Maize MON 87403

Organisation: The European GMO-free Citizens (De Gentechvrije Burgers)
Country: The Netherlands
Type: Others…

a. Assessment:
Others

Fragment: Dr Mae-Wan Ho: ‘The notion of an isolatable, constant gene that can be patented as an invention for all the marvellous things it can do, simply did not occur to the [scientists in the field of genetics between around 1975 to 1985]. And if it had occurred to them, they would have recognised it for what it really was: the greatest reductionist myth ever perpetrated, flagrantly conflicting with all scientific research data.’ 255 13. **Genetic contamination** The application of a materialistic, fragmented, reductionist worldview has brought about contamination in every field. Its application in the field of genetics is the cause of genetic contamination. New biotechnology is presented as the technology of the future. However, it is the belated product of a paradigm that has long been superseded. New biotechnology is based on the premise that each particular characteristic of an organism is encoded in one or a few constant genes. It is assumed that the transfer of these genes results in the transfer of the specific characteristics. This reductionist view has been rejected by numerous biologists and scientists from other fields because it overlooks the extremely complex interactions between genes and their cellular, extracellular and external environment. The psychological aspects are not taken into account either. The development of the characteristics of a species or individual involves all these factors. There is a limited capacity for so-called recombinant DNA techniques to transfer certain molecular characteristics from one species to another. This does not, however, in any way mean that we have a comprehensive and reliable system to predict what the effects of gene transfer will be. This is because the overall environment in which the gene functions is not transferred. If you try to start the car with the key to the letter box this is also unlikely to produce the desired result. **13.1. Parasites** Genetic manipulation involves ‘updating’ the heritable material - the DNA - of organisms. This process uses pieces of heritable material from parasites and other organisms from different species. The foreign DNA can end up anywhere in the heritable material of the plant and begin to produce foreign substances, often in a manner that the organism cannot control. **13.2. Natural order breached** Thousands of species of animals, plants and micro-organisms have now been genetically manipulated. The intelligent order that nature has built over millions of years of evolution is thus irreversibly distorted with reckless disregard. There are also serious risks to health associated with this. All the important food crops, including rice, wheat, soya and maize, sunflowers, walnuts, rapeseed, sugar beet and potatoes are genetically modified in order to generate ‘attractive commercial characteristics’. Most genetic engineering involving plants is intended to produce resistance to a given herbicide. The attempt is often made to create built-in resistance to viruses or fungi or to alter the chemical composition for the purposes of the food, pharmaceuticals or other industries. Micro-organisms and animals are manipulated to serve as ‘production systems’ for all kinds of substances. Genetic manipulation also has medical applications, such as the production of vaccines and various forms of gene therapy. There are serious concerns about all of these applications. **13.3. Genetic engineering is based on pseudo-science 13.3.1. Purely**

