Annex 5: Online Survey Health

BEETLE

Biological and Ecological Evaluation
towards Long-Term Effects

Long-term effects of genetically modified (GM) crops on health, biodiversity and the environment: prioritisation of potential risks and delimitation of uncertainties

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1. Introduction

One of the objectives of the project was the prioritisation of potential long-term effects of GM plants on animal and human health as well as the effective identification of areas of greatest scientific uncertainty. To achieve this goal, the BEETLE approach included consulting an extended expert panel and conducting a stepwise assessment. The conclusions of this allowed a ranking of potential long-term effects to be established, aimed at supporting the Commission in the ongoing task of improving GMO risk assessment and management.

In Steps 1 and 2, an initial and preliminary assessment of potential risks of GMOs and an identification of areas of greatest scientific uncertainty was performed by the BEETLE team based on a literature review (Annex 4 Literature Review Health). General mechanisms ('processes') were extracted that potentially could lead to adverse long-term health effects. Several specific processes were analyzed and preliminarily ranked in terms of probability for certain crop/trait combinations. The Step 2 results were the basis for Step 3: the development of questions to a broader scientific audience in the Online Survey Health (OSH). Representatives of different stakeholder groups were invited to participate in the online survey, but taking into account that a basic requirement was their scientific expertise. The extended expert panel had the following tasks:

(i) proof the completeness of the listed processes,

(ii) approve or correct the preliminary ranking, and

(iii) identify areas of uncertainty.

The experts specifically assessed whether the listed processes are relevant for the crop/trait combinations cultivated today or in the near future in the EU (Bt maize, HT oilseed rape, HT sugar beet, HT soybean, SM potato). It is important to emphasize that this evaluation did not lead to an absolute or quantitative but to a relative ranking and prioritisation among the processes. The expert contributions in the Online Survey Health helped to identify

a) processes with a high potential to cause adverse long-term effects, and on which there was good agreement among members of the panel;

b) areas of uncertainty highlighted by an ambiguous response or a high proportion of the answer 'don't know, insufficient data'.

2. Material & Methods

Based on the Literature Review nine processes (without the questions looking at stacked events) were identified as potentially causing adverse long-term effects. The experts were asked in the first part of the survey whether the list for each category was complete. In an open response option they had the opportunity to add possibly unrecognized processes or to comment on the general process list. In the second, more detailed part of the survey, the experts were asked to evaluate the relevance of the potential long-term effects in relation to crop/trait examples. Furthermore in the categories (A) 'Nutritional value' and (B) 'Toxicity' the experts were asked how the quality of the risk assessment might be improved. Different scenarios were proposed, and the experts were asked to indicate for each of them one of the following likelihoods: 'negligible', 'low' or 'high'. If the experts did not feel competent nor had the impression that the data basis was insufficient, they had the opportunity to answer 'don't know'. In some cases the experts' responses were differentiated into 'don't know, no expert' and 'don't know, insufficient data' respectively. The experts were also asked whether they would change their assessment if they had to assess stacked events. Finally, the experts were asked which field of research regarding long-term effects of GMOs on livestock and consumers should have the highest priority for financial support.

The structure of the Online Survey Health allowed a relative assessment based on the experts' knowledge and their personal interpretation of the probability of occurrence of adverse long-term effects. It has to be considered that the results reflect a frequency distribution of the personal assessment of experts. It is not possible to deduce directly a probability of incidence of potential long-term effects.

The BEETLE team analysed the expert assessments in detail. An overview of how conclusions were drawn is given in Table 1. The BEETLE team defined the decision criteria for the overall assessment of the responses in Table 2.

Altogether 185 experts were invited to participate in the Online Survey Health. The majority of the experts were scientists from research institutions and universities. They came from 17 different European and 7 different overseas countries. The participants were selected based on three major criteria: (a) known expertise substantiated by relevant scientific publications cited in the ICGEB database, (b) added value for the requested field in the BEETLE project (due to the area of specific competence) and (c) known representativeness for important stakeholder groups (see Table 3). In particular experts from countries outside the EU with a long experience of using GM feed and food were invited to participate.

Table 1: Assessment options in the Online Survey Health and corresponding BEETLE team interpretation regarding processes

Assessment options:	**BEETLE team interpretation**
negligible	The occurrence of the process causing adverse long-term effects is negligible (can be excluded with a high confidence). Therefore, no need for additional measures is given, remaining risks are covered by general surveillance (monitoring).
low	The occurrence of the process causing adverse long-term effects is possible to a low extent, on a case by case basis additional research or additional measures should be taken into account.
high	The occurrence of the process causing adverse long-term effects is possible to a relatively high extent, risk management measures are necessary to protect health.
don't know, insufficient data	An assessment of the process is not possible due to insufficient data. A high percentage of this answer to the survey question highlights an area of higher uncertainty; therefore more research is needed to close knowledge gaps.
don't know, no expert	An assessment of the process is not possible due to a lack of personal expertise; this answer was inevitable given the wide field of health-related disciplines addressed.

The ICGEB database[1] is a scientific bibliographic collection of studies on 'Biosafety and Risk Assessment in Biotechnology'. On 11 December 2007 the database held a total count of 6,166 records and 11,828 authors. The database is updated monthly and contains scientific articles (full reference + abstract), published in international scientific journals or conference proceedings from 1990 onwards, selected and classified by ICGEB scientists for the main topics of concern regarding the environmental release of GMOs. All records have been extracted from the internationally renowned applied life sciences database CAB ABSTRACTS [TM], and AgBiotechNet, the online service for Agricultural Biotechnologists from CABI Publishing. The CABI choice is based on the concept of avoiding 'any unnecessary duplication' but collecting very broadly available scientific information. CABI holds the main collection of data on biosafety which are not focused only on human health (main topic of PubMed, free accessible database of scientific bibliographic information, developed by NCBI primarily from MEDLINE and PreMEDLINE).

In addition, some experts were selected based on single publications in a field that was not sufficiently covered by the ICGEB database. Membership in a European Commission Working Group, or participation in EU funded research projects highly relevant to BEETLE or national Biosafety Commissions were other selection criteria.

