PROGRESS IN DEVELOPMENT AND IMPLEMENTATION OF A STRATEGY FOR COMMERCIALISATION OF DNA MARKER TECHNOLOGY FOR THE AUSTRALIAN BEEF INDUSRTY

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SUMMARY

This paper outlines the strategy which is being implemented to support commercialisation of DNA technologies for the Australian beef industry. The strategy includes a national database for phenotypic and genotypic information, information nucleus population for validation and research, integration of DNA results with BREEDPLAN evaluations and a close cooperation between commercial companies and other industry players. Various risks of this strategy and their control are discussed.

INTRODUCTION

Genotyping technologies have evolved rapidly over the last 10-15 years, and offer significant potential benefits for the beef (and other) industries. Australian research effort for this technology has a focus within the CRC for Beef Genetic Technologies, with significant activity within both the public and private sectors. The Beef CRC developed a strategy for the commercialisation of its DNA marker technology, in consultation with industry, research, development & extension (RDE) partners and providers, and with service companies. That strategy has four core elements:

- that information on the value of marker tests of various sorts, ranging from single genes or single nucleotide polymorphisms (SNPs) through to multi-snp panels or whole genome evaluations, should be made public,
- that industry will need an independent reference population to support the evaluation of markers,
- that a national database and matching DNA bank will be required to store phenotypes, genotypes and DNA from commercial and seedstock cattle; and
- that where possible, results of marker tests should be integrated within the existing genetic information framework provided by BREEDPLAN.

Recognising that the emerging technologies would require more than the resources of the Beef CRC alone for effective industry implementation, Meat and Livestock Australia (MLA) and Beef CRC agreed in 2008 to work together firstly to determine the feasibility of the proposed strategy, and, subject to that feasibility evaluation, on its implementation. A working party was established initially to consult on the feasibility of the strategy, and more recently to progress implementation. This paper outlines progress being achieved, plans for the immediate future, and briefly discusses some risk considerations.

FEASIBILITY ASSESSMENT

Two dimensions of feasibility assessment were explored: the technical requirements, and the implementation requirements (including longer-term governance).Technical requirements include:

- methods and skills in place to estimate the effects of markers, and
- whether or not methods and software exist for the integration of marker information into BREEDPLAN genetic evaluations.

Both questions were answered by the success of the SmartGene project (Johnston and Graser 2008), where effects of the DNA marker tests derived principally from the CRC program, were estimated for a number of breeds, and for a limited set of markers, integration into marker-enhanced EBVs was achieved (Johnston *et al.* 2008).

A continuing challenge with regard to the integration into EBVs will be the rapid evolution of the DNA tests themselves, and the format of the results. The latter is likely to vary between providers, at least in the short-term.

The SmartGene project included considerable consultation with industry and one genotyping provider, and provided a basis for addressing a second set of questions relating to implementation challenges. These implementation challenges include:

- what infrastructure is to underpin regular estimation of marker effects,
- what incentives exist, or might be established, to encourage integration of marker results with EBVs, and
- whether new governance systems might be required.

It was concluded that the core infrastructure required is of two forms: a) a database which can receive and hold data on ID, pedigree, performance and genotype, and b) suitable reference populations. The Beef CRC I&II research databases provide at least an initial version of the first requirement. It is clear that consolidation and development of the types of genotype and genotype test data that can be stored, will be needed.

Consideration of the requirements for reference population(s) is complicated by the fact that as research proceeds, the effects of or due to individual SNPs have in general become smaller, meaning in broad terms that larger numbers of performance recorded animals will be needed for "validation" or calibration of effects, and further by the fact that considerable differences may exist between populations in terms of allele effect(s) and frequencies.

Not withstanding this complication, a number of industry groups, focussed mainly amongst breed societies, are keen to explore and establish appropriate populations. The challenge will be to fund the necessary populations. The MLA Donor Company mechanism, whereby Commonwealth Government funds can match commercial funds in appropriate projects, was identified as a potential avenue for at least some of the support needed.

Consultation around the issues of engagement and governance suggested that in the short term at least, no specific new regulatory approach is required. However, ongoing consultation will be needed on data transfer and exchange protocols, and how results are reported to industry.

The overall assessment was that the strategy is technically feasible, but that new investment will be required, particularly in phenotypes, and that coordination of information flow and communications will be essential.

PLANS FOR NEXT PHASE IMPLEMENTATION AND INDUSTRY DEVELOPMENTS

From October 2008 to mid-2009, most activities have focussed on developing proposals for establishment of reference populations building on the large industry-based progeny tests in Beef CRCI and II (Upton *et al*. 2001; Burrow and Bindon 2005), and drawing on the model established in the sheep industry known as Information Nucleus (IN) (Banks *et al.* 2006). At the time of writing this paper, one breed-based project proposal for a Beef IN had been submitted to the MLA Donor Company for approval, and four others were in preparation. Each is likely to involve utilisation of 300-500 cows in a mix of stud and commercial herds, with male progeny planned to enter a research feedlot for collection of finishing and processing phase trait data, and female progeny retained for recording reproduction traits. To enhance impact on genetic progress, sires sampled will wherever possible be elite and young. In addition, there has been progress in:

- appointment of a manager for the national database, part of whose role is to consult with data and genotyping providers aiming to ensure smooth and secure data exchange;

- continuing analysis of suitable datasets to provide estimates of effects for various marker tests, and posting of the results obtained to an industry website

SmartGene and Pfizer MVP results have been posted on an Australian results website (http://www.beefcrc.com.au/Aus-Beef-DNA-results), and Igenity to follow, and a common reporting format has been developed with NBCEC in North America (www.nbcec.com).