empirical experimentation The genetic manipulation industry likes to create the impression that what it is doing is based on an exact science and that criticism of it is based on purely emotional reactions. However, if one investigates the foundations of genetic manipulation, it soon become clear that this technology is little more than purely empirical experimentation, without any scientific basis. The molecular biologists who promote and carry out the manipulations know a great deal - about almost nothing. In any genetically modified genome only a few dozen out of a total of tens of thousands of genes are known. We have no control over where the foreign genes end up. The effects on organisms of this tampering should not be underestimated. Risk analysis is almost entirely geared to identifying specific risks of a (bio)chemical nature. It is based on the same biased, limited principles as genetic engineering itself. This makes it particularly easy to ignore the damage inflicted. It is as if you let a blind person throw paint around and then let him judge the result. By way of comparison: 'A bacterium contains as much genetic information as the bible contains words, and a human being as much as fifteen bibles. The genetic engineer replaces perhaps one or two or pages and says that this is not dangerous. He keeps quiet, however, about the fact that he hasn't read the table of contents, that he doesn't know which pages have been replaced, that he has not the slightest notion of how important the contents of these page are or of how the contents of these pages fit in with the rest of the book, and moreover has no way of understanding the change of content.' Dr Erwin Chargaff, founder of modern genetic science **13.3.4. The forgotten link** Biophysics tells us that the various levels of biological organisation are characterised by a high level of consistency. Consistent phenomena are not only observed at micro-level and at the level of tissues and individuals, but also in groups of individuals of a species. This consistency is ultimately present throughout the entire ecosystem, and this includes all species. The idea of genomes as a sort of Meccano that becomes lodged in our consciousness via the diagrams in the scientific supplements of newspapers is thus incorrect. Genetic manipulation, the simplistic juggling of DNA fragments, jars with reality and conflicts with our scientific knowledge. **258** Anyone who believes that localised interference with DNA – on this kind of sophisticated and powerful level of biological organisation, without taking account of the infinitely complex connections in and around the given organism – could be harmless, must really have taken leave of their senses. **13.3.5. Viewpoints on living organisms in the mainstream and vanguard of biology** Professor Mae-Wan Ho, the eminent natural scientist whom we have already referred to above, gives a pithy account of old and new viewpoints on living organisms: 'There can be no doubt that the average biologist is an anachronism. Many biologists have fallen far behind the natural scientists, chemists and mathematicians who, one after the other, have stopped seeing the world in terms of static equilibria and linear clockwork mechanisms. Biologists are trapped in the mechanistic era, they refuse to see the reality of organisms as irreducible universes in which genes (and genomes) are changeable and mobile as a result of responses to their cell and body environment, which is ultimately also connected to the external ecological and social environment. […] The majority of biologists clearly do not know that the new key to living organisation – instead of linear, one-way genetic determinism –is non-linear, multidimensional communication. Given the mountain of irrefutable evidence available, to assume otherwise – and this is exactly what the gene manipulators do – is the substance of bad science. What this boils down to is that we are exposing the population to unacceptable risks.' We encounter the same anachronism in various other sciences, for example, medicine and sociology. The same may be said of the prevailing political view of society and its governance. **13.3.2. Unscientific assumptions** Genetic manipulation is based on totally obsolete and downright false, even primitive assumptions. If heritable material were to consist of a number of individual elements that could be cut, pasted and rearranged at will, and if genes were responsible – in an unequivocal, linear manner, in a unidirectional and simple

causal relationship – for each characteristic of an organism, and if the genes themselves were static, and not subject to environmental influences, then yes, genetic manipulation could work. However, this is not the case, as anyone with the slightest understanding of biology is well aware. Thanks to the research of innumerable scientists over the last 20 years, we know that each gene works in tandem with all other genes and with all levels of biological organisation in its environment. Linear relations in living systems are just as rare as lotteries where you always win exactly what you your original stake was. Small causes at a refined level of biological organisation, such as minimal damage to heritable material, can have serious consequences. We also know that heritable material is constantly in motion and that an organism is capable of adapting itself, together with its genetic material, to influences in the environment, through 'adaptive mutation'. DNA determines not only the various levels of its environment, it is also determined by that environment. This kind of interaction is conveniently forgotten by those involved in genetic manipulation. **13.4. Major shortcomings 13.4.1. Irreversible and self-propagating contamination** All living organisms on earth have evolved together over a vast timeframe and are therefore part of the interconnecting fabric of life. Manipulation of any one species carries with it the risk that it can have an impact on all other species. Over a longer period of time changes can occur in the infinitely complex ecosystem the nature and extent of which are impossible to grasp by the current state of science. Once a genetically modified organism is released into the environment, it is no longer possible to reverse that decision. Genetic contamination has the potential to replicate itself. This could threaten the quality of life for all future generations of all forms of life. Major technical difficulties and huge risks are also associated with the – as yet non-existent – medical applications of gene therapy. In this situation there is only one sensible decision to take: no genetic engineering. Instead, research must be undertaken into existing natural technologies which must be applied on the basis of a broader understanding of reality, and developed where necessary. A broader understanding of reality is of the utmost importance. The lack of such understanding alone leads to reckless interventions in the infinitely complex connections between all organisms in the ecosystem, genetic manipulation being one of the most risky examples. **13.4.2. Unlimited risks to health** Leading scientists oppose the introduction of genetically manipulated products. Professor Richard Lacey, microbiologist, physician and professor of food safety, has been one of the best-known figures in the field of food science since he predicted the BSE crisis (mad cow disease) more than seven years ago. Professor Lacey recently spoke out forcefully against the introduction of genetically manipulated foods because of the 'essentially unlimited health risks'. According to Professor Lacey, 'there is no valid reason for the introduction of genetically engineered foods.' Professor John Fagan, a distinguished microbiologist and cancer researcher, argues that the usual risk assessment 'does not even begin to investigate a very substantial category of health risks that are the result of unforeseen side effects of genetic manipulation. With current test procedures,' he says, 'it is completely impossible to discover these health risks.' There are already a number of well-known cases in which genetically manipulated products caused allergies or were downright toxic. There are considerable dangers inherent in any harmful consequences that only become apparent after a long time. Professor Mae-Wan Ho of the Bioelectrodynamics Department at the Open University in London writes: 'The practitioners of genetic engineering biotechnology, the regulators and the critics alike, have all underestimated the risks involved, which are inherent to genetic engineering biotechnology, particularly as misguided by an outmoded and erroneous world-view that comes from bad science. […] It is also meaningless, therefore, to set up Ethical Committees which do not question the basic scientific assumptions behind the practice of genetic engineering biotechnology.' **13.4.3. Either genetic engineering or natural farming — they cannot both exist together!** Genetic manipulation gives rise to genetic contamination. This contamination

