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THE NEXT GENERATION OF GM FOODS:

Good for Whose Health?

GeneWatch UK

Briefing Number 10
April 2000

In a desperate effort to reverse its failing fortunes, the biotechnology industry and its supporters are putting their faith in the 'second generation' of genetically modified (GM) crops. It is claimed that many of these will bring consumer benefits by offering foods with enhanced nutritional value (so-called 'functional foods'). Other genetic modifications to the nutritional composition of crops are intended to facilitate food or animal feed production or provide ingredients for other industrial uses from cosmetics and personal healthcare to biodegradable plastics and biofuels. This briefing reviews what is under development and what the risks and benefits may be.

Why Are Functional Foods Being Developed?

The term, 'functional food' has no clear scientific basis or legal definition. It is primarily a marketing term coined in Japan in the 1980s and such foods may also be referred to as 'designer foods', 'nutritionally enhanced foods' or 'nutraceuticals'. For the purpose of this briefing, functional foods are defined as '*foods with ingredients that claim to provide a health benefit to consumers beyond the nutritional benefits ordinarily provided by the foods themselves*'[1]. Non-GM functional food products already available in the UK include yoghurts with 'bio' cultures, spreads with cholesterol-lowering compounds, bread with fish oil, and soft drinks with added fibre.

The market for functional foods is being developed in response to the growing public interest in the links between diet and health. Foods with enhanced nutritional benefits are seen by companies as a way to achieve added-value growth and profitability in an otherwise highly competitive food market with tight margins and slowly growing food sales. Therefore, food companies around the world are restructuring their operations and spending literally hundreds of millions of dollars to develop and market functional food and beverage products[2]. The real value of functional food to companies is not in their potential to improve the health of the nation (where is the commercial value in that?) but in the '*exciting opportunities*' functional foods offer '*to food manufacturers and retailers to add value and differentiate their products*'[3].

Over recent years, many major food companies and ingredient suppliers have declared their commitment to functional foods. These companies include Nestlé, Kellogg, Unilever, ConAgra, Nabisco, Quaker and virtually every major European dairy company, as well as the 'life sciences' corporations, DuPont, Monsanto and Novartis[2]. Many of these companies have set up 'functional food' or 'human health' divisions to exploit market opportunities. For example, Novartis and Quaker have recently announced the formation of the Altus Foods Company to produce foods with health benefits[4].

Yet there are those who believe that the rhetoric and claims made for functional foods are seriously over-stated: "*To date, marketing hype appears to have outrun scientific evidence, inviting the conclusion that the whole concept of functional foods has been over-promoted, just another food fad for the high-tech era.*" [5]

What's Being Developed?

GM companies such as DuPont, Monsanto, AstraZeneca and Novartis are already developing crops with genetically altered nutritional profiles and foresee a role for biotechnology in developing functional foods and ingredients[2]. The UK Government's research council, the BBSRC, also believes that, *"scientific advances, including those in molecular genetics, now make possible a more rational and systematic modification of raw material"* leading to *"quality enhanced at primary production rather than processing"* [6].

To date, only two GM products with altered nutritional traits have received market approval - both in the USA - although neither is in commercial use. Both are oilseed crops with an altered oil composition - a soybean with increased oleic acid (DuPont) approved in 1997, and a high lauric acid oilseed rape from Calgene/Monsanto approved in 1995. According to Monsanto, the latter is no longer being grown and there are no plans to introduce this crop into Europe[7]. DuPont's product is still under market development in the US, and although the company has sought European marketing approval, it does not expect this to be forthcoming in the foreseeable future[8]. However, neither of these crops are primarily intended to improve human nutrition, but to provide more stable oils to benefit food producers.

GM techniques are being applied to crops to produce altered nutritional profiles

Although no other GM functional food products have yet reached the market, there are several areas where GM techniques are being applied to crops to produce altered nutritional profiles: [9]

- increasing the content of vitamins, minerals and other micronutrients;
- modifying fats and oils;
- altering the starch and sugar content;
- altering protein/amino acid profiles;
- reducing levels of anti-nutritional/allergy factors;
- flavour enhancements.

V*itamins, minerals and other micronutrients*

There has been much recent publicity over the GM rice being developed by Swiss researchers to have enhanced levels of beta-carotene (converted to vitamin A in the body) and iron. This so-called 'golden rice' has been promoted as a means of addressing the problems of vitamin A and iron deficiencies in developing countries (see centre pages). Other work to enhance micronutrient content through genetic modification is likely to be aimed at providing alternative sources of ingredients (e.g. beta-carotene, vitamin E) for the food and food supplements industries, primarily in developed countries.

