS OF THE USE OF GMOS

They are not many national or international organisations who publish information or guidelines about ethical aspects of GMOs. Either the statements are of a very general nature like the corresponding article in the UNESCO Universal Declaration on Bioethics and Human Rights (see Figure 6) or they are integrated in national or international directives and agreements (e.g. the regulations of GMOs in Germany, see chapter 7 or in the European Union, see chapter 8, or the Cartagena Protocol, see chapter 8.4). For an overview about bioethics legislation in different countries see: (The Library of Congress, 2012)

UNESCO - Universal Declaration on Bioethics and Human Rights (2006):

Article 17 “Protection of the environment, the biosphere and biodiversity”: Due regard is to be given to the interconnection between human beings and other forms of life, to the importance of appropriate access and utilization of biological and genetic resources, to respect for traditional knowledge and to the role of human beings in the protection of the environment, the biosphere and biodiversity.(United Nations Educational, Scientific and Cultural Organization, 2006)

Figure 6: Quotation from the Universal Declaration on Bioethics and Human Rights. (United Nations Educational, Scientific and Cultural Organization, 2006)

There are, however, some organisations who published detailed analyses and guidelines about bioethics in connection with GM technologies, like the Nuffield Council on Bioethics or the Australian Gene Technology Ethics Committee. In the following we captured the main ideas of the publications of these two committees as far as they are relevant for DBOX.

Ethics is concerned with what we ought or ought not to do. Ethical principles provide standards for the evaluation of policies or practices, for example, indicating that it would be wrong to carry out a certain genetic modification because to do so would threaten human health or harm the environment.(Nuffield Council on Bioethics, 1999) Thus decisions about gene technology require those involved to assess the ethical consequences of their actions. (Gene Technology Ethics Committee, 2006)

There are three main types of principle that are relevant to the evaluation of policies or practices regarding the introduction of a new technology like GM. The first principle is a principle of general welfare which enjoins governments to promote and

protect the interests of citizens. The second is the maintenance of people's rights, for example their rights to freedom of choice as consumers. The third is the principle of justice, and it requires the burdens and benefits of policies and practices to be fairly shared among those who are affected by them.(Nuffield Council on Bioethics, 1999)

Apart from these three main types of principles there is a fourth issue, namely the ethical status of the natural world itself. Some perceive GM crops as "unnatural" or they have the feeling that we "tinker" with nature. Others argue that it is unethical to treat nature in an industrial fashion, not simply because of the unfortunate consequences of so doing, but because they believe it is intrinsically wrong. On a more general level the question why GMOs transgress natural boundaries has been explored by anthropologists. Some anthropologists refer to the concept of GM pollution, as it seems that all cultures have some conception of pollution – of "things in the wrong place".(Nuffield Council on Bioethics, 1999)

Furthermore, the environment is of great objective value, and humans have legal and ethical duties to protect, conserve and preserve organisms, species, natural ecosystems, natural and physical resources, and the qualities and characteristics of locations, places and areas, both on local and global levels.(Gene Technology Ethics Committee, 2006)

Welfare of citizens

Endangering the health or safety of other people is morally wrong. Thus in the context of GM this ethical issue is linked to the scientific problem of risk assessment. In the European Union the "precautionary principle" is incorporated in the Maastricht Treaty. This puts the avoidance of harm to consumers and the environment at the head of the list of regulatory goals. This rule permits governments to impose restrictions on activities, if there is a risk of environmental damage, even if the risk is not yet scientifically demonstrated.(Nuffield Council on Bioethics, 1999)

People's right

When talking about GM food, adequate labelling and the offering of a choice of products would support the consumer's right. On the other hand this right to choose presents difficulties when it imposes costs on others (the companies) and therefore diminishing their right to choose.(Nuffield Council on Bioethics, 1999) For DBOX this issue is even more difficult. On the one hand the local population should have the right to choose if they accept the risk that the biosensor might "contaminate" genetically the environment of their future farmland. On the other hand the demining organizations should claim their right to use the safest and most cost-efficient methodology available and that includes the use of GM biosensors.

Justice

Usually technological innovation like GM technology produces some gains and some losses. Economists have developed the concept of the compensation test: The new situation is better than the previous situation if the “winners” can compensate the “loosers” and still have something left over.(Nuffield Council on Bioethics, 1999)

For the case of DBOX it is not easy to determine, who the winner is and who the looser. Ideally there are only winners – both the demining company and the local population. The demining company would have a new safe and cheap demining technology at hand. With traditional detection methods the cost to remove one antipersonnel landmine is between 200 and 750 €, which corresponds to a cost between 2 and 8 million Euros to clear 1 km². To tackle this situation all sectors of mine action have to be improved and one step in this direction is to use a cheaper detection technology like biosensing.

The local population would also benefit, as they will get back their farmland earlier. This in turn would open new opportunities for the economic development of the country through agriculture. Also other benefits, like the ease of movement of the people as well as access to school, food, water points, rivers and roads have to be taken into account. All these points will ease and speed up the economic development of the country.

But if the release of the biosensor is somehow unsafe (due to health risks or environmental pollution) or if the local population is left with a feeling of uneasiness or “unnaturalness” regarding the GM biosensor, then the “looser” would be the local population. To decide if the introduction of the biosensor methodology is just we need both a thorough risk assessment as well as the participation of the local population to learn about their attitude towards GM technology.

Researchers and all others involved in gene technology should:

***Principle 1**: treat integrity as the guiding value in the search for and application of knowledge and benefits and in regard to the obligations of, and intentions underlying, the national regulatory system and other relevant guidelines and regulations;*
***Principle 2**: take responsibility for ensuring that activities within their control do not cause damage to the Australian environment or to areas beyond the limits of the national jurisdiction; to achieve this, there must be a thorough assessment of the long-term side effects of applications of gene technology;*
***Principle 3**: minimise risks of harm or discomfort to humans and animals likely to be adversely affected by gene technology;*
***Principle 4**: assess and respect the environmental and health needs of present and future generations;*
***Principle 5**: conduct research in a manner that protects the environment, including protection of genetic diversity, organisms, species, natural ecosystems, and natural and physical resources;*
***Principle 6**: act justly towards others, and demonstrate respect for human beings (as individuals and group members) in all activities associated with gene technology, including obtaining proper consent;*
***Principle 7:** promote equitable access to scientific developments and sharing knowledge, and recognise the value of benefit sharing;*
***Principle 8**: conduct research in a manner that promotes the benevolent and avoids the malevolent uses of gene technology;*
***Principle 9**: conduct gene technology research after appropriate consultation and ensuring transparency and public scrutiny of the processes.*

Figure 7: Ethical principles in gene technology according to the Australian Gene Technology Ethics Committee.
(Gene Technology Ethics Committee, 2006)

6.1 Views of the monotheistic religions

(Omobowale et al., 2009) concluded in his paper that there is no overarching consensus on the permissibility of GM technology, performing of GM research, or consumption of GM foods within the world's three main monotheistic religious traditions. Overall however, it appears that mainstream theology in the world's monotheistic religions accepts the genetic modification of food crops, performing GM research and consuming GM foods as long as there is adequate scientific, ethical

and regulatory scrutiny of research and development of such products, and they are properly labeled.

