Study	Key claims	FSANZ response
Journal articles		
Feeding study in rats		
Zdziarski, I.M., Carman, J.A., & Edwards,J.W.(2018) Histopathological investigation of the stomach of rats fed a 60% genetically modified corn diet. Food & Nutrition Sciences 9: 763 - 796	Rats were fed a diet containing either 60% GM corn (a triple stack comprising MON863, MON810 and NK603) or 60% non-GM corn. After 26 weeks, the rat stomachs were removed and samples were prepared for light microscopy, immunohistochemistry and electron microscopy. The authors reported that the GM diet affected tight junction apposition, gland dilations and dysplasia and concluded that feeding GM corn may have health implications.	FSANZ has reviewed the study and a detailed response is available here.
Feeding study in goats		
Tudisco, R., Calabro, S., Cutrignelli, M.I., Moniello, G., Grossi, M., Mastellone, V., Lombardi, P., Pero, M.E. & Infascelli, F. (2015). Genetically modified soybean in a goat diet: Influence on kid performance. Small Ruminant Research 126 (Suppl): 67-74	The aim of the study was to investigate the effect of GM feeding on colostrum quality in the goats (protein and fat composition; IgG concentration) and on kids fed milk from the goats. The authors also analysed for the presence of feed DNA fragments in the colostrum. The authors report the following findings: • kid weights were significantly higher in the control group at day 30 and at slaughter • kids in the controls groups were significantly taller • colostrum from the treatment groups was significantly lower in fat and protein content although this difference disappeared after day 15 • colostrum and kid serum IgG concentration were significantly lower in treatment groups	FSANZ has reviewed the study and concluded it does not provide convincing evidence that the reduced protein, fat and IgG content of the colostrum fed to the test group is responsible for the reduced growth in the kids, or that the observed differences in milk composition can be attributed to the GM soy present in the diet fed to the dams. The authors also failed to acknowledge and address possible alternative (and more plausible) explanations for the observed effects. FSANZ's full review is available here

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	• transgenic DNA was detected in colostrum from goats fed GM soybean meal in their diet • The authors claim the reported growth delay "was presumably due to the lower percentage of protein in the colostrum as well as in the milk at 15 days of lactation"	
Feeding study in pigs		
Carman *et al.* (2013). A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. *Journal of Organic Systems* **8**: 38 – 54.	Pigs were fed either a mixture of GM corn and GM soy or an equivalent non-GM diet for a period of nearly 23 weeks. The authors claim the GM diet was associated with gastric and uterine differences in the pigs; specifically severe stomach inflammation and enlarged uteri. There were no differences between pigs fed the GM and non-GM diets for feed intake, weight gain, mortality and blood biochemistry parameters.	FSANZ has reviewed the study and a detailed response is available here.
Double stranded ribonucleic acid (dsRNA)		
Heinemann *et al.* (2013). A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. *Environment International* **55**: 43 – 55.	The authors claim that small double-stranded RNAs (dsRNAs) generated in GM plants as a result of using gene silencing techniques can create biosafety risks that are not being adequately assessed by regulators such as FSANZ. They suggest changes to the safety assessment process to address their concerns.	FSANZ has carefully examined the arguments put forward in the article, and has thoroughly researched the scientific literature on gene silencing. The weight of scientific evidence published to date does not support the view that small dsRNAs in foods are likely to have adverse consequences for humans. In formulating their hypothesis, the authors have not taken into account the fact that small dsRNAs are ubiquitous in the environment and in the diverse range of organisms we consume as food, including plants and animals. This establishes a long history of safe human consumption which

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		pre-dates the use of such techniques in GM plants. The authors failed to adequately acknowledge that developing oral therapies based on small dsRNAs targeted against human viruses and other diseases such as cancer has so far been unsuccessful because of the barriers that exist to their uptake, distribution and targeting within the body. The authors have also underestimated the strengths of the GM food safety assessment to detect possible unintended effects, including those that could arise from the use of gene silencing. There is no scientific basis for suggesting that small dsRNAs present in some GM foods have different properties or pose a greater risk than those already naturally abundant in conventional foods. The current case-by-case approach to GM food safety assessment is sufficiently broad and flexible to address the safety of GM foods developed using gene silencing techniques. This approach enables additional studies to be requested should that be necessary to further inform the safety assessment of a particular GM food. A detailed response by FSANZ is available here.

