

# The genetic engineering of microorganisms

*Early in 1988 Monsanto participated in a series of focus groups, or neighbourhood workshops, organised to exchange views on BST [genetically engineered bovine somatotrophin] with farmers, veterinarians, doctors, teachers, nurses and consumers. At the end of one such meeting a local National Farmers' Union (NFU) executive, who had organised that meeting, presented two glasses of milk to two women, representatives of the Townswomen's Guild. He explained that one contained milk from a BST-supplemented cow and the other contained 'normal' milk. He asked them to choose which they preferred. Without hesitation both responded, 'We cannot choose, there is no choice, they're both the same.'*

Deakin (1990)<sup>1</sup>

*Genetically altered micro-organisms pose risks to human health and to the environment. Scientists and regulators promise to keep that risk to a minimum, but our own history warns of the 'whoops' theory of risk assessment (something can go wrong – or perhaps already has – and those affected are left with the apology, 'Whoops, sorry, we made a mistake').*

Spallone (1992)<sup>2</sup>

## Introduction

Microorganisms are, literally, very small organisms. They include bacteria, viruses, yeasts, single-celled algae and single-celled protozoa such as amoebae. To the naked eye they are invisible.

Many of them are of great benefit to humans. For example, if it wasn't for microorganisms, dead animals and plants would pile up. Instead, they decay and their nutrients are returned to the environment to the benefit of other organisms. Other microorganisms harm us. Most diseases are caused by microorganisms. For example, viruses are responsible for colds, flu, mumps and AIDS; bacteria cause cholera, diphtheria and tetanus; while protozoa cause malaria and sleeping sickness.

As we saw in Chapter 1, humans have long since used microorganisms for such processes as bread and alcohol production. Since the 1970s, scientists have learned how to alter the genetic make-up of certain microorganisms through genetic engineering. Genetically engineered microorganisms are already being used for a whole range of purposes. They can be used to synthesise complicated molecules, such as insulin and growth hormone, missing in certain humans; they can be used to manufacture vaccines, antibodies, food additives, bread, cheese and the active component of biological washing powders; they are being incorporated into biosensors able to detect minute amounts of substances for diagnostic purposes; they can even prevent water from freezing.

Looking to the future, the use of genetically engineered microorganisms is likely to increase even further. For instance, designer bacteria are being devised to help clear up oil spills and extract valuable minerals from low-grade ores. In this chapter, though, we concentrate on present practice rather than looking to possible future developments. Five contrasting examples of the use of genetically engineered microorganisms are reviewed. It might be thought that the genetic engineering of bacteria, viruses and yeasts would raise few ethical issues. However, as we shall see, this is not in fact the case.

## Growth hormone from cattle: BST

Cattle produce growth hormone, just as humans do. Cattle growth hormone is called bovine somatotrophin or BST for short.<sup>12</sup> In a dairy cow, BST has two main functions, both to do with the nutrients derived from the cow's food. BST channels some of these nutrients into growth, and it channels some of them into milk production. The details need not concern us. Suffice it to say that BST is a natural hormone produced by cattle. During lactation, BST causes nutrients derived from the cow's food to be diverted to her mammary glands where they are used to make milk. It is this fact that has led to an extraordinary ten year battle over genetically engineered BST.

### Why bother to make genetically engineered BST?

Because BST causes nutrients derived from a dairy cow's food to be diverted to her mammary glands, it was suggested, in the early 1980s, that injecting a cow with BST might increase her milk yield.

The chemical structure of BST was determined in 1973, and by 1982 genetically engineered BST had been made by incorporating the cattle gene for BST into the bacterium *E. coli*. A huge amount of basic and applied research has been carried out on genetically engineered BST by a number of companies including Elanco, Cyanamid and Upjohn, but especially by the multinational Monsanto.<sup>13,14</sup>

Injecting dairy cows with genetically engineered BST increases their milk yields by some 20%. Furthermore, it increases milk to feed ratios by some 15% – that is, the amount of milk made by the cow relative to the food she consumes goes up by around 15%. Monsanto argue that genetically engineered BST offers a number of significant advantages to dairy farmers. The main one is that by raising milk yields and increasing feed efficiency it raises profits. Further, the technology requires no capital investment: the farmer merely injects the cows every 14 days from the ninth week after calving until the end of lactation. This means that the system is, Monsanto maintains, 'immediately self-financing'.<sup>15</sup> In other words, there is no significant lag time between the introduction of the technology and the financial benefits reaped as a result of it. Finally, Monsanto points out that genetically engineered BST is virtually identical to the BST naturally produced by cows, differing by just one amino acid residue. BST is present in milk only in trace amounts and has no physiological effects on humans, as it differs in structure from human growth hormone. In any case, the minute amounts present in milk are digested and so do not pass into the human bloodstream.

