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His work and experience with genetic engineering is comprehensive. He has worked in the field for almost three decades, making him well placed to highlight the dangers and shortcomings of genetically engineering our crops.

Health risks from GMO foods and glyphosate-based herbicides.

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Pleasure to be here and thank you all for coming. I'd like to extend my own personal thanks to Madge and to the sponsors of this event because I know without their generous support we wouldn't all be here this evening.

As Fran mentioned, my background is in basic molecular biology. I use genetic engineering methods as a routine — virtually [a] daily method in my research of gene organisation and control and development of human gene therapy applications. And it is from that background that I view also the developments of genetic engineering; the use of genetic engineering within an agricultural context. And I hope to illustrate to you this evening *why* I am very concerned about the way that genetic engineering, genetic

‘GM produces combinations of genes that have never evolved to work together in a harmonious integrated manner.’



modification as has been used in agriculture — and why we do need to decide if we do need these crops at all, and that's highly questionable in the first place — then we need to go forward with these products extremely in a very cautious manner.

So what I will do this evening: I will look at the sources of mechanisms of the health risks that are associated from GM foods and also their associated pesticides, focusing particularly on glyphosate-based herbicides. Obviously we only have a short period of time this evening. If you wish to follow up any of the points that I'll be raising this evening in greater detail please go onto the Internet... to the Earth Open Source website and download for yourself a free copy of the report that I co-authored, *GMO myths and truths*, which was released last summer [or at least my summer; your winter].

Why should we be concerned about GM foods? I'm sure we've all heard from industry, regulators, governments even, that actually GM foods are the most thoroughly tested foods ever produced in human

history and that they have been passed as safe and that we should consume them with no fear of harm. Is that true or not?

Well, first of all I would like to consider genetic modification GM as a technology. The first thing we need to realise about GM is that it is a purely artificial technology for producing a new crop variety. The fact that it is artificial of course doesn't automatically make it unsafe. It is the consequences of the GM transformation process that gives us cause for concern. And by us I mean scientists like myself around the world. The key points to recognise about the GM transformation process is that, as summarised on this slide, it allows the transfer of genes between totally unrelated organisms — normally transfer of genetic material is between related organisms: strawberries with strawberries; potatoes with potatoes; or wheat with wheat.

But with GM you can transfer genes into a crop from any organism that you like: bacteria, viruses, unrelated plants, animals and so forth. So it crosses species barriers; allows gene transfer across species barriers. And as a result it produces combinations of genes that have never evolved to work together in a harmonious integrated manner.

Now this is a very, very important point so I'm just going to spend a few minutes on that. At the time when GM crops were first conceived and started to be developed in the early 1980s our concept or understanding of gene organisation and function was very, very rudimentary and genes were considered as isolated units of

information, and as a result they could be transferred between species with total predictability. I'm afraid that is simply not the case. We now know gene organisation in DNA to not to be random and that no gene works in isolation. Genes function as part of integrated wholes within a given organism, within a given context, and that therefore when you take a gene from one organism and randomly insert it into the DNA of a totally unrelated organism you're placing a gene in an environment where it has not evolved to work in an integrated manner with the surrounding genes in that organism. As a result of that GM brings with it an inherent unpredictable component in terms of gene function.

In addition to that the GM transformation process, as a whole, is highly mutagenic. What I mean by that is that it produces damage in the DNA throughout the genome, the totality of the DNA of the plant. So what we have is a situation where the combination of effects from the GM transformation process, the combinations of novel genes that normally would not come together, plus the general destructive effect, the mutagenic effects of the GM transformation process, combine to always, to a lesser or greater degree, disrupt the biochemistry of the protein, and biochemistry of the plant. And if you disturb that you run the risks of producing new toxins and new allergens and a disturbed altered nutritional value in the food. These are proven. There is evidence to show this disruptive effect. This is measured. This destructive effect of the GM transformation process is a measured phenomenon. And as a result, for me, this is why we need to thoroughly [and] generically evaluate GM foods.

Especially for chronic – both acute and especially chronic long-term toxicity effects.

But they're highly regulated, are they not? So should we be worried? Unfortunately, yes. GM foods by international law have to be regulated. But regulation of GM foods around the world is very highly variable. In nations such as the United States they've essentially a totally deregulated product. Generally recognised they're safe; or grass? [inaudible] is how they are perceived, and companies can release them with essentially no safety testing whatsoever, near enough. But in Europe we have a much stricter regulatory system. Here in Australia I would put you somewhere in between the two, USA and Europe.