Jewish views

It appears that there is currently no universal agreement within Judaism on whether Jews can eat GM food products or engage in research in the area of GM food technology.(Omobowale et al., 2009)

(Galun, 2000) explained that there are two aspects of GM technology which are relevant to Jewish religious laws: (i) whether genetic engineering can be considered as interference with God's creation, and (ii) whether the transfer of genes from one species to another constitutes a nonpermissible cross-breeding (Kilayim). Currently Jewish religious scholars are not very clear and detailed about the subject of interference with God's creation.

One perspective emphasizes that humanity was created in God's image and this means that humanity can "partner with God in the perfection of everything in the world," and therefore Jewish law accepts genetic engineering to save and prolong human life as well as increase the quality or quantity of the world's food supply.(Omobowale et al., 2009)

Other perspectives hold that GM food technology is a violation of Kilayim, the mixed breeding of crops or livestock, and that because God made "distinctions in the natural world", Jews must honor them.(Omobowale et al., 2009)

Regarding kosher food Rabbis have ruled that simple gene additions that lead to one or a few new components in a species are acceptable for kosher law.(Chaudry et al., 1994; Vogt et al., 2001)

Islamic view

At a seminar in Kuwait on genetics and genetic engineering in October 1998, a group of Muslim intellectuals concluded that although there are fears about the possibility of the harmful effects of GM food technology and GM food products on human beings and the environment, there are no laws within Islam which stop the genetic modification of food crops and animals.(Omobowale et al., 2009)

However, Majid Katme, on behalf of the United Kingdom Islamic Medical Association quotes from the Quran and asserts that there is no need for genetic modification of food crops because God created everything perfectly and man does not have any right to manipulate anything that God has created using His divine wisdom. He also states that the Quran contains several verses, prohibiting man from tampering with God's creation.(Omobowale et al., 2009) and cited herein

Thus, even within Islam, there is no consensus by religious scholars and commentators on whether the Quran accepts genetic modification of food crops and the consumption of GM food products by Muslims.(Omobowale et al., 2009)

Catholic view

The Pontifical Council for Justice and Peace appreciates the advantages of biogenetic techniques, but also demands that the risks and benefits of the applications have to be evaluated accurately (see Figure 8).

Compendium of the social doctrine of the Church

The Church appreciates “the advantages that result — and can still result — from the study and applications of molecular biology, supplemented by other disciplines such as genetics and its technological application in agriculture and industry. [..] It is important, however, to repeat the concept of “proper application”, for “we know that this potential is not neutral: it can be used either for man's progress or for his degradation”.

The Christian vision of creation makes a positive judgment on the acceptability of human intervention in nature, which also includes other living beings, and at the same time makes a strong appeal for responsibility.

The acceptability of the use of biological and biogenetic techniques is only one part of the ethical problem: as with every human behavior, it is also necessary to evaluate accurately the real benefits as well as the possible consequences in terms of risks.

Figure 8: Quotations from the Compendium of the social doctrine of the Church. (Pontifical Council for Justice and Peace, 2004)

In January 2002, the Conference of European Churches (CEC) presented the outcome of the critical examination of the genetically modified food controversy by its Church and Society Commission. They concluded that they have not found a convincing reason of principle against the idea of the genetic modification of food, but admitted that there are many in the churches who would be opposed. They further stated that the uncertainties merit a generally precautionary approach towards environmental and health risks but that a complete rejection of all GM crops on risk grounds would not seem justified. GM applications should only be done if they confer significant human or ecological benefits.(Church and Society Commission, Conference of European Churches, 2001)

The World Council of Churches, on the other hand, has published a document "Caring for Life: Genetics, Agricultural and Human Life" and which concluded in seven key criticisms of genetic engineering in agriculture: GE messes with life, GE messes with the truth, GE messes with our common inheritance, GE messes with justice, GE messes with our health, GE messes with agency (here: food sovereignty) and GE messes with relationships.(World Council of Churches, 2005)

Conclusion

Although most of the above mentioned religious views on GM technology deal with GM food, e.g. if GM food is kosher or halal, it nevertheless appears to be the cases that GM technology in general is acceptable to many religious leaders as long as environmental and health risks are taken seriously and human benefits are clearly visible. Thus apart from the already mentioned general risks and concerns in chapter 5, it can be expected that most religious leaders wouldn't add specific theological based concerns regarding the DBOX biosensor.

7. REGULATIONS OF GMOS IN GERMANY

7.1 Genetic Engineering Act

The national guideline for the Federal Office of Consumer Protection and Food Safety (BVL) in the field of genetic engineering is the Genetic Engineering Act. It implements EU guidelines in national legislation and seeks to protect human and animal health, and the environment, from potential adverse effects of genetic processes and products.(Federal Office of Consumer Protection and Food Safety, 2013c)

Essentially, it regulates activities of development and application of genetically modified organism and also governs deliberate releases of genetically modified organisms into the environment.(Federal Office of Consumer Protection and Food Safety, 2013d; Bundesministerium der Justiz, 2010)

7.2 Genetic Engineering Procedural Regulation

"Ordinance on the documents for application and notification and on the procedure for authorisation and notification, in accordance with the Genetic Engineering Act (Genetic Engineering Procedural Regulation - GenTVfV)"

This ordinance explains in detail which documents the applicant must submit to the competent authority in the authorisation procedure based on genetic engineering legislation.(Federal Office of Consumer Protection and Food Safety, 2013d; Bundesministerium der Justiz, 2008)

8. REGULATION OF GMOS IN THE EUROPEAN UNION

8.1 Directive 90/219/EEC

"Council Directive 90/219/EEC of 23 April 1990 on the contained use of genetically modified micro-organisms" (European Council, 1990)

"Contained use"

Member States are required to regulate the contained use of genetically modified micro-organisms in order to minimise their potential negative effects on human health and the environment.

To do this, the user must adhere to certain principles of safety and health. In addition, before undertaking for the first time in a particular installation the use of genetically modified micro-organisms, the user must submit to the authorities a notification enabling them to ensure that the proposed installation can be used for this activity without danger.

Member States must also ensure that an emergency plan is drawn up to ensure an effective response in the event of an accident and that the persons likely to be affected by an accident are informed about all matters relating to their safety.

To enable the contained use of genetically modified micro-organisms to be monitored throughout the Community, Member States have to provide the Commission with certain information.(europa.eu, 2008; European Council, 1990)

8.2 Directive 2001/18/EC

"Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms"(European Parliament and the Council, 2001)

"Deliberate release"

The European Union (EU) has adopted a legislative framework on the deliberate release of GMOs into the environment and the placing of GMOs on the market in accordance with the precautionary principle.