### Disadvantages of using genetically engineered BST

Despite the apparent financial benefits to farmers of using genetically engineered BST, a number of different arguments have been put forward as to why it should not be used. Four main ones can be proposed.

First of all, who wants or needs more milk? The number of dairy cows kept in Europe and the USA – the two regions where profitable sales of BST are most likely – has fallen over the last 20 years. This is because the demand for milk has failed to keep up

with the dramatic increases that have already taken place in milk yields through selective breeding, feed concentrates and other agricultural practices. Indeed, Europe has seen a surplus of milk production for most of the last ten years, leading to the occurrence of so-called milk lakes. It is likely that the introduction of genetically engineered BST would lead to even more farmers being put out of business. The validity of this argument has been acknowledged, in part, by Monsanto. In some of their promotional literature they argue, rather confusingly, that: 'While it may seem paradoxical to be introducing a new technology into an industry where there is already surplus production, it should be stressed that BST is **not** intended solely to produce more milk. Instead it can be used either for this purpose, or to reduce the cost of milk production in a situation where extra milk is not desired – such as exists in a quota system'.<sup>16</sup>

Secondly, while it is true that genetically engineered BST itself almost certainly poses no health risks to humans, its use is linked to significantly raised levels of insulin growth factor-1 in the cow's milk. The consequences of this are still controversial. It has been argued that the presence of these high levels of insulin growth factor-1, which is chemically identical in cattle and in humans, may trigger premature growth in infants, breast development in children and breast cancer in women. While few scientists regard this possibility as a likely one, Ben Mepham, a physiologist working at the Centre for Applied Bioethics at Nottingham University, has argued that legalisation of commercial use of BST in the absence of more extensive information on these questions could lead to a deterioration in public health, not least if widespread rejection of milk were to result. He has also pointed out that public confidence in biotechnology would be helped by a more open system of regulation and by the use of 'blind trials' in experimental work, as is the norm in the pharmaceutical industry.<sup>17</sup>

Thirdly, does the use of BST injections harm the cow's health? Even the manufacturers of genetically engineered BST accept that its use may increase the incidence of mastitis, cystic ovaries, disorders of the uterus, retained placentas and other health problems, including indigestion, bloat, diarrhoea and lesions of the knees.<sup>14</sup> In addition, its use may result in permanent swellings up

to 10cm in diameter at the injection site.<sup>14</sup> Mastitis, as many women know all too well, is a painful inflammation of the mammary glands. It has the same effects in cows as in humans. (As an ironic twist to the story, research has been undertaken in the hope of producing genetically engineered cattle resistant to mastitis.) Mastitis is commonly treated by giving infected cows antibiotics. Some concern has been raised at the consequences of this for human health, though these fears may be exaggerated as antibiotics have been used on farm animals for decades. A related point is that BST injections possibly put even more pressure on a cow's health in countries where farmers have little or no access to high concentrate feeds.

Fourthly, while everybody knows that dairy farming is big business, for many people the thought that cows will be artificially stimulated by biweekly injections of genetically engineered BST for most of their lives is somehow off-putting. True, genetically engineered BST is almost identical in structure to natural BST, but to some people it seems wrong that it should be used to boost a cow's BST levels beyond what is normal. Is its use analogous to the force-feeding of geese to produce *pâté de foie gras*? For some people, milk still retains a special aura of freshness and naturalness, perhaps because we all start our lives, once born, by living off milk. This image is tarred by the use of genetically engineered BST. It may be hard to reconcile a belief, albeit a naive one, that milk is a 'natural' product with the recognition that genetic engineering is being used to direct the process (see Figure 5.1).

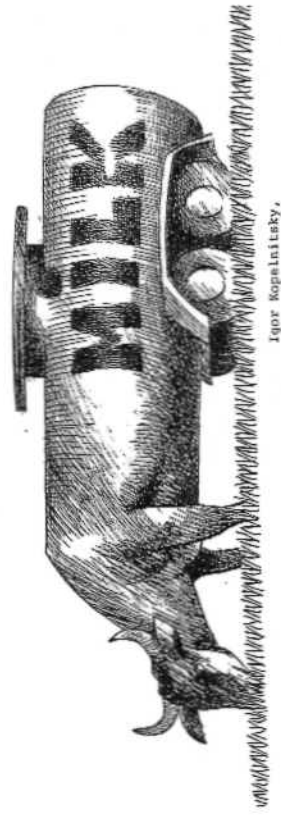


Figure 5.1.