But regardless of which territory we're considering, for me, all regulatory evaluations of GM foods, all regulatory agencies, whatever they do, is totally inadequate. And it's inadequate on many issues but the key ones for me are that they do not fundamentally place, they do not fundamentally question the GM transformation process within our advancing understanding of genetics. They never question the fact that when you move genes around – insert between species, randomly insert them – that this is not the way life has evolved to function. In other words *they never fundamentally question the technology.*

Secondly, they only accept safety data when it's requested and submitted from the developer company. No independent safety evaluation of the GM food is conducted for regulatory purposes. Any

biochemical analysis of the GM food, comparing it to the non-GM equivalent, is very superficial. [It] doesn't go deeply into the proportions, disturbances in proteins and in new small-molecule nutritional components.

And lastly, and this is most important, there is no requirement anywhere in the world by any regulatory agency to conduct long-term toxicity evaluation. And this is important again because GM has unpredictable outcomes. You don't know in advance what the consequences are of the GM transformation process; what that may bring. And because you don't know, the only way to evaluate safety is generically. You basically need to conduct a long-term feeding trial in animals and see what happens. There's no point in just doing a gross biochemical analysis and say, 'Oh, the GM is roughly equivalent to the non-GM, and therefore it's safe'. I'm sorry [but] that's nowhere near good enough. You need to conduct these long-term studies and that's just not going on anywhere in the world for regulatory purposes, at all.

What could be the potential sources of toxicity from GM?

We have, for me, three main sources.

Firstly, the introduced — the foreign GM gene product. One of the GM gene products that's in much of GM crops is this insecticidal protein called Bt toxin. Bt toxin is — the gene for Bt toxin that's introduced into crops is derived from a common bacterium in the environment called *Bacillus thuringiensis*. And a certain subclass of these Bt toxins from these bacteria have potent insecticidal

properties. And these have been engineered into plants. But the way that these engineered Bt toxins are present in the crop is very different to how they exist in the native bacteria which farmers can spray on the crops as a natural insecticide. And with that comes new potential safety concerns.

Secondly, we have of course the fact that 80% of all the GM crops grown commercially in the world have been done so to tolerate application of herbicides, particularly glyphosate-based herbicides, the most common of which is Roundup. What is the outcome of these high levels of exposure, high levels of consumption for farm animals and the consumer?

And lastly there is of course the potential to produce novel toxins, as I'll mention, from the fact that we alter the biochemistry of the plant caused by the mutagenic effects of the GM transformation process and these novel combinations of genes that it brings about.

I would say that there is evidence of toxicity arising from all three of these processes, which I would very briefly like to review to you.

So, controlled animal feeding studies show clear signs of toxicity linked with the consumption of GM crops. What we have seen in studies conducted not only by university-based people but even in some of the industry studies that have been conducted as part of their submissions for regulatory approval in Europe. And this is with crops expressing both the Bt toxin *and* the herbicide Roundup tolerant crops, such as soy and corn. What we've seen in these

animal feeding studies is multiple organ damage; multiple system damage such as liver and kidney damage; functional damage; immune system disturbances; allergic-type reactions; digestive system damage such as proliferation of the cells lining the gut and also other types of lesions.

I don't expect you to read all this — actually I do expect you to read all this because I'm going to test you on it later on at the end of the talk. So what we're seeing from industry studies, for example, we're seeing rats fed these two varieties. If we focus on the commercialised — by the way I'm only going to show you, summarise briefly for you studies on *commercialised* GM crops; in other words things that you and I may be eating now. There are many studies showing toxicity, toxic outcomes from non-commercialised GM crops, but the ones to concern us are the commercialised ones.

If we focus on the Bt insecticide GM crops, corn in particular, industry studies on two varieties of Bt toxin show signs of liver and kidney functional damage after just 90 days of consumption of these products. Academic studies which have used rats, mice, pigs, ewes have shown multiple system and organ damage, ranging from liver and kidney disturbances, immune system disturbances in both mice and in pigs, intestinal damage in ewes and lambs, and this particular worrying study here at the bottom from Egyptian scientists showing that even after just 91 days of consumption there were multiple organ changes in weight, biochemistry, severe damage in structure and function including liver, kidney, testes and

intestines. And this is a variety of maize that's approved for commercial growing in Europe and imported in large quantities.