[1] see http://www.icgeb.org/~bsafesrv/bsfdata1.htm

Table 2: Decision criteria for the overall assessment of processes

Interpretation	Decision criteria	Assessment options	Relative response of the experts
'negligible'	a) The majority (more than 50%) of the experts decided for the response option 'negligible'[1]	negligible low high don't know, insufficient data don't know, no expert	67% 20% 3% 0% 10%
'low'	a) The majority of the experts (more than 50%) responded with the option 'low'	no example found in the online survey	
	b) No option received more than 50% of the experts' votes, but a clear tendency was recognizable. More responses were found for the options 'negligible' and 'low' together than for the options 'low' and 'high' together[2]	negligible low high don't know, insufficient data don't know, no expert	35% 43% 9% 9% 4%
'high'	a) The majority of experts (more than 50%) responded with the option 'high'	no example found in the Online Survey Health	
	b) No option received more than 50% of the experts' votes, but a clear tendency was recognizable. More responses were found for the options 'low' and 'high' together than for the option 'low' and 'negligible' together	no example found in the Online Survey Health	
'area of uncertainty'	a) No clear tendency recognizable for one of the assessment options 'negligible', 'low' or 'high' or 'yes', 'no', 'don't know'[3]	Yes No don't know	38% 38% 24%
	b) A disproportionate percentage of the experts responded 'don't know, insufficient data'[4]	negligible low high don't know, insufficient data don't know, no expert	52% 10% 3% 17% 17%

[1] Example taken from process A.1.1, Bt-maize
[2] Example taken from process D.1.1
[3] Example taken from process A.3.2
[4] Example taken from process A.1.1, starch potato

For completeness, three important stakeholder groups were also invited to participate in the online survey: Companies developing the GM plant applications at the EU level, non-governmental organisations (NGO) contributing scientifically to the GMO debate and regulators working in governmental bodies. Known experts were chosen representing the major companies. Members of NGOs were selected based on recommendations of the Peer

Review Committee. A similar number of industry and NGO representatives were invited to try to ensure balance.

3. Results

3.1. General aspects

At least 52 of the 185 invited experts registered for the online survey (see Table 3). However some of them rejected the Online Survey in principle and did not answer the questions or answered only some questions. On average 27 experts (14.4%) responded to each question (range 23-30). The tendency was observed that the number of answers decreased to the end of the Online Survey. From the stakeholder group 'NGO' no expert answered at all. One NGO expert registered but did not answer any question. The reasons for this reaction were unclear.

In general the number of participants was low, so that conclusions from the Online Survey Health should be interpreted very carefully.

Table 3: Participants of the Online Survey Health. Presented are the number of invited and participating experts for each stakeholder group and the relative proportion.

Stakeholder	Number of participants		Percentage	
	invited	participating	invited	participating
Research institution	108	28	58.4 %	53.9 %
Regulation	33	8	17.8 %	15,4 %
Industry	26	10	14.1 %	19.2 %
NGO	18	1	9.7 %	1.9 %
Other[1]	-	5	-	9.6 %
Sum	185	52	100 %	100%

[1]Differences between the 'invited' and 'participating' stakeholder affiliation are caused by the fact that experts relocated themselves to other stakeholder groups after registration.

3.2. Category A: Nutritional value

In this category the experts were asked whether GM-crops might affect human or animal health by decreased nutritional value or changes in the spectrum of metabolites. Additionally, for some aspects, BEETLE asked for the experts' opinion of how risk assessment procedures might be improved concerning long-term effects. Altogether five processes influencing the nutritional value for feed were identified.

More than 60% of the experts (60% - 69%) were of the opinion that the likelihood of adverse effects on livestock or on (human) consumers due to unintended decreased nutritional value of feed or food derived from the listed crop/trait combinations was negligible. For SM potato more than 50% of the experts (52% - 55%) assessed potential long-term effects as negligible, but 17% were of the opinion that the data basis is insufficient for an assessment.

Concerning the question of how risk assessment procedures might be improved, a majority of experts proposed an increasing number of replications (48% -53%) and additional control groups fed with conventional varieties (63% - 66%). In contrast the extension of studies over the whole life span (50% - 55%) or extended studies over several generations (53% - 62%) of target animals were answered by the majority of the experts with 'no'. The question of whether there should be more studies with GM output traits (GM plants of the 2nd generation) was answered by the majority of experts with 'yes' (63% vs. 17% (no)).

The question of whether genetic modification of plants may result in unintended changes in the spectrum of their metabolites was answered ambiguously. Even though the spectrum of metabolites is tested in the risk assessment (test of substantial equivalence), 45% of the experts voted that increasing modifications could result in unpredictable changes in metabolites. The answers to the question on additive, synergistic or antagonistic effects of gene products showed no clear picture (38% (yes) vs. 38% (no)).

The likelihood of potential long-term effects due to the consumption of food or feed mixtures containing different GM crop/trait combinations was assessed as low: 47 % of the experts decided for the response option 'negligible', but 23% decided for 'low' and 13% for 'high' respectively. Furthermore, 13% of the experts believe that the data basis is still insufficient for an assessment.

3.3. Category B: Toxicity

However, there are currently disagreements about the value and relevance of toxicity tests. The experts were asked about potential improvements in the risk assessment procedure.

Most experts were of the opinion that the toxicity tests should be improved; in particular they voted for a better design and improved statistical analysis. In addition most experts agreed that additional control groups would be useful to demonstrate the biological range of measured parameters. In contrast the experts did not clearly vote for longer exposure tests (46 % (yes) vs. 50 % (no)). However a majority (77%) of the experts believed that data from animal testing are also suitable to assess potential effects on non-target vertebrates.

3.4. Category C: Horizontal gene transfer

In the third category of the Online Survey Health the experts were asked whether horizontal gene transfer to consumer or livestock and to microorganisms in the gastrointestinal tract could have adverse long-term effects on human or animal health. The majority of experts assessed the likelihood of both processes as negligible (75 and 65%). However 13% of the experts answered ‘don’t know, insuff. data’ in relation to horizontal gene transfer to microorganisms in the gastrointestinal tract.

3.5. Category D: Allergenicity

The allergenic potential due to new proteins in crops was assessed as negligible to low by the experts (43% (negligible) vs. 35% (low)). The same opinion was expressed regarding the question of whether allergic reactions are likely to arise due to the increased exposure of consumers.

Regarding the question of whether adverse effects are likely to arise due to increased exposure of consumers to a higher expression of natural endogenous allergens, the experts assessed the likelihood of this scenario as negligible to low (33 % (negligible) vs. 38 % (low)) but in contrast to the preceding questions a higher proportion of the experts assessed the probability of this scenario as high (17 %).

3.6. Stacked events

In each category the experts were asked for their view for stacked events. The majority of the experts (55% to 71% according to the process) would not assess the likelihood of effects from single and stacked events differently. About 8% to 14% of the experts were of the opinion that the data basis is insufficient.

