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Abbreviations

CRI  Crown Research Institute
DHB  District Health Board
DHBNZ District Health Boards New Zealand
DNA  Deoxyribonucleic acid
FRST  Foundation for Research, Science and Technology
FSANZ  Food Standards Australia and New Zealand
GM  Genetic modification
GP  General practitioner
HCA  Heterocyclic amine
HGRP  Human Genome Research Project
MoRST  Ministry of Research, Science and Technology
NHC  National Health Committee
PKU  Phenylketonuria
RNA  Ribonucleic acid
SNP Single nucleotide polymorphism
Executive Summary

Nutrigenomics shares a continuum with biopharming, the major focus of this part of the Constructive Conversations project. Biopharming products may be marketed as nutriceuticals or functional foods. Nutrigenomics research, particularly in New Zealand, aims to provide an evidence base for “functionality” claims for innovative food products such as these.

This is one reason for the selection of nutrigenomics as a topic of research for the Constructive Conversations project. Other reasons are: nutrigenomics potentially has broad societal implications; New Zealand is one of the early movers in the field of nutrigenomics and has made a significant public investment in initiating nutrigenomics as a field of research in NZ; and, given that it is at an early stage, nutrigenomics is an appropriate topic to explore in relation to upstream public engagement. Upstream engagement involves opening up to public scrutiny and deliberation “deeper questions about the values, visions and vested interests that motivate scientific endeavour” before political, economic and organisational commitments that narrow the space for meaningful debate have been made (Wilsdon and Willis 2004).

The field of nutrigenomics (and nutrigenetics) research should be distinguished from its potential applications. The major applications currently promoted or under development are “personalised nutrition” services and novel foods. Commercial “personalised nutrition” services are already available; these have been widely criticised as misleading and scientifically unsubstantiated. Whether or not it will be possible to offer scientifically valid versions of such services in the future is contested.

Similarly, there is disagreement over the feasibility of novel nutrigenomics foods. Nutrigenomics New Zealand aims to develop “completely new, added-value, export-focused, gene-specific foods that will deliver proven health outcomes to consumers.” Some envision that such foods will sidestep the problem of inducing people to change unhealthy eating habits by changing unhealthy foods to make them less unhealthy.

The drivers of nutrigenomics programmes have been primarily economic. In New Zealand, public funding of nutrigenomics has been geared toward increasing New Zealand’s economic competitiveness by enabling the food industry to develop premium products.

The prospect of applied nutrigenomics (and nutrigenetics) raises a number of regulatory and capacity issues. Nutrigenetic testing is one form of so-called genetic susceptibility testing; it screens for gene variants that have been associated with some level of increased risk of developing a disease. There are many uncertainties around the validity and utility of such tests, and it is particularly important to attend to the significance of differences between what is directly or indirectly claimed for the test and what is well substantiated.
New Zealand currently lacks a regulatory framework for nutrigenetic tests. It can be argued that commercial nutrigenetic services should be subject to regulation based on their direct and indirect impacts on public health and their impacts on the public health system. Some argue that the public health service should embrace nutrigenetic testing. The lack of a national framework for assessing the clinical validity and utility of genetic tests means that there is no robust process in place to ensure that scarce health resources are not spent on oversold nutrigenetic screening.

Nutrigenomics and functional foods raise new challenges for regulatory agencies. One of these is the evidence base for health claims for food. Health claims are typically based on association studies that look for a correlation between a particular bioactive compound and reduced risk of some disease. The use of association studies as an evidence base for health claims is not straightforward. The results of many, if not most, association studies cannot be replicated. The problem is exacerbated by the phenomenon known as publication bias: that is, research finding a correlation has a better chance of being published than research that finds no correlation. Many have warned against operationalising findings from association studies without a much greater knowledge than is currently held of gene-gene and gene-environment interactions.

A second challenge is suggested by recent findings showing that increased consumption of bioactive compounds intended for functional foods, such as folate, betacarotene, selenium and vitamins A, C and E, can cause significant harm; in particular, they appear to facilitate the development of various cancers. Nutrigenetic screening is unlikely to be able to address this problem, as the key factor appears to be not genotype but disease state, or timing. That is, it is not genotype that determines whether a particular dosage of a bioactive compound will be helpful, harmful or neutral, but rather whether pre-cancerous or cancerous developments have already occurred.

These findings suggest particular challenges for Food Standards Australia New Zealand and other food regulators. Establishment of efficacy with regard to one nutrient/disease relationship, as difficult as that is, may not be enough. From the perspective of food safety it will also be necessary to establish that the same food will not inflict harm through a different nutrient/disease pathway. The current model of “maximum safe level” used in relation to pesticides or additives is not necessarily useful here, as the concentrations of antioxidants and other substances that have a detectable positive effect on some (persons or pathways) may be the same concentrations that produce harmful effects in others.

The question of whether nutrigenomics should be a topic for upstream public engagement is part of a larger question regarding whether decisions on allocating public research funding are sufficiently accountable to the public. There appears to be a gathering momentum for making nutrigenomics, and particularly research on functional and “gene-specific” foods, priorities for health research. Such a move appears to entail a number of implicit commitments, including: a blurring of the line between economic and public-health priorities such that public-health priorities would be subordinated to economic goals; and the shift to a public-health paradigm that de-emphasises population-wide
interventions in favour of individual responsibility. The implications of such a shift are discussed in relation to public-health interventions aimed at obesity and cancer.

Some of those interviewed for this report voiced concerns that the term “genomics” would result in nutrigenomics getting caught up in New Zealanders’ negative attitudes toward genetic modification. Public engagement was seen as necessary to avoid such an association. This report suggests that the need for public engagement lies instead in the wide social implications of applied nutrigenomics. Further, it demonstrates that public engagement should occur further upstream than is envisioned by the 2008 Agenda for New Zealand Research, Science and Technology; it should occur before high-level research priorities are set.
1. Introduction

1.1. An “upstream” inquiry

The term “nutrigenomics” is less than a decade old. It is one of a number of “-omics” fields that have spun off from research into the human genome. Others include pharmacogenomics and toxicogenomics.

Those involved in the nutrigenomics programmes discussed in this report study aspects of the interactions between food/diet/nutrients and genes or gene expression. The difficulties of defining nutrigenomics precisely are discussed in Chapter 2.

Nutrigenomics shares a continuum with biopharming, the major focus of this part of the Constructive Conversations project. Biopharming is the transformation of plants and animals into bioreactors for the production of pharmaceutical substances. The same processes can be used to produce nutriceuticals or functional foods—indeed, some of the products of biopharming can equally be marketed as nutriceuticals. Nutrigenomics research, particularly in New Zealand, aims to provide an evidence base for “functionality” claims for innovative food products such as these.

Nutrigenomics and related developments have attracted considerable interest and controversy outside New Zealand (Burton and Stewart 2005, Chadwick 2004, Food Ethics Council 2005, Meijboom et al. 2003, Ries and Caulfield 2006, Wallace 2006). This controversy and the wider societal dimensions of nutrigenomics to which it points, together with New Zealand’s investment in nutrigenomics, contributed to the selection of nutrigenomics as a topic of research for the Constructive Conversations project.

However, nutrigenomics was also chosen to explore the possibilities for social research to contribute to the goal of “upstream engagement”. Upstream engagement has been designated, particularly in the UK, as the next stage of developing science-society relations. Wilsdon and Willis (2004: 18) explain the rationale behind moving public engagement upstream:

Processes of engagement tend to be restricted to particular questions, posed at particular stages in the cycle of research, development and exploitation. Possible risks are endlessly debated, while deeper questions about the values, visions and vested interests that motivate scientific endeavour often remain unasked or unanswered. And as the GM [genetic modification] case demonstrates, when these larger issues force themselves on to the table, the public may discover that it is too late to alter the developmental trajectories of a technology. Political, economic and organisational commitments may already be in place, narrowing the space for meaningful debate.
This phase of Constructive Conversations is implementing a new approach to public engagement, one that emphasises the need to incorporate a wider range of knowledge than is normally considered when prioritising science investment and when assessing risks and potential benefits of science and technology development. The products of its research are intended for policy-makers, scientific researchers and technology developers, as well as the wider public. While it is not eliciting generic “public opinion”, it is eliciting knowledge that should be made available to those engaging in wider public debate. The intention when selecting nutrigenomics was to elicit and make available practical knowledge relevant to this area.

This has proved more challenging than expected. While biopharming is currently being carried out in New Zealand and elsewhere in a way that offers clear pointers to the conditions under which it could be more widely implemented, the same cannot be said of nutrigenomics. On the one hand, the field is still in the stage of establishing its own plausibility and importance. On the other hand, commercial operators are already pushing products allegedly backed by nutrigenomics research, and promoters of nutrigenomics more generally are making far-reaching claims as to its benefits. This presented challenges for the Constructive Conversations research, but these challenges may be more or less typical of upstream inquiry.

One possible strategy would be to generate scenarios based upon what nutrigenomics’ promoters envision as the future of the field. However, this runs a real risk of taking too much for granted. A number of recent reports (Food Ethics Council 2005; Burton and Stewart 2005, Wallace, 2006) have cast doubt on the possibility that such an envisioned future of “personalised nutrition” services and products will ever be socially or scientifically robust. For this project, interviews were carried out with members of the nutrigenomics programmes in two of the main centres of nutrigenomics research—New Zealand and the Netherlands. They revealed substantial disagreement about the products and benefits that can realistically be expected to result from it.

As a result, this report retains a scepticism toward claims of future products and benefits of nutrigenomics, while at the same time being mindful of the drivers pushing nutrigenomics research toward societal implementation. Such an approach is also vital to effective upstream engagement, as is a willingness to explore, in Wilsdon and Willis’s terms (quoted above), the “deeper questions” of “values, visions and vested interests”. This report outlines some of the wider social implications of efforts to put nutrigenomics approaches into practice under current conditions, thus facilitating an exploration of the values, visions and vested interests at a relatively early stage in the making of political, economic and organisational commitments to nutrigenomics.

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1 In New Zealand, biopharming is being funded by the Foundation for Research, Science and Technology and developed by AgResearch, which has recently applied to ERMA for a significant expansion of the species and locations involved. See Goven et al. (2008).

2 Eleven interviews were carried out: five from the New Zealand programme and six from the Dutch programme. The interviews ranged from 30 to 90 minutes.
1.2. Centres of nutrigenomics research

This section describes the three major centres of nutrigenomics research that have been established during the past five years: New Zealand’s Centre of Excellence in Nutrigenomics, the Center of Excellence for Nutritional Genomics at the University of California at Davis, and the Netherlands Nutrigenomics Consortium. The Netherlands Consortium is a major contributor to the EU-funded Nutrigenomics Network of Excellence, NuGO (www.nugo.org), the purpose of which is to integrate nutrigenomics researchers across member countries. There are also many individuals, smaller groups and programmes engaged in nutrigenomics-related research at other academic centres and in public and corporate research departments.

1.2.1. Nutrigenomics New Zealand

New Zealand’s nutrigenomics initiative grew out of a call for proposals for a nutrigenomics programme by the Foundation for Research, Science and Technology in 2003. The successful bid involved a team combining researchers from the University of Auckland and three Crown Research Institutes: HortResearch, AgResearch, and Crop & Food Research. The researchers from these organisations formed a virtual Centre of Excellence in Nutrigenomics, otherwise known as Nutrigenomics New Zealand, which describes itself as “tailoring New Zealand foods to match people’s genes” (http://www.nutrigenomics.org.nz/). The focus on linking research to commercial food products is explicit:

*The major aim of this Centre is to determine how foods and food components affect health at the molecular genetic level by using nutritional genomic methods…. This detailed understanding of the molecular mechanisms will ultimately lead to the development of completely new, added-value, export-focused, gene-specific foods that will deliver proven health outcomes to consumers. (http://www.nutrigenomics.org.nz/index/page/26)*

The initial focus of this group has been to demonstrate “proof of concept” through research on Crohn’s disease.

