Discovery, Validation and Commercialisation of DNA Markers in Beef CRC's pipeline

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6 August 2008

Background
Beef CRC is a third-term CRC that commenced operations in July 2005 and builds on two earlier, very successful 7-year terms. It is a collaborative venture between industry and research partner organizations from Australia, New Zealand, USA, Canada and Korea, with associate partners from Ireland, France and South Africa. Centre research is focused on four beef industry priority issues (high quality beef; feed efficiency; adaptation and cattle welfare; and improved reproductive performance) to capture unique opportunities for Australia through world-class genetics and genomics research and accelerated adoption of beef industry technologies to improve profitability, productivity, animal welfare and responsible resource use of Australian beef businesses.

The CRC is targeting an additional 1.5% p.a. increase in gross revenue of the Australian beef industry, estimated at $179 million per annum from 2012, with total expected benefits of the new CRC research being more than $2 billion over 25 years.

New CRC research is focused on *'Gene Discovery and Expression'* to equip Australia for precision cattle breeding and management for quality, efficiency and profitability, using emerging genetic technologies to:

- Improve the capacity to deliver high quality beef to Australia's global markets using cattle of known genetic merit for exacting specifications, without compromising cattle welfare or the environment.
- Enhance beef yield and herd reproductive efficiency, improve efficiency of resource use, reduce production costs, minimise methane emissions and avoid chemical and antibiotic residues through precise application of knowledge about the genes controlling these attributes in cattle, their rumen microorganisms and in parasites that affect cattle productivity.
- Ensure Australia is the number one supplier of beef to meet the growing demand by neighbouring Asian countries to 2020.

Since its inception in July 2005, Beef CRC has initiated a number of new research and industry delivery activities that will potentially impact in a major way on how the beef industry uses DNA technologies in future. These are described briefly below.

"Gene Discovery"
In its third-term, Beef CRC's core business is "gene discovery", which simply means finding genes or DNA markers that are associated with economically important attributes in cattle, developing diagnostic tests for them and effectively delivering those tests to industry so all sectors of industry can benefit from their use.

The aim is to increase the profitability and competitiveness of the Australian and New Zealand beef industries by performing genome-wide association studies (GWAS) using SNP (Single Nucleotide Polymorphism) panels in conjunction with "phenotypes" (accurate measures of very expensive- or difficult-to-measure economically important productive and adaptive traits in thousands of specifically generated, fully-pedigreed cattle) to discover, validate and commercialise DNA markers associated with these traits.

Using GWAS, Beef CRC is aiming to deliver DNA tests that account for up to 50% of the genetic variation for each economically important trait. Specific traits being targeted by Beef CRC include:

- Tenderness; marbling and fat distribution; retail yield percentage; and beef palatability;
- Traits associated with efficient feed utilisation (weight and growth rate, feed intake, feed conversion ratio and net feed intake);
- Adaptation and cattle welfare (resistance to ticks, worms, heat stress and other stressors of tropical and sub-tropical environments; African horn and scur genes to promote breeding for polledness particularly in tropically adapted breeds); and
- Female reproductive performance (particularly age at puberty; post-partum re-conception and lifetime reproduction).

DNA tests for these traits will ultimately be used to identify the best breeding animals for seedstock and multiplier herds, to allocate animals to mating groups (e.g. AI or ET programs or nominate bulls to be joined to particular females to maximise genetic gains etc), to draft animals to best meet particular market specifications (e.g. long- vs. short-fed feedlot vs. pasture finishing systems) and also to underpin the use of decision support and other systems such as Meat Standards Australia. This vision of how the markers will be used over the next decade and beyond will be presented at this Forum by Professor Mike Goddard.

But before industry gets to that stage, there are a number of issues that need to be addressed by the research community, to ensure industry has the confidence it needs in both the value and cost-effectiveness of the technology.

Impacts of rapidly-changing technology

Since Beef CRC commenced in mid-2005, the bovine genome sequence has been delivered freely into the public domain (in 2006) and large panels of SNPs have become commercially available. Their availability has totally changed the way Beef CRC now undertakes its research.

