GENOMIC EVALUATIONS

Research & Development Executive Lucy Andrews-Noden looks at this new tool for genetic improvement to accompany all the great tools you already have (this article first appeared in the February 2012 Journal)

Holstein UK would like to thank DairyCo, and in particular Marco Winters, for providing some parts of the text and a couple of graphics for this article from the Breeding+ Guide to Genomic Evaluations. Much of the rest of this article and graphics represent the views and opinions of Holstein UK and therefore responsibility for the overall view and content is that of Holstein UK

For those who don’t have the time to read the whole article - just make sure you scan over these Dos and don’ts of Genomic Indexes

Do...
• carefully study the bull’s index, just as though he were a conventionally tested sire
• remember that the lower the reliability of the index, the greater the chance the index will change
• ask your AI company to show you how many daughters the bull has and in how many herds
• use a mix of daughter-proven and young genomically evaluated bulls to obtain a balance between risk and reward.

Don’t...
• over-estimate the reliability of genomic indexes, which will be lower than those of most progeny tested bulls
• over-use any young, low reliability bull with or without a genomic index

And remember...
• there’s nothing mystical about genomic evaluations in themselves. A young bull marketed as a ‘genomic young sire’ may be no better or worse than any other bull

Genetic improvement has traditionally been made by measuring an animal’s performance - or more typically that of its offspring and breeding the next generation from the best performing animals. This method has served the livestock industry well for hundreds of years and is, in part, responsible for the dramatic increases that have been seen in not only milk, fat and protein production but also other key important health, welfare and structural changes in the dairy cow.

However, since the advent of genomics, the livestock breeding industry has had the means with which to measure the DNA at the core of every animal’s being. This DNA provides the code for life - for the type, production and even health that each animal (given the right environment and management) has the potential to achieve. As scientists have studied the animals’ genome (or its genetic map), they have learnt what certain codes mean in specific positions along each strand of DNA. They have gained this knowledge by comparing the DNA with the actual performance of thousands of animals over many years. With enough information, it is possible to see clear associations emerge between the animals’ genome and their actual performance. And through knowledge of these associations, genomic indexes or evaluations have been developed. These genomic evaluations are a more accurate prediction of a young animal’s genetic merit than was previously available. Before genomic indexes, the only way of estimating a young animal’s genetic merit was to look at the performance of its ancestors and relatives, most importantly that of its sire and dam.

Pedigree Index/Parent Average in Practice

Figure 1: Illustrates how Parent Average (PA) also commonly knows as ‘Pedigree Index’ works and how this compares to what we see in practice. This is why the reliability of Parent Average is around 35%.
It's not as simple as that though... let's take a look at the genetic material itself. Cows have 30 pairs of chromosomes (60 chromosomes in total) and each parent will pass on one of those pairs to their offspring, including one chromosome which decides the sex of the progeny.

Chromosomes are made up of DNA containing millions of combinations of ‘Base Pairs’. These are combinations of the old ‘A,T,G,C’ or Adenine, Thymine, Guanine and Cytosine that you would have learnt about in biology. Now first message is that ‘YOU DON’T NEED TO KNOW’ all about these really, it just helps to get to grips with the sheer size of the potential information. When you think of the chances of winning the lottery with 6 numbers out of 49, you realise that there are billions of winning combinations. Think of Chromosomes and DNA in the same way – each parent has the possibility of passing on well over a billion different combinations of those base pairs and chromosomes each to the progeny, a total of three billion per offspring!

To give you an example of just how big it is, below is a little piece of the ‘coding’ results for just Chromosome 1 for the famous old bull Elevation. This shows just 864 alleles (interesting locations of the DNA sequence), however if we were to show you all of the base pair results for just Chromosome 1, we would have to show you the same sized snippet, every second for the next three days! The genotype is massive and it’s important to get your head around just how many combinations are possible. Looking at it this way helps to explain why it’s no wonder two full siblings never look exactly the same.

Basic Parent Average assumes that the calf will inherit 50% of genetic potential from the sire and 50% from the dam in equal proportions.

We know in practice however, life isn't that simple! Breeding two animals together creates progeny that 'resemble' their parents in some ways, because they are given basic genetic information from each parent, but they are never identical to either parent.
The numbers 0, 1 & 2 refer to alleles, which are a bits of the gene that are located at a specific position in the chromosome - it’s like coding and shows what CAN be passed onto the next generation, not what necessarily WILL be. Vast portions of the chromosome are what is know as ‘homozygous’ and not really interesting i.e. all animals have the same DNA sequence, but others are Heterozygous and are of interest. 0=Homozygous (for first allele), 1=Heterozygous, 2=Homozygous (for second allele).