There is also nutrigenomics research being carried out outside the Centre, at the Auckland University of Technology, under a project entitled “Nutrigenomics and Biomedical Ontologies”. Its focus is on

*nutrigenomics related to aging and diabetes, with the aims of utilizing genomic data for personalized dietary advice, and managing and organizing metadata related to nutrigenomics ontologies related to diabetes and aging. Microarray data from experiments of diabetic vs healthy and old vs young patients is linked with nutritional data and artificial intelligence methods used to pinpoint genes of interest and diet components of relevance for healthy [sic] and disease-preventing*

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advice.  (http://www.aut.ac.nz/research/research_institutes/kedri/research_centres/centre_for_bioinformatics/)

1.2.2.  The Netherlands’ Nutrigenomics Consortium

The Netherlands Nutrigenomics Consortium is part of the Netherlands Genomics Initiative. Their work is also in the “proof of concept” stage. Its objectives are:

- To demonstrate that nutrigenomics provides powerful tools to show how nutrients and food bioactives work.
- To demonstrate that nutrigenomics allows more comprehensive phenotyping and the identification of early biomarkers for pre-disease states (metabolic stress).
- To provide knowledge and tools for the efficient development of new smart foods to keep people healthy and fit according to their individual needs. (http://www.nutrigenomicsconsortium.nl/res_objectives.html)

Its research projects focus on various aspects of, markers for or responses to metabolic stress.

1.2.3.  The NCMHD Center for Excellence in Nutritional Genomics

While the New Zealand and Dutch centres link their research to potential food products, this centre, sponsored by an award from the National Center for Minority Health and Health Disparities (NCMHD) at the National Institutes of Health and based at the University of California at Davis, describes its “mission” as being “to reduce and ultimately eliminate racial and ethnic health disparities resulting from environment x gene interactions, particularly those involving dietary, economic, and cultural factors” (http://nutrigenomics.ucdavis.edu/).

Our goal is to devise genome-based nutritional interventions to prevent, delay, and treat diseases such asthma, obesity, Type 2 diabetes, cardiovascular disease, and prostate cancer…. The Center is using a multidisciplinary approach to investigate the influence of diet and individual genetic variation as risk factors for health disparities in racial/ethnic populations in the U.S. (http://nutrigenomics.ucdavis.edu/)

1.2.4.  International Society of Nutrigenetics/Nutrigenomics

In addition to these research centres, an international society to promote nutrigenomics and nutrigenetics has recently been established. The International Society of Nutrigenetics/Nutrigenomics intends, in its own words, to:
• promote research on the role of genetic variation and dietary response and the role of nutrients in gene expression;

• define the relationship between genes and nutrients from basic biology to clinical states. This encompasses the areas of (1) genetic variation and dietary response, (2) nutrients in gene expression, and (3) the role of genes in the determination of nutritional requirements;

• establish a Network of Centers on Genetics, Nutrition and Health worldwide;

• encourage the development of programs for genetics and nutrition in departments of nutrition and genetics, and in schools of public health and medicine;

• serve as a clearing-house for the media in disseminating facts regarding the role of genetic variation and dietary response and the role of nutrients in gene expression; [and]

• educate professionals and the public about the role of genetic variation and dietary response and the role of nutrients in gene expression (http://www.isnn.info/)
2. What is nutrigenomics?

2.1. Defining nutrigenomics

The novelty of nutrigenomics, and the complexity of claims around it, is reflected in the fact that there is no consensus on its definition.⁴ According to Dutch nutrigenomics researchers Müller and Kersten, writing in 2003, “[n]utrigenomics is new, it is not yet well defined and there are still relatively few convincing studies in the area”. In 2007, according to Brown and van der Ouderaa, “the way in which [nutritional genomics] is defined is still a topic for debate.”

Recently offered definitions range from the very broad—“the study of the response of humans to food and food components” (Sutton 2007: 117)—to the considerably more specific: “the study of the genome-wide influences of nutrition or dietary components on the transcriptome, proteome and metabolome, of cells, tissues or organisms, at a given time” (Nature Reviews Genetics 2003). Some define nutrigenomics according to the investigative technologies it uses: “Nutrigenomics is the application of high-throughput genomics tools in nutrition research” (Müller and Kersten 2007). Others emphasise a particular set of intended applications:

The new discipline of nutritional genomics (or nutrigenomics) combines various approaches associated with systems biology (including nutrition, molecular biology, bioinformatics and genomics) in order to develop optimized nutrition and foods for individuals based in large part on how specific dietary chemicals affect the variable expression of genes in each person. (Ferguson and Kaput 2004:29)

Nutrigenomics can, and some would argue should, be distinguished from nutrigenetics. From this perspective, nutrigenetics refers to the study of “the effect of genetic variation on the interaction between diet and disease or on nutrient requirements”⁵ (Muller and Kersten 2003), while nutrigenomics studies the impact of diet on gene expression and includes “the study of how nutrients influence the consequences of gene expression, namely the synthesis of mRNA (transcriptomics), protein synthesis (proteomics) and metabolite production (metabolomics)” (Gibney 2006:115). Many research programmes combine the two.

See Box 1 for an early, “pre-nutrigenomics” example of an identified genotype x diet interaction leading to a dietary prescription to avoid disease.

⁴ Some use the terms “nutritional genomics” or “molecular nutrition”.
⁵ Some include within nutrigenetics the effects of genes on an individual’s food-consumption behaviour (in terms of both quantity consumed and foods preferred or avoided) (see, e.g., El-Sohemy 2008).
Box 1: An early example of using genotype x diet therapies.

Many researchers in the field refer to the disease phenylketonuria (PKU) and its treatment as a pioneering example of how an understanding of genotype or genomic response to food can be used both to diagnose and to treat dietary diseases. The diet designed in the 1950s for those suffering from PKU is tailored to the genotype. The foods that have been prescribed for these patients are conventional and readily available, but in current terms could be packaged as nutrigenomics foods.

PKU is caused by hyperphenylalaninemia (HPA), a toxic build-up of the amino acid phenylalanine because it is not efficiently converted by the hepatic cytosolic enzyme PAH into another amino acid called tyrosine (Scriver and Waters, 1999). Those at risk of HPA have mutations, revealed as SNPs, in PAH. This enzymatic activity removes 75% of dietary phenylalanine. So by reducing phenylalanine intake by those who could develop HPA, the amino acid can be prevented from accumulating to dangerous levels. The diet recommended for these patients allows them to ensure that phenylalanine is kept below toxic levels.

PKU is one of the rare conditions linked to a single gene mutation. It is this seemingly uncomplicated relationship between genotype and disease state that made PKU diagnosable using pre-genomics era technologies and distinguishes it from the challenges facing modern-day nutrigenomics researchers. These researchers must link multifactorial causes of disease and multi-gene responses to food and its components.

2.2. Nutrigenomics and nutrigenetics research

It is possible to distinguish the fields of nutrigenomics and nutrigenetics research from their potential applications, such as “personalised nutrition” or new foods. Indeed, some researchers are at pains to do so.

*Can you imagine feasible examples of products that are made specifically to suit certain groups of people sharing certain genetic traits, certain alleles...?*

... [There’s] the MTHFR polymorphism that’s known for folate metabolism ... in which case, if you take enough folate, you won’t have any problems. But we have three million of these SNPs... One of the things I did in my thesis was look at two different [folate-related] polymorphisms together and then it seems somehow, if you have two of them, it might have a different effect than if you

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6 SNP stands for single nucleotide polymorphism, meaning relatively common (present in more than 1% of the population) DNA variations in a single nucleotide.
have only one. So it’s-- in my opinion, it’s too complicated to do that. I think that’s impossible because you don’t know the other effects. (Interview NL)\(^7\)

*If you were asked to give a verdict now on what kind of contribution the nutrigenomics research that you’re aware of, including what you’re doing, what kind of contribution it could, it’s likely to be able to make to public health in the next 10 to 15, maybe even 20 years, what would you say?*

The way we see it, I think mostly we’re contributing to knowledge and, but not, what I do not believe is, which is how nutrigenomics is somehow presented, is that it will cause a shift in how we look at people and how the whole field of nutrition is going to be turned upside down because of our activities. I don’t think like that at all. I often wonder whether the people that actually express those thoughts really have a clear idea of how they see that happening… So personally, I see it mostly as increasing the amount of knowledge that we have on how nutrition acts and also sort of better understand the genetic variation between individuals….The genome is so complex and there’s so many interactions that take place, I mean, what has been done until now is, is less than one percent of what we really should know to be able to make a reasonable recommendation. You can make a recommendation but you could be totally off. I mean, you use genetic information and you pretend it’s actually useful. In the meantime, it’s not--I mean, you lose or you ignore the 99 percent that could have, that actually would change the recommendation entirely. (Interview NL)

In a sense, nutrigenomics remains a “concept” rather than a science in itself. The major research initiatives see themselves as being in “proof of concept” stage. Much of the published literature consists of review articles outlining what the authors see as the promise of the field rather than reports of scientific findings. An interviewee characterised the literature this way:

There’s not much to reflect on because it’s a relatively new field so there’s not a lot of background knowledge. So it’s mostly visionary and a look into the future about what this could mean for us, for society. … And some people really go, take quite a stretch and try to be visionary, in the meantime, losing some sense of realism, whereas others try to be more, more concrete and provide clear examples… and also present the obstacles. (Interview NL)

A comparison drawn by many, particularly in the first few years, has been with pharmacogenomics. However, several factors have tempered that comparison: the results from pharmacogenomics, in terms of new drugs better suited to particular populations, have been disappointing thus far; nutrients are now recognised as having much smaller measurable effects on biomarkers of health and disease than drugs; and nutrient exposures are much more complex (we consume many different foods and each food contains many different compounds). The latter two factors mean that methods used in pharmacogenomics research may not be transferable to nutrigenomics.

\(^7\) In order to preserve confidentiality, interviewees will be identified only in terms of their research programme, that is, either New Zealand (NZ) or the Netherlands (NL).
2.3. Nutrigenetics services: “personalised nutrition”

“Personalised nutrition” services are usually described as genotype-based advice to individuals about which foods to seek out or avoid in order to prevent or ameliorate disease, maximise “wellness”, or enhance performance. It is more properly called nutrigenetics than nutrigenomics, because it is about adjusting diet prescriptions to individual genetic variation. But as Penders et al. (2007) have pointed out, for technical and commercial reasons, “the trend in personalized nutrition leads away from individuality and towards genetic categories of an undetermined minimum size”. Personalisation in practice means categorisation rather than individualisation.

As noted above, such services are already being offered on a commercial basis. They claim, for example, to enable consumers to “identify [their] own unique genetic variations” and to offer consumers “personalized dietary and lifestyle recommendations which enable [them] to take control of [their] own health and well-being” (www.sciona.com). According to another company, “[g]enetic testing combined with a lifestyle assessment, provides you with a scientifically based, personal blueprint for optimizing your health” (www.healthanddna.com/nutrition [Genelex website]). Yet another company, Suracell, “looks at your individual genetic profile and provides exclusive nutraceuticals that work at the cellular level for optimal genetic health” (http://www.suracell.com/how_it_works/). The purported scientific bases of these claims are association studies that look for correlations between particular genetic variants and particular phenotypical outcomes, or between a particular food/nutrient and phenotypical outcome (in the general population or among those with a particular genetic variant). The correlations are not 1:1; rather, positive findings generally take the form of small differences in relative risk of a developing a disease.

The US Government Accountability Office investigated four such Internet-based nutrigenetics services and concluded that the services “mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers.” (US GAO, 2006: 5).

A recent article by Janssens et al. (2008) examines the claims of seven companies selling dietary advice and products on the basis of genetic tests. Using meta-analyses of disease-association studies for the genes or polymorphisms identified by the companies, they found “significant associations with disease risk for fewer than half of the 56 genes that are tested in commercially available genomic profiles.” While “[v]arious polymorphisms of these genes were associated with risk for 28 different disorders [, m]any of these disorders were unrelated to the ostensible target condition, and the associations were generally modest” (Janssens et al. 2008: 595).

The companies are generally not forthcoming about how they derive a “profile” from a series of (questionable) results for single genetic markers. Janssens et al (2008: 597) caution:
To be meaningful, a genetic risk profile should combine information about the disease risk associated with multiple genes, and creating such a profile would require extensive knowledge of gene-gene interactions, which are even less well understood than the disease risk associated with individual polymorphisms.

