Interbull Scientific Advisory Committee (SAC)

Annual report (2007-2008) to the Interbull Steering Committee

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1. INTRODUCTION

Since the 2007 Interbull meeting in Dublin, Ireland, the four SAC members have engaged in e-mail discussions on issues related with the future of (inter)national genetic evaluations. Goddard and Banos met and further discussed during the annual meeting (2008) of the British Society of Animal Science, where Goddard delivered a keynote speech on genomic selection. Banos presented on the same topic at a congress linked to the 50th anniversary of the Italian Brown Swiss Association. Schaeffer worked on a simulation study of genome-wide selection strategies and will make a presentation at the joint Interbull-ICAR session (June 18, 2008).

Discussions among SAC members were dominated by the potential impact of genomic evaluation and selection on animal genetic evaluations, following comments received on the 2007 SAC report and a request from the Interbull Centre.

2. GENOMIC EVALUATION AND SELECTION

2.1. Facts

Following the completion of the Bovine Genome Sequencing Project in August 2006, genome-wide animal genotyping with the use of DNA chip (array) technology is now a reality. Several thousands of bulls are being genotyped across the globe this year[1]. By current farm animal standards, the scale of this application is impressive: at the moment a 54K bovine chip is available[2] meaning that polymorphisms in 54,000 SNP markers are determined for each animal. A new bovine chip, expected to encompass more SNP, is currently under development. Work is in progress in other farm animal species, too, for the development of similar DNA chips.

2.2. Opportunities

The existence of such data opens the door for the calculation of genomic breeding values (GEBV) from the animal DNA profile that can be available at birth (or even before). There is an opportunity to evaluate and select animals early and directly for some breeding goal traits that are otherwise difficult to monitor (e.g. health). Primarily, however, the adoption of GEBV for selection will be economically driven. Theoretical and simulation studies have demonstrated the potential for reduced costs and increased genetic gain.

2.3. Conditions for genomic selection to work

Accuracy of GEBV i.e., its correlation with the true breeding value will be a key concern. At the moment a 0.99 conventional reliability of a proven bull provides the best benchmark.

In order to achieve high accuracy GEBV of bull (and cow) calves, individual SNP and haplotype effects on the various traits of the breeding goal must be properly calculated. This requires an adequate amount of genomic as well as phenotypic data. Simulation work needs to determine the optimal amount and structure of such data.

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[1] http://aipl.arsusda.gov/reference/changes/eval0804.html
[2] http://www.illumina.com/pages.ilmn?ID=256

Although current animal genotyping projects are co-financed by government and public funds, ownership of genomic data will probably lie with the owners of the bulls, that is, the AI studs. Because of market competition, they will be most likely to avoid disclosing or sharing this information. In order to calculate meaningful and accurate SNP effects, however, they will have to join large databases comprising genomic data from other sources as well as pedigree and phenotypic records, possibly from different countries.

Genomic selection constitutes a significant departure from the current modus operandi that has been successfully practiced over the past 50 years. For genomic selection to become the widely accepted norm, all stakeholders must become aware and convinced of its true potential. This implies farmer education and breeder association participation. Dairy breeders are used to getting objective and unbiased information from independent genetic evaluation providers before making selection decisions. They actively participate in the breeding and improvement business and are not accustomed to black box solutions.

2.4. Caveats

As mentioned above, the accuracy of GEBV will be compromised if the amount of data is insufficient. Sharing resources and, above all, SNP chips will likely be needed to attain the appropriate amount and quality of data necessary for accurate SNP effect estimation and GEBV calculation.

Individual SNP and haplotype effects on various traits will likely not be the same across different populations, countries and environments. Genomic data will have to be tested against phenotypic records from many countries in order to establish accurate estimates.

Conventional breeding values (EBV) will most likely continue to be calculated for the years to come based on phenotypic and pedigree records. Such estimates will be used for selection, as before, and also validation of SNP and haplotype effects. However, intense bull pre-selection on GEBV will introduce bias to the EBV calculation procedure. The magnitude of this bias needs to be assessed. If this bias is indeed important, methods to address and reduce it should be urgently derived, otherwise objective comparisons between classical breeding and genomic selection schemes will no longer be possible. This is also essential in situations where GEBV prediction equations are developed using progeny tested bull EBV as proxies to true breeding values.

With the advent of comprehensive DNA chips, it may be tempting to disregard central features of the current breeding schemes (data and pedigree recording, maintenance of national databases and, in some cases, use of known QTL information). Decrease in investment and attention on these aspects would be a mistake. They are critical for the development and evaluation of GEBV equations (for example on lowly heritable or rarely observed traits) and the subsequent validation of the quality of genomic selection schemes in the field.

3. KEY SCIENTIFIC QUESTIONS TO BE ANSWERED

The following are some scientific questions that should be answered before genomic evaluation and selection become widely applicable. The questions concern as much the scientific community as genomic selection service providers. Interbull can play a role here, as discussed in the next section.