Companies are also altering levels of other chemicals which may be connected with health. For example, AstraZeneca is exploring genes (licensed from Japanese company, Kirin) that increase a plant's production of carotenoids, which, it is suggested, could reduce the incidence of heart disease and some cancers[10]. The company is considering introducing these genes into crops such as processing tomatoes, bananas, potatoes and lettuce. DuPont researchers have recently identified one of the key genes coding for isoflavone synthesis in soybeans. (Isoflavone is a natural oestrogen-like compound thought to help prevent cancer, heart disease and the effects of the menopause.) They propose to introduce the gene into crops that do not normally produce these compounds in order to develop functional foods and/or to improve the crop's resistance to disease[11]. However, high intakes of isoflavones may have detrimental health effects for some consumers, such as babies fed on soya infant formula[12].

than the consumption of individual nutrients. The development of the market for functional foods as higher priced niche market products is illustrative of their role in providing companies with new marketing opportunities rather than addressing underlying nutritional problems. Therefore, public policy initiatives and public expenditure should be targeted at encouraging balanced diets and healthy lifestyles rather than supporting the development of GM nutritionally altered foods.

The role of functional foods is to provide companies with new marketing opportunities rather than address underlying nutritional problems

The introduction of GM nutritionally altered foods raises serious safety questions. New systems of safety assessment will have to be developed and regulation of the health claims that can be made for any altered food must be introduced as a matter of urgency. If consumers are not to be misled, all functional foods should be tested to determine whether they provide any real benefit. This should not apply only to the basic ingredient but also to the final product to avoid foods with, for instance, a high fat content being labelled as 'healthy' because it has some added micronutrient.

For the biotechnology industry, an important challenge exists in terms of consumer acceptance. Because there is, in fact, no real consumer benefit that can be detected in the majority of nutritionally altered GM foods being developed, in the present climate it seems unlikely that they would be marketable in the UK. Since GM foods are already so stigmatised, the industry's hope that GM functional foods will reverse their failing fortunes seems rather forlorn.

This briefing is based on a research report '*Biotech - the next generation. Good for Whose Health?*' by Sue Dibb of the Food Commission and Sue Mayer of GeneWatch UK. The full report is available from either organisation for £40 (£10 for individuals and not-for-profit organisations).

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The challenge for safety assessors is that any unintended alterations have to be identified and their significance determined. As one expert has said: *"Safety testing will have to be adjusted for the 'second generation' of food plants, which are modified to improve food-quality traits.... These must undergo extensive toxicological and nutritional assessment with a combination of in-vitro and in-vivo techniques as required for novel foods in general"*.[31] As yet, appropriate testing systems have not been defined or agreed upon.

General safety questions

It is also important to consider the nutritional impact which such altered foods may have on the overall diet of those consuming them - particularly for 'at risk' groups such as infants, young children and pregnant women. Fortification of foods with relatively high levels of a small number of micronutrients may cause an imbalance in dietary intakes and the addition of one nutrient may lead to disturbances in the utilisation of others [32]. It is now becoming clear that plants contain a great many different micronutrients and many interactions take place. For example, vitamin C enhances iron absorption while calcium may reduce it. Potential risks include:

- Consuming high levels of vitamin A during pregnancy may increase the risk of birth defects[33]. Excessive intakes of vitamin A from overuse of supplements are toxic and can cause damage to the liver and cell membranes[34].
- Increased risk of heart disease and cancer are associated with high levels of iron intake.[35]

There is no specific legislation addressing functional or nutritionally altered foods in the UK

Despite such risks, there is no specific legislation addressing functional or nutritionally altered foods in the UK, although the Food Safety Act (1990) prohibits false and misleading advertising of food in general and more specifically prohibits 'medicinal' claims for foods (i.e. that a food can treat, cure or prevent a disease). However, this does not address claims that a food is 'healthy' or has some general nutritional benefit. Therefore, concern is increasing about the proliferation of health claims for 'functional food' products since such claims do not have to be substantiated and the efficacy of the food does not have to be proven.

Conclusions

The claims made for GM nutritionally altered foods and the alleged consumer benefits they will bring are overstated. It is clear that they are a long way from commercialisation and that the first products are targeted at the needs of food processors rather than genuine nutritional advantages for the consumer.

For developing countries, rice genetically modified to contain increased levels of beta-carotene may have a role to play, but it is too early to assess whether it can offer a significant benefit. If GM oilseed crops grown in the developed world are used as substitutes for oils usually produced in developing countries, their economies (and thus their health) will be harmed.