Assuming that in the future the evidence will be strong enough to justify such services (and it is not clear that this is a realistic assumption), most envision that nutrigenomics-based dietary advice would require those receiving the advice to be genetically tested. That is, they would be screened for some number of polymorphisms that are associated with particular (positive or negative) health effects in the presence of particular foods or nutrients.

What you want to do is understand why something biochemically isn’t functioning the same. So can we recommend a different type of fat? Can we recommend more carbohydrates? Or something like that. The moment we understand what that gene’s doing, then we are in a situation where we can often, not always but often, recommend dietary regimes to sort of do it. It might be as simple as: ‘get tested for this gene, and you’re the group of people that will particularly benefit from having broccoli every day, or something like that.’ (Interview NZ)

However, this appears not to take into account the complexities of gene-gene interactions or the potential effects of, for example, high levels of broccoli intake on other genetic/epigenetic pathways not yet understood. Others, such as Fay and German, argue that genotype-based nutritional recommendations are too simplistic:

Humans differ due to a wide range of basic biological variables. These variables are in some cases genetically based chromosomal differences, for example, male, female, or allelic polymorphisms in structural or regulatory regions of specific genes. In other aspects, differences are because of the age and particular lifestage of an individual (e.g. infancy, pregnancy, lactation, pre-menopause and post-menopause, and puberty). In others, variables are due to environmental influences that are either exogenous and random (e.g. exposure to sunlight, toxins, allergens, bacterial inoculum, etc.) or endogenous and volitional, for example, chosen lifestyle (e.g. exercise, athletic training, excess caloric intake and obesity, sedentary behavior, sleep cycle alteration, meal frequency, and temporal variation). Furthermore, each of these variables — if acting at a particular point in an individual’s development or lifestage — may exert effects on various epigenetic or non-genetic elements. These effects may then confer persistence of a particular phenotype through much of that individual’s subsequent life and alter that individual’s response to dietary components. (Fay and German 2008: 122,126)

Some have distinguished between public good health advice and commercialised services as two different types of outcomes that could potentially result from nutrigenomics
research. It is usually assumed that, if nutrigenomics-based public health advice is to produce something more than the dietary advice already freely offered to the public (eat a varied diet with plenty of fruits and vegetables, avoid saturated fats, favour whole grains over refined starches, adjust your calorie intake to your energy expenditure, etc), it would require individuals who wish to make use of this advice to be genetically tested. It would also require the creation of genetic “categories” that would then be addressed by the advice (and, inevitably, by commercial products).

Some nutrigenomics researchers argue that going beyond the population-statistical studies of genetics to the physiological studies of genomics will provide a more robust evidence base for (general or personalised) dietary advice: “Now we give advice just based on association, on correlations, and I think [nutrigenomics] will provide us with evidence-based advice, and I think that’s much better.” (Interview NL)

It is important, however, to understand what is meant here. Nutrigenetics looks for statistical correlations linking gene variants, nutrients and phenotypical outcomes. It works at the statistical level, and its results are probabilistic. Whether or not the correlation applies to any particular individual cannot be determined.

Whether personal risk advice is based on a genetic test, or, for example, on family history, it takes a statistical relationship that holds for the population at large and reinterprets it as an individual probability. Whether this probability is high, middling or low, the implications for individual behaviour are unclear. You only live once, so you cannot develop diabetes, say, x per cent of the time. Either you get it or you do not. So risk information can be useful at a population level but is fairly meaningless for individuals. (Food Ethics Council 2005)

Nutrigenomics studies how gene expression responds to nutrients. This is the “evidence base” referred to by the interviewee. However, it is important to note that this is also not “individualised”. Nutrigenomics cannot be about substituting individual “genomics profiles” for genetic profiles. Gene expression is constantly changing; one cannot derive an individual’s complete transcriptome, proteome and metabolome from a single buccal or blood sample—it would provide instead a necessarily incomplete snapshot of expression activity in that tissue or cell and only at that moment. It would not be possible to provide personalised dietary information on the basis of such a profile. So nutrigenomics can also be seen as producing probabilistic, population-based findings based not on genetic variation but on variations in the amounts of different kinds of physiological (rather than SNP) markers associated with processes of gene expression, namely RNA, protein and metabolites.

This is because there is no determinative relationship between RNA and proteins (transcription and translation) or between proteins and metabolites (translation and catalysis). When researchers measure directional changes in RNA (transcriptome) to protein (proteome), they find that the correlation is poor. Sometimes both RNA and protein levels decrease or increase, sometimes only RNA or protein levels change, and sometimes the change in one has the opposite effect on levels of the other (Chen et al.
2002, Hegde et al. 2003, Ideker et al. 2001). Increasing or decreasing the number of enzymes may not lead to changes in metabolite levels because of complex feedback mechanisms in biochemical pathways. Moreover, only very rarely can a disease be said to be caused by a particular compound. For example, even in the cases of salt and saturated fats which are two of the closest examples of dietary compounds with health implications, some amounts are fully tolerated and other amounts are absolutely necessary for normal health.

Therefore, nutrigenomics itself cannot lay bare the mechanisms of disease-development. The possibility that genomics could reveal the physiology of how a particular person is reacting to a dietary substance seems plausible given the growth in technology for measuring transcriptomes, proteomes and metabolomes. While these technologies are still very much in their infancy, they do have the potential to enable the gathering of this kind of information. However, even this knowledge will not be able to demonstrate disease causation. It only tells us how the food affects transcription, how transcription results in the quantitative or qualitative changes in the RNA pool, how these do or might alter the protein pool, how that might or does alter the metabolome. There is no step in this chain that actually links changes in this pool of molecules to mechanisms of physiology, only to further speculations about how to group people by their particular responses and their final health outcomes.

From this perspective, nutrigenomics, too, is primarily a useful hypothesis-generator. It in effect shifts the “black box” but does not remove it. It does not appear likely to produce the kind of data that would be necessary to “personalise” nutrition. These limitations of genotyping and gene-expression measurement were recognised by one of our interviewees, who favoured a different kind of “personalised nutrition”:

My own definition right now of the personalised nutrition concept is not only looking at the genotype, because the genotype is part of the information, but there is so much between the genotype and the phenotype, knowing about the epigenome and everything, that it’s almost impossible to predict [much] … So it would be better, actually, to measure phenotypes and -- meaning like phenotype after challenges -- and so if you would challenge the system on different levels, you do a kind of function test and you can put people on the bike, see what is your energy, what is your condition actually, what is your fitness? And then you have somewhere, a kind of database and … you can correlate to a certain age …. I want to have, this individualised kind of nutrition, I want to have this a little bit closer to the phenotype. Because this can even change from day to day…Right now, it’s not realistic because you cannot phenotype somebody every day, but also there the developments are rapid and maybe with, I don’t know, with nanotechnology, you can measure certain parameters much cheaper and much easier. (Interview NL)

The difficulties of obtaining tissue from difficult-to-access areas of the body that importantly mediate our reactions to diet, such as the liver, may encourage other nutrigenomicists to look to future developments in nanotechnology to advance their field.
This, of course, would raise a further set of risk, regulation and engagement issues, but they are beyond the scope of this report.

2.4. Nutrigenomics foods

Nutrigenomics New Zealand describes itself as “[t]ailoring New Zealand foods to match people's genes” and sees the purpose of its research as leading to “the development of completely new, added-value, export-focused, gene-specific foods that will deliver proven health outcomes to consumers” (http://www.nutrigenomics.org.nz/index/page/26).

There are currently no foods being marketed as nutrigenomics foods in New Zealand. Such foods could potentially be whole or processed foods, genetically modified (GM) or non-GM foods. They could be “created” simply through a change in marketing rather than a change in the food itself.

In 2004, Ferguson and Kaput maintained that “‘medical foods’ linked with genetic tests (that is, genetic tests that identify individuals who may be helped or harmed by the presence of specific nutrients or dietary chemicals) could be developed in less than 10 years.” In 2007, Sutton again predicts that nutrigenomics foods are likely to appear within a decade and to be “developed in partnership with food industries that will embody the intellectual property developed by research”. Moreover, they “are likely to be processed foods rather than commodities, in order to capture value.” The challenges of formulating such processed foods may require the use of various additives or encapsulation technologies (Sutton 2007). According to this scenario, customers would first need to have themselves genetically tested to discover which, if any, existing genetic food market segments they fit. Whether or not their “risk” is catered to will depend on the economics of the product market; in order to be commercially viable the products would, among other things, need to address gene variants that are common enough to provide a sizeable potential market for the product:

[C]onsumers with specific genetic profiles that may predispose them to particular disease or disease risk can be grouped, and so nutrigenomic foods could be mass customised rather than individualised. The level of differentiation of such products would depend on several factors, including market size and type, profit margins, level of value capture and the level of scientific validation required. (Sutton 2007:120)

A New Zealand interviewee saw product development in these terms:

The first thing I think that nutrigenomics will produce is more an overall dietary advice: do eat this, don’t eat that, off the shelf things. The next would be to be producing new products, so manufactured products that were tailored to a certain disease group, and hopefully, to be true nutrigenomics, to a genotype as well, which is a different level. You can’t say ‘this is what all Crohn’s patients should eat’ because genetically they’re going to be different. It would have to be: get
genotyped, and then we can tell you what you should and shouldn’t eat. (Interview NZ)

Most expect the focus to be on common diseases (such as cardiovascular disease and Type II diabetes), with foods marketed to those with these diseases or those with genetic “risk factors” for these diseases (an even larger number of people). While Crohn’s disease is the focus of the current proof-of-concept research of Nutrigenomics New Zealand, the researchers did not expect that nutrigenomics foods aimed at Crohn’s sufferers would be developed. This is because the number of those with Crohn’s disease, let alone subgroups within that category, does not in their view represent a large enough market to make the commercial development of targeted foods attractive.

It is not only disease or risk of disease that will be targeted, according to proponents. Nutrigenomics foods are also seen as vehicles for “optimizing physical and mental performance (for example, in athletes) [and] retarding aging” (Ferguson and Kaput 2004), as well as for “mood and depression” (Ghosh et al 2007).

Some see nutrigenomics foods as a type of functional foods (e.g., Ferguson and Kaput 2004). It is indeed difficult to make consistent distinctions. One reason for this is the ubiquitous use of the term “functional foods” without consensus on its definition. Food regulatory agencies do not use the term. Most attempts to assign a definition include the notion that functional foods provide health benefits beyond basic nutrition.

Many ambiguities remain: What counts as a ‘health benefit’? Where is the ‘basic nutrition’ line drawn? It could be argued that whole foods such as fruits, vegetables and whole grains fit this definition. Is a food a functional food because it is marketed as such (e.g., pomegranate juice for cardiovascular health, walnuts for cardiovascular health, blueberries for brain function) or because it has been especially formulated, or modified, to deliver specific benefits (e.g., margarines with plant sterols or pigs genetically modified to have omega-3 fats in their meat)? The Institute of Medicine of the US National Academy of Sciences defined functional foods as “those foods in which the concentrations of one or more ingredients have been manipulated or modified to enhance their contribution to a healthful diet” (cited by Katan and de Roos, 2004). Katan and de Roos (2004: 370) prefer “a branded food which claims explicitly or implicitly to improve health or well-being.” In a 2007 Cabinet paper, New Zealand’s Minister of Industry and Regional Development defined functional foods as “foods with scientifically-substantiated health benefits that stem from the foods’ high concentrations of nutrient or non-nutrient substances that promote health and well-being over and above what is normally expected from food products” (Minister of Industry and Regional Development 2007: §15).^8

In terms of target markets, there is a great deal of overlap between nutrigenomics foods and functional foods. One possible way to distinguish them is by whether or not potential

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^8 To confuse things still further, the terms ‘nutriceuticals’ and ‘bioactives’ are also often used in relation to functional foods.
consumers must be genotyped in order to determine whether they are appropriate consumers of the product. However, Sutton (2007:121) argues

[W]here consumers are (generally) more sceptical of genetic technologies, significant efforts will be needed to build consumer confidence in nutrigenomic foods. It is possible that nutrigenomic foods may be advanced by the use of “surrogate markers” for genetic change (for example, a person being obese may be a surrogate marker for an obese genotype), to help circumvent the consumer scepticism [toward genetic technologies].