**Important to remember:** this ‘coding’ shows what CAN be passed onto the next generation not necessarily WILL be – it’s the animal’s genetic potential. The reliability gives a guide to the likelihood of that happening. We don’t, however, know how all of these Heterozygous alleles interact with each other, how they can change over generations or how they are affected by environment, which is why it is VITAL that we continue to progeny test and check to see how these genotyped animals actually perform based on what we know about their genetic makeup.

So, now we know the basics, when can an animal get a genomic index? It is possible to calculate a genomic index from the moment of an animal’s birth. This is done by taking a sample of its DNA, which can be taken from any cell in its body, including blood, nasal swabs or cells at the roots of its hairs.

**How is the information used?**
Like traditional genetic evaluations, which are calculated by blending information (usually from daughters and parents), genomic evaluations are also calculated from a blend of information. This comes from the genomic (DNA-based) information, but still includes Parent Average information and goes on to include daughter performance information once this becomes available some years later.

**What are the benefits of having genomic evaluations?**
There is nothing mystical about genomic evaluations in themselves and a young bull marketed as a ‘genomic young sire’ may be no better or worse than any other bull. However, the significant and only advantages of having genomic evaluations come through their speed and accuracy. By having a more accurate assessment of an animal at a young age, this young animal can be used with more confidence. But REMEMBER, although the Genomic evaluation is more accurate for a young sire than a Parent Average, it isn’t as accurate as a Progeny Test Proof based on real, evaluated daughters. However, by using him earlier, generation interval is also reduced, so potentially increasing genetic gain. The extent of this genetic gain depends on the uptake of genomic evaluations and which sires farmers choose to use. Without genomic indexes, the identification of superior sires is expensive and time consuming because of the need to wait for milking daughters and a progeny test proof. This process generally takes around five years from the bull’s birth.

**Who uses genomic evaluations?**
It is really important to understand that breeding companies such as Genus ABS and Cogent in the UK, plus those throughout the world, have already been utilising genomics for some time to help better target those elite young bulls to take forward to full progeny test with more confidence. This is particularly helpful when selecting between full brothers, which would traditionally have had identical genetic predictions, based on Parent Average information, so one way or another we are all using genomics without realising it. This also means that the young bulls on offer today
and those entering progeny test are already highly selected for all of the functional type, health and fitness and production traits we are seeking, so our genetic potential has already increased without any added selection from us. This information has a variety of uses for females and, just as with bulls, it could help determine which of full siblings to retain in the herd, which to breed to beef bulls, which to breed with sexed semen or which to flush for embryo transfer. Genomic information for females is also playing a growing role in marketing, where high genomic indexes can elevate the value of an animal, embryos and progeny both in the UK and overseas.

**USING GENOMIC EVALUATIONS**

**How are genomic indexes going to be expressed?**
In the UK, a genomic index will be expressed in exactly the same way as a conventional index based on progeny performance. This reflects the fact that indexes are based on a blend of information – they are not genomic indexes one day and progeny indexes the next and even bulls with many milking daughters will have a genomic component to their index, albeit small. For this reason, the UK has opted against the protocol sometimes used to prefix the index with a ‘g’. Instead, farmers are advised to carefully consider the reliability of the index and to establish whether a bull has milking daughters.

**What bull lists will be published in the UK?**
Holstein UK and DairyCo will publish two categories of lists for Holstein bulls from April 2012 onwards. The first will feature bulls with milking daughters contributing to their index and the second will feature young bulls with no milking daughters. Only bulls with a reliability of at least 65% (and 10 milking daughters for production) will feature in the first list while bulls whose indexes have reliabilities of more than 40% will feature in the young sire list.

**What proportion of genomic bulls should be used in a herd?**
There are no hard-and-fast rules governing the use of genomic bulls, although any low reliability bull should be used with caution. Like investment in the stock market, their use is partly governed by the farmer’s attitude to risk and some may prefer to have the security of using only second crop, high reliability bulls. However, although the risks of the second crop strategy are lower, the farmer could be missing out on potential genetic gain that could come from the younger generation. Across a whole herd, it is generally recommended that a mix of proven and young genomic bulls is used to obtain a balance between risk and reward, but the precise amount of each comes down to personal preference. The graph below gives a rough guide that DairyCo recommended for levels of usage of semen from individual bulls at different levels of reliability. In practice, this means that no more than 7% of a herd should be bred to a young sire with no genomic information; up to 12.5% could be bred to a evaluated young bull; around 25% can be bred to a first crop daughter-proven bull and 50% of a herd can be bred to a bull with a highly reliable second crop index.