3.7. Open Comments

The experts were asked whether the list of processes was complete within each category. All comments are listed in the Appendix point II A-D. In general, most of the experts were of the opinion that the listed processes in the different categories were complete (range: 73% to 91%).

As in the Online Survey Environment (see Annex 2) no principally new processes were added by those experts who had the feeling that the categories were incomplete. The majority of these critical experts expressed general doubt on the usefulness of the approach.

Single comments were made that

- the questions in the survey were inherently biased,
- all questions had already been answered in the environmental risk assessment and posed no additional risk to animal and human health,
- the Online Survey Health was limited to potential effects in relation to unintended phenotypes, and that
- benefits of GM crops e.g. in relation to mycotoxin content should be considered.

3.8. Final Question

At the end of the Online Survey Health the experts were asked: ‘In which field of research regarding long-term effects of GMOs on livestock and consumers should the highest priority for financial support be given?’ The answers were expected to provide additional hints regarding areas of uncertainty. All answers are listed in the Appendix II E. However, the experts did not agree on a favoured research topic. Answers were more or less equally distributed. Experts would invest money into the following areas

- improvement of toxicity tests,
- development of prediction methods for allergenicity,
- nutritional value of GM plants,
- horizontal gene transfer,
- effects caused by stacked events,
- benefits of GM plants on animal and human health, or
- in other research fields, because there is no need for additional money regarding potential long-term effects on human or animal health.

4. Summary

The Online Survey Health provided additional information for the prioritization process and helped to identify areas of uncertainty. However, due to the small number of participants the results of the Online Survey must be interpreted carefully, in particular due to the relative high proportion of representatives from companies. Nevertheless the experts came to clear

assessments for most processes and cases. Potential long-term effects are likely in relation to allergenicity. In all other categories the likelihood of adverse long-term effects was assessed as negligible by the majority of the experts.

The experts voted for methodological improvements in the risk assessment procedure. In particular the design of the tests should be improved by using a larger number of replications and additional control groups to demonstrate the biological range of measured parameters. In contrast the Online Survey Health could not support with a clear answer whether the risk assessment should be improved by extended studies over the whole lifespan or over several generations of the target animals. The answers suggested that the experts tended to consider this approach as less important. One area of uncertainty identified in relation to potential adverse effects on health was the possibility of unintended changes in the spectrum of metabolites of genetically modified crops. Even though the spectrum of metabolites is tested in the risk assessment (test for degree of equivalence to a known comparator), nearly half of the experts believed that increasing modifications of complex pathways in plants could result in unpredictable changes in metabolites. In addition the Online Survey Health could not support with a clear answer whether additive, synergistic or antagonistic effects of gene products and/or the produced metabolites are likely long-term effects.

In addition, uncertainty was indicated in the case of potential adverse effects due to decreased nutritional value of the SM potato: 17% of the experts felt that the data basis is insufficient. It should be kept in mind that the SM potato has not been designed for food or feed purposes.

In the case of adverse effects due to a higher allergenic potential of GM crops, the scenario of an increased exposure of consumers to a higher expression of natural endogenous allergens deserves some attention. Even though a high proportion of experts assessed the probability of this scenario as negligible to low (33 % (negligible) vs. 38 % (low)) a relatively high proportion of experts (17%) assessed this scenario as high.

The results of the Literature Review Health were confirmed in most cases. The expert assessment gave helpful additional information for the prioritisation process and identification of areas of uncertainty.

Appendix

I. Assessment of processes and cases (crop/trait combinations)

A. Category A: Nutritional value

Step 1: Collection of important biological processes caused by the intended phenotype of the GMP that may lead to long-term effects.

A.1	Decreased nutritional value of feed results in decreased growth and/or adverse health effects on livestock.			
A.2	Decreased nutritional value of food results in malnutrition and/or adverse health effects on [human] consumers.			
A.3	Genetic modification of plants results in unintended changes in the spectrum of their metabolites.			
A.4	Mixtures of different events in feed and food may cause additive adverse effects.			
A.5	Stacked events: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes.			
	Is the list for this category complete?	[2]Σ	30	100%
		Yes	24	80%
		No	6	20%
	If not, other important processes to assess? Please explain your answer.			

[2] The table presents response options (column 1, row 2ff), the total number of participants (column 2, row 1), the distribution to the different response option (column 2, row 2ff) and the percentage of the different response options (column 3).

Step 2: Prioritization of long-term effects

A.1 Decreased nutritional value of feed results in decreased growth and/or adverse health effects on livestock.

Scenario: Assessing long-term effects of GM plants on livestock is only relevant for dairy cattle or **breeding** animals, because lifespan of livestock for meat production ranges between 35 and 500 days, depending on the species.

Case (theses): Adverse long-term effects will arise due to unintended decreased nutritional value (**digestibility**, bioavailability of nutrients, anti-nutritiva) resulting in decreased growth and/or adverse health effects on dairy cattle and breeding animals for...

A.1.1	…Bt-**maize**.	Σ	30	100%
		Negligible	20	67%
		Low	6	20%
		High	1	3%
		insuff. data	0	0%
		no expert	3	10%
	…HT-maize.	Σ	30	100%
		Negligible	20	67%
		Low	5	17%
		High	1	3%
		insuff. data	1	3%
		no expert	3	10%
	…HT-soybean.	Σ	30	100%
		Negligible	20	67%
		Low	5	17%
		High	1	3%
		insuff. data	1	3%
		no expert	3	10%
	…HT-oilseed rape.	Σ	30	100%
		Negligible	20	67%
		Low	6	20%
		High	1	3%
		insuff. data	1	3%
		no expert	2	7%
	…HT-sugar beet.	Σ	30	100%
		Negligible	18	60%
		Low	5	17%
		High	1	3%
		insuff. data	2	7%
		no expert	4	13%
	…starch potato.	Σ	29	100%
		Negligible	15	52%
		Low	3	10%
		High	1	3%
		insuff. data	5	17%
		no expert	5	17%

Quality of risk assessment: The nutritional assessment might be improved by...				
A.1.2	…increasing number of replications.	Σ	30	100%
		Yes	16	53%
		No	11	37%
		Don't know	3	10%
A.1.3	…additional control groups with conventional varieties (not only the near isogenic counterpart) to demonstrate the biological range of measured parameters.	Σ	30	100%
		Yes	19	63%
		No	9	30%
		Don't know	2	7%
A.1.4	…extended studies over the whole lifespan of the target animals.	Σ	30	100%
		Yes	13	43%
		No	15	50%
		Don't know	2	7%
A.1.5	…extended studies over several generations of target animals.	Σ	30	100%
		Yes	11	37%
		No	16	53%
		Don't know	3	10%
A.1.6	…more studies with GMP with output traits (GMP of the 2nd generation).	Σ	30	100%
		Yes	19	63%
		No	6	20%
		Don't know	5	17%