RISK CONSIDERATIONS

The strategy proposed by the Beef CRC seeks to maximise the benefits for the industry. That strategy carries its own internal risks, faces potential external risks, and its implementation will be within the context of some wider challenges facing the industry. Each of these risks is examined briefly, together with discussion of potential responses.

The main "internal" risk is that no markers (or marker-based tests) will be discovered that offer any real value, expressed as the proportion of genetic variance explained for one or more traits in one or more breeds. Although this risk is considered small, Beef CRC is mitigating this risk by undertaking specific research aimed at understanding reasons for the failure of most existing markers to provide value across breeds, by investing in development of larger SNP panels to overcome the problem and using its international collaborations to share resources and agreeing on common approaches to overcoming problem areas..

The second internal risk is that whatever tools become available are too expensive to be funded within the financial capacity of the Australian beef industry. This reflects the relatively low margins for seedstock operations, the almost complete absence of vertical integration in the industry, and the relatively poor flow of price signals from consumer through the value chain to the breeder. Should this risk become real, industry as a whole will have a serious strategic issue, particularly if beef industries in competitor countries are able to adopt the technology. Careful assessment of the degree of market failure and potential responses using collective funding will be required.

A third internal risk is that availability of marker tests undermines confidence in BREEDPLAN. The CRC's mitigating strategy aims to inform the market by placing full results of objective assessment of marker tests into the public domain and integrating marker data into EBVs. But the second element of the strategy depends on choices made by breeders. Accordingly, clear communication about the value of integration into EBVs is essential.

The fourth internal risk is that the amount of phenotype data required for useful calibration of markers proves to be too large for industry to achieve. This risk will be mitigated through development of denser SNP panels that allow discovery of markers that are closer to the causative mutation and where effects are more consistent across breeds.

There are two external risks. The first is that commercial genotyping companies offer products that have insufficient value for industry or provide a diversity of products with a wide range of claimed attributes, causing confusion in industry. The strategy that has been developed by the working group aims to encourage independent testing of all markers by the companies with information on test results made publicly available. The commercial companies may choose not to use such an approach and hence, industry's use of the independent information will be critical to the success of this strategy.

This approach is regarded as a win-win where industry phenotyping resources are used as a pre-release screening or "validation" step, in a manner analogous to progeny testing of young dairy bulls. This approach reduces risk for both buyers and sellers, but may take some time to evolve.

A second external risk is that the joint effects of R&D provider, industry and commercial company behaviour are inadequate in providing customer protection. In that case, some form of independent regulatory approach may be required ("independent" in this sense meaning independent of industry, with government as the obvious possibility). It would be preferable that this does not become necessary, since introduction of an external regulatory framework would introduce substantial new costs, both financial and time.

Finally, there are wider challenges facing industry, related to the effectiveness with which existing technology is used. There is evidence that the Australian beef industry makes no better use of BLUP technology than its competitors (McDonald 2008), and that this reflects less than optimal data collection coupled with lower than potential sire selection differentials (Johnston 2007). While marker technologies may assist in making genetic improvement easier, this is automatic, since that progress ultimately depends on recording and selection efficiency: if these are not optimised, marker technology could just as easily lead to reduced progress. This risk must be addressed through coordinated and effective extension and training at the seedstock and commercial levels.

The other wider risk is that the combination of accelerating genetic progress using either existing technologies, or those augmented by marker technology, coupled with the potential explosion of DNA-based products and likely new value-chain relationships, will result in a period of heightened confusion and turbulence in the market for genes, resulting in reduced investment effectiveness. In addition, it is very likely that new industry structures will emerge, potentially around co-investment in phenotyping and genotyping, and these will challenge existing ways of delivering genetic evaluation, of delivering genetic material, and of both investing in and managing the industry genetic improvement "system".

The risk of confusion is real, and would be very damaging for the Australian beef industry, since the industry does not in general have large reserves of capital, and needs to accelerate progress in both production efficiency and product quality differentiation in order to maintain or achieve higher prices than competitors in world markets. Minimising this risk from cheaper undifferentiated beef requires effective coordination of effort across all sectors of industry. Finally, the strategy must be flexible enough to allow response to the changing technology.

CONCLUSIONS

The Australian beef industry, along with others, is investing heavily in development and implementation of DNA-based technologies. The strategy developed initially by the Beef CRC for that implementation is now moving out of a feasibility evaluation phase and into implementation. The strategy calls for development and utilisation of new information and infrastructure, and its success will depend in part of wide and effective coordination across industry coupled with capacity for rapid response to evolving technology. The risks around the implementation are manageable but significant. The Australian beef industry seems inevitably to be entering a phase of rapid and potentially valuable evolution, but at the same time one which could lead to great loss if these risks are not managed effectively.

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