The main aim of this Directive is to make the procedure more efficient and more transparent, to limit such consent to a period of ten years (renewable) and to introduce compulsory monitoring after GMOs have been placed on the market.

It also provides for a common methodology to assess case-by-case the risks for the environment associated with the release of GMOs, common objectives for the monitoring of GMOs after their deliberate release or placing on the market, and a mechanism allowing the release of the GMOs to be modified, suspended or terminated where new information becomes available on the risks of such release.

Notes providing detailed guidance regarding the environmental risk assessment are provided in Commission Decision 2002/623/EC of 24 July 2002.(European Commission, 2002b)

Public consultation and GMO labelling are obligatory under the new Directive. The Commission is obliged to consult the competent scientific committees on any question which may affect human health and/or the environment. It may also consult ethical committees. The Directive requires registers to be established for the purpose of recording information on genetic modifications in GMOs and on the location of GMOs.(europa.eu, 2010; European Parliament and the Council, 2001)

Experimental releases of GMOs into the environment are mainly carried out for the purposes of study, research, demonstration and development of novel varieties. The behaviour of the GMO in an open environment and its interactions with other organisms and the environment are studied. The experimental releases are subject to the provisions of Part B of Directive 2001/18/EC.

If the results of the experimental release are positive, the company may decide to place the GMO on the market, i.e. make it available to third parties either free of charge or for a fee. The placing on the market of a GMO is mainly governed by the provisions of Part C of Directive 2001/18/EC.(europa.eu, 2005)

A number of Member States have invoked the so-called 'safeguard clause' of the Directive 2001/18/EC (Article 23). This safeguard clause provides that where a Member State has justifiable reasons to consider that a GMO, which has received written consent for placing on the market, constitutes a risk to human health or the environment, it may prohibit the use and/or sale of that product on its territory.

The safeguard clause was invoked on nine separate occasions, three times by Austria, twice by France, and once each by Germany, Luxembourg, Greece and the United Kingdom (by now UK has withdrawn its ban). The scientific evidence provided by these Member States as justification for their measures was submitted to the Scientific Committees of the European Union for opinion.(European Commission - DG Health and Consumers, 2009)

8.2.1 DECISION 2002/811/EC

"Council Decision of 3 October 2002 establishing guidance notes supplementing Annex VII to Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC" (European Council, 2002a)

"Guidance notes - monitoring"

Notifiers are required to submit as part of the notification a plan for monitoring in accordance with Annex VII of Directive 2001/18/EC. This should include a proposal for the time-period of the monitoring plan. Annex VII describes in general terms the objective to be achieved and the general principles to be followed to design a monitoring plan.

8.2.2 DECISION 2002/623/EC

"Commission Decision of 24 July 2002 establishing guidance notes supplementing Annex II to Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC" (European Commission, 2002a)

"Guidance notes – environmental risk assessment"

Notifiers must submit a notification including an environmental risk assessment (ERA) for deliberate release or for placing on the market.

This guidance note outlines the objectives and principles as well as the methodology for the ERA. The objective of an ERA is to identify and evaluate potential adverse effects of the GMO, direct and indirect, immediate or delayed, on human health and the environment which the deliberate release or placing on the market of GMOs may have.

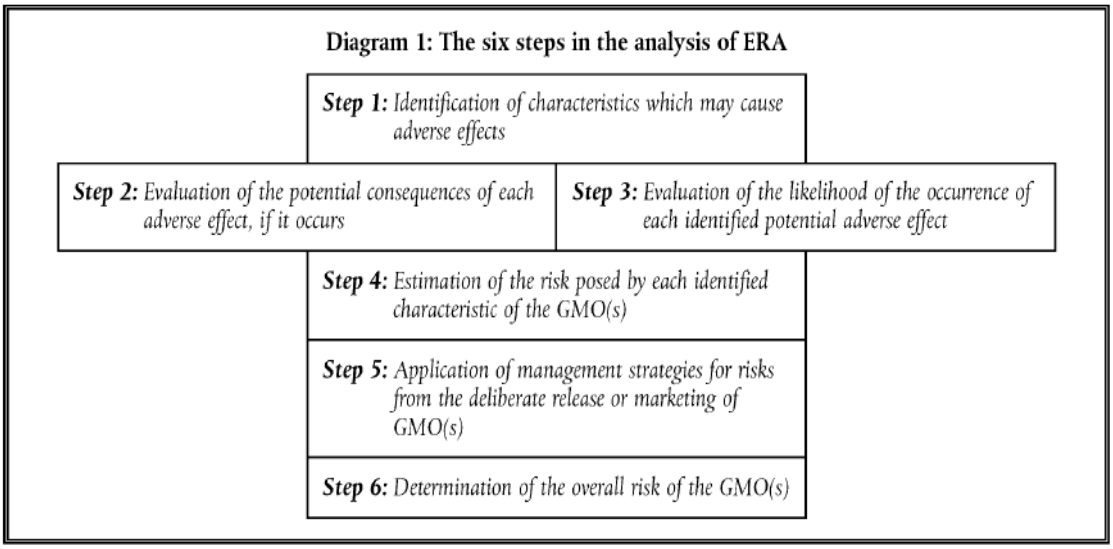

Figure 9: The six steps in the analysis of the environmental risk analysis. (European Commission, 2002a)

8.2.3 DECISION 2002/813/EC

"Council Decision 2002/813/EC - The summary notification information format for notifications concerning the deliberate release into the environment of genetically modified organisms for purposes other than for placing on the market"(European Council, 2002c)

"Summary notification information format (SNIF)"

In accordance with European notification procedures, applicants must complete a Summary Notification Information Format (SNIF). Article 11 of Directive 2001/18/EC stipulates that there has to be an exchange of information between the competent authorities and the European Commission. This means that the competent authorities must send a summary of the application form (SNIF form) to the Commission. The SNIF form can be found on the website of the Joint Research Centre of the European Commission Other Member States can then comment on it within 30 days.(Gene Therapy Office, 2013)

The Summary Notification Information Format consists of a Part 1 and a Part 2.

Part 1 applies to products consisting of or containing genetically modified organisms other than higher plants and contains the following sections:

- General Information

- Information relating to the recipient or parental organisms from which the GMO is derived
- Information relating to the genetic modification
- Information on the organism(s) from which the insert is derived (donor)
- Information relating to the genetically modified organism
- Information relating to the release
- Interactions of the GMO with the environment and potential impact on the environment
- Information relating to monitoring
- Information on post-release and waste treatment
- Information on emergency response plans

In Part 1 the information entered should adequately reflect the information submitted to the competent authority[8].

Part 2 applies only to products consisting of or containing genetically modified higher plants. The term "higher plants" means plants which belong to the taxonomic group Gymnospermae and Angiospermae.(European Council, 2002c)

8.2.4 DECISION 2002/812/EC

"Council Decision 2002/812/EC - The summary information format relating to the placing on the market of genetically modified organisms as or in products"(European Council, 2002b)

"Summary information format – placing on the market"

This summary information format must be used for notifications concerning the placing on the market of a GMO as or in products.