A.2 Decreased nutritional value of food results in malnutrition and/or adverse health effects on [human**] consumers**				
Case (theses): In the long term, consumers are potentially affected by unintended decreased nutritional value of the GM crops or the derived products of…				
A.2.1	…Bt-maize.	Σ	29	100%
		Negligible	20	69%
		Low	6	21%
		High	0	0%
		insuff. data	1	3%
		no expert	2	7%
	…HT-maize.	Σ	29	100%
		Negligible	19	66%
		Low	6	21%
		High	0	0%
		insuff. data	2	7%
		no expert	2	7%
	…HT-soybean.	Σ	29	100%
		Negligible	19	66%
		Low	7	24%
		High	0	0%
		insuff. data	1	3%
		no expert	2	7%
	…Starch potato.	Σ	29	100%
		Negligible	16	55%
		Low	5	17%
		High	0	0%
		insuff. data	5	17%
		no expert	3	10%

Quality of risk assessment: The nutritional assessment concerning long-term effects might be improved by...				
A.2.2	…increasing number of replications.	Σ	29	100%
		Yes	14	48%
		No	12	41%
		Don't know	3	10%
A.2.3	…additional control groups with conventional varieties (not only the near isogenic counterpart) to demonstrate the biological range of measured parameters.	Σ	29	100%
		Yes	19	66%
		No	9	31%
		Don't know	1	3%
A.2.4	…extended studies over the whole lifespan of the target animals.	Σ	29	100%
		Yes	12	41%
		No	16	55%
		Don't know	1	3%
A.2.5	…extended studies over several generations of target animals.	Σ	29	100%
		Yes	9	31%
		No	18	62%
		Don't know	2	7%

A.3 Genetic modification **of plants results in unintended changes in the spectrum of their metabolites.**				
Scenario: Adverse long-term effects may arise due to unintended changes in the spectrum of metabolites despite the conducted risk assessment (test for substantial equivalence).				
Case (theses): Adverse long-term effects will arise due to…				
A.3.1	…the increasing modifications of complex pathways resulting in unpredictable (and undetected) changes of metabolites.	Σ	29	100%
		Yes	13	45%
		No	11	38%
		Don't know	5	17%
A.3.2.	…additive, synergistic or antagonistic effects of the gene products and/or the produced metabolites.	Σ	29	100%
		Yes	11	38%
		No	11	38%
		Don't know	7	24%

A.4 Mixtures of different events in feed and food may cause additive adverse effects.				
Scenario: The number of GM crops with different traits is increasing. Mixtures of different crop/trait combinations in food and feed may occur. Consumption of different traits may result in additive or synergistic adverse effects on humans or livestock.				
Case (theses): Adverse long-term effects will arise due to…				
A.4.1	…consumption of a food or feed mixture containing different GM crop/trait combinations.	Σ	30	100%
		Negligible	14	47%
		Low	7	23%
		High	4	13%
		insuff. data	4	13%
		no expert	1	3%

A.5 Stacked events: GM crops **with stacked traits need a different assessment of the above mentioned long-term effects and processes**				
Case (theses):				
A.5.1	Concerning the processes mentioned in A1 to A 4: Would you change your assessments if you look at GMO with stacked traits (for maize: combination of IR/HR; for oilseed rape and sugar beet: combination of different HT traits); in comparison to GMO with single traits?	Σ	29	100%
		Yes	8	28%
		No	16	55%
		insuff. data	4	14%
		no expert	1	3%

B. Category B: Toxicity

Step 1: Collection of important biological processes caused by the intended phenotype of the GMP that may lead to long-term effects

B.1	Consumers or livestock are affected adversely by toxicity of GM plants and derived products due to chronic exposure.			
B.2	Stacked events: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes.			
	Is the list for this category complete?	Σ	26	100%
		Yes	19	73%
		No	7	27%
	If not, other important processes to assess? Please explain your answer.			

Step 2: Prioritization of long-term effects

B.1 Consumers or livestock are affected adversely by toxicity of GM plants and derived products due to chronic exposure**.**				
Scenario: So far no toxic effects have been observed after consumption of Bt crops or derived products. However, there are presently disagreements about value and relevance of tests. A harmonised approach for the statistical analysis of data obtained from animal experiments and their interpretation is not available. Therefore, the results are discussed controversially (example MON863: Seralini et al. 2007 vs. Hammond et al. 2007/EFSA 2007).				
Quality of risk assessment: The nutritional assessment might be improved by...				
B.1.1	…better designed, appropriate and diversified toxicity tests.	Σ	26	100%
		Yes	18	69%
		No	6	23%
		Don't know	2	8%
B.1.2	…better statistical analysis of data from animal toxicity studies and interpretation of the results regarding their biological relevance.	Σ	26	100%
		Yes	16	62%
		No	9	35%
		Don't know	1	4%
B.1.3	…longer duration of exposure to the test animals taking into account chronic intake of various GM crops at low levels.	Σ	26	100%
		Yes	12	46%
		No	13	50%
		Don't know	1	4%
B.1.4	…additional control groups with conventional varieties to demonstrate the biological range of measured parameters.	Σ	25	100%
		Yes	17	68%
		No	7	28%
		Don't know	1	4%
B.1.5	Do you agree that data from animal testing for food & feed safety are suitable to assess potential effects on non-target vertebrates?	Σ	26	100%
		Yes	20	77%
		No	3	12%
		Don't know	3	12%

B.2 Stacked events: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes				
Case (theses):				
B.2.1	Concerning the processes mentioned in A1 to A 4: Would you change your assessments if you look at GMO with stacked traits (for maize: combination of IR/HR; for oilseed rape and sugar beet: combination of different HT traits); in comparison to GMO with single traits?	Σ	26	100%
		Yes	8	31%
		No	15	58%
		insuff. data	3	12%
		no expert	0	0%

C. Category C: Horizontal gene transfer

Step 1: Collection of important biological processes caused by the intended phenotype of the GMP that may lead to long-term effects

C.1	Horizontal gene transfer to consumers or livestock causes unintended adverse effects.			
C.2	Horizontal gene transfer to microorganisms living in the gastrointestinal tract of human beings or livestock causes unintended adverse effects to human or animal health (e.g. transferred antibiotic resistance to pathogenic microorganisms).			
C.3	Stacked events: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes.			
	Is the list for this category complete?	Σ	23	100%
		Yes	21	91%
		No	2	9%
	If not, other important processes to assess? Please explain your answer.			