- What is the minimum amount of data (number of animals, number of SNP, number of and nature of phenotypic records) required for SNP effect estimation and calculation of accurate GEBV for the various goal traits? This will likely differ for different traits and methods.
- How do SNP estimates differ in different countries and environments? International joint analysis of SNP, phenotypic and pedigree data will be needed for this matter.
- How often should SNP effects be re-estimated?

- What is the best way to combine data from different sources (phenotypic records, pedigree, SNP, QTL)? This may range from a simple selection index approach combining conventional EBV and GEBV to an elaborate integrated analysis of all data.
- When and how will the superiority of genomic selection over classical selection schemes based on progeny tests be confirmed and how large will the superiority be? Will there still be a place for progeny testing programs afterwards?
- Exactly how much bias does genomic pre-selection introduce to an EBV calculation that does not include any SNP data? This will primarily affect national EBV and be a function of the intensity applied to young bull selection. An EBV including SNP information on which selection is based would probably alleviate much of this bias. On the other hand, an international evaluation with MACE requires conventional national EBV without any DNA (SNP) information in them. If such information on a bull were added to his national EBV in all countries where the bull had daughter data, then these figures would not be independent since the bull DNA is the same in all cases.

The best answers to many of the above questions could be derived from joint international analyses of all DNA and phenotypic data available worldwide, under the auspices for Interbull. The likelihood of such a study will largely depend on these data being accessible to Interbull and collaborators.

4. THE ROLE OF INTERBULL

4.1. Opportunities

The following constitute possible opportunities for Interbull to emerge as a doer in the new order of affairs:

- A need to offer and monitor the sharing of genomic and other information in order to increase the accuracy and acceptability of GEBV: at first, this may mainly concern small breeds and/or countries/regions which want to reach a critical size for their genomic selection scheme.
- A need to calculate SNP effects across different countries and monitor their periodic re-estimation: this will be fueled by the continuing belief that genotype-by-environment interaction is important and that breeding goals differ across country.
- A need for independent, international validation of SNP effects and, possibly, new phenotype collection protocols (e.g. health traits) for this matter.
- A need for independent monitoring and international evaluation of breeding value estimation regardless of selection method.
- A need to ensure farmers and breeder associations continue to participate in the genetic improvement business.

Although intuitive to an extent, the above prospects need to be well understood and communicated to stakeholders involved, including member organizations, AI studs and the breeding industry as a whole. The benefits must remain mutual in all cases.

4.2. Threats

Although conventionally calculated EBV at national and international level will most likely continue to be required (possibly after adjusting for genomic pre-selection), the new momentum and developments in genomic selection will leave Interbull lagging behind if it does not manage to seize the opportunities mentioned above. If/when conventional EBV do no longer constitute the primary selection tool or at least a sought-after independent comparison tool, the future of the organization will be severely compromised and its very existence threatened.

Furthermore, there is a high probability that "top" members of the breeding industry, in countries with advanced genomic selection capacity, will not opt for a collaborative approach and, driven by the urge to protect their competitive advantage, decide to keep SNP data to themselves. The long-term implications of this must be well understood and quantified both in scientific and economic terms.

4.3. Roles

Interbull has repeatedly demonstrated its ability to adapt, evolve, prosper and lead. From an international forum for information exchange to a reference centre for conversion equation and international genetic evaluation services, Interbull has managed to negotiate new methodology development and produce widely acceptable data sharing protocols. The potential advent of genomic selection presents another, albeit potentially steeper, inflection on the organization's 25-year old trajectory. The following are some possible roles for Interbull to contemplate:

Service: Conventional EBV will still be required, at least for a certain time-frame, but this should not be the only product in the pipeline. Interbull is in a unique position to negotiate and offer estimates of SNP effects across country for the many traits on the various breeding goals. This will require successful solicitation of SNP data from breeding companies, which will not be straightforward. At first, a pilot study considering a numerically small breed and/or an economically non-critical trait will probably be more realistic. There may also be a need for conversion equations of GEBV from one county to another. Furthermore, Interbull may conduct independent feasibility studies for genomic evaluation and selection. All this implies strong investment on new methodology and expertise.

Monitoring/coordination: Interbull can organize and monitor collaborative research that is needed to address the scientific questions mentioned in the above section. Interbull can be involved in the concept, design, fund solicitation, management and implementation stages, while providing administrative expertise for the coordination and dissemination of results. As a well-recognized international independent entity, Interbull is in a good position to negotiate and oversee acquisition and sharing of sensitive data.

International forum: Interbull meetings have enjoyed a constant scientific attendance by representatives of most genetic evaluation units and farmer associations around the globe. These meetings can further evolve and become international fora for the exchange of ideas, experiences, perspectives and techniques among scientists and industry leaders. We could even envisage an expansion of some of these meetings to include research and business representatives from other farm animal species areas where similar DNA technological tools are being used and valuable experiences are being gained. Now more than ever scientific principles and commercial realities can and must be placed together on the same table for the development of mutually profitable synergies and the benefit of animal breeding worldwide.

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for the Interbull SAC

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Convener