The Summary Information Format is divided into Parts 1 and 2. Part 1 applies to products consisting of or containing genetically modified organisms other than higher plants and contains the following sections:

- General Information
- Nature of the GMOs contained in the product
- Predicted behaviour of the product
- Information relating to previous releases

[8] in accordance with Articles 6 and 7 of Directive 2001/18/EC under the conditions specified in the preface to Annex IIIA

- Information relating to the monitoring plan

Part 2 applies only to products consisting of or containing genetically modified higher plants. The term 'higher plants' means plants which belong to the taxonomic group Gymnospermae and Angiosperma.(European Council, 2002b)

8.3 Regulation 1946/2003

"Regulation (EC) No 1946/2003 of 15 July 2003 of the European Parliament and of the Council on trans-boundary movement of genetically modified organisms"(European Parliament and the Council, 2003)

"Trans-boundary movement"

This Regulation aims to implement the provisions of the Cartagena Protocol on preventing biotechnological risks. The aim of the Protocol is to ensure an adequate level of protection for the transfer, handling and use of genetically modified organisms (GMOs) that may have adverse effects on the environment and human health, and specifically focusing on trans-boundary movements.

This Regulation distinguishes between GMOs intended for deliberate release into the environment and GMOs intended for use as food or feed, or for processing.

Exporters of GMOs intended for deliberate release into the environment must notify, in writing, the competent national authority of the country of import prior to the trans-boundary movement. The notification must contain the information specified in Annex I to the Regulation. Under no circumstances may trans-boundary movements take place without prior written consent from the importer.

Exporters must keep the notification, the acknowledgement of receipt and the importer's decision for at least 5 years. They must also notify the transit of the GMOs to any country upon request.(European Parliament and the Council, 2003; europa.eu, 2007)

8.4 Cartagena Protocol on Biosafety

The Cartagena Protocol on Biosafety to the Convention on Biological Diversity is an international treaty governing the movements of living modified organisms (LMOs) resulting from modern biotechnology from one country to another. It was adopted on 29 January 2000 as a supplementary agreement to the Convention on Biological Diversity and entered into force on 11 September 2003.

The Protocol seeks to protect biological diversity from the potential risks posed by living modified organisms resulting from modern biotechnology. It establishes an advance informed agreement (AIA) procedure for ensuring that countries are provided with the information necessary to make informed decisions before agreeing to the import of such organisms into their territory. The Protocol contains reference to a precautionary approach and reaffirms the precaution language in Principle 15 of the Rio Declaration on Environment and Development. The Protocol also establishes a Biosafety Clearing-House to facilitate the exchange of information on living modified organisms and to assist countries in the implementation of the Protocol.

At the time of writing 166 parties have signed the Cartagena protocol. The EU Member States and the Community signed the Cartagena Protocol in 2000. In June 2002, the Council published Decision 2002/628/EC concerning the conclusion, on behalf of the European Community, of the Cartagena Protocol on Biosafety.(Secretariat of the Convention on Biological Diversity, 2012; europa.eu, 2007)

9. RELEVANT ORGANIZATIONS WHEN DEALING WITH GMOS

9.1 European Food Safety Authority (EFSA)

EFSA's core task is to independently assess any possible risks of GMOs to human and animal health and the environment. EU Member States participate throughout the risk assessment process while EFSA's GMO Panel is responsible for preparing and adopting the GMO risk assessments. EFSA does not authorise GMOs, which is done by the European Commission and Member States in their role as risk managers. EFSA's role is strictly limited to giving scientific advice.

EFSA's assessments are carried out by the GMO Panel, which is composed of independent scientific experts supported by a number of specialised working groups drawing on a pool of more than 40 external experts in fields such as allergenicity, ecology, microbiology, toxicology, plant physiology and molecular genetics.(European Food Safety Authority, 2013b, 2012)

9.2 Biosafety Clearing House (BCH)

The Biosafety Clearing-House (BCH) is a mechanism set up by the Cartagena Protocol on Biosafety to facilitate the exchange of information on Living Modified Organisms (LMOs) and assist the Parties to better comply with their obligations under the Protocol. Global access to a variety of scientific, technical, environmental, legal and capacity building information is provided in all 6 of the UN languages. (Biosafety Clearing-House, 2013)

A Party has obligations under the Protocol to make some information available through the BCH. Article 20 of the Cartagena Protocol lists the specific information that a Party must provide to the BCH:(Convention on Biological Diversity, 2010)

> *"(a) Any existing laws, regulations and guidelines for implementation of the Protocol, as well as information required by the Parties for the advance informed agreement procedure;*
>
> *(b) Any bilateral, regional and multilateral agreements and arrangements;*
>
> *(c) Summaries of its risk assessments or environmental reviews of living modified organisms generated by its regulatory process, and carried out in accordance with Article 15, including, where appropriate, relevant information regarding products thereof, namely, processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology;*

(d) Its final decisions regarding the importation or release of living modified organisms; and

(e) Reports submitted by it pursuant to Article 33, including those on implementation of the advance informed agreement procedure."

Access to this information is provided through the "Finding Information" page of the BCH website.(Biosafety Clearing-House, 2013)

In the following three examples are given to demonstrate the utility of the BCH information portal:

Example 1: Database of National Contacts – Search term: "Germany"

ID	Description	
3 record(s) found		
8673	**Germany** National Focal Point	Volker Matzeit Biosafety Clearing-House Focal Point, Cartagena Protocol on Biosafety National Focal Point
12096	**Germany** Competent National Authority	Federal Office of Consumer Protection and Food Safety
43897	**Germany** National Database or Website	German Biosafety Clearing House Information regarding contained use, deliberate release and placing on the market of LMO in Germany. The site offers information regarding the German legal framework of technology, describes the administrative procedures of deliberate releases and placing on the market of LMO, houses the German location register that informs about the sites where LMO are grown, informs about sampling and detection of LMO, informs about the number of contained use and number of LMO laboratories, the duties and results of consultations of the German advisory body for biological safety (Central Commission for Biological Safety [Zentrale Kommission für Biologische Sicherheit, ZKBS]). The website offers access to databases with information about field trials in Germany and the EU, about the risk assessment of oncogenes, organisms, vectors and plasmids as well as cell lines that are used under conditions of contained use in Germany. To date, most of the information is offered in German language. The translation into English of summaries and information of interest is under way.