What could be causing these signs of toxicity? This is when we come back to this list. Is it the Bt toxin or is it some other aspect of the product caused by the mutagenic effect of the GM transformation product? That is an unresolved question. What we do know is that there's something wrong with these GM crops.

What I want to focus on in the rest of my presentation are the consequences of the higher exposures to herbicides in weed killers that are used in conjunction with the cultivation of the GM crops, especially the glyphosate-based formulation such as Roundup.

Why?

Because most of the GM crops are engineered to tolerate glyphosate application and this is the world's most used pesticide.

And the vast majority of GM soy is genetically engineered to tolerate glyphosate and as a result, not surprisingly, you find worryingly high levels of glyphosate in GM soy. So if you're importing GM soy from North America here in Australia — I know you grow your own non-GM soy, very good, I would favour that if I were you — but if you're importing it then you can expect to find a worryingly high three milligrams per kilogram of glyphosate in the GM soy from North America.

From South America measurements have been done to show that some batches can have up to a hundred, almost a hundred milligrams per kilogram. Very worrying high concentration.

And these are worrying amounts because what I hope to show you later on is that the doses, the safety levels of glyphosate are wrongly set too high by regulators.

But maybe some of you use Roundup in your home. How many of us use Roundup in our gardens? See, I'm not gonna put my hand up. A few of us. No, no, don't be embarrassed because the regulator says it's safe and maybe this is how you look [pointing to image on screen], you know, don't have to put on any special clothing, no masks, no gloves — just spray it away in the weeds in your garden because it's safe, the regulator says it's safe. But is it?

Industry study. Let's turn to the industry studies first of Roundup tolerant GM corn NK603. Ninety-day feeding studies in rats showed signs of liver and kidney damage, functional damage. Studies conducted by Manuela Malatesta in Italy with Roundup-tolerant GM soy. What she found was that in mice-fed GM soy there was a disturbance in liver, pancreas, testes and testes function. And when she fed the soy, basically for the lifetime of the mice, 24 months, there were more acute signs of ageing in the liver.

The question is, is [it] the GM process or the Roundup residues in the feed that are causing these effects, or maybe a combination of

the two? An unknown quantity. But the finger can point to both; both the Roundup residues and the GM process.

What are we allowed? If we focus on the Roundup, the glyphosate right now, what do our regulators say we can consume and still be safe? In the European Union and in Australia we have the same set limit of daily exposure; what is known as the 'acceptable daily intake'. Acceptable daily intake is what our regulator says we can consume on a daily basis, day in/day out, and not suffer any damage to our health. And as I say, in Europe and Australia that value is 0.3 milligrams per kilogram body weight per day. For somebody like me that's a little over 20 milligrams per day in Europe. You all know your own weight; you can do your own calculation. In China and Russia that value is up to 1 milligram per kilogram body weight per day. In the United States where clearly regulators think Americans are more hardy, even [moreso] than good tough Australians, they say you can consume 1.75 milligrams per kilogram body weight per day and still be healthy.

Question is: Are these exposures really safe? What is the evidence behind this, bearing in mind that all these regulatory agencies have looked at the same scientific data, and all come to a different conclusion as to what is safe to consume on a daily basis or not. For me that's already very suspicious.

Well, when we looked at the data that the German regulator used in Europe to set the safety limits for us we actually came to a different conclusion. We thought they ignored very important evidence of

birth defects — teratogenicity arising in certain animals, animal tests, and that we thought they'd set the level three times too high. So already we were suspicious years ago about the data behind these safe limits.

And also what the regulator ignores is the fact that glyphosate is a multiple toxin, as you heard from Michelle before me. Glyphosate is not just a weedkiller: it is an antibiotic, it binds nutrient metals and makes them unavailable. At certain concentrations it's a DNA mutagen. What does that mean? It damages DNA. If you damage DNA you mess up your gene function and this could lead to cancer.