Initially Beef CRC expected to deliver 5-10 DNA markers for each economically important trait, with those markers collectively accounting for around 50% of genetic variation for the trait. However with the availability of whole genome scans based initially on 10,000 SNPs and now on 50,000 SNPs, it is clear that very few DNA markers of large effect will be discovered. Rather, CRC scientists have literally found hundreds of DNA markers associated with the traits of interest, though each one of those markers has a relatively small size of effect. Not all these markers will be commercialised, but it is likely the CRC will commercialise perhaps hundreds of DNA markers by 2012.

Currently, discovery of DNA markers is well ahead of schedule. But validation of those markers in totally new cattle populations is proving more difficult, we believe because a denser SNP panel is needed. Until a panel of around 200,000 or 300,000 SNPs is available, it is most likely that Beef CRC will deliver markers that are most suited for use within breed types (e.g. British, Brahman and tropically adapted composites) rather than across breeds.

Instead of delivering commercial markers on a marker-by-marker basis as occurred in the past, Beef CRC will in future deliver panels of SNPs associated with one or more economically important traits. The aim is to find enough DNA markers to explain up to 50% of the genetic variation for each trait and deliver the markers collectively as panels of markers, thereby delivering significant potential economic impact in industry herds.

In 2006 and 2007, Beef CRC's gene discovery research used data from the Affymetrix 10,000 SNP panel. In mid-2007 though, the CRC's gene discovery research was put on hold pending the availability of the new "Infinium" assay (Bovine SNP50) from Illumina, which screens for about 54,000 different SNPs for each animal being tested. The new SNP panels will potentially speed up the rate of discovery, improve the quality of DNA tests and considerably reduce the cost of individual DNA tests.

In June 2008, the CRC received its first genotypes from Illumina for the 50+K SNPs on ~2,600 animals that had been carefully selected by Beef CRC scientists for all traits of interest to Beef CRC. Data analysis is now underway, with timeframes and processes for discovery, confirmation, validation and commercialisation of DNA markers derived from these analyses outlined below.

International Genomics Collaborations

In January 2008, a workshop was held in San Diego, USA between Beef CRC, the US Department of Agriculture (USDA), US National Beef Cattle Evaluation Consortium (NBCEC), US Beef Improvement Federation (BIF), the Canadian Universities of Alberta and Guelph and AgResearch New Zealand to scope areas of mutual public research interest around DNA marker discovery, validation, and delivery to industry for beef cattle, to determine whether opportunities existed for new international collaborations that would speed up or enhance the quality of diagnostic DNA tests for use by the beef industries of the collaborating countries, and if those opportunities exist, to determine how best they could be captured.

Five major areas of potential research collaboration were identified and formally endorsed by the Beef CRC and MLA Boards in March 2008. They are:

- Discovery of markers and their validation;
- Validation of existing markers;
- Coordinated resource populations;
- Methods for delivering DNA markers to industry; and
- Development of larger SNP chips.

1. <u>Discovery of markers and their validation</u>

This is the area with the greatest benefit to collaborators because it will lead to better panels of markers for commercialisation and use by industry. The availability of the 50k SNP chip from Illumina is an opportunity to greatly improve the power to discover useful markers. For the foreseeable future, GWAS will be undertaken using the same Illumina 50k chip across all countries (i.e. all research groups will be using the same panel of markers that are already in the public domain). It is proposed that Australia, USA and Canada will each undertake an independent GWAS ***(discovery phase)*** on ~1,000 animals for carcase and meat quality and feed efficiency in steers. USA and Australia will collaborate separately to discover DNA markers associated with female reproductive performance. New Zealand does not plan to undertake GWAS over the next 1-2 years, but could provide cattle resources to assist in the validation of markers.