Example 2: Laws and regulations – Search term: "Tajikistan", "Intentional introduction into the environment"

ID	Description		
2 record(s) found			
8414	**Tajikistan** All functions pursuant to the Cartagena Protocol on Biosafety	National Biosafety Framework	
10347	**Tajikistan** All functions pursuant to the Cartagena Protocol on Biosafety	Law on Biological Safety	

Example 3: LMOs, genes and organisms – Search term: "pseudomonas", Registry: organism

ID	Description	
5 record(s) found		
14934	Organism	Pseudomonas chlororaphis
48835	Organism	Pseudomonas fluorescens
103677	Organism	Stenotrophomonas maltophilia - S. maltophilia, Stenotrophomonas
103754	Organism	Vibrio harveyi - Vibrio, V. harveyi
104803	Organism	Delftia acidovorans

9.3 German Federal Office of Consumer Protection and Food Safety (BVL)

Since 2004, the Federal Office of Consumer Protection and Food Safety (BVL) is the leading federal authority responsible for the field of genetic engineering in Germany. The BVL fulfils the mandate as national competent authority according to the Genetic Engineering Act (Gentechnikgesetz) and Ordinances of the European Union.(Federal Office of Consumer Protection and Food Safety, 2013c)

The release of genetically modified organisms (GMO) for scientific trials needs to be approved by the BVL. If GMOs are to be cultivated commercially, the BVL will provide a statement in the Community approval process of the EU. Furthermore, the BVL manages the international information exchange on GMOs in the Biosafety Clearing House for Germany. (Federal Office of Consumer Protection and Food Safety, 2013c)

9.4 German Central Committee on Biological Safety (ZKBS)

The Central Committee on Biological Safety (ZKBS) is an expert committee comprising twenty members and twenty deputy members. The ZKBS examines and evaluates questions relevant to safety in genetic engineering according to the regulations of the Genetic Engineering Act (GenTG) and advises the Federal Government and Federal States (Bundesländer). The ZKBS is based at the Federal Office for Consumer Protection and Food Safety (BVL).(Federal Office of Consumer Protection and Food Safety, 2011)

10. APPROVAL PROCEDURE FOR GMOS

The notification of GMOs for the experimental release into the environment as well as for the commercial placing on the market of GMOs are subject to an assessment and approval process.(Federal Office of Consumer Protection and Food Safety, 2013c)

Depending on the place and the use of GMOs one has to distinguish between four different cases:(Leggewie, 2010)

1. Experimental release within in EU
2. Experimental release outside the EU
3. Placing on the market inside the EU
4. Placing on the market outside the EU

In the first case the national genetic engineering act applies in connection with directive 2001/18/EC – part B (see chapter 8.2).(Leggewie, 2010) As the research work on the genetic modified organisms is done in Germany, only the German approval procedure is described in this deliverable (see chapter 10.1).

Step 1: Experimental release in Germany → German national genetic engineering act & Dir. 2001/18/EC part B

At this stage of the D-BOX project it is not clear, if it is necessary at all to test the biosensor in non-EU states. However, if after the completion of D-BOX the researchers need to test biosensors outside the EU, the Biosafety Clearing House (see chapter 9.2) is a good starting point to obtain information about the relevant national genetic engineering acts in 3rd countries.

If the results of the experimental release are positive, the GMOs maybe can be made available to third parties either free of charge or for a fee ("placing on the market"). The placing on the market of a GMO is governed by the national genetic engineering act and the provisions of Part C of Directive 2001/18/EC (see chapter 8.2).(Leggewie, 2010; europa.eu, 2005) The approval process for this case is described in chapter 10.2.

Step 2: Placing on the market inside EU → German national genetic engineering act & Dir. 2001/18/EC part C

In case 4 the applicants have to follow the national regulations of the 3rd country. As it is still unknown in which country the biosensors might be placed on the market, it is not possible to describe the legislation of possible 3rd countries in more detail. At a later stage the information platform of the Biosafety Clearing House (see chapter 9.2) might be helpful.

Step 3: Placing on the market in a non-EU country → Respective national genetic engineering act

Apart from the placing on the market itself the applicants have to observe the export laws. Hereby regulation (EC) No 1946/2003 on transboundary movement of genetically modified organisms (see chapter 8.3) implements the provisions of the Cartagena Protocol on preventing biotechnological risks.(Leggewie, 2010) Chapter 10.3 explains the export regulations in more detail.

Step 3b: Exporting to non-EU countries → Reg. (EC) No 1946/2003

10.1 Approval Procedure for experimental release in Germany

Shall GMOs during an experiment be introduced into the environment for a limited period of time and in a limited area it is a matter of “deliberate release”. According to the German genetic engineering act (GenTG) one must apply for approval for every intended release which can be granted if the planned release will present no hazard to humans and the environment.(Federal Office of Consumer Protection and Food Safety, 2011)

In Germany the Federal Office of Consumer Protection and Food Safety (BVL) is responsible as the overall Federal Authority for approving the release of GMOs. The BVL reaches its decisions in conjunction with the Federal Office for Nature Conservation (BfN), the Federal Institute for Risk Assessment (BfR) and the Robert Koch Institute (RKI). The Central Commission for Biological Safety (ZKBS), the Julius Kühn Institute (JKI) and the relevant authorities of the Federal States involved provide position statements on the planned release. Other EU member states are informed about the release application and can take a position on it.(Federal Office of Consumer Protection and Food Safety, 2011)

In the following the different phases of the approval process for the experimental release of GMOs is described (see Figure 10):(Federal Office of Consumer Protection and Food Safety, 2013c; Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL), 2010a)

1. *Completeness check*: All involved federal authorities check the application for completeness.
2. *Public Participation*: The Federal Office of Consumer Protection and Food Safety (BVL) is responsible for the public announcement of the application. Citizens can submit their objections to the BVL. The objections are verified and considered in the final decision.
3. *Assessment of the application*: This step includes the scientific evaluation of molecular, health, and ecological data by experts in the particular fields and consultation with further federal and state agencies. The BVL also asks for an opinion of the Central Commission for Biological Safety (CCBS), which hosts experts in the field of bacteriology, virology, plant breeding, medicine and ecology, as well as industrial and environmental safety.
4. *Approval*: If all the requirements are met, the Federal Office of Consumer Protection and Food Safety (BVL) submits the decision of approval to the applicant. The whole process from the application to the approval usually takes 6 to 9 month.
5. *Monitoring*: The regional authorities are responsible for the monitoring of the release. Three days before the planned release the release has to be registered in the GMO Location Register.
6. *Informing the EU member states*: The applicant has to submit a summary notification information formate (SNIF) to the Federal Office of Consumer Protection and Food Safety (BVL). This information has to be entered into the data base of the Joint Research Centre (JRC) and is published on the internet to inform the other EU member states as well as the public.