There is little evidence to support the role of functional foods in reducing diet-related disease and improving public health

For developed countries, there is little evidence to support the role of functional foods, whether genetically modified or not, in reducing diet-related disease and improving public health. However, there is considerable evidence to support the health benefits of consuming more fruits and vegetables and other foods naturally rich in vitamins, minerals and other micronutrients, rather

Assessing the health benefits of levels of individual chemicals in foods is difficult. Epidemiological data supports the need for greater consumption of fruit and vegetables and other foods rich in micronutrients in diet-related disease prevention. However, in general, evidence to support the health benefits of increasing the consumption of individual micronutrients (the approach taken with GM nutritionally altered foods) is less convincing[13].

Modifying fats and oils

Efforts to modify the oil composition of oilseed crops such as oilseed rape and soybean have largely focused on producing sources of more stable oils to reduce the need for blending or processing, or alternative sources of speciality oils[14]. Some of these novel oils are intended to substitute for tropical oils (e.g. palm or coconut) or existing speciality oils (e.g. fish oils, evening primrose oil). Such developments are primarily intended to benefit food processors and producers or other industrial users rather than consumers. Even those intended to eliminate the need for chemical hydrogenation in processing (which results in the production of harmful trans-fats) are unlikely to offer a significant health benefit as this is achieved by increasing the level of unhealthy saturated fats.

Any benefits will be limited to those able to afford the higher prices

Much of the early optimism for producing designer oilseeds has been tempered by setbacks in obtaining high yields of specific novel fatty acids in GM crops[14]. Any products will have to be processed separately from conventional crops and the costs of harvest segregation and separate transportation will add considerably to the price. The final product will therefore only be applicable to specialist niche markets that bring a premium and any benefits will be limited to those able to afford the higher prices.

Altering starch and sugar content

Most research into genetically modifying the starch content of sugar beet, potatoes and maize is primarily aimed at producing alternative sources of specialist starches for industrial purposes. However, spin-off research claims that it could be possible to produce 'healthier' chips from potatoes which have been modified to have a higher starch content and so absorb less fat. Another area of interest to the food industry is that of fructans found in artichokes, onions and garlic. Although sweet-tasting, these are non-digestible (and therefore non-calorific) carbohydrates. Fructan-encoding genes have been introduced into chicory[15] and also into sugar beet[16] to produce sugar that has half the calories of conventional sugar and is intended for the lucrative 'low calorie' or 'slimming' foods market.

The removal of allergens from allergy-triggering foods such as peanuts, rice and milk is also under research

Other applications

It has been proposed that biotechnology could be used to improve the protein content of staple crops in developing countries. Some success has been reported for sweet potato and future work may involve cassava, rice and plantain.[17] Modifying protein composition is also being used to improve the dough-making characteristics of wheat with potential benefits to the baking industry[18] and to improve the quality of animal feeds[19]. Proteins are also of interest to the pharmaceutical and infant formula markets. Biotechnology is being used to produce the human milk protein, lactoferrin, found in colostrum (the first breastmilk) which has antibacterial properties. The removal of allergens from allergy-triggering foods such as peanuts, rice and milk is also under research [20,21] although no such products are close to being marketed.

In 1994, 3 million pre-school age children had eye damage due to vitamin A deficiency

Can GM Rice Tackle Vitamin A Deficiency in Developing Countries?

Vitamin A deficiency (VAD) is an important cause of illness in developing countries, resulting in night blindness, total or partial blindness, and reduced resistance to infection. In 1994, the World Health Organisation (WHO) reported that 3 million pre-school age children had eye damage due to vitamin A deficiency. Annually, an estimated 250,000 to 500,000 pre-school children become blind from this deficiency and about two-thirds of these children die within months of going blind. VAD is also thought to contribute to the 1.1 million childhood deaths from measles each year.

Rice is being genetically modified to increase its beta-carotene content (a precursor for vitamin A that is absorbed and converted into vitamin A in the body)[22,23]. Can the GM rice end VAD and prevent this suffering?

Why vitamin A deficiency occurs

VAD is associated with poverty and an inadequate, unbalanced diet. Vitamin A is obtained either by ingesting the preformed vitamin or by its production in the body from the precursor beta-carotene. Vitamin A itself is found in foods of animal origin such as eggs, whole milk and meat. Beta-carotene is found in plant foods and especially in green leafy vegetables and fruit. The majority of people with VAD are in those countries where rice predominates in the diet - south and southeast Asia - since polished rice is low in beta-carotene because the naturally beta-carotene rich husk is removed during milling. Women and children are most at risk because of their increased physiological needs during pregnancy and growth.