spreads and self-propagates and there is no way at all of stopping or reversing it. If we truly want to farm naturally, then we have to stop genetic manipulation. **1. Bad science, defective technology, disappointing results** Again and again, genetically manipulated crops create problems if they are exposed to stressful situations. In the US we have seen ‘insect-resistant’ manipulated cotton fields devoured by worms, plus a herbicide-resistant species whose cotton bolls are deformed and fall off the plant. Even worse are the unforeseen side-effects that pose a risk to human and animal health and which threaten natural farming and the balance of the environment. **2. Genetic contamination through cross-breeding** Genetically manipulated crops can spread their foreign gene constructs far into the environment through cross-fertilisation. Scientific research undertaken in California, Scotland, Denmark, France and Germany shows that this occurs much often and more rapidly with genetically manipulated crops, and over greater distances and with greater persistence than was previously assumed. Scottish researchers have found contamination from genetically modified pollen up to 2.5 km from the source. From their findings it can be deduced that this contamination can spread more than 4 km. Bees and other pollinating insects carry nectar and pollen up to three kilometres The Dutch authorities have, however, issued licences for field trials using genetically manipulated oilseed rape, while 'for safety reasons' prescribing an isolation distance of only 400 metres! Farmers and producers who do not wish to have anything to do with genetic manipulation cannot escape it. Their harvests are contaminated. Pollen pollinates. Genetic contamination is impossible to contain. **3. Genetic contamination by horizontal transfer** Horizontal transfer is a second source of genetic contamination. Heritable material is spread not only by cross-breeding and propagation. Many organisms can pass on copies of heritable material to and exchange them with one another, just as we would copy a cassette tape and give it to a friend. As early as the 1920s it was discovered that bacteria do this among themselves, even from one species to another, but recently it has been found that heritable material is also transferred horizontally between organisms that belong to different natural kingdoms. It has also already been established that genetically manipulated organisms exchange heritable material much more frequently than natural organisms. Making plants resistant to a virus by genetically manipulating them is a particularly short-sighted practice. It involves inserting heritable material from the virus into the plant’s genome. The virus can then no longer attack the plant. This sounds like an advantage. However, it appears that within a very short period of time other viruses are able to absorb the foreign virus material from the plant. The new form of virus that arises from recombining this material is more virulent that natural viruses and is capable of attacking a greater number of plant species. So what did you do? You simply created a more serious disease. Author: Jan Storms Meer at: http://www.natuurwetpartij.nl/download/programma98.pdf

---

4. Conclusions and recommendations

We read: ‘The nutritional value of food and feed derived from maize MON 87403 is not expected to differ from that of food and feed derived from non-GM maize varieties.’ How can you claim this. The DNA has been interfered with, and this has disturbed the natural order of things. It is incredible that you as a scientist dare claim this. We don’t want to eat your defective genetically modified crops and we don’t want to feed them to our cattle.

Organisation: Testbiotech
Country: Germany
Type: Others…

---

a. Assessment:
Molecular characterisation

The comments from the experts of the Member States (EFSA, 2018b) show that much more detailed information would be needed to understand the exact molecular mechanisms involved in the expression of AtHB17Δ113, which influences ear biomass at an early development stage and, therefore, potentially the yield at harvest. For example, experts from the German authority BVL (EFSA, 2018b) request, "in this regard molecular mechanism, genes regulated and the role of environmental factors should be addressed."