Up to know there have been three approvals of a release of genetically modified microorganisms: (Federal Office of Consumer Protection and Food Safety, 2013b)

- Az 6786-01-0020, University of Bielefeld, 1994 – 1998, Rhizobium meliloti
- Az 6786-01-0071, University of Bielefeld,1997 – 2000, Sinorhizobium meliloti
- Az 6786-01-0213, Intervet International B.V., 2012 – 2014, live bacterial vaccines against equine disease (Rhodococcus equi RG2837)

The Federal Office of Consumer Protection and Food Safety has collected some information about the approval procedure on its homepage:

- Application Guide (Federal Office of Consumer Protection and Food Safety, 2012)
- Sample Application (Federal Office of Consumer Protection and Food Safety, 2013a)

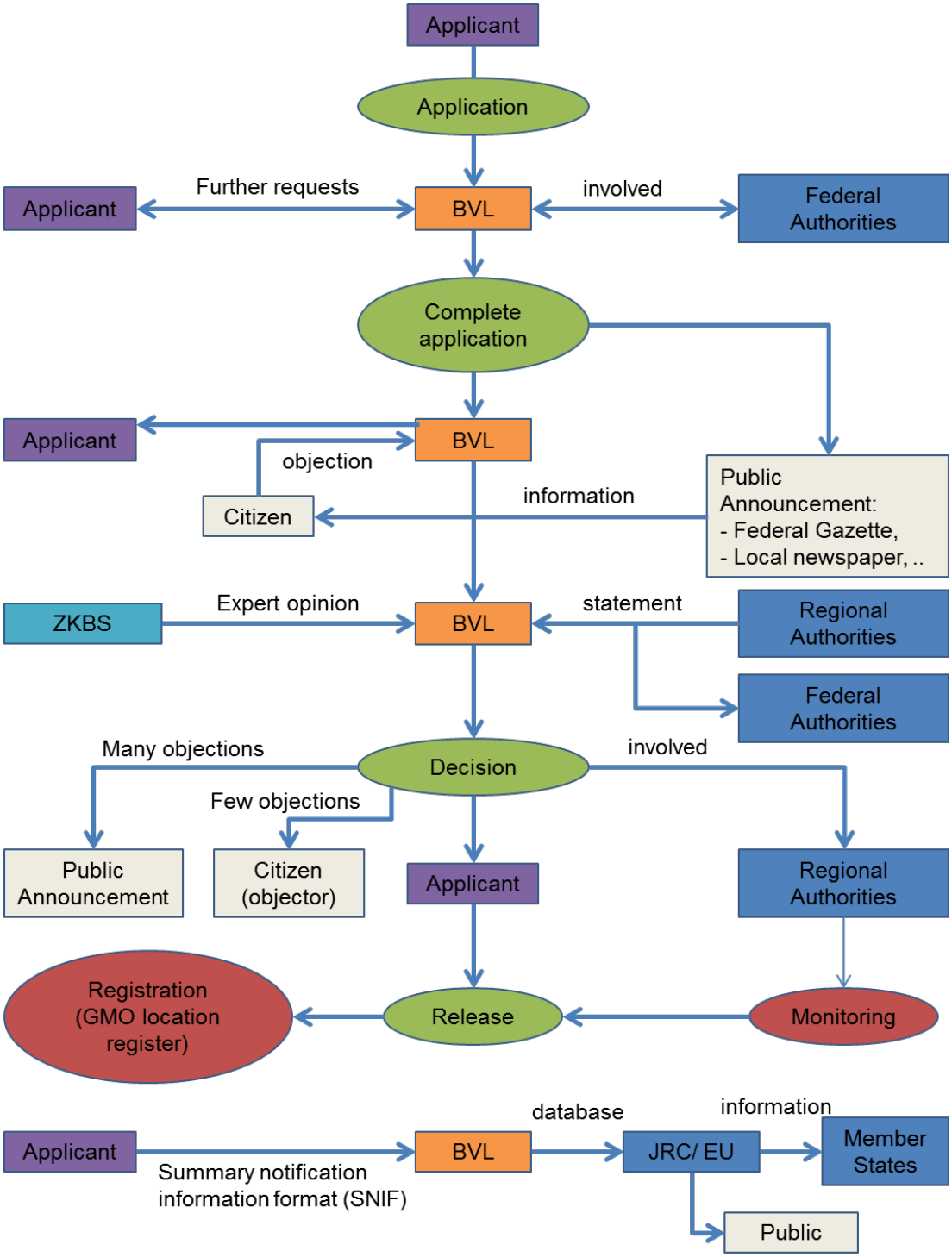

Figure 10: Notification procedure for the experimental release of GMOs in Germany. (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL), 2010a)
BVL - Federal Office of Consumer Protection and Food Safety, Involved Federal Authorities: BfR - Federal Institute for Risk Assessment, BfN - Federal Agency for Nature Conservation, JKI – Julius Kühn Institute, RKI – Robert Koch Institute, ZKBS - Central Commission for Biological Safety, JRC – Joint Research Centre of the EC

10.2 Approval Procedure for Placing on the Market in the EU

"Placing on the market" of GMOs or products containing GMOs refers to each kind of propagation like giving away or selling, unless they are not intended to be used for a genetic engineering operation in a genetic engineering installation or for an approved deliberate release.(Federal Office of Consumer Protection and Food Safety, 2011) In the following the approval procedure is described in more detail – also see Figure 11.

Placing GMOs on the market requires approval. Since an approval for placing a GMO on the market is met through an EU-wide procedure, it applies to all member states of the EU. (Federal Office of Consumer Protection and Food Safety, 2011) The applicants must apply to the competent authority of the EU country where the GMO is going to be marketed for the first time. That country prepares an assessment report within 90 days. It sends the applications to the European Food Safety Authority (EFSA) if at least one other EU country reasonably objects to the assessment report.(European Commission - DG Health and Consumers, 2012c)

EFSA assesses the risks the GMO presents for the environment, human health and animal safety. It may give instructions on labelling or conditions on the use and sale of the products including the GMO. Normally, EFSA performs the risk assessment within 6 months of receiving the application and issues a scientific opinion published in the EFSA Journal. It takes longer if it has to request more information from the applicant. EFSA submits its opinion to the European Commission and to EU countries. The opinion is made available to the public, except for certain confidential aspects.(European Commission - DG Health and Consumers, 2012a)

Once EFSA publishes its risk assessment, the public has 30 days to comment on the Joint Research Centre website on the assessment report of the "lead" EU country for applications under Directive 2001/18.(European Commission - DG Health and Consumers, 2012a)

Within 3 months of receiving EFSA's opinion, the Commission grants or refuses the authorisation in a proposal. If it differs from EFSA's opinion, it must explain why. National representatives approve the Commission's proposal by qualified majority in the Regulatory Committee under Directive 2001/18/EC.[9] The proposal is adopted if the Committee agrees with it.(European Commission - DG Health and Consumers, 2012b)

[9] if the application was submitted under Directive 2001/18. Applications for genetically modified food and feed have to be submitted under Regulation 1829/2003.