Once the independent GWAS are complete, the collaborating groups will meet to share the results and agree on a common panel of promising markers. Ideally, those promising markers will then be confirmed ***(confirmation phase)*** by each of the countries in a different ~1,000 animals each, using the 50k assay if economical, and funds are available.

Thereafter prediction equations for use in each country will be developed based on these first two steps. A list of all markers that occur in any of the prediction equations will be drawn up and used in the ***industry validation phase*** by genotyping up to 5,000 animals for this list of markers to provide an unbiased estimate of the correlation between prediction and breeding value or phenotype. This will also allow validation of any Genotype x Environment interactions (GxE) at the SNP level discovered in the first two phases.

Traits included in the collaborations will be those traits common across countries. Traits available only to one organisation or one country are exempt from the collaboration.

2. <u>Across-country validation of existing markers</u>
Public or private research has yielded a number of markers of potential value to the beef industry. The value of these markers in differing production/marketing environments across countries needs to be confirmed for the common good. Sharing cattle phenotypic resources across countries will most efficiently accomplish this goal. This will be done by the group with the marker IP genotyping cattle belonging to the group with the cattle phenotypes and DNA. Results will be analysed by the group with the cattle and made available to the other party. The results would be made public. No transfer of IP would occur.

3. <u>Future resource populations</u>
A major realisation by research groups globally from the availability of the bovine genome sequence was that discovery and validation of DNA markers with relatively small sizes of effect requires many more animals with accurate phenotypes and matching DNA than are currently available to any one group, including Beef CRC, although Beef CRC still leads the world with the size and scope of its bovine phenotypic databases. Although existing resources are sufficient to conduct initial GWAS, they are insufficient for validation for many traits. And for economically important traits that are difficult or expensive to measure (e.g., efficiency of feed utilisation, female fertility and disease resistance), they may not even be sufficient for marker discovery and confirmation.

With rapid developments in genomics, the critical bottleneck in making use of these technologies is the lack of deeply phenotyped populations. International collaboration is most likely to overcome this gap and foster synergies previously not possible (for example to investigate the nature and magnitude of GxE interactions). Each country will aim to establish fully pedigreed diverse (ideally multiple breed) cattle populations relevant to their country, with a good sampling of animals from within each breed. Those cattle populations will then be measured for as many industry-relevant traits as possible and DNA collected and stored from every animal in the population. A common breed or breeds will be used across countries to provide linkages. Trait definition will be very important as common measurement protocols will need to be applied to evaluate GxE interactions across-countries.

4. <u>Delivery of DNA markers to industry</u>
Results of the research in (1) and (2) above will be published. This might mean that enough information is in the public domain that commercial companies can provide a service without any agreement from the organisations that conducted the research. However, it is likely there will still be some benefit to commercialisers in obtaining information from the research organisations (for example, the exact prediction equation for each trait). This information could be provided by a licence, trade secret or simple Material Transfer Agreement approach. The aim would be to ensure that genotypes derived from commercial testing are returned to the “national database” in each country to allow generation of marker-assisted breeding values or commercial values.

One product being targeted by the international collaborators is a panel of about 1500 SNPs that covers a range of traits. If it was available for $US45 it would be attractive for stud cattle. Another product being targeted is smaller panels of markers (e.g. 200 SNP) for commercial cattle for US$10 per animal. In the longer term, the aim of technology development research is to reduce the cost of the larger panel sufficiently to allow routine testing of all calves in a herd early in life (e.g. at branding), so selection and management of individual animals for breeding and commercial purposes throughout their lives is based on knowledge of the different forms of genes they carry.

The value of markers to cattle breeders will be maximized if they are used to calculate EBVs comparable to existing BREEDPLAN EBVs and also comparable across companies providing the markers. This implies national databases that contain phenotypes and genotypes and are used to estimate prediction equations and to calculate EBVs. Under this model, genotypes derived from DNA testing simply provide additional data from which to estimate breeding values and commercial values. The international partners will collaborate in research on methods to develop prediction equations and use them to calculate EBVs.