Step 2: Prioritization of long-term effects

C.1 Horizontal **gene transfer to consumers or livestock causes unintended adverse effects.**				
Scenario: There are some reports that DNA fragments were found in animal tissue. However, there is no evidence that either functional DNA fragments were introduced in the genome or that transgenic DNA will be transferred to progeny.				
Case (theses): Adverse long-term effects will arise due to…				
C.1.1	…horizontal gene transfer of transgenic DNA to consumer or livestock.	Σ	24	100%
		Negligible	18	75%
		Low	4	17%
		High	1	4%
		insuff. data	0	0%
		no expert	1	4%

C.2 Horizontal gene **transfer to microorganisms living in the gastrointestinal tract of human beings or livestock causes unintended adverse effects to human or animal health.**				
Case (theses): Adverse long-term effects will arise due to…				
C.2.1	…increasing antibiotic resistance due to horizontal gene transfer to potential pathogenic microorganisms in the gastrointestinal tract.	Σ	23	100%
		Negligible	15	65%
		Low	2	9%
		High	1	4%
		insuff. data	3	13%
		no expert	2	9%

C3 Stacked events**: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes**				
Case (theses**)**:				
C.3.1	Concerning the processes mentioned in C1 to C2: Would you change your assessments if you look at GMO with stacked traits (for maize: combination of IR/HR; for oilseed rape and sugar beet: combination of different HT traits); in comparison to GMO with single traits?	Σ	23	100%
		Yes	5	22%
		No	14	61%
		insuff. data	3	13%
		no expert	1	4%

D. Allergenicity

Step 1: Collection of important biological processes caused by the intended phenotype of the GMP that may lead to long-term effects

D.1	Newly expressed proteins have high allergenic potential.			
D.2	The potential allergenicity of the whole plant and derived product is increased due to e.g. over-expression of natural endogenous allergens as an unintended effect of the genetic modification.			
D.3	Stacked events: GM crops with stacked traits need a different assessment of the above mentioned long-term effects and processes.			
	Is the list for this category complete?	Σ	24	100%
		Yes	20	83%
		No	4	17%
	If not, other important processes to assess? Please explain your answer.			

Step 2: Prioritization of long-term effects

D.1 Newly expressed proteins have high allergenic potential.				
Scenario: 1. Genetic modification results in the expression of new proteins in crops. 2. Genetic modification results in the expression of known proteins from not (or seldom) consumed crops in staple foods.				
Case (theses): Adverse long-term effects will arise due to ...				
D.1.1	…the unpredictable allergenic potential of such new proteins which might become manifest only after long-term exposure and resulting sensitization of certain population groups.	Σ	23	100%
		Negligible	8	35%
		Low	10	43%
		High	2	9%
		insuff. data	2	9%
		no expert	1	4%
D.1.2	…the development of allergic reactions due to the increased exposure of consumers to such proteins.	Σ	23	100%
		Negligible	8	35%
		Low	10	43%
		High	2	9%
		insuff. data	2	9%
		no expert	1	4%

D.2 The potential allergenicity of the whole plant and derived product is increased due to e.g. over-expression of natural endogenous allergens as an unintended effect of the genetic modification.				
Case (theses): Adverse long-term effects will arise due to…				
D.2.1	…increased exposition of consumers due to a higher expression of natural endogenous allergens.	Σ	24	100%
		Negligible	8	33%
		Low	9	38%
		High	4	17%
		insuff. data	2	8%
		no expert	1	4%

D.3. Staked **events**				
Case (theses):				
D.3.1	Concerning the processes mentioned in D1 to D 6: Would you change your assessments if you look at GMO with stacked traits (for maize: combination of IR/HR; for oilseed rape and sugar beet: combination of different HT traits); in comparison to GMO with single traits?	Σ	24	100%
		Yes	4	17%
		No	17	71%
		insuff. data	2	8%
		no expert	1	4%

E. Final question

E.1.	If you had 100,000 Euros available, which field of research (according to our four categories) regarding long-term effects of GMOs on livestock and consumers in the EU would you give highest priority to financial support?

II. Open field answers

A. Step One Answers for Category A

It is questionable, whether only decreased nutritional values of food may lead to adverse health effects. "Over-nutrition" appears to be a big problem in well developed societies.
The questions are not focusing on intended effects as stated in the title but on unintended and unexpected effects that are ruled out by testing during crop development. Unintended effects and potential effects are well addressed in the case by case risk assessment in the specific application.
Other processes to consider: - Changes giving rise allergic sensitization and/or allergic responses, such as when a new protein introduced into the GMO becomes a new allergen or when the genetic modification has changed the intrinsic allergenicity of the recipient organism (NB so far the fist scenario is known to have occurred only in an experimental GMO, i.e. soybean modified with 2S globulin from Brazil nut) - Antibiotic resistance of pathogens caused by potential horizontal transfer of antibiotic resistance genes from a GMO to the pathogen. So far, this has only been a hypothetical scenario for which a very remote likelihood exists.
From the beginning of the survey I feel that there are bias: for me the first questions are: does these processes are plausible or not, in which cases, why? Based on which existing data? In relation with which specific dossiers? This starting point of the survey has no sense for me! I refuse to continue this survey, the results of which could be interpreted only in one sense: the present evaluation of existing GMP is not sufficient, the risk for human and animal health is not correctly presently assessed .... There is no relevant, validated methodology to test long-term effects of feed or food which is a totally different question than the assessment of a drug, a pesticide, a food contaminant, substances chemically defined and for which the human or animal exposure is very low. If you know how to do, I am very interested to receive your proposal. Sorry but I have more than 40 years of experience as a researcher and as an expert involved in the food safety assessment at the national, European and international level (WHO) and I have no found the solution. New methodologies (not still validated) are developing for answering the question but obviously there are not traditional methodology which can be the solution.
These issues are not unique to GM crops. So called conventional breeding techniques also may affect the above. Any approach to GM crop ingestion should also apply to other methods of crop modification
Decreased levels of mycotoxins due to improved health of crop results in improved growth and overall health of livestock. *Improved test weight of grain due to improved health of crop results in improved growth and overall health of poultry. Equal time should be given to unintended benefits of the biotech product. Furthermore, none of the negative impacts listed have actually occurred whereas the positive ones are real examples. If a crop has been shown to be substantially equivalent, then none of the examples listed are valid. To date that is the case with all approved biotech products.
Extended studies with treated groups should be necessary (same number of individuals in treated and control groups, which is not the case today).
new metabolites and different degradation products (for example in the context of herbicide resistant plants)of herbicides and bt toxins with long term health impact not only additive but also synergistic effects (of 3 different herbicides and their metabolites