All applications for marketing GMOs or releasing them into the environment must have a monitoring plan. This plan is part of the authorisation decision. The applicant must implement it and regularly report to the authorities.(European Commission - DG Health and Consumers, 2012d)

The overall process usually takes 3 to 4 years.(Leggewie, 2010) Then, an approval for placing on the market is initially limited to ten years. (Federal Office of Consumer Protection and Food Safety, 2011)

Up to know there have been two product approvals of genetically modified microorganisms:(EU Commission - DG Health and Consumers, 2013)

- pCABL- Bacterial biomass, Ajinomoto Eurolysine SAS[10]
- pMT742 or pAK729-Yeast biomass, NOVO Nordisk A/S

EFSA's Panel on Genetically Modified Organisms (GMO) produces guidance documents that assist companies and other organisations in the preparation and presentation of applications. At the time of writing 12 guidance documents can be downloaded from EFSA's homepage.(European Food Safety Authority, 2013a)

Unfortunately, at the moment there are only guidance documents available about the placing on the market of microorganisms for the use as food and feed. But these documents still give some information about the applications for genetically modified organisms for other uses than food and feed.

[10] To our knowledge both the bacterial and the yeast biomass have been heat-treated and therefore do not contain any living organisms.

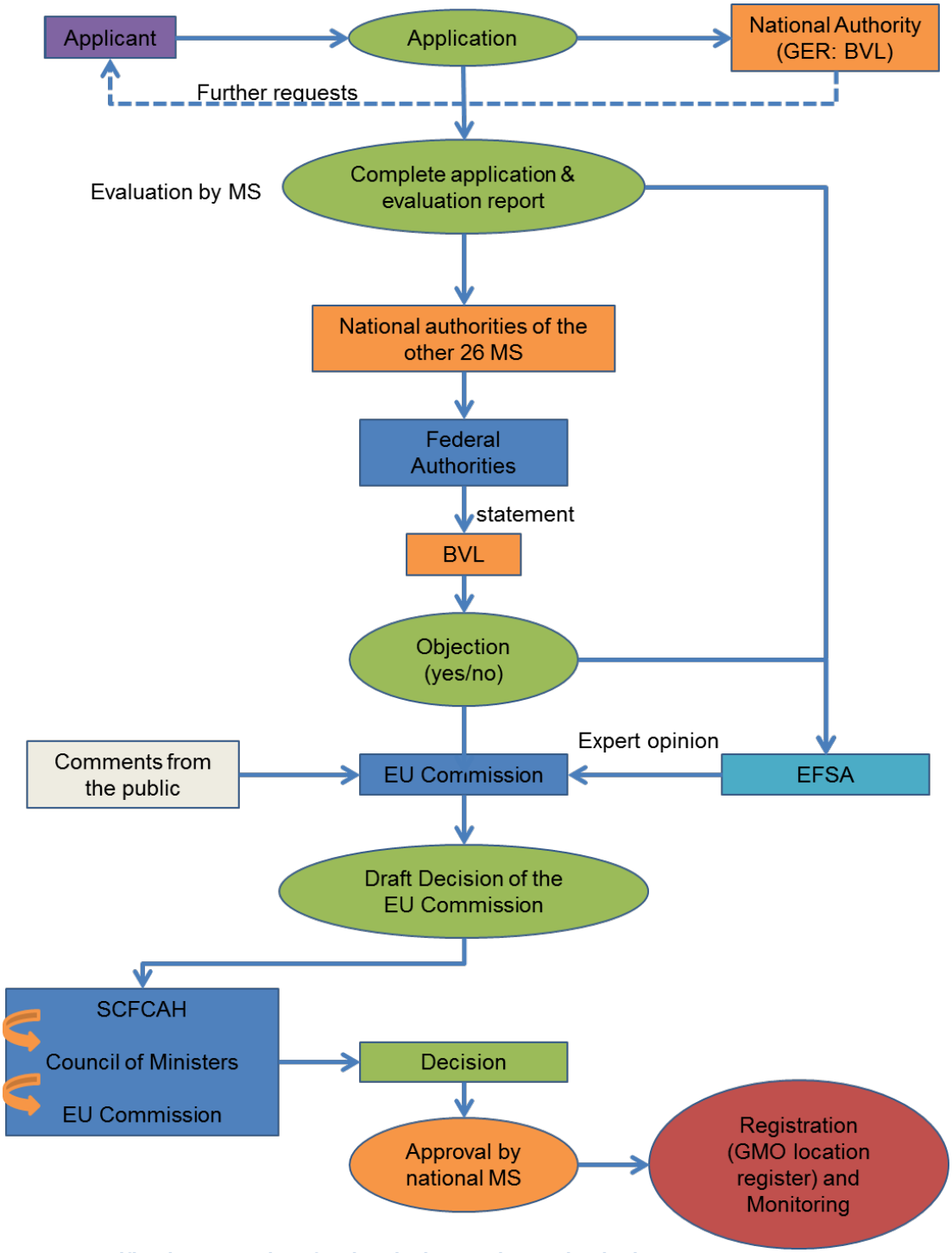

Figure 11: Notification procedure for the placing on the market in the EU. (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL), 2010b) BVL - Federal Office of Consumer Protection and Food Safety; Involved Federal Authorities: BfR - Federal Institute for Risk Assessment, BfN - Federal Agency for Nature Conservation, JKI – Julius Kühn Institute, RKI – Robert Koch Institute; EFSA – European Food Safety Authority, SCFCAH - Standing Committee on the food chain and animal health, Council of Ministers, EU Commission.

10.3 Trans-boundary movement of GMOs

Regulation EC 1946/2003 regulates trans-boundary movements of GMOs and transposes the Cartagena Protocol on Biosafety into EU law (see chapter 8.3).

The regulation establishes the procedures for the trans-boundary movement of GMOs including:(European Commission - DG Health and Consumers, 2010)

- notification to importing parties;
- information to the Biosafety Clearing House;
- requirements on identification and accompanying documentation.

11. CONCLUSION

The conducted interviews in combination with our desktop research have shown that the public opinion about GMOs for the detection of explosives is divided.

In general there are two different attitudes. The first group generally disapproves of the use of a GM biosensor. They regard the possible risks as too high and have also doubts whether this demining technique will be better than conventional methods or if it will work at all.

The second group sees the GM biosensor as generally positive. They think that this technique is a promising way to complement and improve the already established demining technologies. As long as the EU law or a similar strict national law is complied, they have no further objections.

The most serious risk is seen in a possible antibiotic resistance marker gene. Several interview partners think that an approval process could fail due to an antibiotic resistance of the bacteria. Other mentioned risks are for example a negative impact on the ecosystem, gene transfers to other organisms and especially the non-reversibility of the release of the biosensor.

11.1 What are the next steps?

1. **We have to develop a "safer biosensor".**

   The experts offered suggestions how the safety of the biosensor could be improved. For instance, it was suggested to use suicide genes, $RecA^-$ mutants, auxotrophic bacteria or transient gene expression.

2. **We have to develop a demonstrator to be able to compare the quality of the biosensor with conventional demining techniques.**

   A serious objection to the biosensor is the lack of experimental data, which could demonstrate the demining capabilities (number of false positive/ false negative results, costs, speed, quality in different environments, etc.) of the biosensor. A further involvement of the public doesn't make sense before we could present more experimental data.