5. Development of a larger SNP chip

It is likely the current 50K SNP chip will not provide dense enough SNPs to generate equations that predict breeding value across breeds. Efforts are therefore underway through the international collaborations to enhance the 50k SNP panel to around 200-300k.

Aim of the international genomics collaborations

The agreed aim of the international genomics collaborations is entirely to provide greater benefits to the beef industries of the collaborating countries (i.e. decisions were made on the basis of value-add to industry, not on potential returns to the research provider organisations or the commercialising companies). As a result there are unlikely to be patent claims over the traits that are researched collaboratively. Traits available only to one organisation or country are exempt from the collaboration and could still be exclusively licensed. Causative mutations or candidate genes are also exempt from this type of approach, as they would most likely be identified by individual research groups. Once the collaborative model is established, the collaborations will be opened to other participants or countries, with the proviso the other participants can work with the existing model.

Impact of the international genomics collaborations

Discovery and confirmation of new markers over the next 12-36 months will be achieved by simultaneously genotyping 6,000 animals for carcase and meat quality and feed efficiency attributes (~2,000 each from USA, Canada and Australia) and another ~4,000 animals for female reproductive performance (across USA and Australia) and by validating final marker panels across countries in several thousand more totally independent animals. By comparing results of the much larger numbers of genotypes and agreeing on confirmation of a common panel of markers, the impact will be to:

i) significantly increase the accuracy of the estimated markers effects and the accuracy with which breeding values can be estimated by a panel of markers;
ii) at least halve the time it would otherwise take to complete these phases and have sufficient faith that the results are useful to industry; and
iii) provide additional information about the value of the markers in different environments that would not otherwise be available to any country in the absence of the collaboration.

Independent validation of existing markers or those discovered outside this collaboration by sharing phenotypes across countries will lead to more accurate estimates of their effects and better use by industry.

New cattle resources will help to close the “phenotype gap” especially for traits where current resources are inadequate (e.g. feed efficiency and female reproductive traits).

Shared research on methodology and industry structure to deliver marker assisted EBVs will lead to adoption of better and more uniform methods in all countries.

A 200-300k SNP chip will lead to panels of markers that can be used to predict breeding value across breeds rather than the breed types currently being targeted by Beef CRC.

Beef CRC’s Preferred Commercialisation Model

Beef CRC has also been examining a range of options by which it could “commercialise” (where “commercialise” implies delivery and utilisation by industry) DNA markers developed and validated for industry use by Beef CRC researchers. It developed an entirely new model for commercialising DNA markers aimed at increasing the level of uptake of DNA marker technologies by industry. As the architect of this model, Professor Goddard will briefly describe it during this Forum.

In February 2007, the CRC Board endorsed the new commercialisation model and authorised its further development and refinement in conjunction with MLA, BREEDPLAN, breed societies and other relevant beef industry organisations to maximise uptake of genetic technologies for the benefit of the Australian and New Zealand industries, generate competition and responsiveness to commercial drivers at a number of levels and promote collaboration across beef industry sectors nationally and internationally.

In March 2008, an independently-facilitated workshop was held in Armidale to provide industry and research providers with a first-hand opportunity to examine the CRC’s commercialisation model, to identify problems with it and potential solutions to those problems and to recommend to the CRC the next steps in implementing the refined commercialisation model.

Following the workshop, the Boards of MLA and Beef CRC formed a DNA marker commercialisation Working Committee and a Board-level Steering Committee to oversight it. Progress achieved by this Committee to date is described at this Forum by Dr Rob Banks.

SmartGene for Beef Project

Beef CRC’s preferred commercialisation model requires the use of Marker-Assisted EBVs (MA-EBVs). Beef CRC is therefore a key partner in the “SmartGene for Beef” project that will integrate BREEDPLAN EBVs and DNA diagnostic tests into a single genetic tool known as MA-EBVs. Progress in the SmartGene Project is described at this Forum by Mr Don Nicol and Dr Hans Graser.