This, however, would seem to undermine the claim that nutrigenomics (or nutrigenetics) represents an advance because genetic diversity within phenotypic categories is key to devising effective nutritional treatments. In other words, nutrigenomics is supposed to look beneath phenotypes with multiple causes to target those individuals with phenotypes that are crucially genetic rather than behavioural or social.

Another distinguishing factor could be the mechanism by which nutrigenomics foods work. According to Sutton (2007: 120): “Nutrigenomic foods could down regulate damaging genes, up regulate useful genes and/or over regulate genes to enhance performance.” However, many if not all foods would have such effects, so nutrigenomics foods might then be distinguished by being enabled to make a claim to a health benefit based on specific evidence of up-, down-, or over-regulation of specific genes. For example, the same omega-3-oil containing products may be marketed to those with gene variants that have been associated with a greater need for, or ability to utilise, omega-3 oil (nutrigenomics food) or they may be marketed as generally beneficial (non-nutrigenomics functional food).

It is assumed by some that the point of nutrigenomics or “gene-based” foods (or, for that matter, functional foods) is to permit people to avoid having to change their unhealthy eating habits by supplying them with foods that are engineered (genetically or otherwise) to include components associated with healthy outcomes and/or omit components associated with unhealthy outcomes. According to Ferguson and Philpott (2003:202):

[A]s the Western worlds [sic] increasing obesity problem demonstrates, it can be extremely difficult to convince an individual to change their diet, even when specific causative foods have been identified. Therefore, the development of functional foods, guided by nutrigenomics research, offers a solution whereby people can continue to consume the foods they recognise and enjoy, which have had their nutritional content altered to better meet the needs of various identified subpopulations.

This was also raised in interviews, for example:

There’s going to be plenty of money to be made by the Nestle’s and things of the world as they work out how to make a Big Mac burger that won’t make you obese. Because people don’t want to have to change. …The diabetes epidemic
shouldn’t happen, it’s a hundred per cent preventable. We know exactly how to prevent it at the moment. We don’t need nutrigenomics to prevent obesity, we just need to get people to eat a bit less. And the functional foods are already there, it’s just fruit and vegetables and all those sorts of things – stop eating the high fat processed foods. But, no, it’s human nature. People keep eating those things and they’re waiting for that pill to come along that means they can eat those things anyway. (Interview NZ)

This suggests that the purpose of nutrigenetic tests, rather than or in addition to advising consumers as to what types of foods to include or avoid in their diet, would be to direct consumers toward proprietary nutrigenomics foods. Alternatively, the food manufacturer could depend on marketing to attract those with particular genetic profiles. This implies that a standardised set of categories or genetic types would be developed by the food and genetic testing industries in order to allow marketers to make their claims and guide consumers toward their ‘gene-specific’ nutrigenomics foods.

Some envision that consumers will enter supermarkets with their genetic profile encoded on a card. The card would be inserted into a machine that would produce a printout advising the shopper of the location of particular items that are suitable for their genotype. This could potentially apply to whole foods as well as processed foods. But ‘custom-made’ foods are also envisaged:

There’s people that talk … of this idea of sort of point-of-sale manufacture of things, and you walk in with the equivalent of your Foodtown card and zap your genotype, they make your food, and by the time you’ve finished walking around, those bits are ready for you. (Interview NZ)

There was much diversity among interviewed researchers regarding their evaluations of the feasibility of nutrigenomics foods. On the one hand there were those who simply answered “No” to the question: do you see nutrigenomics foods as something that we can expect to happen? Others were carrying out research aimed at producing such foods, and still others argued that they were already available. Some of the difference hinges on the definition of nutrigenomics food:

There are many examples … The whole approach in industry at the moment [is] … the modification of food to get it more bioavailable. That means that you need enzymes for that, and this is all based, the selection of enzymes nowadays, is all

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9 See also Boland (2006): “POSIFoods™ (point of sale individualised foods) is a novel system that is being developed by Fonterra to cater for individual health needs and sensory preferences, while at the same time providing the convenience of fast food. The project involves research collaborations with BASF and the Riddet Centre (involving three New Zealand universities). POSIFoods adheres to the principle of mass customisation with which the consumer should be involved in the design of the final product, involving the customer’s specific nutritional needs (functional performance) as well as personal food preferences (sensory performance), and owes its development to a combination of smart ingredients and special software and hardware that can design and manufacture a customised food product on the spot for the customer who has done a one-time entry of all the necessary health and preference data.”
based on nutrigenomics… So far I think the idea was that nutrigenomics only had to do with what is the reaction on a personal level in relation to food intake. That’s part of it. That’s the personalised nutrition. But that’s only a very small part of what genomics can bring to better understanding of what nutrition is doing in your body. (Interview NL)

Here the emphasis is on nutrigenomics as the use of transcriptomics, proteomics and metabolomics to increase understanding of physiological processes, and nutrigenomics foods are foods that have been produced through the use of this knowledge, regardless of whether they are aimed at particular genetic categories.

As noted above, nutrigenomics or functional foods may or may not be GM foods. GM technology is one strategy for enabling intellectual property to be “captured” and capitalised upon. However, GM was not a direction embraced by most of the researchers interviewed. It was seen as unnecessary, as risking consumer rejection, or both.

I don't think it makes the slightest sense in this. A: because there’s an emotional component in it. But, B: our task is really to identify components. And you can put them together as a yoghurt or a drink or a cereal bar. Why would we go to all the time and expense [of using GM]? It’s a whole other programme. So I don't think we should go there. I’m actually quite strongly opposed to going there. We don’t need to. (Interview NZ)

There’s no doubt we have the potential to [use GM], and we could if we wished to do that. But we also want to be guided by what’s going to be acceptable for both our customers… and also by the wider food community. So I guess the short answer is we have the capability to do that, we choose not to because we don’t believe at the moment there’s good reasons for doing that…. I think we’ve got plenty of things to work on without having to go down any kind of GM route right now. (Interview NZ)

Others, however, are utilising GM in this area; see, e.g., Diaz de la Garza et al. (2007), Dixon (2006), Qi et al (2004), and examples cited in Powell (2007).
3. Why nutrigenomics?

3.1. Drivers

3.1.1. Food industry

Author affiliations in the published research literature confirm observations made by interviewees that major international food companies, such as Nestle, Unilever, Danone and DSM, are pursuing food research related to nutrigenomics. It can be assumed that this research is intended to underpin new product lines. It is not clear if such products would be ‘nutrigenomics foods’ in the sense of targeting a specific genotype, having claims grounded in nutrigenomics research, or neither. There is thought to be a wider market for ‘wellness foods’ that may fall short of nutrigenomics claims.

Hasler (2002) reports on a survey of thirty-eight Chief Research Officers of major food companies who indicated that much more research was going into “the development of foods considered to be healthful [than into] research efforts directed toward food safety, or toward the development of either organic or reduced fat foods”. As have many others, New Zealand’s Food and Beverage Task Force (2006: 10) claims that “the functionality of food is the fastest-growing segment of the global market” and sees supplying this market as key to future profitability. Hasler (2002: 3779)) attributes the strength of this market to “consumer interest in self-care, aging demographics and increasing healthcare costs”. A key to its attractiveness to industry is the ability to capture IP and increase profit margins by charging considerably higher prices for these products than for their “non-functional” counterparts.

The nutriceuticals and dietary supplements industry should also be included here. Some (e.g., Fenech 2008, Kaput 2006) see targeted dietary supplements as a likely outgrowth of nutrigenomics research. Among existing commercial nutrigenetics testing companies are those already selling dietary supplements that are claimed to address the individual needs purportedly identified by their tests.

3.1.2. Governments

The example of Nutrigenomics New Zealand highlights a second set of actors driving the nutrigenomics field: governments and their affiliated agencies. The Foundation for Research, Science and Technology played an unusually direct role in fostering nutrigenomics in New Zealand. In response to the results of its Innovative Foods Review, advice from MoRST and discussions with CRIs, FRST made a fund of approximately NZ$20 million available for a nutrigenomics programme in 2003.11 This was noted by New Zealand interviewees:

10 All food is in some sense functional.
11 Interview, FRST.
Government put up the idea of nutrigenomics a few years ago. It just literally put
the idea up. Nobody really quite knew what nutrigenomics was, or what it meant.
And then we all came flocking around to see how we could access this money. …
Why government chose that area, I don't know…. But they must have had some
internal report that this was an area to invest in. Everybody formed into little
teams around the country [to bid for the money]… Put up $20 million,
everybody’s going to become very enthusiastic! (Interview NZ)

I’d like to think it was, you know, a Ministry of Health and government push. But
the Foundation for Research, Science and Technology were the ones in New
Zealand that recognised the need for this, they’d taken external advice. And they
set up the centre. [Do you have any sense of what persuaded them, what was the
telling argument for them?] I think there were some visits from some key people
that just seemed to come to the right ears at the right time. But I think they
listened, and they took external advice. (Interview NZ)

According to our interviews, the process that initiated the Dutch Nutrigenomics
Consortium was not dissimilar.

In New Zealand as elsewhere (e.g., the UK and the EU; see Food Ethics Council 2005),
public investment in nutrigenomics is part of a strategy to enhance economic
competitiveness. The New Zealand Government’s vision for a ‘transformed food and
beverage sector’ includes “a diversified product base, stemming particularly from the
space where food, nutrition, health and wellness intersect” (Minister for Industry and
Regional Development, 2007: Annex 2). A New Zealand interviewee also put the
Nutrigenomics New Zealand initiative in the context of international economic
competitiveness:

Presumably people down at FRST have had their group sitting around, and
nutrigenomics has been identified as of economic importance. And I think that’s
where it does sit, particularly for someone like New Zealand. When we go to the
food conferences you hear things like: New Zealand is no longer the biggest
producer of kiwifruit – apparently Chile is and then China, and I think we’re third.
And that’s because we’re a little country both in land area and people, and we’re
never going to feed the world, we’re never going to keep up. And since the
agricultural industry is still New Zealand’s biggest industry, they either need to
innovate or the whole country’s going to have serious problems because the
biggest industry’s going to disappear. Already, apparently, it’s cheaper to import
your kiwifruit from China than it is to buy local grown ones….So for a small New
Zealand agricultural sector the only way in the future is to stay ahead of the game.
They have to have the next kiwifruit, or the next whatever it is that’s some sort of
innovative product that the Chinas and Chiles of the world are going to take 10
years to ramp up production of, and they have to stay ahead of all of that. So that
was the rationale behind nutrigenomics, is that it is with a 10-20 year view of
when these actual new products and cultivars and things are going to be produced. (Interview NZ)

3.1.3. Technology

The development of high-throughput ‘-omics’ technologies has helped to pull researchers into the nutrigenomics area. The tools available shape the questions that can be asked. The development of these tools in the context of the Human Genome Project and commercial biotechnology has led to attempts to apply them to a large number of research areas. As noted above, the field of nutrigenomics is often defined in terms of these tools.

3.1.4. Scientific researchers

Research scientists in the public sector must compete for research funding by convincing funders of the value of their proposed research. Increasingly the orientation of public as well as private science funders has meant that scientists must convince funders that their work will lead to specific, near-term economic benefits. This provides an incentive for researchers even in basic or theoretical areas to link their work to, or formulate it as, a more “applied” programme (such as one that promises economic benefits for food producers) in order to attract funding for work that might otherwise be seen as too “blue skies”. Most of those interviewed referred to this imperative, which may help to explain the early linking of basic nutrigenomics research to claims of economic and health benefits. Even if the impetus for the initial funding does not come from researcher “pull”, once a field of research is created, the researchers involved may have a strong incentive to attempt to persuade funders of the continuing importance of the area.

