A SHORT HISTORY OF THE REGULATION OF GENETICALLY MODIFIED ORGANISMS (GMO) IN AUSTRALIA

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In 1972 scientists in the USA reported an experiment in which two unrelated DNA molecules were joined together by a process called homopolymer tailing. One of these molecules was a bacterial virus (lamda *dv*) and the other was a mammalian virus SV40. Although SV40 was regarded by many as a harmless virus extensively studied in the laboratory for many years there was some questions as to whether or not it had oncogenic properties. When the experiment was first reported some scientists expressed concern as to whether introducing this molecule into the bacterium *Escherichia coli K12* could produce a novel strain able to transmit oncogenes between humans by a novel route. This experiment created speculation about possible unpredicted outcomes associated with mixing genes from different species. In the next couple of years scientists developed new methods involving restriction enzymes and plasmids that greatly simplified the introduction of novel genes into *E.coli* and by extension to many other organisms.

In 1974 a group of American scientists called for a temporary halt to all experiments involving these new recombinant DNA techniques until a meeting could be called to consider possible implications of the work. In Australia the Academy of Science immediately established an ad hoc committee on Recombinant DNA to alert Australian scientists to the situation and to ascertain the extent to which work of this nature was being undertaken in Australia. It also agreed to send two delegates, Jim Peacock and myself, to the International Meeting being held in Asilomar USA in February 1975. Bruce Holloway from Melbourne was separately invited to attend. The conference had 86 participants from the USA and 53 from some fifteen other countries. The meeting ran for four and a half days and was a period of frenetic activity. Part of the time was spent listening to the latest exciting developments in this field to be followed by intense sessions in which an attempt was made to formulate guidelines for the absolutely safe and secure development of this new science. For many scientists attending who thought that this would be a possible opportunity to discuss possible hazards it was a shock to find that pressure from the legal and media representatives at the meeting made it obligatory to either state that all experiments using these techniques were entirely safe or to produce a set of guidelines that would guarantee safety. Most of the participants were molecular biologists and in retrospect it was a major error not to have a greater representation of scientists well versed in the study of infectious diseases and others involved in the industrial use of microbes. At this point in time most of the experiments involved introducing novel genes into the bacterium *Escherichia coli* K12. Because some strains of *E.coli* were known to be human pathogens, vague fears were expressed about the possibility that strains of *E.coli K12* receiving genes from other organisms might acquire new properties of pathogenicity or oncogenicity. There was no evidence presented at that meeting relevant to these hypothetical or conjectured risks. Furthermore each group, virologists, microbiologists, cancer specialists, while expressing complete faith in the safety of their own work expressed some apprehension about the experiments of their colleagues. This environment unfortunately encouraged a solution which in some ways has provided ongoing obstacles to any rational consideration

of novel risks associated with this work. The meeting basically said, we don't know whether any of these hypothetical risks are real but in order to get on with the work let us assume a worst case scenario for every experiment and design conditions of biological and physical containment that would still ensure safety.

For example, let us assume that the gene we want to introduce into *E.coli* will make it a pathogen. We will introduce it on a plasmid or phage that cannot be transferred to other strains and we will weaken the *E.coli* recipient so that it can not survive outside of the laboratory and we will carry out all these experiments under strict conditions designed to prevent the infection of lab workers by the organism. Some of the systems of biological containment were extremely elegant and that also aided their acceptance. What no-one realised at the time was that this acceptance of worst case scenarios without any justification would forever enshrine these possibilities in the psyche of many members of the public including our political masters.

The conference concluded that the moratorium should be lifted but that future work with recombinant DNA should be carried out in accordance with guidelines for biological and physical containment being produced by NIH. In Australia the academy appointed a standing committee on recombinant DNA (ASCORD) to establish a set of Guidelines, collect and disseminate information in this field, review research proposals and recommend appropriate conditions and liaise with national committees of other countries. Professor Gordon Ada was chairman. Although compliance with the guidelines which were published in 1976, was voluntary, the committee quickly established agreement with the heads of Universities, Research Institutes, CSIRO, ARGC and NHMRC that they would enforce compliance with the guidelines. Conditions stipulated in the guidelines were modified towards a more relaxed stringency in '78, '79 and '80 as new information became available.

In 1979/80 the Council of the Academy set up a new committee under the chairmanship of Professor Frank Fenner to prepare an authoritative report on all aspects of recombinant DNA research. Nancy Millis was an important member of that committee chosen for her acknowledged expertise in applied Microbiology and the interface between Academia and Industry and also Agriculture.

The committee produced a report entitled Recombinant DNA: An Australian Perspective. The main recommendation of this report was that the Federal Government should set up a new surveillance committee with a scientific subcommittee to oversee developments in this area.

It is worth noting that the report also states "Early concerns about conjectured hazards to human health that might be associated with recombinant DNA research have proved to have been misplaced"

The need for a new Federal Government committee arose (a) because some believed the entry of industry into this area may require a committee with more clout than ASCORD and (b) because having failed to obtain financial support from the government of about $10,000 for secretarial support for ASCORD, it was believed to be appropriate for the government to take over.