Standards Prior to Commercial Release of Beef CRC’s DNA markers

Beef CRC already has a small number of DNA markers for different traits that have been validated within particular breeds or breed types. However these markers have not yet been released to industry because they do not meet Beef CRC’s standards or principles against which commercial release is assessed. These standards include:

- The markers have been discovered in at least 1,000 appropriately-recorded animals. The individual and combined effects of the SNPs are confirmed in another 1,000 animals that do not include the original (discovery) animals. The false discovery rate is calculated and reported. The markers are further validated in up to another 5,000 totally independent industry-relevant animals. At the validation stage, the SNPs are also evaluated for antagonisms with other productive and adaptive attributes and the nature and magnitude of any antagonisms are also reported where possible. The Beef CRC’s Underpinning Science Committee reviews results of all phases of discovery, confirmation and validation and make recommendations on industry release or otherwise to the CRC Board. An implication of this model is that Beef CRC retains control of the discovery and validation processes to a greater extent than occurred in the past. This also means that Beef CRC funds a greater share of the costs than occurred in earlier models of DNA marker commercialisation.
- To avoid confusion in industry through the release of DNA markers that may account for only a small proportion of genetic variation for each individual trait, Beef CRC is planning not to release the first suite of its markers for any trait until a minimum amount of genetic variation for that trait is accounted for by the markers (e.g. 15-20%) based on the assumption that a statistically significant correlation between the DNA marker(s) and the phenotype of interest can be detected. Using “back-of-the-envelope” calculations, this assumes a correlation of 0.4 between the breeding value and the

DNA marker(s) for a trait with a heritability of 0.25. Some adjustment for the economic weighting of the particular trait may be applied to allow an earlier release of markers for traits with a very high economic weighting, but the new standards will be documented by Beef CRC at the time of commercial release.

- Wherever possible, Beef CRC will not release its markers commercially until the extent of antagonisms is known. By way of example, Beef CRC already has a small panel of about ten DNA markers that are associated with age at puberty in Brahman and tropical composite cattle. However before the tests are released to industry, Beef CRC wants to be sure that reducing the age of puberty will not compromise the cow or the calf's survival or the future breeding ability of the animal. This requires additional information (still being collected) on later-life reproductive performance of these cattle.
- Beef CRC is considering releasing its new DNA markers under a trademark that provides some form of guarantee of efficacy and value of the markers to industry if they are used in the manner recommended by Beef CRC.
- To promote integration of DNA markers and other industry schemes, as well as transparency of CRC operations, the Beef CRC's commercialisation model promotes the use of routine reporting of size of effect of individual and collective markers and accuracy of MA-EBVs through schemes such as BREEDPLAN. This could see for example, the routine reporting of the impact of the markers in industry herds each time a new BREEDPLAN analysis is undertaken.
- Beef CRC regards such routine reporting of the impact of the markers in industry herds as more preferable than the independent validation of DNA markers as currently applied by the US NBCEC system, mainly because of the very large costs (both of scientists' time as well as financial costs) of independent validation and the need to fund and develop even greater animal resources than are currently available to the research partners through the international genomics collaborations.
- Possible licensing and accreditation of genotyping laboratories authorized to use Beef CRC's DNA markers.

Best-case Timeframes for Delivery of CRC's DNA markers

Beef CRC is currently continuing to validate DNA markers for a number of traits arising from its earlier 10K SNP panel. Those markers are not validating as well as originally anticipated, primarily due to the relatively small numbers of animals used in the discovery populations (ranging from ~200 to ~600) and the uneven and often large gaps between DNA markers along the bovine chromosomes. Those difficulties have been addressed with the much larger discovery and confirmation populations in GWAS using the Illumina 50K panel. Nevertheless, it is still possible, though perhaps unlikely, that DNA markers arising from the 10K panel could meet Beef CRC's commercialisation standards and be delivered to industry before results from the 50K panel are available.