Study	Key claims	FSANZ response
The Cauliflower mosaic virus (CaMV) promoter		
Podevin & du Jardin (2012). Possible consequences of the overlap between the CaMV 35S promoter regions in plant transformation vectors used and the viral gene VI in transgenic plants. *GM Crops and Food: Biotechnology in Agriculture and the Food Chain* **3(4):** 1 - 5	The authors analysed the 35S promoter region used in a number of approved GM crops and found that it included some of the sequence of Gene VI, a viral gene with multiple functions. An online commentary was published shortly after the publication of the paper: Latham, J. & Wilson, A. (2012). Regulators Discover a Hidden Viral Gene in Commercial GMO Crops, *Independent Science News,* 21 Jan 2013. In this commentary, the following claims were made: • Researchers have "discovered" viral gene sequences in GM crops that were previously unknown to regulators. • Serious ramifications for crop biotechnology, regulatory agencies, consumers and farmers. • Could present an unidentified safety risk to humans and could disturb normal functions of crop plants.	Podevin & du Jardin did not raise any concerns about the implication of their analysis for the safety of food derived from GM crops in which the CaMV has been used. The claims by Latham and Wilson that the presence of viral gene sequences was unknown to regulators and presents a safety concern are incorrect. All DNA sequences introduced into GM plants are described and fully characterised before approval is granted. The presence of parts of Gene VI from CaMV is not a food safety concern. This virus infects common vegetables such as cauliflower and broccoli and has been consumed naturally by humans without adverse effects. The 35S promoter in various forms has itself been used safely in GM crops for nearly 30 years. The European Food Safety Authority has reached similar conclusions and has released a statement in response.
Ingestion of microRNAs		
Zhang *et al.* (2012) Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA. *Cell Research* **22**: 107 – 126.	This study reported that naturally occurring plant microRNAs (miRNAs) in food can be detected in the bloodstream of mammals, including humans, following ingestion. It appears also from experiments in mice, that these small	The study dealt with miRNAs found in conventional (non-GM) rice, indicating that this is a natural phenomenon. No specific association was made in the study with GM crops.

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	molecules may have the potential to modulate mammalian gene expression. Following publication of the study, concerns were raised in some quarters that DNA ingested from GM crops could inhibit the expression of important human proteins e.g. Heinemann (2012). Evaluation of risks from creation of novel RNA molecules in genetically engineered wheat plants and recommendations for risk assessment. Heinemann (2013) Update on "Evaluation of risks from creation of novel RNA molecules in genetically engineered wheat plants and recommendations for risk assessment". Both reports above are available online here.	Some of the findings in this study, and the interpretation of results, have been disputed e.g. Petrick, J.S., Brower-Toland, B., Jackson, A.L. and Kier, L.D. (2013) Safety assessment of food and feed from biotechnology-derived crops employing RNA-mediated gene regulation to achieve desired traits: A scientific review. *Regulatory Toxicology and Pharmacology* **66**: 167 – 176. Zhang, Y., Wiggins, B.E., Lawrence, C., Petrick, J., Ivashuta, S. and Heck, G. (2012b) Analysis of plant-derived miRNAs in animal small RNA datasets. *BMC Genomics* 2012, open access(13):381. Witwer, K.W., McAlexander, M.A., Queen, S.E. and Adams, R.J. (2013) Real-time quantitative PCR and droplet digital PCR for plant miRNAs in mammalian blood provide little evidence for general uptake of dietary miRNAs. Limited evidence for general uptake of dietary plant xenomiRs. *RNA Biology* 10(7):1-7. Wu, J., Liu, Q., Wang, X., Zheng, J., Wang, T., You, M., Sheng Sun, Z. and Shi, Q. (2013) mirTools 2.0 for non-coding RNA discovery, profiling, and functional annotation based on high-throughput sequencing. *RNA Biology* 10(7):1087-1092. Therefore, further confirmation and evaluation is required to determine whether uptake of miRNAs from the diet is a real and common phenomenon. In the meantime, the weight of