### The current legal position

By 1994, genetically engineered BST had been licensed for use in a number of countries including South Africa, India, Mexico, Brazil, the former USSR and, in February 1994 – and after a long battle – the USA. Endless debates have taken place within the European Union but in December 1994 agriculture ministers from European Union countries agreed to continue the ban on its use until the year 2000. Britain alone advocated lifting the ban, but was outvoted 11 to 1. A UK government consultation in 1994 showed that three-quarters of the organisations that responded, including consumer groups, animal welfare organisations, environmental pressure groups, organisations representing farmers and four of Britain's largest supermarket chains, wanted the ban to remain in place.<sup>18</sup> The organisations that wanted the ban lifted were mainly biotechnology companies and scientific institutions. One of the most remarkable features of the lifting, in the USA, of the ban on the use of genetically engineered BST was that the Food and Drug Administration produced guidelines stating that any company proclaiming that its milk was produced without the use of genetically engineered BST would have to carry a long statement explaining that there is no advantage to BST-free milk.<sup>19</sup> The first two American dairies that advertised their milk as 'hormone-free' were promptly sued by Monsanto.<sup>20</sup>

### Genetically engineered viruses to control insect pests

The three examples we have considered so far – genetically engineered human insulin, human growth hormone and BST – have been examples of substances made by genetically engineered bacteria and injected into individuals – humans or cows. A very different example of the use of genetic engineering is provided by the case of genetically engineered viruses, used to control insect pests.

### The control of insect pests

Worldwide, somewhere around a third to a half of all agricultural production is lost to pests and diseases. Insect pests are amongst

the most important pest organisms and chemical insecticides are widely used to reduce their effect. Since the early 1980s, there has been a resurgence in the use of so-called 'biological control'. Biological control is where one organism is used to control another. Biological control was practised by the Chinese some 4000 years ago when ants were used to kill leaf-eating insects, thus protecting valuable crops such as oranges.

Perhaps the most famous example of biological control was the use of a moth called *Cactoblastis cactorum* to control the prickly pear cactus (*Opuntia*) in Australia. The prickly pear cactus is not native to Australia. It was introduced there by a certain Dr Carlyle who grew the plant in his garden because he thought it looked nice and might do well. It did. By 1910, the cactus was spreading at a rate of over 300 000 hectares a year. The Australian government responded by trying to find an animal that would eat it. In 1925, eggs of the moth *Cactoblastis cactorum* were introduced into Australia from Argentina. These proved a great success. Within a few years almost all the prickly pear cacti had been destroyed.

### Why use genetic engineering?

Genetic engineering is being used to try and improve the effectiveness of biological control. Some of the most thorough work to date has been carried out by David Bishop and Jennie Cory in the UK.<sup>21</sup> Bishop and Cory work on viruses known as baculoviruses. Baculoviruses attack insects. Natural (non-genetically engineered) baculoviruses have been used for decades to protect crops simply by spraying the viruses onto crops infected with insect pests such as aphids or caterpillars. One of the great advantages of baculoviruses is that they have absolutely no effect on vertebrates. This means that there is no danger to humans from eating crops treated with them. Given the widespread concern over the effects of chemical pesticides both on human health and on animals such as sparrowhawks and fish, baculoviruses hold out the hope of safe, effective insect control.

However, one problem is that natural baculoviruses are relatively slow in their effect. This is a common problem with biological control agents. They need time to multiply up in the field. Because

of this, Bishop and Cory are carrying out a series of experiments in which insect-specific toxins or insect-specific hormones are introduced into the viruses through genetic engineering. The idea is that the virus will be even more effective at killing the insect pests. Either it contains a toxin that poisons the insect or it contains an insect hormone that causes the insects to fail to develop normally.