<u>**Best-case**</u> scenario timeframes that apply to the 50K panel research are:

June 2008	Genotypes received from Illumina by each international research group.
August 2008	Beef CRC Underpinning Science Committee meets to evaluate the several independent analyses (across CRC programs) of the 50K WGAS data and to make recommendations on further or different analyses etc.
Oct 2008	The international collaborators meet to share results of their independent (USA, Canada, Australia) analyses of WGAS data using the Illumina 50K panel and to agree on the DNA markers that will be independently confirmed by each of the countries.
Oct 2008 – April 2009	Each of the countries undertakes further independent genotyping and data analyses to confirm the selected DNA markers within their own countries
April 2009	The international collaborators meet to share the results of their

	confirmation studies and agree on the DNA markers that will be independently and collectively confirmed by each of the countries and also across countries. The two collaborating commercial companies (Merial and Pfizer) will participate in this meeting, which will also scope the extent of new data analyses to occur across countries to estimate the size of GxE interactions and to test for antagonisms that exist between markers for different traits.
April 2009 – Oct 2009	Each of the countries undertakes further genotyping and data analyses to validate the selected DNA markers in their own countries using industry datasets where possible. A combined (across-country) data analysis will also investigate the nature and magnitude of GxE interactions at the DNA marker level. During this period the commercial companies will develop and test commercial assays to allow release of the marker-based tests to industry once the markers have been independently confirmed.
Oct-Nov 2009	The international collaborators, commercial companies and industry collaborators meet to share the results of the validation studies and studies to identify antagonisms between markers and to detect GxE interactions that impact across countries. At this stage the project will have evaluated the SNP panel(s) and equations to predict performance of cattle for economically important traits within and across Australian, US and Canadian environments and will agree on the best methods of delivering the project outcomes to the beef industries in all countries. Direct industry involvement in the validation process will provide a unique opportunity to trial the new markers with leading industry partners, as well as educating them about the best use of the marker panels for their particular enterprises.
Early 2010	A panel of novel DNA markers with strong industry validation and knowledge about which markers have similar effects in Australia and North America and which markers need to be used specifically for Australian or North American production systems will be commercially available from two commercial companies. It is highly likely that these panels of markers will have specific application to particular breeds or breed groups (e.g. British, Brahman and tropically adapted composites) rather than applying across all breeds.

These best-case scenario timeframes will necessarily be deferred if difficulties arise with:

- the standards of quality assurance around the genotypes (believed to be a much reduced risk relative to the earlier 10K panel data because of recent rapid advances in technology development);
- methods of analysis of combined phenotypes and genotypes (Beef CRC spent considerable time over the past year or so while waiting for the 50K panel investigating these methods and is hopeful any difficulties in this area have been identified and a solution to overcome them found); and/or
- the number of animals available for confirmation and validation are insufficient – this is potentially the greatest risk to industry commercialisation, particularly for traits such as feed efficiency and female reproductive performance and particularly if the size and magnitude of GxE interactions are sufficiently large to prohibit the use of international animal resources for confirmation and validation.

The urgent need for an Australian "Beef Information Nucleus"

The current lack of phenotypes for some hard-to-measure traits, together with the likelihood that industry will stop recording altogether if genomic selection proves to be viable, suggests a very urgent need for Australia to establish a "Beef Information Nucleus" that builds on the

CRCI, II and III and other industry databases (e.g. BREEDPLAN, MSA, NLIS). This issue is being directly addressed by the DNA marker commercialisation working group, with the aim of having new breeding programs underway in the next breeding season if at all possible.

Beef CRC's short-term focus on delivery of markers to industry

Beef CRC has made a deliberate decision to focus its bovine genomics research efforts over the next year or so almost exclusively on discovery, confirmation and validation of panels of SNPs from the Illumina 50K panel through the international genomics collaborations. The only Beef CRC research over this period aimed specifically at identifying candidate genes will be undertaken through post-graduate student research projects.