Nonetheless, some researchers are somewhat baffled by the sudden surge of interest in nutrigenomics:

[I]t has kind of surprised me how this whole concept has caught on, and I still don’t understand where it comes from. It’s, sometimes people just want to have something new and [are] just so desperate to pick it up without actually putting a lot of effort into it. (Interview NL)

3.1.5. Consumer genetics industry

A fourth set of actors involved in driving the development of nutrigenomics is the consumer genetics industry. Companies seeking to sell diet and other lifestyle advice or supplements on the basis of genetic tests have proliferated (see section 2.3 above). In New Zealand, the project team listed on the website for the Nutrigenomics and Biomedical Ontologies project includes Brent Ogilvie of Fidelity Genetics, which appears to be a consumer genetics company.12

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12 Ogilvie is also Director of Pacific Channel Limited, a private investment company specialising in biotechnology, which is a New Zealand affiliate of US ‘life sciences venture firm’. In March 2008, a
3.1.6. GM food industry and research sector

While nutrigenomics does not necessarily entail the development of GM foods, there are indications that some in the sector see nutrigenomics as a way to break through consumer resistance to GM foods (Warren 2007). The argument is that the industry made a strategic error in first introducing GM products aimed at growers but which did not offer benefits to the consumer. Nutrigenomics or functional foods are said to provide the opportunity to offer consumers GM foods that have been modified in a way that will be seen as beneficial to the consumer. Proponents of this view argue that this will erode consumer opposition to GM foods in general.

3.2. Projected benefits

3.2.1. Population health and reduced health-care costs

The nutrigenomics research literature is replete with descriptions of nutrigenomics’ promise for improving the health of individuals and populations. There is a particular emphasis here on multifactorial, lifestyle-related conditions that are prevalent in wealthier societies, such as Type II diabetes, cardiovascular disease and obesity; some also include cancers.

[T]he benefits associated with personalized nutrition will include those linked to our state of health and disease prevention and amelioration of many of the ‘lifestyle’ diseases. (Ghosh et al. 2007: 570)

More ambitiously, Ferguson and Philpott (2003) nominate cancer, obesity, cardiovascular disease, diabetes, osteoporosis and arthritis as appropriate targets for nutrigenomics research in New Zealand.

In addition to combating a range of diseases, nutrigenomics is said by proponents to offer further (potential) benefits, including combating social disparities in health; improving mental health; optimising mental and physical performance; and retarding aging. It is claimed that the net result of these benefits will be to reduce healthcare costs (Ferguson and Kaput 2004, Ghosh et al. 2007).

3.2.2. Food industry profits

The other major benefit emphasised in the literature is that provided to the food industry. According to Ferguson and Kaput (2004:29-30):

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partnership between Pacific Channel and the publicly funded Crown Entity Company New Zealand Venture Investment Fund was announced, which will invest $8-12 million into new biotech ventures.
The field [of nutrigenomics] has the potential to create novel market opportunities for customized, nutrient-enhanced or toxicant-reduced crops or food products, and products customized for individual nutritional needs. Such developments have the potential to increase the value chain from agricultural crops through to consumer products.

One way in which nutrigenomics can provide such benefits is through the removal of obstacles to marketing through health claims:

Getting such food products on to the market with an associated health claim depends upon establishing proof of efficacy. If there are gene-diet interactions, one would anticipate that the full potential of a new food product may be unrecognized or deemed ineffective if efficacy studies neglect to relate genetic polymorphisms to the associated physiological influences. (Ferguson and Kaput 2004: 34)

Moreover, it is argued, “individual consumers diagnosed with a disease or early disease indicators, and who have consequently received specific dietary advice, are highly motivated and will pay premiums for branded foods with specific health claims” (Ferguson and Philpott 2003: 201).

3.2.3. New Zealand’s advantage

It has been claimed that New Zealand is well placed to benefit from nutrigenomics research. According to Nutrigenomics New Zealand researcher Dr Julian Heyes:

New Zealand’s advantage in this area of research is our access to raw food ingredients which are either unique to this country, or we have a competitive advantage in producing them. This includes such things as novel fruit varieties, protected arable cultivars, dairy and deer products and seafood. (http://www.nutrigenomics.org.nz/index/news/12)

It is argued that New Zealand would be particularly suited to the production of functional foods that may result from nutrigenomics research:

Given New Zealand’s strong background in agricultural and horticultural research and the recent emphasis by local funding agencies on innovative foods …, New Zealand is ideally positioned to be at the forefront of functional food development. (Ferguson and Philpott 2003: 201)

And according to an interviewee:

The functional foods business is a collection of niches. It’s a very niche business. That suits New Zealand. (Interview NZ)
Nutrigenomics is also said to offer particular benefits to New Zealand. One example involves the implication of well-cooked red meat in the development of cancer. High consumption rates of red meat, and particularly that which is fried, grilled or barbecued, are associated with increased risk for various cancers. Some genetic variants have been identified as being implicated in some of these cancer risks. Given that “New Zealand produces much meat, which is eaten in high amounts domestically as it is a relatively cheap protein source,” Ferguson and Kaput (2004:32) argue that genetically testing the population for these variants would be of particular benefit, as the “meat industry and indeed the health of the nation could be adversely affected by a blanket recommendation to reduce the consumption of red meat”. (See section 5.2.2 for further discussion of this proposal.)
4. Regulatory and capacity issues

4.1. Services

The regulatory and capacity issues associated with nutrigenetics services depend in part on the nature and context of those services. This discussion will distinguish between, on the one hand, commercial services that are currently available and may be expanded, and on the other, the possibility of offering nutrigenetics services through the public health system.

Nutrigenetic testing is one form of so-called genetic susceptibility testing; it screens for SNPs that have been associated with some level of increased risk of developing a disease. There are many uncertainties around the validity and utility of such tests (Haga et al. 2003, Hall et al. 2004, Hunter et al. 2008, Janssens and van Duijn 2008, Offit 2008), and it is particularly important to attend to the significance of differences between what is directly or indirectly claimed for the test and what is well substantiated.

4.1.1. Commercial services

Commercial nutrigenetics services can currently be accessed directly by consumers through the internet. The establishment of a New Zealand-based service would presumably increase consumer take-up in New Zealand. There appears to be nothing preventing the establishment of a commercial nutrigenetics, or other “consumer genetics”, enterprise in New Zealand, and no suitable framework for regulating this activity.

In Australia, the Therapeutic Goods Administration will regulate nutrigenetic tests (and genetic tests more generally) as part of its new regulatory framework for in vitro diagnostic devices (Therapeutic Goods Administration 2007). Had the planned joint Australia-New Zealand therapeutic products authority been created, this new framework would have applied in New Zealand as well. With the failure of that initiative, New Zealand remains without an overarching framework capable of regulating nutrigenetic tests.

The focus of National Health Committee and other policy discussion in New Zealand has primarily been around the adequacy of public provision of genetic testing services. There has been little or no discussion of private provision and particularly of direct-to-consumer provision. As Hopkins and Nightingale (2006) have argued, “the uncertainties involved in the diagnosis of some conditions and ignorance about their implications generates personal risk for consumers, which can translate into commercial risk for firms”; private genetic testing businesses respond by “relocat[ing] a portion of their commercial risk onto a third party”, particularly through “trusted third parties acting as gatekeepers.”
many cases, those gatekeepers would be General Practitioners (GPs). In New Zealand, Australian company Genetic Technologies has used this strategy by attempting to recruit clients through advertising to GPs and oncologists (Johnston and Walsh, 2005). As noted above, other companies market their tests directly to consumers, but address some of the commercial risk by carefully wording the description of what their services deliver. In either case, a number of other costs that can be expected to arise from nutrigenetic testing are also likely to be “relocated” onto the public health service, as discussed below.

4.1.1.1. Should commercial nutrigenetic testing be regulated?

Commercial providers argue that private genetic testing companies can provide access for people currently unable to access genetic testing through the overstretched public services, or can provide it more quickly, or can provide access to tests not included in public genetic services. It has also been argued that direct-to-consumer services enable people to obtain genetic information without the danger of it being accessed by insurance companies or employers. Moreover, it is argued, people have a right to access such services. The strength of these arguments very much depends on the quality of information delivered by the commercial service, which in the case of nutrigenetics is problematic.

It has been suggested (Ries 2008) that the lack of adequate science underpinning direct-to-consumer nutrigenetic services and their resulting inability to deliver clinically useful information means that the risk associated with such services is primarily the economic risk to the consumer of wasting his or her money. Were this the case, a “buyer beware” approach might be appropriate. However, the impacts of commercial nutrigenetic services can be expected to extend beyond consumers’ wallets.

**Direct and indirect impacts on health:** Nutrigenetic services currently give clients scientifically un- or under-substantiated advice regarding gene-related disease risk and actions that can be taken to mitigate it. This advice may be consistent with freely available generic public health advice; if this delivery pathway elicits greater compliance with the existing advice, it could have a beneficial effect on the health of those using such services. Where this advice deviates from generic public health advice, however, it could potentially be harmful to health. This may particularly be the case where the service also recommends and provides supplements. As will be discussed further below, the concentrations of bioactive substances contained in supplements can be harmful to health. Moreover, recommendations that focus on particular nutrients may undermine the general advice to eat a varied diet (if some of x is good, more of x must be better). Indirectly, the mere existence of such allegedly “personalised” nutrition advice may act to undermine the effectiveness of public health messages even among those who do not purchase such services.

**Impacts on the health system:** All tests that purport, directly or indirectly, to identify disease risk have the potential to impact adversely on the public health system by placing unnecessary demands on the system. The first site of impact is likely to be GPs.
[P]eople [will] start going along with test results to their local GP, and say ‘look, I’ve just been told I’ve got this and that. What can you do for me?’ They’ll have to re-test them because they don’t even trust the company. There’s a whole lot of fall-out because of that…. (Interview NZ)

Under any circumstances dealing with such test results would be difficult to manage in a typical 10-minute consultation. This would be exacerbated by many GPs’ lack of comfort, preparation or competence in this area (White and McLeod 2003). This, in addition to the assertiveness of patients ‘empowered’ by direct-to-consumer test results, could well result in an increased loading not only on GPs, but also on public testing services and referrals to specialists. All of this would consume healthcare resources for questionable ends.

Arguing that the use of genetic tests for susceptibility to common diseases is currently inadequately regulated in Europe and the U.S., Melzer et al. (2008a) note:

If tests provided to consumers, patients or doctors perform differently to what is claimed or implied in promotional literature or test reports, then the results have the potential to seriously mislead clinical decision-making. In areas such as pharmacogenetics, misleading performance can result in direct harm. In other areas the main effects of false positive and negative results may be a cascade of unnecessary follow-up testing and treatments. (See also Melzer et al. 2008b)

Offsetting benefits?: Some argue that even if “personalised” nutrition recommendations offer nothing beyond what is already offered freely, they can have a positive effect. This rests on the contention that people are more likely to follow “personalised” advice. This could result in a healthier population—albeit only that sector of the population who can afford such tests. However, there is as yet little evidence supporting this contention and some evidence to the contrary (Hunter et al. 2008, Marteau and Lerman 2001).

It should be noted that the researchers interviewed were generally not supportive of current nutrigenetic services, seeing them as under-substantiated and potentially damaging to the field.

4.1.2. Nutrigenetic services through the public health system

Some advocate public provision of nutrigenetic services. From both a regulatory and a capacity perspective, New Zealand is underprepared for this. According to the Human Genome Research Project (HGRP) 2007 report, “despite a number of reports and recommendations from the National Health Committee (NHC) over the last ten to fifteen years calling for a national strategy and greater coordination of primary, secondary and tertiary services in the area [, t]here is no clear Ministry of Health policy on genetic testing services…” (HGRP, I:15). As Goold et al. (2006) note,
New Zealand has not introduced a formal system for validating new genetic tests and the [Ministry of Health] has no formal role in assessing new tests. Rather, new tests are introduced in response to clinical demand, or as a result of the individual interests of each laboratory. Each DHB is responsible for funding genetic tests, and are therefore responsible for the quality of testing in their regions. Genetic tests are also not listed on the Laboratory Services Schedule, which lists tests available for public funding in New Zealand, as determined by the Laboratory Services Advisory Group. There is also no advisory body in New Zealand responsible for determining whether a genetic test should be publicly funded.