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		evidence published to date does not support the view that small RNAs ingested as part of the human diet have an impact on human gene expression.
Cry1Ab in blood		
Aris & Leblanc (2011). Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology* **31**: 528 - 533	· The Cry1Ab protein can be detected in the blood of pregnant and non-pregnant women and in umbilical cord blood of newborns. Study has been cited as evidence that GM foods are unsafe for human consumption.	The authors analysed blood from healthy pregnant and non-pregnant women, as well as umbilical cord blood from babies subsequently born to the pregnant women, for the presence of the herbicides glyphosate and glufosinate, plus the insecticidal Cry1Ab protein. FSANZ identified a number of significant limitations in the design and conduct of this study which means that the results, as published, do not support the interpretations of its authors. FSANZ's full response is here. A letter to the Editor of the journal, by FSANZ staff, was also published: Mueller, U. and Gorst, J. (2012) Comment on "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada" by A. Aris and S. Leblanc [Reprod. Toxicol. 31 (2011) 528-533]. *Reproductive Toxicology* 33:401-402.

Study	Key claims	FSANZ response
Séralini Studies		
(a) Statistical re-analyses of rat feeding studies with MON863, MON810 and NK603 corn Séralini *et al*. (2007). New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. *Archives of Environmental Contamination and Toxicology* **52**:596 – 602. de Vendomois *et al*. (2009). A comparison of the effects of three GM corn varieties on mammalian health. *International Journal of Biological Sciences* **5**:706 – 726.	The consumption of the GM corn lines is associated with adverse effects mainly in the kidney and liver.	Séralini and colleagues have used a non-conventional statistical approach to analyse and interpret data from animal toxicity studies with three different GM corn lines. FSANZ considers Séralini and colleagues have placed emphasis on statistically significant differences while ignoring the absence of supporting histopathology or other relevant toxicological evidence of an adverse effect. Reliance on statistics alone to determine treatment-related effects in toxicity studies is not regarded as indicative of a robust toxicological analysis. FSANZ is confident that the minor differences observed between test and control groups in the toxicity studies are neither sex- nor dose-related and are primarily due to normal biological variability. The statistical analyses published by Séralini and colleagues therefore provide no grounds to revise previous conclusions regarding the safety of food derived from GM corn lines MON863, NK603 and MON810. FSANZ comments on feeding studies undertaken with MON863 corn is available here.

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(b) Review of animal feeding studies with herbicide tolerant or insect-protected soybean and corn. Séralini *et al*. (2009). How subchronic and chronic health effects can be neglected for GMOs, pesticides or chemicals. *International Journal of Biological Sciences* **5**:438 – 443. Séralini *et al.* (2011). Genetically modified crops safety assessments: present limits and possible improvements. *Environmental Sciences Europe* **23**:ePub.	90-Day studies are insufficient to evaluate chronic toxicity. Claim that data from several different animal studies with herbicide tolerant and insect-protected corn and soy lines show liver and kidney effects which may indicate the onset of chronic disease. Suggest that long-term, multigenerational and reproduction feeding studies be made compulsory for GM foods containing herbicide-tolerant or insect protection traits.	Séralini and colleagues reviewed animal feeding studies undertaken with various herbicide-tolerant and insect-protected GM corn and soy lines. Many of the lines included in the analysis are those previously assessed and approved by FSANZ. The authors criticise conventional toxicology testing, as applied to GM food and interpreted by food regulators, but this criticism appears to be based on a limited understanding of toxicology which, in FSANZ's view, invalidates the conclusions reached by the authors. The authors also re-state that their statistical methodology is appropriate for interpreting toxicity studies, without any regard to clinical pathology and historical control data (see above). The arguments presented by Séralini and colleagues provide no grounds for revising conclusions regarding the safety of food derived from previously approved herbicide-tolerant or insect-protected GM corn and soy lines. Nor do they provide sufficient rationale for revisiting FSANZ's position on the use of animal feeding studies in GM food safety assessment (available here).
(c) Long term feeding study	The authors claim that a wide range of adverse effects occurred in rats fed NK603 corn in their diet, including • A higher mortality rate • Development of tumours	The claims of a link between a range of adverse effects and a GM corn diet over a two year period in rats are not supported by the evidence. There are no rational scientific grounds for attributing the findings to the GM diet, and the authors make no attempt to