This is because Beef CRC recognises a need to very urgently deliver DNA tests that industry can use, as soon as that can possibly be achieved. Discovery of candidate genes will ultimately improve the accuracy and the use of DNA tests, particularly for application across breed types (as well as giving our Beef CRC researchers a higher international scientific standing through prestigious scientific publications). However candidate genes are likely to take longer to deliver and will require considerably more resources than panels of SNPs associated with the particular traits of interest.

Hence Beef CRC will not discontinue its candidate gene research totally, particularly over subsequent years. But in the short-term, our goal is very strongly and very specifically on delivery of panels of SNPs associated with a range of economically important productive and adaptive traits required to value-add the Australian and New Zealand beef industries as soon as that can feasibly be achieved.

Glossary of Terms

Abbreviation	Definition
ABRI	Agricultural Business Research Institute - based at UNE, ABRI provides a wide range of agribusiness information services, including delivery of BREEDPLAN
AGBU	Animal Genetics and Breeding Unit - based at University of New England (UNE), AGBU is a joint venture of UNE and NSW Department of Primary Industries
allele	One variant of a gene
bioinformatics	The computational and mathematical backgrounds to modern biology and genomics; bioinformaticians can be database specialists, statisticians and/or computer programmers
Bos indicus	Breeds of cattle originating from the Indian sub-continent; sometimes called Zebu breeds and includes Brahman and Sahiwal.
Bos taurus	Temperate British and European breeds of cattle e.g. Hereford, Angus, Charolais
BREEDPLAN	Australian's beef genetic evaluation system that estimates the genetic merit of animals for economically important traits
candidate gene	Gene that is thought to be directly involved in a particular cell's, tissue's or animal's characteristics.
confirmation	Confirming the significance and existence of an association between a DNA marker and an economically important trait in a totally independent cattle population. Beef CRC will confirm in at least 1,000 animals that are measured for the trait of interest and that are totally unrelated to the animals in the discovery population.
CRC	Cooperative Research Centre
CSIRO	Commonwealth Scientific and Industrial Research Organisation
discovery	The discovery phase of DNA markers occurs when an association between a DNA marker and an economically important trait is first identified in a population of cattle that has been accurately measured for the trait of interest. Beef CRC will undertake its discovery phase in at least 1,000 animals.
DNA	Deoxyribonucleic acid - contains the genetic information that is passed from one generation of animals to the next. It is a long double-stranded molecule made up of nucleotides A,T, G and C.
DNA fingerprinting	A method of determining the parentage of animals using DNA extracted from samples such as blood or tissue obtained from the animals. Each animal has a unique genetic makeup (DNA fingerprint). By comparing the DNA fingerprint of progeny with potential parents, it is possible to determine actual parentage.
DNA marker	DNA markers - stretches of DNA closely linked to the genes that underlie an economically important trait. They are used to detect different forms of genes. Tests based on DNA markers are used to predict the breeding performance (genotype) or the lifetime performance (phenotype) of animals for the particular traits. They use a wide range of tissue samples such as blood, skin, hair or muscle collected at any age after conception.
EBV	Estimated Breeding Value – an estimate of an animal's genetic value for measurable traits such as growth rate, meat tenderness etc. EBVs are calculated from the measured performance of animals and their close relatives compared to other animals measured in an identical way.