In its 2003 report on genetic testing in New Zealand, the National Health Committee noted that “there are no mechanisms for assessing and evaluating new tests for safety or for their effectiveness in improving health outcomes” and that consequently “[a]n increasing number of new genetic tests are coming onstream with little or no mechanism in place to assess or evaluate their clinical validity and utility.” As there are no formal processes for assessing a test’s clinical validity, “[t]ests are being used when their clinical validity is uncertain” (NHC 2003: 12-14).

While “[c]linical geneticists have a greater understanding of the clinical validity of genetic tests than other health professionals,” clinical geneticists (as well as genetic counsellors) are in short supply in New Zealand (NHC 2003: 14, 5). The NHC expected GPs to be increasingly involved in genetic testing referrals and counselling in response to a predicted increase in demand for genetic testing, while evidence (White and McLeod 2003) suggested that “many GPs have little experience or knowledge of less common genetic conditions and lack of confidence to know when to refer or to whom” (21). It is likely they are also underprepared to interpret for their patients the meaning or significance of a test result showing increased or decreased probabilistic risk for a multifactorial late-onset disease. It recommended the urgent development of protocols “to assist practitioners to assess when and how different tests should be used” and to “address which practitioners are most appropriate to order which tests” (22).

These protocols have not been developed (HGRP I:17), nor has the recommended national framework for assessing the clinical validity and utility of genetic tests been developed. Instead the Ministry of Health passed responsibility for considering the NHC recommendations onto the DHBs (NHC 2005) and then onto the co-ordinating body of the DHBs, DHBNZ, which as of late 2007 reportedly had not progressed the matter (NZORD 2007). There are also unresolved issues around the management of information derived from genetic testing more generally, particularly with the ongoing implementation of an electronic medical records system accessible by multiple parties.

All of this suggests that there is no robust process in place to ensure that limited resources are not spent on oversold nutrigenetic screening. It can be argued, and was in our interviews, that there are other genetic tests that are better established scientifically, have greater clinical utility and are more urgently needed. Beyond that is the larger question of
how (nutri)genetic screening stacks up in terms of clinical utility against other currently unfunded or underfunded health service interventions.

Answering this question requires, first of all, a realistic assessment of what nutrigenetic screening can actually deliver. This is partly a matter of robust scientific/clinical substantiation and partly a matter of social practice: that is, how are the people most in danger of developing diet-related disease likely to respond in practice to this sort of intervention? Answering this question requires an understanding of what currently deters people from following the public health advice that is already available. (This is discussed further in Chapter 5.)

Nutrigenetics could also be utilised within the public health service as a source for freely available public health advice. Nutrigenetics-based advice would presumably need to address genetic categories, so would require those who want to use the advice to have themselves genetically tested. This could generate the pressures on the health system referred to above.

### 4.2. Nutrigenomics foods and functional foods

Functional foods raise new challenges for regulatory agencies; ‘gene-specific’ foods, were they ever developed, would do the same. These foods straddle the food/drug boundary. While efficacy is a criterion normally applied in drug regulation, it has not been seen as relevant to food regulation. Food manufacturers’ desire to market specific food products as health-promoting has moved food regulatory agencies to develop rules and protocols in this area.

Food Standards Australia New Zealand (FSANZ) has recently released its draft proposed standard on “nutrition, health and related claims”, which has been under development for four years and is currently undergoing review as requested by the Ministerial Council. The proposed standard would create three categories of claim: nutrient content claims, general level health claims, and high level health claims. A health claim is one that directly or indirectly refers to a relationship between (a) food or a property of the food; and (b) a health effect.”(FSANZ 2008). While ‘performance enhancement’ foods may fall under the general level health claims category (being claims that “[do] not, directly or indirectly, refer to a serious disease or a biomarker”), the kinds of foods discussed here would be likely to fall into the high level health claims category, which are claims that directly or indirectly refer to a serious disease or a biomarker. The proposed standard would require manufacturers to obtain pre-market approval from FSANZ to make such claims by providing scientific evidence to substantiate the claims (except in those cases where the cited food component/disease relationship is already recognised in the Standard) (FSANZ 2008).
On the issue of appropriate levels of regulation of health claims, there were differences between the New Zealand and Dutch researchers. Some (though not all) New Zealand interviewees expressed the view that functional foods may be over-regulated by FSANZ. For one, the danger lay in denying some consumers benefits out of a preoccupation with risks: “they [FSANZ advisors] were so conservative that it was actually dangerously conservative… I think it’s important that the population is protected, but the population probably needs protecting against itself sometimes, too.” For another, the issue was whether food regulators should be considering the efficacy of functional foods at all.

Food regulation policy philosophy has always been around safety of food. Pesticide residues, all of that kind of thing. So you have this positive list of things that are approved to go into food, and everything else that isn’t on that list is not approved. But they struggle immensely, and have struggled for the last however many years that this has started to come onto the horizon, with: how do we work around health claims? Because of where they come from, they’re always going to be thinking: how can we protect people from these health claims? And the problem is, I think for them, personally, is they can’t. Because people will make a decision about whether they want to eat it and whether they believe it’s going to work in terms of health claims or not. So the regulators now are coming from a position of saying: what’s safe? … But whether it does what it says it’s going to do is not a food safety issue. … So I think regulators are struggling with this issue. They’re coming from a food safety point of view, and now they’re being asked to adjudicate on whether something is efficacious or not. And that’s not really a food regulators’ place. (Interview NZ)

Interviewees from the Netherlands had, if anything, the opposite concern:

We have now health claims, nutritional claims, and the companies could send in their claims to the European Food Safety Authority. And I think they have received, I think 12,000 claims…And now people need to select the claims that are evidence-based. I mean, the importance for the industry is so tremendous. … Q: And do you have confidence in the Food Safety Authority, to apply the right sort of criteria? Yes and no. The task is so huge and relevance for the industry is so large that it will be a very difficult process. If you reject a claim, you know you have to defend yourself for years, and that’s a difficult process. (Interview NL)

Evidence for such claims is typically based on association studies that look for a correlation between a particular bioactive compound and reduced risk of some disease. This has led to the formulation of products with increased concentrations of such compounds and to the development of plants and animals genetically modified to contain them, or to contain higher concentrations of them than they would ordinarily (see, e.g., Diaz de la Garza et al. 2007, Lai et al. 2006, Newell-McGloughlin 2008, Powell 2007, Yusuf and Sharin 2007).
The so-called “golden rice”, a variety genetically engineered to produce the vitamin A precursor beta-carotene, provides a well-known example (Schubert, 2008). This rice has been under development for over eight years. However,

few studies have measured the most important parameter to determine the eventual success of conventionally bred foods or genetically modified lines; namely, whether these foods are actually functional foods [that is, the effects of the foods on the consumer]. The most notable example of this gap between the technology used to grow transgenic plants and the measured nutritional efficacy is the case of ‘golden rice’, which was engineered to produce $\beta$-carotene in the edible portion of the grain… Unfortunately, the lack of nutritional assessment of biofortified foods is the norm rather than the exception.” (Hirschi 2008: 459)

In the case of beta-carotene fortification and probably other kinds of food enhancements, the overall nutritional state of the consumer will influence his or her ability to absorb the nutrient. In the case of golden rice, which is suggested for use in developing countries,

absorption of pro-vitamin A depends on overall nutritional status, which in turn depends on the diversity of the food consumed. People in the Third World, who stand to gain the most from golden rice, eat predominately plain rice out of necessity and do not have the luxury of a diversified diet. Thus, the nutritional impact of golden rice needs to be assessed using diets that will not favor optimal absorption of the nutrient. (Hirschi 2008: 459)

Similar contextual issues can be expected for products designed for consumers in different socio-economic groups or ethnic diets in New Zealand.

Many have warned against operationalising findings from association studies without a much greater knowledge than is currently held of gene-gene and gene-environment interactions (Haga et al. 2003, Hall et al. 2004, Hunter et al. 2008, Janssens et al. 2008, Offit 2008). The complex actions and interactions of food are also still poorly understood.

[Even the most innocuous of dietary components—fats, proteins and carbohydrates—have wide ranging effects on the overall regulation of genomic expression. Unavoidably, designing foods that contain functional ingredients for one targeted benefit cannot be guaranteed to have no potential deleterious side effects on other pathways of metabolism….This means that, in both research on and implementation of dietary modification through food choices, the effects of dietary change on metabolism must be examined comprehensively. (German et al. 2006:87)

There are particular concerns around the effects of purified compounds being added into foods, as expressed by two Dutch interviewees:

[If you] take a kind of classical food and put a little bit of micronutrient X or selenium-rich, this, I think can even be dangerous. Because we never, in
evolution, have been exposed to, for example, pure sugars or pure, even, PUFA [polyunsaturated fatty acids]. I mean, it’s always in the context of the foods we have eaten. So even if you would take olive oil, for example and you pull away all the polyphenols, you lose a lot of effects. I mean clearly, oleic acid is something which appears to be beneficial, but if you have only oleic acid, it’s not that beneficial any more. Because the cells need to deal with it in an efficient way. It needs a lot of other factors, too. (Interview NL)

People want to see food as drugs, and if you purify a nutrient, then, yeah, then you can have these harmful effects as well. Because in nature, in the food, it’s never present on its own. So there are maybe, for every active compound, there may be counteractive compounds as well. But if you purify them, then yeah, then you may generate problems also… For every compound, I think if you really look, there are people who somehow suffered from these purified compounds. (Interview NL)

This area presents some sharp challenges to food regulators.

**Association studies:** The use of association studies as an evidence base for health claims is not straightforward. The results of many, if not most, association studies can not be replicated (Hirschhorn et al. 2002, Pearson and Monolio 2008). The problem is exacerbated by the phenomenon known as publication bias: that is, research finding a correlation has a better chance of being published than research that finds no correlation (PLoS Medicine 2005).

It is argued that replicability of epidemiological studies looking for health/disease effects of diet has been hampered by the failure to take genetic diversity into account, and that stratifying by genotype will give stronger diet-disease relation results. While this may well be true, genotype-stratified research has also produced contradictory results. For example, Johnson (2007) reports on contradictory findings of a number of studies measuring effects of cruciferous vegetable consumption, stratified by genotype, on the risk of developing colorectal cancer. This points to the complexity of gene-gene, gene-nutrient, and nutrient-nutrient interactions, and the impact of wider environmental factors on both genes and nutrients (Aires et al. 2006).

**Unsafe for some:** More worrying than the inability to replicate study results are recent findings suggesting that increased consumption of bioactive compounds intended for functional foods can cause serious harm. This is illustrated by studies on folic acid. In New Zealand and several other jurisdictions, folic acid is required to be added to bread and flour as a public health measure, because maternal folate deficiency during pregnancy can result in the development of neural tube defects in the foetus. In addition, past studies have suggested that dietary intake of folate is protective against a number of diseases, including cardiovascular disease and colorectal and other cancers.

Folate (a water-soluble B vitamin that is present naturally in foods) and FA [folic acid] (the pharmaceutically packaged form of this vitamin that is used
commercially in supplements and in fortified foods) have been considered nutritional stars for a decade. Folate has been generally regarded as safe and has long been presumed to be purely beneficial and an ideal functional food component for disease prevention. (Kim 2007:504)

Recently, however, a number of animal, in vitro and human studies have indicated that increased consumption of folic acid can promote the development of disease. The evidence is particularly strong with regard to colorectal cancer. It now appears that “whereas folate deficiency in normal tissues increases the rate of neoplastic transformation, high doses of folic acid may accelerate the progression of existing neoplastic lesions to cancer.” (Powers 2007:666) Cole and colleagues, whose study was one of those showing an association between folate supplementation and increased rates of more advanced colorectal cancer, also found evidence for an association with increased rates of other cancers (Cole et al. 2007).

Mechanisms for these results have been hypothesised: “Rapidly proliferating tissues, including tumors, have an increased requirement for nucleotides; thus many cancers up-regulate folate receptors…” (Ulrich and Potter 2007: 2408). Essentially, the extra folate helps the cancer to grow faster. A paper by Wright et al (2007) postulates that folic acid (the form of folate used in supplements and fortified foods), as opposed to the folate naturally occurring in foods, is metabolised in the liver, which is unable to reduce high concentrations of folic acid, which then enters the bloodstream, where it can contribute to colorectal cancer as well as leukemia and arthritis (see also Powers 2007). Both pathways may have parallels in other bioactive substances.