Study	Key claims	FSANZ response
Séralini *et al.* (2012). Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically-modified maize. *Food and Chemical Toxicology* **50**:4221 – 4231 **NOTE: This study was retracted by the journal in November 2013**	• Pituitary 'dysfunction' in females • High level of liver congestions and necrosis in males • Deficiencies in kidney function • High level of kidney nephropathies in males They also claim that administration of glyphosate in the drinking water of the rats at concentrations well below officially set safety limits, induced severe hormone-dependent mammary, hepatic and kidney disturbances.	discuss possible mechanisms of toxicity to explain their findings. FSANZ does not believe the study provides any grounds to revise its previous conclusions on the safety of food derived from NK603 corn. A FSANZ review of the study is given here.
CSIRO Peas Study		
Prescott *et al*. (2005). Characterisation of the structure and immunogenicity of bean α -amylase inhibitor (α AI) when expressed in peas. *Journal of Agricultural and Food Chemistry* **53**:9023 – 9030.	The authors claim that: • the expression of a bean α AI in peas can lead to the synthesis of a modified form of the protein with altered antigenic properties; • exposure of the GI tract in mice to the modified α AI along with heterogeneous food antigens cross-primes and elicits immunogenicity. Study often cited as evidence that GM foods can cause allergic reactions.	The GM peas were still in the research and development phase and were never submitted to FSANZ (or elsewhere) for food safety assessment and approval. The α AI protein was therefore never assessed for potential allergenicity, as would be standard for any GM food safety assessment. Following publication of this study, the developer of the GM peas, CSIRO, announced they were ending the research program. While the results show that a modified form of the α AI protein had been produced in the GM peas, and this modified protein produced an altered immune response when fed to mice, they do not show that the mice became 'allergic' to the modified protein, as is often asserted. The animal model used by the study authors has not been validated to predict human

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		immune or allergic responses and the authors make no such predictions. It is therefore not clear what relevance (if any) the findings have in relation to human food allergy. The results of a study released in 2013 cast doubt on the findings of the Prescott *et al*. (2005) paper: Lee *et al.* (2013). Genetically modified α-amylase inhibitor peas are not specifically allergenic in mice. PLoS ONE 8(1): e52972. Lee *et al.* repeated the experimental work of Prescott *et al.* (2005) but were unable to duplicate the results. They concluded that transgenic peas containing αAI are not more allergenic than either beans or non-transgenic peas in mice, since beans and peas (both GM and non-GM) all elicit an allergic response in mice. The authors concluded it is still not clear that these immune responses are biologically relevant for humans.
Pusztai Study		
Ewen & Pusztai (1999). Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine. *The Lancet* **354**:1353 – 1354.	Authors claim that rats fed GM potatoes expressing a plant lectin had stunted growth and a depressed immune system.	The GM potatoes were in the research phase and were never submitted to FSANZ (or elsewhere) for food safety assessment and approval. FSANZ has not formally reviewed the results of this study. The UK Royal Society undertook a review of data on the possible toxicity of GM potatoes in 1999. They could find no convincing