Abbreviation	Definition
GxE	Genotype x environment interaction - GxE interactions occur when a breed or DNA marker (genotype) ranks differently in different environments e.g. British breed cattle grow well but *Bos indicus* breeds grow relatively poorly in temperate environments. In tropical environments, where levels of environmental stress are high, better adapted *Bos indicus* breeds grow much faster than British breeds. This same scenario could occur when DNA markers rank differently in different environments.
gene	The basic unit of heredity. Each gene has two or more forms which can be the same or different.
gene expression	The process by which a gene code is transcribed into messenger RNA and exported to the nucleus for translation into proteins. Beef CRC uses this term to describe research aimed at understanding the function of the genes associated with expression of economically important genes and identifying non-genetic approaches (for example, changed management practices, modified diets, water medications, vaccines etc) that can be used to 'switch on' favourable genes or 'switch off' unfavourable genes in cattle where the form of the gene has been identified, so the cattle can be individually managed to better comply with market specifications.
gene marker	See DNA marker.
genetic correlation	Extent to which two attributes are determined by the same genes. Genetic correlations range from -1.0 to +1.0. A high negative relationship means an increase in one trait leads to a decrease in the other; a high positive relationship indicates an increase in one trait leads to an increase in the other trait. A low or zero correlation indicates there is little genetic relationship between the two traits.
genomic selection	Simultaneous selection for hundreds or thousands of DNA markers covering the entire bovine genome with the markers alone accounting for a significant proportion of the targeted genetic variation (i.e. selection will be based only on knowledge of the markers in the absence of pedigree and phenotypic selection as required to calculate MA-EBVs)
genotype	Genetic makeup of an animal, but is also sometimes used to indicate the breed composition of an animal.
heritability	Proportion of variation for a measurable trait attributable to variation in genetic factors and is therefore passed on to offspring. Heritabilities (h^2) range from 0.0 to 1.0. A $h^2 = 0$ means the trait is not controlled by genetic factors and $h^2 = 1.0$ means the trait is under total genetic control. In general, traits that have $h^2 > 0.4$ are considered to be highly heritable.
in vitro	Literally "in glass" and it refers to experiments that mimic life in a test tube or by tissue culture.
in vivo	Examining the reactions of life by experimentation with the living animal.
link sire	To validly compare the performance of animals across herds, it is necessary for those herds to be genetically linked. The usual method for linking these herds is to use a common (or link) sire in all herds where performance of animals is to be compared.
microarray	An ordered array of thousands of gene probes, printed onto glass slides.
microsatellite	A genetic marker that is highly polymorphic, that is it has many alleles.
MA-EBV	Marker-assisted EBV – an estimated breeding value calculated using pedigrees and phenotypes for direct and indirect selection traits) and also DNA marker information

Abbreviation	Definition
MLA	Meat and Livestock Australia a beef-industry owned company with responsibility for red meat industry R&D and for promotion and marketing of red meat within Australia and internationally
molecular techniques	Laboratory procedures that allow a researcher to investigate a scientific problem at the level of individual molecules. The term normally refers to nucleic acid techniques but is equally valid for protein techniques.
MSA	Meat Standards Australia, Australia's new meat grading scheme based on guaranteed beef eating quality
NFI	Net Feed Intake - a measure of feed efficiency that refers to variation in feed intake between animals after differences due to weight and growth rate have been accounted for. Low (more negative) NFI is desirable.
phenotype	The appearance, structure or biochemical characteristics of an organism, contrasted against genotype, which refers to sequences within the DNA. In the context of discovery of DNA markers, it means the accurately measured record of an animal for a particular trait of interest.
QTL	Quantitative Trait Loci – stretches of DNA that are closely linked to the genes that underlie an economically important trait (see DNA marker)
Sanga	Adapted *Bos taurus* breeds that evolved in Southern Africa independent of the European *Bos taurus*. They retain the productive attributes of the European *Bos taurus* but have resistance closer to that of the *Bos indicus*.
sequencing	DNA, RNA, protein or oligosaccharide structure determination
SNP	Single nucleotide polymorphism. A polymorphism at a specific base or nucleotide in the DNA sequence. For instance, at a point in the DNA sequence where one allele contains an 'A', another allele contains a 'T'
trait	Attribute or characteristic of animals that can be improved genetically (for example, growth rate, fertility, carcase or meat quality etc.)
UNE	University of New England
USDA	United States Department of Agriculture
validation	Validation of DNA markers occurs after the discovery and confirmation phases, when prediction equations from those phases are tested independently in another set of cattle that have been measured for the trait. Where possible, Beef CRC plans to use at least 5,000 animals to validate the prediction equations to provide an unbiased estimate of the correlation between prediction and breeding value or phenotype.