Nutrigenetics approaches are unlikely to be able to address this problem, as the key distinction appears to be not genotype but disease state, or timing. That is, it is not genotype that determines whether a particular dosage of folic acid will be helpful or harmful, but rather whether pre-cancerous or cancerous developments have already occurred in the body. Indeed, it may be particularly hazardous for those with an identified genetic risk factor for the relevant cancer to consume high levels of folic acid as they are more likely than others to have undetected neoplastic lesions.

Similar findings have recently been produced in relation to beta-carotene, vitamins A, C, and E, and selenium. Beta-carotene is an antioxidant that has been promoted as protective against cancer. It is taken as a supplement as well as being the target of functional food development (e.g., Giorio 2006; see also the “golden rice” example above). A large cancer study has found an association between aggressive prostate cancer and high levels of beta-carotene. In 2002 a Finnish study of male smokers found that taking beta-carotene as a supplement was linked to an increased risk of developing lung cancer (BBC News 2008).

Selenium has been promoted as being protective against prostate cancer. In addition, because “[f]indings from animal models suggest that selenium supplementation improves glucose metabolism”, its effectiveness in preventing the development of Type 2 diabetes was investigated (Stranges et al. 2007). However, the study’s findings
indicate no overall efficacy of selenium supplementation in the primary prevention of type 2 diabetes; conversely, they suggest that long-term supplementation with 200 μg of selenium daily may adversely affect glucose metabolism. The findings are potentially important because selenium supplements in doses of 30 to 200 μg are widely used by the public in the United States and other Western countries (Stranges et al. 2007:221; see also Bleys et al. 2007).

Vitamin E, another antioxidant, is said to be “implicated in decreasing the risk of several types of cancers, coronary heart disease and a number of degenerative human conditions, when taken in excess of the recommended daily allowance” (Yusuf and Sharin 2007). However, a recent U.S. study on supplements and lung cancer concluded:

Supplemental multivitamins, vitamin C, vitamin E, and folate were not associated with a decreased risk of lung cancer. Supplemental vitamin E was associated with a small increased risk. Patients should be counseled against using these supplements to prevent lung cancer. (Slatore et al 2008)

A meta-analysis by the Cochrane Collaboration found that taking supplements of the antioxidants beta-carotene, vitamin A, vitamin C, vitamin E, and/or selenium did not lower mortality rates, and that a significant increase in mortality was found for Vitamin A (16%), beta-carotene (7%) and vitamin E (4%). They concluded:

Future randomised trials could evaluate the potential effects of vitamin C and selenium for primary and secondary prevention. Such trials should be closely monitored for potential harmful effects. Antioxidant supplements need to be considered medicinal products and should undergo sufficient evaluation before marketing. (Bjelakovic et al 2008)

A common lesson drawn from these findings is that one should eat a varied diet rich in fruits and vegetables, rather than use supplements, to get the benefits of antioxidants. However, as noted earlier, one purpose of functional foods is to substitute for a good varied diet on the assumption that people will not change current unhealthy eating habits. Moreover, researchers are engaged in modifying the foods themselves to increase the concentrations of these substances, or to introduce into foods substances that they would not ordinarily contain; examples include a high-beta-carotene tomato (Giorio et al. 2007), high-beta-carotene rice (Hirschi, 2008), a high-folate tomato (Diaz de la Garza et al. 2007), “a transgenic oilseed crop with high α-tocopherol [vitamin E] levels, which can provide a feasible, innocuous, and inexpensive way of taking the beneficial effects of high α-tocopherol intake to the masses” (Yusuf and Sharin 2007), and a pig whose meat contains omega-3 oils (Lai et al. 2006).

These findings suggest particular challenges for food regulators faced with health claims for foods like these. Establishment of efficacy with regard to one nutrient/disease relationship, as difficult as that is, may not be enough. From the perspective of food
safety it will also be necessary to establish that the same food will not inflict harm through a different nutrient/disease pathway.

Nor is the current model of “maximum safe level” used in relation to pesticides or additives necessarily useful here, as the concentrations of antioxidants and other substances that have a detectable positive effect on some (persons or pathways) may be the same concentrations that produce harmful effects in others. Whereas, currently, different subpopulations may be addressed with labelling (e.g., indicating that a food is not suitable for pregnant women, infants, allergy sufferers, or those with phenylketonuria), in this case those who would be harmed may well be unaware of their vulnerable status. (Nor could their vulnerability be identified through genetic testing.) This raises the question of whether high concentrations of bioactive substances should be permitted in the food supply. How high is too high, and how will this be determined?

These regulatory concerns also raise capacity issues. The Australia and New Zealand Food Regulation Ministerial Council (2008) expressed concern about the ability of FSANZ to enforce the proposed standard and noted that “[s]ubjectivity in the weight of evidence to substantiate a food-health relationship and the onus on regulators with limited capacity to adequately assess claims provides an environment for food companies to market food products in a way that contradicts public health messages.” It also creates an environment in which the “potential deleterious side effects on other pathways of metabolism” (German et al. 2006) may not be adequately considered; the science is not well developed, and producers may have little incentive to invest in complex research that would look for negative effects.
5. Upstream engagement

[Deep]er questions about the values, visions and vested interests that motivate scientific endeavour often remain unasked or unanswered. … [W]hen these larger issues force themselves on to the table, the public may discover that it is too late to alter the developmental trajectories of a technology. Political, economic and organisational commitments may already be in place, narrowing the space for meaningful debate. (Wilsdon and Willis 2004)

The question of upstream engagement on nutrigenomics is part of a larger question regarding whether decisions on allocating public research funding are sufficiently accountable to the public. In its recently released Agenda for New Zealand Research, Science and Technology (MoRST 2008), MoRST lists “connect[ing] New Zealanders with science” as one of four challenges to be addressed through public investment and/or policy development, more specifically: “To connect New Zealanders more closely with science, supporting a strong sense of ownership of RS&T [research, science and technology] and innovation and improving outcomes from RS&T.”

This is said to require “engagement”, where engagement is defined as “a broad term that includes a range of communication styles with different intents,” namely,

- dialogue, typically used to understand the views of others, develop shared views and help guide research, particularly at its early stages
- awareness, typically used to develop an understanding of the state of knowledge in a particular area of research, and
- promotion, typically used to enhance uptake of research knowledge or influence support for research. (55)

Effective engagement is said to require “a broad culture of innovation, across society” (54).

In addition to increased funding for science education and promotion, a focus from 2009 will be on “support for public engagement at early stages of research”. The emphasis is on “science teams and research organisations” having funding as well as “best-practice tools and techniques” for public engagement.

There are two clear limitations to this approach. One is that it does not take into account the problems inherent in simultaneously promoting technoscientific innovation and attempting to engage in “dialogue” on it. The second, more relevant here, is that engagement is seen as something that happens after high-level research priorities have been set. It is seen as the responsibility of science teams and research organisations. Nutrigenomics illustrates the difficulties with such an approach, as set out below.

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13 The other three are: sustain our science base; focus new science; and propel business R&D.
5.1. Setting public research priorities

Following on from its Growth and Innovation Framework (New Zealand Government 2002), in 2004 the Government set up a Food and Beverage Taskforce, which “mark[ed] the beginning of a Government and industry-led initiative to capitalise on one of the country’s fastest-growing sectors” (Anderton 2004): “The taskforce will ensure that the whole range of government activities that impact on the sector are coordinated and aligned, and that policies support the sector’s growth.”

When the taskforce reported in 2006, among its “action points” was: “Research into the health effects of food and diet modification, essentially looking at food as a preventative medicine, is required and should be considered as eligible for health research funding” (Food and Beverage Taskforce 2006:28). This was translated into a recommendation:

8. Align scientific effort with the productive potential of the sector—to support innovation in the food and beverage sector

…

8.5. Assess the value of increasing research into how food and diet modification influences the health of a population and consider establishing this as a formal area of health research eligible for [health] funding. (Food and Beverage Taskforce 2006: Appendix One)

Government duly incorporated this recommendation into MoRST’s research programme, pledging to “bring key stakeholders together from research and government to discuss how this research is funded, the barriers and limitations that may exist to this research, and possible actions” (Minister of Industry and Regional Development 2007: Annex 1).

This theme has been pursued further in FRST’s 2008 Food Domain Review and MoRST’s work on its Food Research Roadmap (scheduled for release in 2009). As in the case of the Food and Beverage Taskforce, in neither of these cases was public dialogue, as defined by MoRST above, incorporated into these processes.

The Food Domain Review noted:

[L]inkages to medical research should be encouraged…. Given this is an area of increasing interest to stakeholders, MoRST and the Ministry of Health should be asked to consider the interface of research for economic/health outcomes invested by FRST and HRC [Health Research Council]…. The Foundation should take the lead in building linkages between food and medical research as a means of facilitating food-related health research broadly (as it pertains to all of NZ’s key markets), [including] the validation of health benefits from export food products. … The Foundation should note that this has been identified by stakeholders as important area for convergence that will need to be addressed in the Food Research Roadmap. (FRST 2008: 17, 21)
Among the issues identified by MoRST in its stakeholder consultations around its Food Research Roadmap (described as having “a focus on ever more value-added food products and ingredients with Sustainability and Health & Wellness as key drivers”) was:

> Government needed to acknowledge that the same capabilities can result in dual economic/health outcomes and there is a need to take a more strategic approach to investing in these research areas. (FRST 2008: Annex 3)

What this illustrates is a gathering momentum for making nutrigenomics, and particularly research on functional and “gene-specific” foods, priorities for the health sector. Given the wide-ranging implications of such an approach, this is an issue suitable for wider public engagement.

### 5.2. Blurring the line between economic and public-health priorities

While it is not clear whether nutrigenomics will ever provide a basis for personalised nutrition or gene-specific foods, the attempt to bring this about would require a major research effort. The rationale for such an investment—as the policy discussion above makes clear—straddles economic and public health arguments. The benefits claimed for investment in nutrigenomics by its proponents include the development of high-value foods as well as improved population health and reduced health costs.

The economic argument focuses on what is seen as a growing market for food products branded as healthy. While public health advice already points to a number of foods, such as fruits, vegetables, whole grains, and oily fish, as health-promoting, such whole foods do not provide opportunities for large profit margins. As has already been noted, the focus is on the development of “completely new, added-value, export-focused, gene-specific foods”, or “branded foods with specific health claims” for which “individual consumers diagnosed with a disease or early disease indicators … will pay premiums.” Moreover, such foods “are likely to be processed foods rather than commodities, in order to capture value” (see sections 2.4 and 3.2.2).

The public health argument adduced in support of this strategy focuses on the claim that nutrigenetics screening and new foods will make it possible to prevent the development of common multifactorial diseases, especially cardiovascular disease, Type 2 diabetes, and various cancers, as well as obesity, which is associated with these diseases. Dietary advice that would be effective for most people is already freely available; the problem is lack of compliance. It has been argued by New Zealand nutrigenomics researchers that foods can and should be developed that make compliance unnecessary: “people can continue to consume the foods they recognise and enjoy, which have had their nutritional content altered to better meet the needs of various identified subpopulations” (Ferguson and Philpott 2003:202).

Apart from the question as to whether a diet of functional foods can ever provide the overall health benefits of the generally recommended balanced diet, there is a major flaw
in this approach: in New Zealand and many other relatively wealthy countries, these “lifestyle” diseases are disproportionately concentrated among the poorer parts of the population. They can ill afford to pay premiums for new, branded health foods. This raises serious questions as to whether it is appropriate to invest health funding in such research. These are the kinds of questions, which entail “the values, visions and vested interests that motivate scientific endeavour,” that Wilsdon and Willis have in mind for upstream engagement.