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		evidence of adverse effects. Where the data seemed to show slight differences between rats fed predominantly on GM and non-GM potatoes, the differences were uninterpretable because of the technical limitations of the experiments and the incorrect use of statistics. The review by the Royal Society is available here.
Schubbert Studies		
Schubbert et al (1994). Ingested foreign (phage M13) DNA survives transiently in the gastrointestinal tract and enters the bloodstream of mice. *Molecular and General Genetics* **242**:495 – 504. Schubbert et al (1997). Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA. *Proceedings of the National Academy of Sciences USA* **94**:961 – 966. Schubbert et al (1998). On the fate of orally ingested foreign DNA in mice: chromosomal association and placental transmission to the fetus. *Molecular and General Genetics* **259**:569 – 576.	A series of studies which showed that, when fed to mice at high doses, M13 bacteriophage DNA could be transiently detected as fragments in blood, various cells, organs and tissues, including fetal tissue. These studies often cited as evidence that ingested recombinant DNA could represent a risk to human health.	The fate of ingested DNA has been thoroughly studied. DNA is extensively broken down during digestion and this process is the same for both recombinant DNA and non-recombinant DNA. Some studies, such as the Schubbert studies, have shown that not all ingested DNA is completely degraded. Some DNA fragments may remain which can be detected in the digestive tract, and which have also been shown to pass into the bloodstream and other body tissues. This is a normal biological phenomenon that can be expected to occur with both non-recombinant and recombinant DNA and there is no evidence that this represents a human health or safety concern. The cells of the human body have effective mechanisms of defence against the uptake, integration and continued expression of

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		foreign DNA from food or from the environment. A FSANZ Fact Sheet on the safety of ingested recombinant DNA is available here.
Netherwood Study		
Netherwood et al (2004). Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. *Nature Biotechnology* **22**:204 – 209.	Authors showed that a small proportion of recombinant DNA from GM soy survived passage through the upper gastrointestinal tract but was completely degraded in the large intestine.	See above.
Internet publications		
'Austrian' Study		
Velimirov et al (2008). Biological effects of transgenic maize NK603 x MON810 fed in long term reproduction studies in mice. Study available from the website of the Austrian Ministry of Health, Family & Youth: Download the study as a PDF (908kb).	Authors claim the feeding of GM corn to mice is associated with adverse reproductive effects, namely statistically significant reductions in the number of offspring of mice allowed to breed continuously, but only in the third and fourth litters.	The study was commissioned by the Austrian Government and conducted predominantly at the University of Vienna. FSANZ examined the published report released on the internet and considers the conclusions drawn in the report are not supported by the results because they incorrectly calculated pup losses in a continuous mouse breeding study. When corrected, no differences of biological significance in reproduction parameters or longevity were evident in the mice irrespective of their dietary group. The European Food Safety Authority has also examined the results of the Austrian study and was critical of the methodology and authors' calculation errors. EFSA reached a similar conclusion to FSANZ and

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		has dismissed the findings of the study as being of minimal scientific value. The Austrian Government announced on 19 October 2010 that it had formally withdrawn the study because the researchers had failed to deliver a satisfactory statistical analysis of the data.
Conference presentations		
Ermakova study		
Ermakova (2005). Influence of genetically modified soya on the birth-weight and survival of rat pups. Available from: Download the study as a PDF (1.64kb).	Claims that rats fed diets containing glyphosate-tolerant GM soybeans gave birth to pups with low survival rates, stunted growth, abnormal testicles (male pups) Study often cited as evidence of the potential toxicity of GM foods	The study remains unpublished in the peer-reviewed scientific literature and full details are not available. In the absence of detailed information on the study conduct it is difficult to interpret the study results. No information is available on the source of the GM and non-GM soy or the nutritional adequacy of the test diets. Moreover, mortality of the animals in this study, including the non-GM control animals, was very high, which raises questions about the conduct of the study. The results from this research are not supported by other studies on the safety of glyphosate-tolerant soybeans.