3. **After or during a successful demonstration we have to involve the public.**

   The "public" should consist of organisations or institutions, which have the trust of the population. Thus, possible organisations could be consumer organisations, environmental groups, renowned scientists and also demining organisations. These persons should also have a good knowledge of gene technology, so that technical details, safety measurements and remaining risks could also be discussed.

   The approval process of the experimental release and especially the placing on the market of a GMO is a complex and time consuming task and furthermore it also involves the public. Thus, this step is only advisable if the safety measurements and the benefits of biosensor easily convince (the majority of) the public. Several interview partners already think that the GM biosensor could be a very valuable tool for humanitarian demining, but we need facts and figures to convince the others.

4. **After a successful approval procedure, care has to be taken to involve the local population in the demining process.**

   Although there are serious doubts that "education the public" or other information strategies raise the public acceptance of the use of GMOs, it is nevertheless recommended to involve the public in GM projects. This means that the demining organisations should encourage transparency and that affected populations should be in the position to make an informed decision about the use of GM biosensors in their environment. Depending on the community it could also make sense to involve the religious leaders in the decision making process.

12. ANNEX

12.1 Information sheet for volunteer participants

INFORMATION SHEET FOR VOLUNTEER PARTICIPANTS
Regarding research undertaken for Project
D-BOX (EU FP7 funded project No: 284996)

PRELIMINARY RESEARCH IN THE CONTEXT OF Project D-BOX, INFORMATION ON THE OVERALL PROJECT, THE RESEARCH INTERESTS AND YOUR INVOLVEMENT

We invite you to participate in this research project. You should only participate if you want to; choosing not to take part will not disadvantage you in any way nor will it affect any aspect of your employment. Before you decide whether you want to take part, it is important you understand why the research is being conducted and what your participation will involve. Please read the following information carefully and discuss it with others if you wish and ask if there is anything that is not clear or if you would like more information.

The D-BOX project: Landmines and the cluster munitions still kill or maim civilians every day in an indiscriminate manner long after conflicts are over. Project D-BOX will tackle the issue of anti-personal landmines and cluster munitions remaining from armed conflicts. This will be achieved through the development of innovative solutions that will be interfaced and integrated in a comprehensive toolbox to provide demining stakeholders the best tools, methods and procedures. The Toolbox will be aimed at all demining activities including the preparation of the mission, the elimination of the mines and communication to the general public and stakeholders. It is hoped that the Toolbox will help operators and end users have the best, least expensive and “easy to use” tools for a specific task during the different steps of demining activities.

Project D-BOX starts with an assessment of existing state of the art technologies, processes, procedures and related on-going-activities and scenarios. The requirements and specifications for different tools will be conducted with a strong involvement of end-users. The project will incorporate tools for human and ethical procedures, technologies for mapping and identifying landmines and cluster munitions, neutralisation, protection, education and training. The project will culminate in two validation exercises to evaluate performance and a CEN Workshop Agreement.

One part of the D-BOX project involves the use of highly-sensitive biosensors for the detection of explosives. This emerging technology exploits the ability of living cells to sense trace amounts of explosive chemicals like TNT and to convert this input into visual output signals that can easily be measured. D-BOX follows a new approach, in which the common soil bacterium Pseudomonas putida was genetically modified to produce red fluorescent proteins upon recognition of TNT-signatures in liquids or soil. The specific response is achieved by a genetic switch that is activated by TNT or its derivatives and induces the production of fluorescent proteins. Laboratory results and field tests using sensor beads revealed a feasible detection range of up to 300 m using a 300 mm high aperture LIDAR-system. Recent developments on airborne laser scanners for mapping of coastal regions and seawater analysis could be the basis of a detection system. This type of laser scanner can be modified for the specific requirements of the fluorescent proteins.

If you agree to take part, you will be interviewed by one of our researchers. The interview should take no longer than one hour. There are no right or wrong answers to the questions. Any quotes used in the report or future publication will be anonymous. You are free to end interview at any time and withdraw from the research.

Personal information will be in accordance with the Bundesdatenschutzgesetz (BDSG). Interview transcriptions may be shared with other researchers, but this will be anonymous.

If you decide to take part you will be given this information sheet to keep and asked to sign a Consent Form.

We hope that your involvement in this study will be both interesting and enjoyable. If you would like to take part or have any further questions or comments related to this project then please contact the researcher Sonja Grigoleit (sonja.grigoleit@int.fraunhofer.de, +49-(0)2251-18-309).

12.2 Consent form

CONSENT FORM in relation to participation in research being undertaken for Project D-BOX (EU FP7 funded project number 284996)

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research. Thank you for considering participation in this research. The person organizing it will explain the project before you agree to take part.

If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to proceed. You will be given a copy of this Consent Form to keep and refer to at any time.

The information you provide as part of this interview will be used as part of the EU FP7 funded research Project D-BOX (Demining tool-BOX for humanitarian clearing of large scale areas from anti-personal landmines and cluster munitions). The output of this project includes research reports and peer-reviewed journal articles. Confidentiality and anonymity will be maintained and it will not be possible to identify you from any publications.

Participant's Statement: I _____(your name) agree that the research project named above has been explained to my satisfaction and I agree to participate in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves. I have had the opportunity to consider the information, ask questions and had these answered satisfactorily.

I understand my participation is voluntary and I am free to withdraw from this study at any time during the period of data collection or engagement with the researcher without giving a reason and without my medical care or legal rights being affected.

I understand any information collected during this study will be held confidentially and will be shared within the Project D-BOX consortium anonymously. I understand that the outcomes of this study may be published in ERW & Mine Action journals and academic journals, as well as project reports. I also understand that individuals participating in the study will not be identified in any of these reports.

I consent to the processing of my personal information for the purposes of this research study. I understand that such information will be treated as strictly

confidential and handled in accordance with the provisions of the Bundesdatenschutzgesetz (BDSG).

I consent to my answers to be noted or video-recorded and transcribed.

I agree that the research team may use my data for future research and understand that any use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).

I agree to take part in this research.

Signed Date

Researcher's Statement: I, _____ (name of researcher), confirm that I have carefully explained the nature, demands and any foreseeable risks (where applicable) of the proposed research to the volunteer.

Signed Date

12.3 Interview Guide

1. Do you support the use of GMOs in general?

2. Do you support the use of GMOs in biosensors for the detection of explosives in landmines?

3. Which risks or drawbacks do you see in the use of GMOs in biosensors?

4. Who should be responsible for these risks?

5. Do you think the benefit of the detection of explosives in landmines outweighs the risks?

6. Which conditions must be fulfilled so that the use of GMOs in biosensors is ethically justified?

7. On the level of:

a. EU and national governments

b. Industry

c. Research Institutions

d. Media

8. Nearly all landmines are located in states outside the EU. Are there additional conditions which must be fulfilled so that the use of GMOs in these countries is ethically justified?

13. LITERATURE

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