The new committee had a new acronym RDMC (Recombinant DNA Monitoring Committee). Its new chairperson was Professor Nancy Millis and for the next five years it worked hard at overseeing developments in this area, revising the *Guidelines for Small Scale Work* on three occasions, producing a set of *Guidelines for Large Scale Work* and another for the planned release of *Live Organisms Modified by Recombinant DNA*. The production of these guidelines required a great deal of negotiation and careful consideration in order to achieve regulations that made sense and that would be accepted and acted on by all those involved with this work. Nancy had played a very important role during these developments not only as an excellent chair of the committee but as someone able to drive the various developments and establish a general respect for the committee and the task that it had to perform. As suggested in the Fenner report, five years after its establishment a further review was produced. This report recommended continued monitoring to deal with some potential hazards and with new systems that were constantly being introduced. However it should also be noted that amongst its conclusions were (a) The majority of experiments using the recombinant DNA technique in Australia are of very low risk (b) In the case of those experiments with potential risks, the containment specified by the Guidelines provides safe working arrangements.

In response to this report, and after dragging the chain for a couple of years, the government set up a new committee Genetic Manipulation Advisory Committee (GMAC) again with Professor Nancy Millis as Chair in 1988. This committee and its four subcommittees, the Scientific Subcommittee, the

Planned Release Subcommittee, the Large Scale Subcommittee and the Public Liaison Subcommittee continued to oversee and offer advice on work involving genetic manipulation for the next 14 years, after which its activities were taken over by the new Office of the Gene Regulator (OGTR). During this period Nancy worked tirelessly as Chair of the main committee and a member of each of the subcommittees and as a spokesperson interacting with the media, institutional biosafety committees, and state and government bodies.

The main committee was now quite large and contained some members who were there to represent the interests of different government departments, which meant that often the free exchange of views had to first uncover all the hidden agendas that came uninvited to the meetings. Nancy handled all this with remarkable patience and firmness, demonstrating also a sharpness of wit that dissuaded most from pursuing hypotheticals that strayed too far from the acknowledged facts. The committee was kept focused on the task at hand and rationality spiced with a little humour provided the means for resolving most of the committee's disputes. To give you some idea of the extensive activities undertaken by Nancy on behalf of the committee I would like to quote from her 1996/97 report.

> "In the area of public communication, I have had the opportunity to speak to reporters for the national daily papers and the rural press, as well as to a number of talk-back interviewers for radio and Late Night Live. I have addressed a wide variety of audiences from children at school to undergraduates, social clubs and farmers organisations. Specialist lectures were presented to an international conference on wood technology as well as to Australian plant biotechnologists. Extensive discussions were held with a delegation from the Phillipines who were investigating options for a regulatory system for genetic manipulation in their country. There was considerable favourable comment on the Australian model."

In 1990 the government set up a House of Representatives Standing Committee to "identify and report on any national issues unique to the contained development and use of genetically manipulated organisms and their release into the environment; and inquire into and report upon the adequacy of the current arrangements, and advise on future desirable legislative frameworks for the regulation of the contained development and use of genetically manipulated organisms, and their release into the environment, including imported material."

The committee called for public submissions, held public hearings and produced a report entitled *The threat or the glory* in February 1992. Although this detailed report failed to identify any real hazards associated with genetic manipulation or point to any major disasters arising from 17 years of active research in this area, it nevertheless recommended that observance of the GMAC guidelines should be made mandatory. Because of our Federal system of government it took another ten years before a mechanism to implement this recommendation was agreed on. In 1999 the Interim Office of Gene Technology was established.

The Interim Office of the Gene Technology Regulator (IOGTR)

The IOGTR was established as a branch of the Therapeutic Goods Administration within the Commonwealth Department of Health and Aged Care in May 1999.

The decision to establish the IOGTR followed the 1999 Federal Budget decisions to:

- Establish Biotechnology Australia to coor-dinate the Commonwealth's non-regulatory activities in biotechnology; and
- Establish a new national regulatory framework, including an independent regulator, by 3 January 2001.

Need for a new national regulatory system

The GMAC and its predecessors have provided scientific advice regarding any risks posed by the application of gene technology and how such risks should be managed for the past 25 years. Experience with this system indicates that organisations dealing with GMOs have maintained a high level of compliance with the GMAC recommendations.

The major weaknesses of the existing system relate to the fact that, as an administrative system, there is:

- insufficient capacity for independent legally enforceable auditing and monitoring;
- insufficient capacity for the imposition of penalties or other action in the event of a breach; and

- inadequate transparency of decision making, including terms of statutory time frames and obligations.

These problems under the current voluntary system will be addressed and overcome by the implementation of a comprehensive, transparent and accountable regulatory system, involving the enactment of legislation in each State and Territory, and by the Commonwealth.

Eventually the bill was passed and the office of the gene technology regulator was established with three new committees, Gene Technology Technical Advisory Committee (GTTAC), Gene Technology Consultative Committee (GTCC) and Gene Technology Ethics Committee (GTEC). When GMAC was closed down in 2001 Nancy did not offer herself for election to the new system.

As an aside one of the reasons offered for the new development by government was to ensure an efficient and cost effective approach to the regulation of gene technology. ASCORD ran for five years requiring only some secretarial assistance, RDMC had an initial budget of about $80,000 and may have extended to about $200,000. GMAC ran for about fifteen years on an annual budget of between $300,000 and $400,000. The current annual budget for the OGTR is approximately $8,000,000.

Thank goodness for Nancy Millis and all her hard work between 1980 and 2001.