So far so good. However, in 1994 a major row broke out over the research.<sup>22</sup> The research group had been given permission to spray some of the genetically engineered virus in a field near Wytham in Oxfordshire. However, this field is only 100 metres from a nature reserve inhabited by rare moths. The viruses had been modified by having a scorpion gene inserted into them – the gene making a venom lethal to insects. Although Bishop and Cory had already, in 1993, carried out a very similar experiment, the new experiments sparked off a major controversy amongst scientists and led to articles with such headings as ‘Will the scorpion gene run wild?’<sup>22</sup>

On the one hand, the UK government’s Advisory Committee on Releases to the Environment, which evaluates all proposals for outdoor tests with genetically engineered organisms, approved the experiment. On the other hand, a number of ecologists have subsequently expressed concern. Might some of the viruses escape from the test site? David Bishop counters this fear by pointing out that the enclosures that surround the experimental plots consist of tough, fine netting designed both to stop the wind blowing the virus out and to prevent animals from getting in. This netting has been extensively used and proved effective.

The major fear is the effect that the viruses might have if they do come into contact with native insects. In the 1993 experiments, Bishop and Cory found that the genetically engineered viruses killed caterpillars of the cabbage looper moth faster than the normal virus. As a result, the genetically engineered virus afforded significantly greater protection to the cabbage crop on which the cabbage looper moth caterpillars were feeding. What is not really known is the effect that the genetically engineered virus might have on native moths. There is genuine academic disagreement about which moth species are attacked by the natural, let alone the genetically engineered, virus. Work carried out by Bishop suggests

that only a very small proportion of British moths are susceptible to the virus. However, Alan Wood, who studies baculoviruses at the Boyce Thompson Institute for Plant Research in New York, believes that these figures are too low and points out that there have even been reports of the virus infecting termites and beetles.<sup>23</sup>

A related fear is that the use of the genetically engineered virus might allow the scorpion gene to be picked up by other viruses. Again, academic disagreement exists as to how likely this is in the field, though it has been demonstrated in the laboratory.

### Other issues

The row over Bishop and Cory’s research with genetically engineered viruses has focused exclusively on the issue of safety. As we saw in Chapter 2, it is virtually impossible to predict the risks of an action before the action is carried out. Bishop and Cory’s research has to be undertaken if we are to evaluate the risks of the procedure – though it would perhaps be wiser to carry it out rather further from a nature reserve.

However, the use of such viruses to control crop pests raises issues that go beyond safety. Suppose we knew that the widespread, commercial use of genetically engineered baculoviruses would increase the value of crops by, say, £10 million a year but carry a 1% chance each year of leading to the extinction of a native species of moth. How do we decide whether, given this clear-cut scenario – and in life the alternatives will never be as definite as this – we should legislate for the use of genetically engineered baculoviruses or ban them?

## Vegetarian rennet

The final example we shall consider of the use of genetically engineered microorganisms raises a different set of ethical issues from those we have addressed so far. It concerns the making of cheese.

Cheese has been made by people for at least 5000 years. The fundamental principles have changed little over the millennia. During cheese making, a number of substances are added to sour milk. One of them is rennet. Rennet is a crude extract of enzymes, of which much the most important is chymosin, also known as rennin. These enzymes act on a milk protein called casein. Their effect is to cause the milk to form a soft curd, also known as junket. Without rennet, most cheeses cannot be made.

Traditionally, rennet has been obtained from the stomachs of young calves (or piglets, kids, lambs or water buffalo calves). Rennets can be of vegetable origin, but, until recently, by far the most important source was young calves. Calves' stomachs were ground up in salt water – ten of them being required for one gallon of rennet.<sup>36</sup> Of course, calves' stomachs contain a lot of stuff in addition to rennet, so the purity wasn't very high. However, the gene for calf chymosin has now been inserted, by genetic engineering, into a yeast, which produces a ready supply of chymosin in commercial quantities. As a result, the use of rennet obtained directly from animals has greatly decreased. In addition, genetically engineered chymosin is cheaper than traditional rennet and considerably purer.

The original gene used in the genetic engineering of the yeast came from an animal source. However, the Vegetarian Society of the United Kingdom decided to endorse genetically engineered chymosin on the grounds that its use would significantly decrease the slaughtering of calves. Accordingly, manufacturers that produce cheese through the use of genetically engineered chymosin can put a V-symbol on the cheese and state that the product is suitable for vegetarians on the packaging. It is also approved by Muslims and Jews.

In the UK, the Co-op supermarket chain was the first retailer to announce a policy on the genetic engineering of food. It has produced a free leaflet called *The Right to Know: Your Guide to*

*Genetic Engineering*, which is available from its stores and also from its Customer Relations Department.<sup>37</sup> Key points within the policy are:

- No food product containing modified human genetic material will be sold by the Co-op
- Co-op Brand products will not contain vegetables or fruits which have been modified with genetic material from animal sources
- All Co-op Brand products known to contain modified genetic material from non-related species will be clearly labelled

By 1994 the only product in the Co-op's range that had used genetic engineering was Co-op vegetarian cheese. This product is labelled 'Produced using gene technology, and so free from animal rennet'.