These items are of THEORETICAL importance, but of little practical importance given the routine assessment of nutrient and anti-nutrient composition and animal wholesomeness. A number of theoretical issues here are at least as valid for conventionally derived traits as for GM traits, if not more so- See the US NAS report on unanticipated changes in GM foods and Crops.
1) I read the question as asking for health issues related to the INTENDED phenotype. I doubt that decreased nutritional value (A.1 and A.2) will commonly be an intended phenotype. The same comment is relevant for A.3, where the issue is unintended effects when the question specifies intended effects. 2) A more likely data gap would be to verify that the intended phenotype actually results in the intended effects. For example, modifying the ratio of saturated to trans-fatty acids is assumed to be heart healthy. However, verifying that the intended pheontype actually is associated with improved cardiovascular health is less certain.
Extended studies with treated groups should be necessary (same number of individuals in treated and control groups, which is not the case today).
The above list assumes all long term effects to be negative. Evidence from Bt corn in studies conducted in both Italy and the United States indicates reduced levels of Fumonisin with beneficial effects on both human and animal health. A.6 Enhanced nutritional value through reduction in fungal pathogens
Unfortunately long term effects can not be categorizes in simply nutritional, toxicological areas. Most unintended effects will arise from complex interactions between toxicology, nutrition and environmental effects such as by changes of agricultural practices and consequent problems possibly addressing all aspects (see conclusions from the UK large scale trial). Unfortunately the format of the questionnaire does not address these interactions. People should learn from environmental health areas and ways to analyse interactions between toxicology, nutrition, environment.

B. Step One Answers for Category B

The effect of long term feeding of GM plants/transgenic protein and their presence or influence in/on vital organs vis-à-vis in milk/meat and their products need to be assessed.
The questions are not focusing on intended effects as stated in the title but on unintended and unexpected effects that well addressed in the case by case risk assessment in the specific application.
Indirect effects of the genetic modification can also be considered, e.g. chronic exposure to lower levels of mycotoxins due to less insect damage, and thus less mould infestation, in Bt maize and other Bt crops could lead to less cancer caused by these mycotoxins in consumers.
Toxicity testing of most GM crops will not only be a waste of time and money but unjustifiable from an animal ethics perspective because they cannot yield interpretable data. Need to look at the results from pharmaceutical carcinogenicity studies with dual control groups where statistically significant differences, purely artificial, are routine.
The attempt to address the indicated risks by specifying only classes of GM crops such as GM maize without differentiating the only relevant specific single transformation events does make answers possible.

I'm sorry, but I find the statements listed here very influenced. B.1 There will be no toxic GM plants on the market, because this is clarified in the pre-market safety assessment.
*Improved health of farmers due to decreased exposure to pesticides because of reduced application requirements. *Improved health of non-target insects due to decreased need for nonspecific pesticide applications. *Decreased petroleum product consumption due to reduced need to make chemical applications. Consumers or livestock are NOT adversely affected by consumption of biotechnology products. There is no data to support the question, GM plants are NOT toxic. Living is not good for your health as the eventual end-point for all organisms is death. However, there are multiple benefits to the farmer, to the environment, to non-target organisms, etc.
1) As with the nutritional assessment questions, B.1 relates to unintended effects when Step 1 specifically asks about an INTENDED phenotype. I doubt that the intended phenotype of a GMP would be to cause long-term health effects. Perhaps Step 1 should have been worded "caused by an unintended phenotype resulting from a changed genotype." 2) For an intended phenotype, the consensus of nutritionists is constantly evolving. As such, what nutritionists feel is advantageous today may change tomorrow. As such, the benefits and risks of nutritional modification of plants should be backed by data rather then simply by inference from separate nutritional studies (e.g., just because a GMP has less saturated fat does not necessarily mean is more healthy than the parental variety).
The question should be: What tests are necessary to assess chronic health effect of GMOs ? The access to raw data (blood and organ analyses) for all animals having eaten commercialized GMOs should be rendered public.

C. Step One Answers for Category C

Horizontal gene transfer is a very rare event and therefore effects are negligible at all if the transgenes exist in the environment
Horizontal gene transfer for GM crops is no more likely than for non GM crops.
In this case, it appears that the word phenotype is inappropriate. Considering C.1, C.2, and C.3 all deal with gene transfer, the issues have little to do with the phenotype and a lot to do with the genotype of the plant. For genotype, the major health issues were originally identified as related to gene transfer. However, after years of practical experience and molecular research, this has not happened and has been widely discredited as a potential unintended effect from currently employed gene transfer technologies.
Questions about assessment of stacked events are unclear for me: They need the same level of assessment but new aspects considering more complex fitness characteristics. A: Toxicology studies need better standardisation, methods for testing unintended effects (combination of rodents feeding whole food and molecular methods; this avoiding public concern about different interpretation of data by different committees. Genetic instability and loss of markers in intended and unintended stacked events and further breeding might be the most problematic aspect in the GM field.

D. Step One Answers for Category D

Allergenicity is no long-term effect and any potential effects are better addressed than with any conventionally bred variety.

Newly expressed proteins per se (just because they are newly expressed) do not have a higher allergenic potential than any other protein. Very few proteins are actually allergens; allergens are frequently very highly expressed proteins (>1% by weight). Novel proteins are usually expressed at very low levels (<0.01%). There is a state-of-the-art weight-of-evidence approach taken to evaluate the potential allergenicity of the novel protein as part of the overall safety assessment of the product. Organic carrot varieties have been shown to have higher levels of allergens when grown organically than when grown under conventional conditions. These allergens have as their role in the carrot to protect the carrot from pathogens that they are more likely to encounter when grown organically than conventionally. These carrots have been purposely bred for growth under organic conditions. On the other hand, biotech products have not been bred with this in mind. Very little work has been published regarding the variability of the levels of endogenous allergens across conventional genotypes, growing conditions or locations. This information is needed prior to making any conclusions about the impact of a transformation event on levels of endogenous allergens.
These issues, to the extent they are meaningful at all, are equally applicable to conventional breeding technologies. There are tens of thousands to millions of dietary proteins and variants (recalling that many would consider even a single amino acid change novel... probably millions) vs a tiny handful of significant allergens. The a-priori probability of any protein being a major food allergen is nearly nil and after exclusion of known allergenic homologies and allergenic gene sources, is likely to be utterly inconsequential. At birth, NONE of these proteins has been consumed by the individual- thus every human being has exposure over a lifetime to immense numbers of "new" proteins, with consequences being exceedingly rare. This is a grossly overblown and entirely theoretical issue.
D.1 relates to allergenicity, which is widely recognized as an acute exposure phenomenon. As such, the potential allergenic potential of GMPs should not be included in a category devoted to assessing long-term effects. As such, the question would be much more relevant if it were directed toward acute or intermediate-term effects, rather than long-term effects.
I don't agree to point D.1. For me the list is not complete because the first statement is not correct.
Conjugative processes need enhanced attention. Molecular assessment have considerably improved recently. Allergenicity assessment needs combined toxicological and environmental (environmental health) assessment (e.g. looking for groups of farmers, citizens and their interaction with potential proteins). Subsequent D need a case by case approach.