But what is emerging as well very recently is this last point, which worries me most, and that is increasing evidence that glyphosate is what is known as an endocrine or hormone-disruptive chemical. We all know what hormones are because we hear about them all the time. Insulin is a hormone, growth hormone is a hormone, and steroids are hormones, and we've all got these in our bodies. Females have a different complement of hormones to men. And the crucial thing about hormones is that they control just about every function in our body. All our organ functions. They're communicating molecules and they're controlling immune system function, organ function and so on and so forth. And the balance of hormones in the body is absolutely crucial for health. If you disrupt them with this class of chemicals known as EDCs and the endocrine-disrupting chemicals you can end up causing extremely severe illness.

But if you go on the Monsanto website today you will find categorically stated, without any shame, ‘**There is no evidence of endocrine disruption**’. You [can] see that at the bottom. Is that right or not? We'll see just shortly whether Monsanto is correct or not.

Endocrine disruptive chemicals are very worrying because they can work at very low doses — well below what a regulator may have said is safe. And that's because they work by this mechanism: **Non-linear dose response**. (And excuse me if I revert to university lecturer. This is what I do to the medical students. I go to the board sometimes.)

I'm just going to quickly draw you a graph where on this [upper right] side is ‘toxicity’ and this [lower left side] is ‘dose’. Regulators all over the world work by an archaic principle (I call it ‘our cake’ and you'll see why in a minute) called *the dose makes the poison*. That means, simply, the more of the poison you take, the more toxic, the more poisonous it is. And so it's a linear relationship — that's what they say. The higher the dose, the more the toxicity, until eventually you come down to a range where things are non-toxic. And it's in that range — the regulator will therefore set a dose down here [lower left] to say that's what you can be exposed on a daily basis and you'll be fine.

But what we now know is that many chemicals don't work that way. Past a certain point what's been found with these endocrine-disruptive chemicals is that you come down and suddenly the

toxicity shoots up again. And what the regulator does... in other words a regulator chooses a safe dose and it could end up right in the middle of a potent endocrine-disruptive range of toxicity.

(You got that? Right. Very good. Excellent.)

Non-linear responses — *and* these endocrine-disruptive effects at these incredibly low doses begin in the womb. Very, very important, and they don't *stay* in the womb. So the foetus gets exposed to this and then the effects of that carry forward after birth, the consequences of which may not manifest for many years later.

Why is this worrying? Every regulatory agency in the world ignores non-linear endocrine-disruptive effects such as these in evaluating the toxicity of a chemical, any chemical, including glyphosate.

Why is that worrying? Endocrine disruption is now linked with a whole spectrum, a whole plethora, of incredibly serious illnesses: hormone related cancers, ADHD, learning disabilities, infertility, heart disease, diabetes, obesity. You can read this chart for yourself. If this isn't worrying I don't know what is.

Just to illustrate the point to you, the mouse on the left, as you look at that, the mother was fed normal water. No problem. The mouse on the right — same strain, same calories, same activity but during pregnancy the mother was fed one part per billion in the drinking water of an endocrine-disruptive chemical called Bisphenol-A. And look at the difference!

It resulted in massive obesity after birth with consequent ill health, as you can imagine. Bisphenol-A is a common plastic ingredient. (Don't see any plastic bottles here tonight, I'm proud of you. I strongly recommend you avoid Bisphenol A [in] plastic bottles.)

The point is all classes of pesticides in agriculture have herbicides, fungicides and insecticides [and] are now known to have endocrine-disruptive effects. And they can be very costly. This is obviously a speculative study conducted by scientists in America looking at the European Union situation. And look, in a limited range of outcomes such as male reproductive disorders, premature deaths, obesity [and] neurological impact, they estimated that endocrine-disrupting chemicals were costing Europe around €150 billion a year. Not insignificant.

And since we have one paediatrician sharing the panel, sharing the platform with me tonight, I thought I would quote to you another American paediatrician commenting on these findings. Dr Leonardo Trasande, a paediatrician at New York University School of Medicine (isn't that where you studied? Anyway, doesn't matter). He said that these results suggest that regulating endocrine-disrupting chemicals could produce substantial economic benefit (but what about the health benefit?) that would be less than the cost of implementing safer alternatives and producing economic benefits.

Clearly we need further research but there is a greater than a 99% probability that these chemicals contribute to disease. He's absolutely right. The science is behind him.