In part, the situation has been exacerbated by the Green Revolution because the high-yielding varieties of rice, maize and wheat are low in vitamins and minerals and have displaced local fruits and vegetables from diets. Therefore, the overall intake of micro-nutrients - such as vitamin A, iron and zinc - has actually declined in many groups even though energy intake may have increased[24].

Is GM rice the answer?

Beta-carotene production in the GM ‘golden rice’ is made possible by the introduction of three genes from a narcissus plant which complete the biochemical pathway needed for beta-carotene production in the rice endosperm (the rice grain remaining after milling has removed the outer layer which naturally contains beta-carotene)[23]. However, changing the metabolism of the endosperm may alter the levels of other components if there is a trade-off in how basic chemicals are processed in the rice grain. In other words, the increase in pro-vitamin A may come at the expense of other compounds of nutritional importance. There could also be unexpected products that prove harmful. Rice can form a very large proportion of the diet in developing countries, so even small alterations will need rigorous evaluation. There is also no information yet on how well the pro-vitamin A will be absorbed - this varies enormously according to the type of food involved.

Because the GM rice is yellow and people have been encouraged to believe that polished white rice is best, there would also need to be an education programme to persuade people to eat it. Furthermore, whilst the inventors of the GM rice are giving the technology to plant breeders in developing countries, it will still have to reach the people most in need at a price they can afford – even public plant breeding comes at a cost.

Alternative methods of control

Technically feasible, relatively cheap and effective ways of reducing VAD are already available and practised. These include:

- **Supplementation** programmes using high dose vitamin A capsules - ideally twice yearly – which are now extensive.
- **Fortification of foods** – adding vitamin A to foods before they are purchased – can also be very effective and this approach is expanding[25]. However, as with supplementation programmes, this strategy requires external inputs, foreign currency and a sustainable distribution system.
- **Dietary diversification** – where a wider based diet is encouraged - is considered an important dimension of control and is likely to be a more sustainable approach in the long term. Home gardening and women’s education have both been shown to improve long-term consumption of foods that are rich in vitamin A[26].

However, the WHO and UNICEF’s goal of virtually eliminating VAD by the year 2000 has not been achieved. The WHO consider VAD to be *“..a test case of political will, and managerial capacity to implement known technologies and known solutions”* [27]. Continuing VAD would therefore seem to demonstrate a failing on both counts.

The goal of virtually eliminating VAD by the year 2000 has not been achieved

Conclusion

Encouraging the growing and consumption of more fruit and vegetables and animal products such as eggs and cheese would have wider nutritional benefits than the GM rice. Improving incomes, education and sanitation or giving supplements to those in need could prevent deaths and disability arising from reasons other than vitamin A deficiency alone.

However, in the same way that GeneWatch UK has argued that people in Europe should have a say over what they eat, those who are at risk from vitamin A deficiency have to be included in the process of finding the best and most sustainable solutions - they understand their problems far better than any scientist. Rather than being used as pawns in a distant political debate about the pros and cons of GM foods, it is the poor and disadvantaged who must be centrally involved in weighing up the options.

Altering nutritional composition raises important questions about the safety of the final food

Will GM Nutritionally Altered Foods be Safe to Eat?

Altering nutritional composition raises important questions about the safety of the final food in two respects – does the genetic modification result in any unexpected, potentially harmful changes and are there any problems with nutritionally altered foods more generally (however they are produced)?

GM and the potential for new toxins

The application of GM to the nutritional composition of foods involves altering the plant’s basic biochemical process by modifying the synthetic pathways which determine its chemical composition. This may alter other metabolic pathways and lead to the production of not only the expected compound but also unexpected ones. Some unexpected and unintended effects have already occurred:

- When Monsanto introduced genes to produce beta-carotene and other carotenoids in oilseed rape, this resulted in a decrease in tocopherol (including vitamin E) levels and alterations to the fatty acid composition which were unexpected and which are so far unexplainable[28].
- When researchers in Germany tried to reduce the sugar levels and increase the starch content in potatoes (using genes from yeast and a bacterium), starch levels were actually reduced. Many unexpected compounds were also produced as a result of disturbances to the potato’s metabolism[29].
- In high-stearate oilseed rape, the stearic acid was found to be present not only in the storage oil but also in the membrane lipids of the seed. The seeds tended to have relatively poor germination rates and the high-stearate properties were gradually lost when the GM plants were grown on a field scale[30].

The application of GM to the nutritional composition of foods has had some unexpected results