E. Final Question Answers

Horizontal gene transfer
C. Horizontal gene transfer as the response to common critical comments from ecologist, biologist, politicians who are expressing their negative attitude to GMO.
Nutritive value and toxic effect of GMOs on livestock and consumers.
Building awareness amongst experts and public for the topic food safety as such with all its limitations and the rationale of testing and analyzing testing results in the current manner Focusing on benefits of GM technology by decreased amounts of anti-nutrients as mycotoxins

Research into prediction methods for allergenicity
This survey is a scandal! It is a "scenario catastrophe" not based on any relevant scientific data. The huge amount of scientific literature on the subject seems ignored. All the potential effects mentioned are taken into account in the present evaluation of GMP by hundred of competent scientists all around the world. Only a few people, without any competence verify on the basis of their scientific publications contest this evaluation. This survey is totally directed to obtain the wished results, which can be on no account considered as scientific and objective. I dispute it formally! If I had 100,000 Euros available I will try to avoid wasting them in a long term study on GMO, but I will identify actual public health problem on an epidemiological basis like food behaviour in relation to overweight and obesity and all the diseases associated: CVD, Diabetes, certain types of cancer. We are living in a real life and we have serious problems of public health in developed and essentially developing countries; please don't forget the priorities for the protection of public health. I should be obliged to react personally to your initiative at the level of the European Commission and the European Parliament! I will diffuse largely this survey for information of the scientific community!
Environmental issues such as loss of genetic diversity or effect on native animals and insects. Toxicity testing of GM crops is not only a waste of money but ethically unjustifiable. Given their inevitable failure to distinguish between GM and native foods the use of experimental animals for such a purpose is clearly unethical. The inability to establish: meaningful dose escalation, significant margins of exposure with respect to human intakes and to adequately compensate for inevitable dietary imbalances makes such studies uninterpretable. Experience form the pharmaceutical regulatory area where dual control groups have been commonly used in carcinogenicity studies for some years demonstrate that statistically significant, but artificial differences between rats fed a GM crop and others fed the native crop would arise. These results would be irreproducible, uninterpretable and serve only to confound rather than inform the debate around GM foods. Nutritional studies are also unlikely to reveal very much of value as GM modification is no more likely to unintentionally affect this aspect of food than is conventional breeding.
I would not like to take the grant because I do not envision that there will be long term effect if there are no differences between GM or non-GM product in chemical components including protein. The effect of target protein could be performed in a rather simpler way.
Since the GMO proteins are digested in the gastrointestinal tract and are not absorbed into the bloodstream and thus not found in any tissue outside the GI tract, what is the scientific justification for long-term feeding studies? When the tissues are not exposured to the GM protein why would one spend money to look at long-term effects. Are microbial products, enzyme products, herbal products containing many different and foreign compounds to the animal evaluated to the same level and rigor as the GM products? Those advocating for long-term studies for GM products need to provide sound scientific justification and treat all protein products in a similar. Regarding horizontal gene transfer in animals and microbes, animals and humans have been consuming plant, insect, animal, viral, microbial, etc. DNA since the beginning of time when animals starting occupying this earth. There is agreement within the scientific community that consuming DNA from any source is not a safety issue. Therefore, I would spend no money in this area. Regarding allergenic proteins, existing safety assessment would identify any new proteins. These proteins go through a rigorous assessment to determine allergenic potential before they are even considered for use. There are no definitive models in place that can predict allergenicity in humans 100% of the time regardless of the protein. If I had 100,000 Euros, I would spent it on how the use of GMO's can reduce mycotoxins in food and feed. Mycotoxin consumption is a major problem in food and feed and can result negative short and long-term effects in humans and animals. The use of GMO's especially maize can help mitigate the costly and devastating known food and feed safety effects of mycotoxins in non-GMO maize that is seen in the EU today.

In the 12 years since biotechnology products have been on the market, there have been no examples of adverse effects on livestock and the consumers to date. Why? - because the safety evaluations of these products have been thorough and complete. No product has been approved for which there has been even the remotest safety concern. The first generation products have expressed either a new protein (in addition to a selectable marker) or turned off the expression of an endogenous protein. Proteins are inherently safe and indeed are a dietary requirement for humans (and livestock). They are broken down in the digestive system that has been designed and has evolved over the years specifically to break down our dietary components to their building blocks which are then absorbed and used to produce the organism's own protein, for instance. There are some known protein toxins that are easily screened for prior to seeking regulatory approval (those proteins would immediately be dropped from consideration). Understanding the natural variability of endogenous allergens in various crop plants would be important to understand, however, since a threshold for sensitization as well as one for elicitation is not known, it would be hard to apply that data to answering the question about how a transformation event will impact the inherent variability of a known allergenic food. In my opinion, the best use of 100,000 Euros would be to educate the consumer regarding the true benefits of products produced through biotechnology. These benefits include benefits to the farmer (lower pesticide exposure, improved yield, lower cost), environment (improved production on arable land, hence saving the rainforest, less input of chemicals into the environment, reduced petroleum product use) AND consumer (healthier products, lower mycotoxin levels, less food borne disease, less expensive food, more available food).
Allergenicity. The key to many of these questions that have been proposed is an assessment of the trait that is being expressed. This would have to be evaluated on a case by case basis. Introduction of traits that specifically alter nutrient composition (e.g., fatty acid profile) are far more likely to have an impact on the livestock that consume it. Likewise modification in the meat or milk quality of livestock as a result of consumption of such GM modified crops could have consequences for human health. I do not see these risks arising from presently approved IR or HT traits.
It should be the effect of GMP's with stacked traits and their effect on reproductive parameters in experimental animals (as a predictor for the effect on consumers).
A. Nutritional value
Start to develop an in vitro detection system for food/feed allergenes. However 100,000 Euro is not suitable to establish new research activities especially when investigating long-term effects.
Advanced studies on GMP’s of the second generation for nutritional evaluations including: • Long and short term feeding studies • Monitoring of adverse side effect (allergenic or morphologic variances)
I would sponsor an effort to develop harmonized mammalian toxicity test guidelines for both acute and subchronic (90-day) tests with GMPs. Currently, most toxicity tests with GMPs are not in full compliance with world-wide guidelines (e.g., OECD, USEPA, JMAFF). There are some valid reasons for the differences. However, a consensus on when the tests are needed and how they should be performed is currently lacking.
Chronic Toxicity tests in mammals.
Animal model for predicting allergenicity of proteins. This is the only test that will help for predicting potential sensitization potential.