What's the evidence for glyphosate and Roundup as an endocrine-disruptive chemical? There is quite a lot. A lot of the data however uses for me unrealistically high doses in those studies. But there are some very good studies that show that, really indicate that even at low doses glyphosate can act as an endocrine-disruptive chemical.

In frog and chick embryos it can interfere with retinoic acid [in the immune] system. Retinoic acid, as you may know, is vitamin A, which we need for vision. But actually retinoic acid connects as a hormone-like molecule and it's very, very important during early development of the foetus. And if you interfere with its function it can result in birth defects and that's exactly what was found in this study by Carrasco & colleagues published in 2010. They got birth defects in their chick and frog embryos that were similar to what's been seen in the Argentinian rural population, which is exposed to large amounts of Roundup because they're growing so much GM soy in that country these days.

And then in these tissue culture cell experiments, glyphosate for me has been shown very, very clearly to mimic the effect of oestrogen and augment the function of oestrogen, resulting in hormone-dependent human breast cancer cell growth. So in other words not only some human breast cancers, as some of you may be aware, are dependent on growth [of] oestrogen. Glyphosate can replace it and *boost* that affect. Very worrying. And of course if you disrupt the oestrogen system you can also end up with organ damage.

In addition to — and I must say this because this is another major concern, because again, the regulators are not incorporating this into their evaluation of toxicity — glyphosate formulations:

Adjuvants.

If you take a solution of glyphosate in water and spray onto your plant nothing happens because the glyphosate can't get into the plant to exert its weed killing properties. So what the manufacturer has to do is they have to add additional chemicals in the mix, collectively known as *adjuvants*. So, turns out that particular classes of adjuvants, particularly those collectively known as POEAs, which are claimed to be inert (at least that's what the industry says) are... There is increasing evidence to show that these adjuvants can be even more toxic than the active ingredient, in this case glyphosate itself, up to a thousand, a hundred to a thousand times more toxic. And the regulator doesn't regulate for these.

When a farmer sprays the crop, or when you use your Roundup or some other pesticide spraying your garden, you're spraying a mixture [of] all these adjuvants. And so what we are exposed to is not just glyphosate but these adjuvants. And these have not been evaluated for toxicity at all by regulators because they've essentially believed the industry when it says they are inert, non-toxic. This is again a failing of our systems.

Quickly, a study released just late last week from again scientists at Flinders University in Adelaide. They basically... these human placental, human placenta type cells were exposed to Roundup and

glyphosate, and again they showed that the Roundup formulation as a whole was a hundred times more toxic than glyphosate alone in killing these cells. And that the level of toxicity began at a glyphosate equivalent concentration that is permitted in Australian drinking water. Not a good thing.

In terms of what's generally present in the human population you'll hear more from the following speaker on this but just to say that there are very few studies that have been conducted looking at our body burden of glyphosate in different regions around the world. But what generally we're finding is that North American levels are much higher than European levels by as much as say a 10-fold. We don't know what's in the Australian population because no one has been looking.

Collectively what the regulator has done (and this is from a paper by German regulators) is that they dismissed these levels. They simply dismissed them. Why? Because it's well below the safe regulatory safe limits, therefore nothing to worry about. These are studies of human subjects in Germany. If you look at the top right here [pointing to graphs titled *Detection of glyphosate Residues in Animals and Humans*, Kruger et al.] people on a conventional diet [had] about two nanograms, two parts per billion in urine, much higher than those on an organic diet. But in the same paper from Professor Kruger's lab in eastern Germany, if I can just focus your attention to the right top, left sorry, top left again, what we see here is the glyphosate levels in urine of dairy cows in Germany: around 20 parts per billion, 20 nanograms per meal there. The worrying thing is

when you look at the bottom here in the organs of the same animals. What you find is roughly the same amount of glyphosate in kidney, liver, lungs, spleen, muscle, intestines in these dairy cows as you find in their urine.

So claims by the industry and regulators that glyphosate is very quickly cleared from our bodies and there's no evidence of accumulation is completely wrong, basically. And that means that you can accumulate glyphosate in your body, and if you eat these meats from these dairy cows, of course, you're not only going to be getting glyphosate from soy, corn, whatever products, you're going to also get it from meat products as well.