5.3. Nutrigenomics and public-health paradigms

5.3.1. Obesity

Rising rates of obesity are seen as a major public health challenge due to obesity’s links to major diseases such as cardiovascular disease, Type 2 diabetes, and some cancers. As noted above, it has been argued by some New Zealand nutrigenomics researchers that people are unwilling to make the dietary changes required, and the problem should therefore be addressed by modifying problem foods to make them less unhealthy (see section 2.4). When the problem, noted above, of the inability of people on low incomes to purchase premium branded health foods was raised, the reply of one New Zealand researcher was to call for the public health sector to adopt a nutrigenomics approach:

[this] is why the public health people have got to buy into this. Because I actually think,… I mean, is it cause or effect? Is it that they are having more of a problem with obesity--the FTO gene’s also involved in diabetes--is that the reason that perhaps they’re not getting such high-profile jobs, and other things? And I suspect unless there are public health recognitions that some of these genes are actually important and unless they’re helped in some way—the foods and the approaches don’t have to be all that incredibly high tech. Once we can focus down and learn which ones are really important then I think we’re in a position to go out and say: OK, I think there are probably about 30 genes that are really important, and it may be that there’s a public health initiative that we need to help the people in South Auckland or something like that, and help them think about just what they need to do and practically put it into play. (Interview NZ)

This approach points to the nature of the paradigm choice involved in adopting a nutrigenomics approach in public health policy toward obesity and related diseases. This approach assumes:

- that obesity is due largely or entirely to individual lack of self-discipline;
- and/or that obesity is due to genetic causes;
- and/or that only those interventions aimed at addressing individual motivation are legitimate.

This takes an individualist approach to public health.

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14 The quotation also suggests applying a genetic paradigm to understanding and addressing poverty; this would be widely contested and would also have wide-ranging social implications.
Those who contest the adequacy of this paradigm point out that the fact that rates of obesity have been rapidly rising since the 1970s in wealthy countries argues against either a genetic or characterological explanation. Evolution works slowly; genetic change cannot account for changing rates of obesity. Also, as many submissions to the Health Select Committee Inquiry into Obesity and Type 2 Diabetes (2006) argued, the population of New Zealand has not suddenly and collectively lost its willpower to exercise and eat a healthy diet. What has changed, they argue, is the social and physical environment.

Submissions to the Committee showed a remarkable degree of consensus among health researchers and practitioners around which strategies are most likely to be effective. It was repeatedly emphasised that individual-focused approaches would not be successful without policy or legislative measures to address the social and physical environment. People make food choices within a larger environment, and the current environment places obstacles in the way of healthy choices. This is particularly true for people with low incomes, among whom obesity and diabetes are disproportionately concentrated. The obstacles consistently highlighted by submissions included:

- Affordability: e.g., many low-income New Zealanders find healthy choices unaffordable, and must prioritise quantity over quality in order to put food on the table; healthier choices are more expensive than unhealthy alternatives (e.g., soft drinks v. milk, fatty meats v. lean meats, white bread v. whole-grain bread, processed foods v. fruits and vegetables);
- Availability: e.g., school vending machines, tuck shops and sponsored events tend to feature energy-dense (high-calorie), low-nutrient foods, contradicting nutrition education; opportunities for unhealthy food choices (e.g., fast food outlets) are more prevalent in low-income communities while good-quality fruits and vegetables are less available as well as less affordable;
- Creation of demand for the wrong foods: e.g., extremely high levels of advertising of energy-dense, low-nutrient food to children

Personalised advice or functional foods can be seen as a solution to the “obesity epidemic” if obesity is seen as caused by an unwillingness of individuals to take up generic dietary advice—either because they lack sufficient knowledge/motivation or because they strongly prefer the taste of unhealthy foods. However, affordability, availability and socialisation are structural constraints; personalised, gene-specific approaches will not address them. Focusing on individual choice in this way removes responsibility from those who shape the menu of choices available to individuals. Those who point to changes in the environment as a key factor in rising obesity rates advocate societal-level measures, such as restricting advertising of energy-dense, low-nutrient food; removing vending machines for such foods from schools and making school canteen offerings healthier; and removing GST from fruits and vegetables while levying

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15 For a detailed discussion of structural/environmental factors in an Australian context see Dixon and Broom (2007).
additional taxes on sugary drinks and other energy-dense, low-nutrient foods. While a genetic approach may be helpful to some of the small minority for whom following the generic advice would not be effective, the overall public health effect of pursuing such an approach at the expense of addressing structural constraints, these submitters argue, is likely to be a widening health gap between rich and poor and a failure to curtail the increasing rates of obesity and diabetes.

Plans to direct health funding toward nutrigenomics/functional food appear to contain within them the choice of the individualist paradigm. This choice has embedded within it further, political choices (e.g., regarding the appropriate roles for markets and regulation) and deserves wider public scrutiny.

5.3.2. Cancer

As noted above, genetic screening has been proposed as a public health measure and a substitute for general dietary advice with respect to consumption of red meat. Ferguson and Kaput (2004) note that seven-eighths of the population “may be unaffected by” the heterocyclic amines (HCAs) produced during high-temperature cooking of red meat, whereas the one-eighth of the population “who are not only fast acetylators but also have a rapid CYP1A2 phenotype” have been shown to have an increased risk of developing colorectal cancer from HCAs. They go on to argue:

The meat industry and indeed the health of the nation [i.e., New Zealand] could be adversely affected by a blanket recommendation to reduce the consumption of red meat, especially well done red meat. However, there is a specific group of the population (the one eighth referred to above) that is likely to continue to be at high risk if interventions are not made. High-throughput genetic testing for these metabolic phenotypes is increasingly becoming a reality… and (debatably) might be considered as a public health priority. (Ferguson and Kaput 2004: 32)

The public (and indeed, individual) health benefits of such a measure would depend on a number of factors, including: those found to have the identified characteristics would be motivated to stop consuming (well-cooked) red meat; only those with the identified characteristics are at increased risk of colorectal cancer as a result of high consumption rates of red meat; and high consumption rates of red meat do not have other negative health effects on those without the identified characteristics.

This example illustrates some of the difficulties of applying genetic susceptibility studies to public health. When is an association sufficiently robust to be incorporated into public

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16 See e.g., submissions from Simmons (Waikato Clinical School, University of Auckland), Mann et al (University of Otago), Scragg et al (School of Population Health, University of Auckland), Weber et al (Institute of Food, Nutrition and Human Health, Massey University), Crampton et al. (Department of Public Health, University of Otago), Community Child Health and Disability Service (Auckland District Health Board), Connor (Diabetes Otago), National Pacific Diabetes Initiative, Nutrition Services of Canterbury District Health Board, and Pacific Islands Heartbeat Programme.
Shortcomings in study design (Haga et al. 2003), publication bias (see section 4.2) and the complexity of gene-gene, gene-environment and even environment-environment (e.g., smoking and red meat intake) interactions (see section 2.3) complicate such an evaluation. Even apparently straightforward associations turn out to be rather more complex on closer examination (see Box 2).

Box 2. PKU is a single gene disease that illustrates the complexity of linking genotype or genomic responses to cause and treatment.

Even in this special case of PKU (Box 1), the link between genome and disease state is easily oversimplified. This is because of “(1) widely different phenotypes that can be accounted for by allelic variation in a single gene; (2) the blurring of predicted relationships between genotype and phenotype in [monogenic disorders; and] (3) modifier genes and non-genetic factors that contribute to the phenotypes of monogenic disorders” (p. 267 Scriver and Waters, 1999).

In the case of phenylketonuria, it can be diagnosed using either a genetic marker (SNPs in the PAH gene) or a metabolic marker (HPA). There are three distinct phenotypes that can be associated with HPA and not all need occur in any particular patient whether treated or not (Scriver and Waters, 1999). The first is retardation due to excess phenylalanine during brain development. The others are individual variation in metabolic tolerance for elevated phenylalanine levels and possibly differences in the activities of the mutant PAH enzymes, which derive from complex genotype x phenotype effects involving many other genes and environmental factors that could be well beyond what nutrigenomics techniques will be able to survey (Scriver and Waters, 1999). While in the case of this monogenic trait an effective treatment through diet is achievable, the complexity suggests that the majority of diseases which derive from multigenic traits, or quantitative traits in which multiple genes contribute to varying degrees, may not be amenable to genotype- or genomic-response-based prescriptions.

In relation to the red meat example, a 2008 study notes that evidence of “the interaction between polymorphisms in carcinogen-metabolizing enzymes and red meat intake/doneness is inconsistent” (Cotterchio et al 2008). More importantly, this study found that red meat consumption was associated with increased colorectal cancer risk regardless of genotype.

On what grounds, then, could this be considered a public health priority? It is not clear how (as argued by Ferguson and Kaput) an overall decrease in red meat consumption would result in adverse effects on the health of New Zealanders. On the contrary, it currently appears more likely that there would be beneficial effects from such a decrease.

Two significant societal choices would be embedded in any decision to invest health funds looking for those assumed to have enhanced susceptibility to well-done red meat consumption: the first is the use of health policy to accomplish economic goals, as
discussed above; the second is the choice of an individualist paradigm for public health. That is, do we take population-based measures to improve public health (e.g., a “blanket recommendation” to limit red meat consumption; the creation of infrastructure promoting physical activity and healthy eating; anti-smoking measures and subsidised quit-smoking programmes; general and workplace pollution controls) or do we invest in research that may eventually lead to an ability to identify higher-risk individuals and make it their responsibility to protect their own health on an individual basis? Should workplaces be generally safe, or should individuals with genetic variants associated with a higher-than-average risk of developing cancer from a workplace chemical be responsible for avoiding such workplaces? Should public funds be invested in determining in each case whether the association is robust and reflects causation; whether those found to have the identified characteristics would be able to act on the advice; whether only those with the identified characteristics are at increased risk; and whether the pollutant, food, etc., does not have other negative health effects on those without the identified characteristics? Should this be done in order to avoid having to take population-based measures? Surely these are questions of broad public interest.

New Zealand interviewees voiced concerns that the term “genomics” would result in nutrigenomics getting caught up in the New Zealanders’ negative attitudes toward GM. Public engagement was seen as necessary to avoid this association. The discussion above suggests that the need for public engagement is of a different nature and that opportunities for “dialogue” and for public accountability should occur further upstream than is envisioned by MoRST (2008). They should be brought to bear on the work of MoRST itself.
6. Conclusions

Nutrigenomics/nutrigenetics research will not necessarily lead to the use of nutrigenetic screening, to genotype-linked personalised nutrition services, or to gene-specific foods. These outcomes are the aim of some, but certainly not all, researchers in the field.

The problems flagged in this report apply not to nutrigenomics as a field of research but to “applied” nutrigenomics. Nutrigenomics has made an extremely rapid leap from bench research to market (see, e.g., Trivedi 2007; Hill 2008). It is the current environment for scientific research (including the expectations of research funders and regulatory environments that permit premature commercialisation), rather than the degree to which nutrigenomics research is ready for application, that has determined this.

New Zealand currently lacks an appropriate regulatory framework for nutrigenetic services and nutrigenomics foods. It also currently lacks the capacity for adequate oversight in these areas.

Nutrigenomics New Zealand has been created with the expectation that it will eventually produce economic benefits for New Zealand’s food industry. Recently it has been suggested that this would be facilitated by making nutrigenomics and functional food research eligible for health funding. It has also been suggested that a nutrigenomics approach be employed in public health. Neither of these suggestions has as yet been seen as suitable for public debate, yet both would commit the New Zealand research and health sectors to a trajectory with significant socio-political implications.

Constructive Conversations research is premised on the assumption that in order to evaluate the risks and benefits, the desirability and ethics of a technology, we must know how it is likely to interact with its context. The primary focus of this research is biopharming; its aim has been to identify the contexts relevant to the implementation of biopharming in New Zealand and to use this information to evaluate the likelihood of benefits as well as the nature of the risks and their prospects for adequate management. It has done this by eliciting relevant knowledge from people who have experience and expertise in the identified contexts. Its focus is not public attitudes toward a technology, but rather the widely distributed knowledge that is relevant to assessing a technology.

This assumption, we believe, remains valid. The research on nutrigenomics has, however, shown that an approach to public engagement that focuses on engaging the public only in relation to the potential harms and benefits of a deployed or about-to-be deployed technology has serious limitations. These limitations arise from the fact that commitments with significant socio-political implications may have been made well before that point. The policy lesson to be learned from this, in our view, is that the processes through which high-level public research priorities are set should be transparent and open to public scrutiny.
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