At this time, the examination of GM food, feed, and crops vastly exceeds the evaluation provided for conventionally derived materials and existing foodstuffs, for many of which virtually no data or long term risk assessment is available. Nutritional and anti-nutritional compositional assessments make nutritional deficiency in livestock or humans extremely unlikely. Significant public health impacts related to nutrition have to do with overall micro- and macro-nutrient intake from the general diet and, more importantly, to dietary intake choices such as fat composition, fiber intake, consumption of cruciferous vegetables, trans-fat intake, etc. If you are worried about human nutrition related to public health, these would be far better places to put your money. As noted in comments above- the idea that the ingestion of a novel dietary protein never previously consumed by a particular individual represents some type of significant hazard (short of recognized classes of protein toxins which are readily identifiable)is unjustified based on human experience with tens of thousands of proteins. I understand that there are population issues, i.e.- that there may be some proteins that are dominant allergens in populations. There is no reason to believe that the a-priori risk for any protein is high, and if allergenic sources and homology to major allergenic sequences is excluded, this risk is fundamentally negligible. Further- the major food allergens causing problems in human populations (eggs, milk, "nuts" (including peanut- which is not a nut), seafood) are due to EXISTING allergens, about which, evidently, there is no desire to do anything at all. Why waste resources on an entirely theoretical and fundamentally tiny risk when there is a manifest occurrence of significant allergy which you are willing to ignore? Gene transfer issues related to antibiotic resistance markers are a phantom risk, given the huge presence of antibiotic resistance genes in the population of bacteria at large. Risks associated with antibiotic resistance are, like the existing food allergens, being ignored. I see little real action on needless prescribing of antibiotics, overuse of new antibiotic categories, or the use of antibiotics for non-therapeutic purposes in agriculture. The risks of these actions are clear. Gene transfer has not been demonstrable save for the rescue of deletion mutants in highly selective environments in the absence of other bacterial flora. Real world transfer risks for ARMs are simply too small to matter. Gene transfer for enzymatic variants or synthetic enzymes unrelated to bacterial pathogenicity are of little concern even if such transfers should occur. Further, bacteria have had ample access to the whole panoply of genes in living organisms, up to and including the entire human genome (gut bacteria and dead intestinal cells). The bacterial world has, it seems, found little of any utility in the genomes of higher organisms. Existing data, in conjunction with background accessibility of plant and animal genes, fungal genes, bacterial genes, etc, strongly suggests that any risk of real concern as a NOVEL risk (not already a risk due to existence in bacterial populations or readily accessible to bacteria now) would need to focus on NOVEL gene constructs not currently present in nature at any meaningful frequency, and then only upon those constructs which could plausibly contribute in some way to bacterial pathogenicity or are likely to alter overall bacterial ecology. Experience to date would lead one to conclude that the present pre-market assessment for substantially equivalent crops is quite sufficient to assure foods as safe as, or safer than, existing foodstuffs. Nutritionally altered crops will require pre-market scrutiny of altered composition and related effects on the human diet. Stacking of agronomic traits related to herbicide tolerance appears to carry negligible health risks to humans or animals. Stacking of pesticidal traits can be rationally assessed based on known principles of toxicology. Finally, environmental impacts related to farming practices in general are vastly larger than the differential impacts of crop choice, which are in turn vastly greater than the impacts of choice of production methods (including GM vs non-GM) for a given crop. If you want to spend 100,000 Euros to improve human health and the environment, you need to limit GM assessments to a rational, science-based, risk- appropriate paradigm rather than endlessly pursuing largely phantom risks. Want to address food allergy- study and consider reduction of EXISTING food allergens. Want to improve nutrition and human health- study food choices and move to improve them. Want to help with antibiotic resistance- do something about prescribing habits and animal husbandry practice. Want to help the environment- study sustainable practices and crop/production choices in farming as well as broad land-use considerations. I am not suggesting that …

… we discontinue rational evaluation of GM crops- especially of those with altered nutritional composition, nor am I suggesting the above as a diversionary measure to avoid such a rational evalution. What I am suggesting is that we have actual problems that are already KNOWN to exist and which are of vastly greater importance to human and environmental health, making the use of scarce resources to chase infinitesimal or theoretical risks above and beyond those considered in the current pre-market evaluation paradigm a mis-allocation of time and resources. My personal belief is that much of the current evaluation will prove to be overkill- but it is at least rational and defensible, and provides good public assurance of safety. Endless pursuit of small, theoretical risks related to GM while ignoring both similar theoretical risks in conventional crops and known, larger, EXISTING risks is irrational scientifically, economically, and in regards to public health.
Horizontal gene transfer will be my priority research topic.
Allergenicity tests might be most important because it might be expected that on long exposure and broad populations, eventually some unintended or unanticipated events will occur. It's just the curse of the larger sample size: if something is 99.99% safe, you won't see any negative effect until marketing and when it hits larger populations. At the end, there is not a single risk-free technology, but one has to weigh benefits and potential risks.
Physiological effects in animals over long term studies
I would not spend the money for research regarding long term effects of GMOs or food/feed product derived from them, because in this field basic research on the interaction between food, nutrition and impact on health is missing. To overcome this 100.000 Euros are by far not enough. I would spend the 100.000 Euros for tasks related to the pre-market safety assessment of novel/GM food e.g. - define criteria to evaluate the allergenic potential of food - harmonize the design of animal feeding tests and statistical data management - improve the statistical data management from composition and nutrition analyses
CMO Allergenicity compared to standard food.
I would invest in high tech (GM) crops expressing cash proteins in contained or well monitored areas and stick to integrated pest management farming and marker directed breeding. For GM crops I would monitor to see the first unintended problematic aspects coming up from intended and unintended cross breeding and study epigenetic aspects.