UK Genomic indexes can be obtained for female Holsteins, and Holstein UK will be able to offer this service (as well as every major milk recording organisation in the UK - CIS, NMR and UDF), which will be launched during 2012 based on work undertaken as part of an industry collaboration. The calculation of the indexes is carried out by both Holstein UK for type traits and DairyCo Breeding+ for production, fitness + PLI.
Rule of thumb (DairyCo);
50% - Second crop
25% - First crop
12.5% - Genomic Young Sire
6.24% - Young Sire

Source: DairyCo

The above graph, provided by DairyCo, illustrates a guide to proportion of semen usage for a single bull at different levels of reliability. However, it is always important to remember that the younger generation does not necessarily give greater genetic gain. There are some young bulls on the market with very mediocre genomic indexes and there will be little argument in favour of using them. If they are no higher or offer little gain over a more reliable proven product, Holstein UK would recommend using the proven product based on real progeny test daughters, to reduce the risk of disappointment.

Will there be any young sires without genomic indexes?
Because of international collaboration and high levels of investment by various industry partners, ground rules have been established to protect participating interests. This means that breeding companies that have invested in the project are eligible to obtain a genomic index for any of their sires. While this covers almost every bull being used in the UK, there are likely to be small numbers from independent companies which have not taken part in the process and will not obtain genomic indexes. In these instances, the bulls will be published with Parent Average information as in the past, and the reliability of their indexes will be lower.

What makes a genomic evaluation change over time?
As with any genetic evaluation, genomic indexes can change over time. This can seem surprising when the animal’s genetic makeup does not itself change. However, the key factors which cause the indexes to change are the addition of more family (such as parent) information to the calculation of the index and the addition of more animals to the reference population.

How reliable are genomic indexes?
The reliability of any genetic index is expressed as a percentage and gives an indication of how likely the index is to change over time. A low reliability index of around 30-40% is typically based on Parent Average information. At the opposite extreme, a bull with a genetic index based on the performance of thousands of daughters (so called ‘second-crop’ indexes) could have a reliability of 99%. Genomic indexes have reliabilities somewhere between these two extremes at around 55 to 65%. When more information goes into the calculation of the genomic index, and when the heritability of the trait is high (such as production traits), the reliability will be at the higher end of the scale.
**Understanding reliability and risk**

While Canada, the United States, the UK and Italy are using a common pool of genotyped animals for estimating genomic evaluations, the final genomic results in each country around the world may often be different. These discrepancies come from different Parent Averages (PA) or weights in the national indexes in each country as well as slightly different technical details associated with the calculation of reliability and different modelling methods.

Gains in reliability with genomics vary by trait and sub-group of animals in the population, however on average reliabilities achieved for genomic evaluations on young bulls are currently around 60-65%, which is a gain of around 30-35 reliability points over the average of around 35% for traditional Parent Average. While this increase in accuracy is significant and young sires with genomic evaluations can be used with a little more confidence than Parent Average young sires previously, caution is still warranted. The genomic evaluation reliability is less than an evaluation based on an actual progeny performance, which can be up to 99% reliability. As an animal accumulates actual progeny information, so the genomic (and Parent Average) component contributing to its index gradually diminishes.

Table 1: Helps to summarise the differences in bull reliabilities. Source: Holstein UK

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Average Reliability</th>
<th>No. Daughters/Herds</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA = Parent Average</td>
<td>35%</td>
<td>0 dts/0 hds</td>
<td>This is a straight average of the genetic potential for both sire and dam. No daughters have been born, milked or classified.</td>
</tr>
<tr>
<td>PA + Genomics</td>
<td>60-65%</td>
<td>0 dts/0 hds</td>
<td>The increase in reliability is said to be equivalent to approx: 10 daughters (on average over all traits), however - No daughters have been milked or classified.</td>
</tr>
<tr>
<td>Progeny Test</td>
<td>70-99%</td>
<td>Start at approx 40 dts/25 hds upwards</td>
<td>At this stage the impact of the PA and genomic evaluation diminishes and is replaced by information taken from real cows milked and classified.</td>
</tr>
</tbody>
</table>

To gain a little real world perspective on this, let’s imagine a world where genomic evaluations didn’t exist. Truthfully answer two simple questions:

1) How many AI companies would launch and aggressively market a young bull, in some cases at upwards of £30-35 per straw with only 10-11 daughters in his proof?

2) How many of you out there would have paid for it?

Having said that, it is also important to understand the benefits of increasing genetic progress. The graphic below, kindly supplied by DairyCo, helps to give an understanding of the rate at which genetic progress can be made by using Genomics. Essentially it may take up to five years before a young bull moves from a Parent Average reliability up to a much more reliable first crop proof with progeny milking and classified. Genomics helps to reduce that generation interval by providing the farmer with a little bit more reliability to base their decision on a few years in advance of that first crop proof.