One important factor in the Vegetarian Society's decision to approve genetically engineered chymosin was the fact that, in practice, the rennet actually used by cheese manufacturers will not contain the original calf chymosin gene, but copies of it. However, something of a diversity of views exists on this point among vegetarians:

The concept of copying rather than direct transfer was important in our decision to allow chymosin manufacturers to use the V-symbol. However, vegetarians are obviously not a homogeneous group and will have divergent views on this issue. Some will accept the copying stage as meaning a host containing a gene from an animal source is acceptable whilst others will view its animal origin as meaning that the product is not acceptable.<sup>38</sup>

By 1994, approximately one half of the market for rennet worldwide was being supplied by genetically engineered chymosin. It is tempting to see this example of genetic engineering as a way of saving the lives of the millions of four- to ten-day-old calves that, until recently, were killed for their rennet each year. The reality, though, is that these calves continue to be produced so as to keep their mothers, dairy cows, producing milk. Female calves generally

themselves become dairy calves. Male calves are usually reared for meat, either as veal calves or as beef cattle.

### WHAT'S WRONG WITH GENETICALLY ENGINEERING MICROORGANISMS?

The genetic engineering of microorganisms does not at first sight look to be a subject capable of arousing much moral concern or controversy. After all, we cannot even see these organisms (without a microscope) and so do not normally devote much time and effort to considering their welfare. However, the previous six case studies have already shown that the issues raised are far from being purely scientific and, in fact, often contain a clear moral dimension. Following the distinctions drawn between 'moral' and 'ethical' in Chapter 3 (pp. 45-7), we can now examine the possible areas of moral concern highlighted by these case studies and subject them to some ethical scrutiny. Where relevant, religious and theological considerations will also be included.

The range of moral concerns implicit in these case studies is extremely wide, too wide in fact to be dealt with in one section of a single chapter. Therefore, as each chapter in Part 2 will conclude with a separate ethical analysis, certain topics will be reserved for certain chapters, where they can be given fuller treatment, rather than attempting to deal with every ethical aspect of every case study in every chapter, which would inevitably lead to repetition. In this chapter, for example, the use of human growth hormone poses serious ethical and theological questions about the extent to which human differences should be regarded as 'defects' to be remedied or even prevented by genetic engineering, while BST has aroused much moral unease on grounds of animal welfare. Although these examples involve the genetic manipulation of microorganisms, the ethical and theological issues will be more conveniently dealt with not here but in Chapters 7 and 8, where the focus will be upon animal and human applications of genetic technology.

This still leaves plenty of ethical work to be done in this chapter. The genetic engineering of microorganisms in general and the case studies in particular illustrate graphically many of the basic

distinctions and arguments introduced in Chapters 3 and 4. Following the framework developed there, we can see that moral concerns arising from the case studies may fall into either the intrinsic or the extrinsic category.

### Respect for nature

Intrinsic concerns that the technology is wrong in itself and so ought not to be used can of course be expressed about *any* application of genetic engineering, irrespective of the possible advantages and disadvantages in particular cases. We offered a general ethical and theological assessment of such arguments in Chapters 3 and 4 and pointed out some of the weaknesses and confusions that they may suffer from. These points will not be repeated in detail in this or the following three chapters. However, intrinsic objections to the genetic engineering of microorganisms carry with them some more specific implications which help to clarify and further develop the general comments already made.

Moral or religious qualms about 'interfering with Nature' or 'playing God' are strictly speaking as relevant to the manipulation of laboratory bacteria to produce insulin as they are to work on animal or human genetic material, for DNA ('the stuff of life') is being genetically altered in all such cases. Despite this logical equivalence, however, intrinsic objections do seem, intuitively at least, to carry less weight when the object of the manipulation is an invisible microbe than when it is a pig or a person.

If we probe this intuition further, we can see that important questions have to be asked about intrinsic objections to genetic engineering that are based on an alleged lack of respect for 'Nature' or for 'life' itself. To put the problem at its simplest, what are the boundaries of 'Nature' or of 'life'? Do they extend to the world of microorganisms? No doubt the microbiologist would maintain that they do, but this scientific categorisation creates serious difficulties for those who wish to attribute moral or religious value to *all* of 'Nature' and to *all* 'living' beings and who consequently object to any genetic interference with them.