In addition, experts from the German Federal Agency for Nature Conservation (BfN) spell out some unknowns in detail: "Currently the mechanisms that regulate the transcriptional activity of HD-Zip I and HD-Zip II transcription factors in vivo are largely unknown (Harris et al. 2011, Turchi et al. 2015). It has been shown however that environmental and stress conditions such as water status, light conditions, nutrient status, temperature and the concentration of toxic compounds play a crucial role in its regulation. In addition evidence is emerging that these transcription factors are integrated in phytohormone-regulated developmental networks. (Harris et al. 2011). Thus for the characterization of the genetic modification plant material from different growth conditions should be examined and the mode of action of the trait should be characterized."

Indeed, the most relevant publication prepared with experts from Monsanto and Dupont (Rice et al., 2014) does not answer crucial questions regarding the underlying mechanisms. This publication shows that the expression of several plant genes and related proteins are changed in the genetically engineered maize. Some of these natural proteins have similarity with heat shock proteins, others are regulatory proteins; some are involved in cell wall organisation or are just of hypothetical nature. The exact mechanisms causing the supposedly intended effects and their possible side effects remain a matter of uncertainty and non-knowledge. As the authors conclude: "It is not yet clear what role these proteins may play in ear growth and development in maize." Further, the overall effects are described as minor: "Overall, the observed effects of AtHB17Δ113 on the maize ear inflorescence and ear transcriptome were very small."

Furthermore, the outcome of the field trials shows that the observed effects were not only small, but also inconsistent. As an analysis of the data from the field trials shows, ear biomass and kernel weight developed differently and were dependent on the specific site of the field trial. In several of the field trials, no statistically significant effects could be observed in regard to the expected effects. EFSA summarises: "The GMO Panel acknowledges that the change due to the intended trait is known to be of limited amplitude, and that the AtHB17Δ113 protein is expressed in maize MON 87403, which suggests that the manifestation of the trait may depend on environmental conditions in the field trials."

In conclusion, risk assessment on a molecular level shows several major uncertainties regarding the intended molecular mechanisms and unintended changes in biochemical pathways. Furthermore, gene expression depends on environmental conditions. No data were

provided on whether gene expression also depends on the genetic background of the specific varieties.

Risk assessment cannot concluded under these circumstances. To reduce uncertainties, the plants should be investigated under a wide range of defined environmental conditions taking into account potential extreme stress conditions, such as those caused by ongoing climate change. In addition, more varieties should have been included in the trials since it is known that the genetic background of the varieties can influence the level of expression of any inserted genes. Furthermore, much more data would be needed to assess the effects of the additional DNA on the genome of the plants, the transcriptome, proteome and metabolome.

EFSA GMO Panel (2018b) Comments from the experts of the EU Member States on the Scientific Opinion on the assessment of genetically modified maize MON 87403 for food and feed uses, import and processing, under Regulation (EC) No 1829/2003 (application EFSA-GMO-BE-2015-125). EFSA Journal 2018;16(3):5225, 28 pp, accessed via the register of EFSA http://registerofquestions.efsa.europa.eu/roqFrontend/login?1

Harris JC, Hrmova M, Lopato S and P. Langridge (2011) Modulation of plant growth by HD-Zip class I and II transcription factors in response to environmental stimuli. New Phytologist 190, 823–837

Rice EA, Khandelwal A, Creelman RA, Griffith C, Ahrens JE, et al. (2014) Expression of a Truncated ATHB17 Protein in Maize Increases Ear Weight at Silking. PLoS ONE 9(4): e94238. doi:10.1371/journal.pone.0094238

Turchi L., Baima S., Morelli G. and I. Ruberti (2015) Interplay of HO-Zip II and III transcription factors in auxin regulated plant development. Journal of Experimental Botany, Vol. 66 No. 16, p 5043-5053.

Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

As EFSA (2018a) points out, the data from the field trials indicate that the magnitude of the effects is dependent on environmental factors.