So, other levels detected to date in humans which are below regulatory safe limits. Are they safe or not? There's only one study that has been published which has actually addressed this. And this is a study from Professor Seralini's lab in France [*Long-term toxicity of a Roundup herbicide and a Roundup-tolerant GM maize*], which basically was an extension of the 90-day feeding study with the same GMO corn conducted by Monsanto. But what he incorporated in this study was the very first evaluation of Roundup (of full formula, not just glyphosate alone, but a full Roundup herbicide formulation) at incredibly... including a very low dose [of] 50 nanograms per litre (50 nanograms per litre is 50 parts per trillion) and he chose that because it's what we may find in European drinking water as a contaminant. I think you allow much more than that, by the way, as we will see.

So the question is, if you're exposed daily to these minuscule doses of glyphosate, is there any health consequence? Well, I'm afraid there was. Not only was the GMO corn, the GMO corn plus Roundup showing toxic effects, but the lowest dose Roundup group also showed signs of liver and kidney toxicity, escalation of these signs of toxicity, [and] well beyond what Monsanto saw in their 90-day feeding study. There was especially damage and failure of organs in males leading to premature death. There was testosterone/oestrogen imbalance in the females, suggesting endocrine disruption. And, there was a trend increase in mammary tumour incidence in the females. This was a two-year study. The black line here shows the trend increase in mammary tumours in the control group, not receiving this tiny dose of Roundup in their drinking water, and the red line is the tumour incidence in females receiving 50 parts per trillion glyphosate on a daily basis in their drinking water. This is a statistically significant finding. I don't find that surprising. There's a report from the World Health Organisation's international agency for research on cancer. They have included glyphosate in their evaluation of five organophosphate pesticides [*Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate*]. You'll see glyphosate in the title there and what they came... They're looking at the animal studies that have been conducted to evaluate cancer — of glyphosate. They came to the conclusion, and I think correctly, that these animal studies suggest that glyphosate is a *probable* (this is the word that was used), a probable carcinogen. That means it's not insignificant.

And to come back to the Seralini study — with this

very surprising finding, by the way, [as] it was thought that there would be no effect from taking 50 parts per trillion glyphosate in your drinking water. However, the amount in the drinking water that was fed is half the dose of what's permitted in drinking water in Europe; half the level permitted in drinking water in Europe. It's 14,000 times lower than what's permitted in drinking water in the United States. But I'm afraid it is 20,000 times lower than what your regulators here in Australia say; the Australian Drinking Water Guidelines of 2011 says can be permitted. And when you look at the daily intake in these rats that still suffered these extreme illnesses — the liver and kidney damage, the pituitary damage, the hormonal imbalance, and then increase trend in tumour incidence — when you look at what these rats were actually consuming on a daily basis they were tens to hundreds of thousands of times lower than what the regulator has set for us as an acceptable daily intake, as something safe to consume on a daily basis.

So, how do I account for this? I believe it's because [of] glyphosate; these minuscule doses are acting as an endocrine-disruptive chemical. I don't have another mechanism where this can come about, but we're conducting more research to try and really nail that, for sure.

So, is Monsanto right to claim there is no evidence of endocrine disruption from glyphosate? I will say that is highly questionable. Is the regulator up-to-date with the science to say that we can consume this on a daily basis and it not be toxic and safe? I would also say that is also highly questionable.

So, in conclusion, in summary, I would say that based on the current evidence alone, say a safe dose for glyphosate or Roundup is actually unknown, and that we should simply withdraw it from the market.

And in terms of GMOs in general, because that's our theme this evening, for me this evening too, I believe that the studies conducted to date show clear evidence of toxicity, especially to liver and kidney function in controlled animal feeding studies, including even on a short-term basis. What is causing this toxicity from GMO consumption? It can be from the GMO transient product Bt toxin, the herbicide, especially glyphosate in the adjuvant residues, or the mutagenic effect of the GM transformation process. I believe there is evidence that it's a combination of all of these three but particularly the glyphosate adjuvant residues, I believe, are a major contributing factor.

And so on that note, I would say that we need to conduct, we need to withdraw — I would go as far to say that since it has not been possible, you cannot claim, based on the inadequacy of the tests requested by regulators, and on the available evidence at present, no GMO crop and food can be categorically be stated as safe to consume, especially on a long-term lifelong basis. And as we published and as a result, we say there is no scientific consensus on GMO food safety, despite what the industry and the pro-GM lobby may say.

So thank you very much.

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