Now the thing to remember here is the risk. Remember the genomic evaluation at 55-65% is NOT as reliable as waiting for that first crop proof and the reliability figure reflects this. If you want to take the risk and have the hot new genetics, then that’s a choice you have to make, but be aware of the facts, which are that it’s not 100% accurate. With the addition of daughters that proof WILL on average move - and you won’t know if that’s up or more importantly down!
This next graphic illustrates in very simple terms the general risks involved and the likelihood of a bull’s Genomic Index changing from the one you see when you buy the semen. On the left hand side you can see that a second crop highly reliable bull has a ‘normal’ distribution and that the risk of the bull moving either up or down from the Index they have been given is very low. If you take a first crop sire, the potential is that the genetic merit for the population in which he was selected has moved on, so, he has the potential to make a little bit more improvement at the top end. However there is also a greater risk that the bull will drop and his initial index move. The next risk group up are the genomically evaluated bulls sired by highly reliable second crop sires – this increases the risks further, but likewise offers the potential to make more progress but at a higher risk of disappointment. As you move along the graph, you can see the really high risk situations, where young Genomic bulls are being offered for sale that are not only sired by Genomic, unproven young bulls, but are realistically also out of the world’s highest genomic maiden heifers. This leaves the potential to use a bull with a sire stack that doesn’t have a single lactation record amongst several generations.

This is where the serious risks are present and you need to use your eyes and knowledge of good pedigree families and sires so that you not only understand but also limit your risk. It is from this group that the very highest elite Genomic genetics will be moving to gain ever higher and higher Genomic values as quickly as possible. The higher the number for marketing the better, but remember you can go a very long way in the wrong direction very quickly and, as we have said for many years at Holstein UK, it takes a moment to put that straw of semen into a cow and a lifetime to breed out a problem!
It wasn’t long ago that AI companies were getting heavily criticised for only contracting bulls out of young maiden heifer bull dams – that changed at your request and more solid, older proven females and families started to emerge over the past several years. Genomics does offer the chance to move forward much more quickly and take advantage of genetic potential but do we want to undo all of the hard work that has been done in establishing the UK proven and progeny tested product as one of the best in the world? Just be aware of the risks and the rewards.

**Will genomic evaluations take over from traditional progeny evaluations?**

Genomic evaluations clearly offer the potential to increase genetic progress. However, their accuracy depends entirely on having performance measurements for large reference populations for on-going calibration. Progeny testing of dairy bulls therefore remains the gold standard and many farmers out there wanting to reliably achieve consistent, easy-to-manage cows will continue to demand a rock solid and reliable proven product. In order to increase the scope and accuracy of genomic evaluations into the future, it is essential that milk producers continue to participate in recording programmes and classify their cows. In the era of Genomics, data and the Phenotype is king as you cannot prove one without the other. We need to keep collecting high quality information for production, type, health, calving, fertility and management traits for genomics to continue being a useful new tool in the future.

**Summary**

Genomics has given breeders and AI organisations an incredible new tool in their breeding toolbox with which to select and market animals more accurately, nationally and internationally. The most appropriate use of genomic information remains in combination with traditional evaluations using pedigree and performance data. It has been evident overseas that young animals tend to have a large variation in how their Genomic indexes compares to their traditional Parent Average. On average, the Genomic indexes in heifers and young bulls are lower than their Parent Average. Genomics pulls the breeding value of these young animals closer to how we would expect them to perform in the future long before their own or daughter performance can be recorded. At this stage it is important to remember that proofs, by nature of the very word, for domestically proven sires in any country are extremely reliable with or without the inclusion of genomic information – remember there is no such thing as a ‘genomic proof’ they are Genomic Evaluations or Indexes - the proof of the pudding is always in the eating!

Genomic Indexes will be available for bulls on Tuesday 3 April from Holstein UK for all Holstein Type traits and from DairyCo for Holstein Production + fitness traits as of the April 2012 Genetic Evaluation run. Check out those respective websites for information in April.

Holstein UK would like to thank DairyCo once again for providing parts of the text and a couple of graphics for this article, from their Breeding+ Guide to Genomic Evaluations
**Genomic Evaluations are not the equivalent of a bull’s proof**
Genomic information added to a Parent Average gives a genomic evaluation equivalent to approximately 10 daughters (average over all traits).

In most countries, genomic information is combined with traditional proofs to give a ‘blended’ proof of genomic information, pedigree information and daughter information. As the animal gains more real progeny, the weighting of parent average (pedigree information) and genomics diminishes.

**There are still only two types of bulls**

1. **Progeny proven**
   - Can be used individually or in large volumes
   - Ensures consistency of females and profit within a herd
   - More likely to see the gains promised by the proof (especially high reliability)

2. **Young sires**
   Addition of genomic data improves prediction, but
   - Individual bulls should only be used in low volumes
   - Lower reliability and higher risk than progeny tested proven sires