However, the maize was only grown for one year and all the field trials were carried out in the US, leaving aside other important maize producing countries. As a result, the plants were grown under a too narrow range of environmental conditions that do not allow any conclusions to be drawn upon the quality and safety of the plants under different conditions, such as those related to climate change. Furthermore, according to EFSA, the data on biotic and abiotic stressors occurring during the field trials were not statistically analysed.

Remarkably, EFSA raises the question of whether the data from these trials can be used for risk assessment at all, since the intended effects were only observed in some of the field trials: “Based on the provided data, four out of seven sites from which samples were taken for the compositional analysis, phenotypic manifestation of the intended trait was realised. For these sites, the ear biomass (at the R1 or R6 stage) [explanation by Testbiotech: these are specific

stages of growth] was higher. However, only for one site the increase in ear biomass was statistically significant at the R1 and R6 stages, which raised the question on whether compositional data obtained from the field trials would allow a thorough risk assessment."

Indeed, the relatively low number of differences in plant composition derived from comparison with the conventional plants might be due to failure of the intended additional gene function.

In conclusion and in awareness of the uncertainties in the assessment on the molecular level, the risk assessment cannot be completed. Any assumptions that products derived from MON87403 do not show unintended effects that would raise safety concerns are not based on sufficient evidence. In light of the facts, EFSA´s final conclusions on comparative assessment are nothing more than a kind of guessing game in a situation of profound non-knowledge: "The GMO Panel concludes that the agronomic, phenotypic and compositional analysis did not identify issues requiring further assessment regarding food and feed safety and its environmental impact."

---

b. Food Safety Assessment:
Toxicology

The maize used for the 90-day feeding study was not sufficiently assessed in regard to its biological characteristics and the magnitude of the intended effects. It is unclear whether the maize used in the diet is representative for the products that might be derived from MON87403 grown under practical conditions.

Consequently, the data provided from feeding studies cannot be considered to be sufficient to show the safety of the product.

Allergenicity

No tests were conducted to assess whether the concentration of known maize allergens was increased due to the insertion of the additional gene construct. Since the introduced trait interferes with the plants metabolism on several levels, more data are needed to show to which extent the maize is changed in regard to its allergenic properties.

Nutritional assessment

The maize used for the feeding study with poultry was not sufficiently assessed in regard to its biological characteristics and the magnitude of the intended effects. It is unclear whether the maize used in the diet is representative for products that might be derived from MON87403 grown under practical conditions.

Consequently, the data provided from the feeding studies cannot be considered to be sufficient to show the nutritional quality of the product.

Others

Metabolic pathways which interfere with plant growth are multifunctional and complex. They are connected to plant characteristics such as stress reactions, fitness and composition of the plants constituents. Under these circumstances, risk assessment has to be driven by the hypothesis that the biological characteristics of the plants as a whole will be changed by the genomic intervention.

The risk manager and the risk assessor need to be aware of these challenges. The pending application should be stopped and a comprehensive methodology of risk analysis for this category of plants should be developed.

---

3. Environmental risk assessment

EFSA discusses the risk of gene flow from maize MON87403 to teosinte plants. These plants have been found growing in Spain for more than a decade and are wild relatives (ancestors) of cultivated maize. Depending on the subspecies of teosinte, gene flow is more or less likely to occur. However, the subspecies occurring in Spain has not been fully identified and seems to be a hybrid between maize and teosinte. Its actual potential for gene flow with maize in the fields is not known Trtikova et al., (2017).

MON87403 is not allowed for cultivation in the EU, however, spillage of imported kernels might lead to spontaneous transgenic plant populations. Pollen from these plants – under some circumstances - could enable gene flow to teosinte plants.

Without having any data on gene expression and possible effects on teosinte plants, EFSA, nevertheless, indicated that gene flow from maize MON87403 to teosinte would not cause problems because, as yet, teosinte has only been observed in the fields and not outside cultivated fields. “Vertical gene transfer from maize is limited to Zea species. Wild relatives of maize outside cultivation are not known/reported in Europe (…). Therefore, potential vertical gene transfer is restricted to maize and weedy Zea species, such as teosintes and/or maize-teosinte hybrids, occurring in cultivated areas.”

A paper published by Devos et al (2018) was one of the publications used for the EFSA assessment. It was written by Yann Devos, who works for EFSA, together with Alan Raybould, who works for biotech-company Syngenta, which sells genetically engineered maize. Other experts from EFSA were also involved, including Antoine Messéan, Jeremy Sweet and Elisabeth Waigmann. It is remarkable that Devos, Sweet and Messéan were also involved in the risk assessment of MON87403. There are clearly several reasons why this kind of expert involvement needs to be regarded as a conflict of interest.

Whatever the case, the assumptions of EFSA and of Devos et al. (2018) are biased and lead to the wrong conclusions. Devos et al. (2018) acknowledge that currently there is no "information of the expression of the transgenes in the hybrid plants". They do not deem such data to be necessary. Instead, they simply state that a "worst-case assumption is that any teosinte × GM maize hybrids will express/manifest the traits that the transgenes confer".

Thus, these experts assume that once the transgenes have escaped to teosinte they will somehow preserve the intended biological trait originally inserted. They seem to think of the transgene as an inert BioBrick, which has a predictable function that is independent of the rest of the organism and its interaction with the environment. This is wrong. For example weedy rice, derived from Bt rice (Cao et al., 2009) and from glyphosate resistant rice (Fang et al., 2018) is known to show enhanced fitness that is not related to the intended trait.

Currently, there are neither EFSA guidelines nor methods for making detailed assessments of the risks associated with genetically engineered plants emerging from unintended crossings and next generation effects. Risk assessment as performed by EFSA only considers genetically engineered plants that are grown for just one season and are re-sown every year.

Devos et al (2018) try to escape this factual complexity by stating that risk assessment "focuses the assessment on the phenomena that are important for decision-makers and away from the multitude of other changes that may interest scientists, but which are irrelevant for ERA". This approach is clearly failing by design: In many cases, there is no clear cut difference between environmental risk assessment (ERA) and basic research on the biological characteristics of genetically engineered plants.

Genetically engineered plants are mostly grown for just one season and re-sown every year. This enables the company to check the seeds in regard to their most relevant economic characteristics before they go into the fields. However, potential teosinte × GM maize hybrids and their offspring will not undergo any additional quality or safety checks before they appear in the fields. Instead, they are simply new, untested, never risk assessed transgenic plants. Therefore, they cannot be allowed to emerge and persist in the environment. This problem does not depend on the question of whether teosinte will spread beyond sites of agricultural production.

Therefore, the ERA of EFSA has to be rejected due to significant methodological flaws and due to the bias caused by conflicts of interest.

Cao, Q.-J., Xia, H., Yang, X., Lu, B.-R. (2009) Performance of Hybrids between Weedy Rice and Insect-resistant Transgenic Rice under Field Experiments: Implication for Environmental Biosafety Assessment. J. Integr. Plant Biol. 51, 1138–1148. https://doi.org/10.1111/j.1744-7909.2009.00877.x

Devos, Y., Ortiz-García, S., Hokanson, K.E., Raybould, A. (2018) Teosinte and maize × teosinte hybrid plants in Europe−Environmental risk assessment and management implications for genetically modified maize. Agric. Ecosyst. Environ. 259, 19–27. https://doi.org/10.1016/j.agee.2018.02.032

EFSA GMO Panel (2018a) Scientific Opinion on the assessment of genetically modified maize MON 87403 for food and feed uses, import and processing, under Regulation (EC) No

1829/2003 (application EFSA-GMO-BE-2015-125). EFSA Journal 2018;16(3):5225, 28 pp https://doi.org/10.2903/j.efsa.2018.5225

Fang, J., Nan, P., Gu, Z., Ge, X., Feng, Y.-Q., Lu, B.-R. (2018) Overexpressing Exogenous 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) Genes Increases Fecundity and Auxin Content of Transgenic Arabidopsis Plants. Front. Plant Sci. 9. https://doi.org/10.3389/fpls.2018.00233

Trtikova, M., Lohn, A., Binimelis, R., Chapela, I., Oehen, B., Zemp, N., Widmer, A., Hilbeck, A., (2017) Teosinte in Europe – Searching for the Origin of a Novel Weed. Sci. Rep. 7, 1560. https://doi.org/10.1038/s41598-017-01478-w

4. Conclusions and recommendations

The EFSA opinion does not identify the true range of uncertainties and the current limits of knowledge. The risk manager should therefore reject this opinion and not allow import of maize MON87043.