

Genomics for Pedigree and Cross-bred Beef Cattle Populations; Some experiences from Ireland

A.R. Cromie¹, F Kearney¹, R Evans¹ and D.P. Berry².

¹ Irish Cattle Breeding Federation, Bandon, Co. Cork, Ireland, ²Teagasc, Moorepark, Co. Cork Ireland,

ABSTRACT:

Multi-breed genomic selection in beef cattle in Ireland is expected to be launched in 2014 based on a population of >3000 high reliability purebred AI beef sires, ~30,000 natural mating beef sires and 100,000 commercial crossbred beef cows. Breeding companies (AI bulls) and breeders/producers (natural mating bulls and cows) will have open access to the genomic proofs based on our custom dairy-beef genotyping platform with 19,000 SNPs which also monitors lethal recessive mutations, congenital defects and major genes. Producers and breeders will be able to more confidently select genetically elite animals on either of our two beef national breeding goals; dairy farmers will be able to select genetically elite beef bulls (AI or natural mating) for use on their dairy herd.

Keywords; imputation; single nucleotide polymorphism; genomic selection

Beef cattle breeding in Ireland

Beef cattle breeding in Ireland is built around three core components; (i) the ICBF database, (ii) genetic indexes focused on profit, and (iii) the GENE IRELAND breeding program, which helps ensure that the very best of animals are returned as parents of the next generation.

i. The ICBF database. All cattle herds in Ireland operate off the ICBF database for the provision of cattle breeding services (some 81,000 herds and 2.1 m calf births/annum). There are now over 34 million animal records in the ICBF database which was first launched in 2002. The Irish genetic evaluation systems are as large (i.e., data numbers) and complex (i.e., multi-breed genetic evaluations for some 20 different cattle breeds) as anywhere in the world. The fact that the ICBF database routinely collates information from so many sources, including livestock auctions, abattoirs, animal health laboratories etc., is also unique and places Ireland in an envious position with regard to especially its beef breeding potential (Evans, 2014).

ii. Economic Indexes. Economic indexes have been developed along with Teagasc, the government funded, research, extension and education organisation. Currently three economic indexes have been identified for the Irish beef industry: (i) *Maternal Index* - for a producer wishing to also keep female replacements and sell surplus female and all male calves for slaughter, (ii) *Terminal Index* - for a producer who is purchasing replacements and is therefore looking for a bull that is easy calving but with good carcass attributes, and (iii) *Dairy Beef Index* - for a dairy farmer looking an easy calving bull for the dairy herd with good calf value and short gestation. An important aspect of these indexes is the on-going demonstration of their ability to accurately identify more profitable animals for breeding. Indeed latest results from Teagasc, indicate

that high genetic merit animals based on terminal index, have the potential to leave an additional €300/animal value at slaughter than low genetic merit animals (Connolly et al., 2014); this ignores the fact that higher terminal index animals are slaughtered, on average 60 days younger, and expect to eat less feed per day (Connolly et al., 2014). The economic values (and genetic evaluations) are evaluated for relevance annually and, if necessary, updated.

iii. Breeding program. The GENE IRELAND beef breeding program has recently undergone a major over-haul in an attempt to increase the number of young bulls being progeny tested, from the current 10 bulls/year (based on maternal index) to a target of 80 bulls within the next 2 years (current numbers for 2014 is 30). The key driver of change was a realisation amongst all stakeholders, that despite a steady decline in genetic merit for maternal traits (Figure 2), there was still only a limited interest amongst bull breeders (and commercial beef farmers) in bulls with good maternal attributes; this is because maternal and terminal characteristics are antagonistically correlated (Berry and Evans, 2014). As a consequence, it was agreed that ICBF should become directly involved in procuring young bulls for the breeding program, in addition to AI companies. As a result ICBF now purchase young beef bulls for the breeding program but then sells these bulls to AI companies and/or farmers, once the bull has generated a target of 1000 straws for the program (i.e., 500 for the progeny test and 500 for potential elite matings to generate the next generation). The decisions around all aspects of the program (including the purchasing of young bulls) is made by ICBF in consultation with key stakeholders including AI companies, herdbooks, pedigree bull breeders and commercial farmers. An added advantage of the program is that it will help provide the key data on which ICBF and Teagasc will look to further exploit the potential of genomics, as the value of this technology is highly dependent on the quality of the underlying data on which the genomic predictions are based. Obviously genomic selection will greatly aid this breeding program through greater accuracy of selection and more importantly also greater intensity of selection.

Research and implementation model

The success of the Irish dairy genetic and genomic selection program owes itself to the relationship between the organization charged with genetic improvement in the Irish cattle breeding herd, the Irish Cattle Breeding Federation (ICBF), and the Irish research, extension and education authority for the Agri-Food industry, Teagasc – the latter include quantitative geneticists, molecular geneticists, economists and livestock systems researchers.

ICBF was formally established in 2000 with the objective of increasing profitability for Irish beef farmers and the wider industry. Its shareholding is made up of (i)

farm organizations (46%), (ii) milk recording organizations (18%), (iii) AI organizations (18%) and, (iv) beef and dairy herdbooks (18%). The annual ICBF budget is €5m, with some 50% of this coming from services and producer contributions (levy of compulsory calf ear tag) and the remaining 50% from Irish National Development Plan support programs and Department of Agriculture Food and Marine (DAFM) directly, in terms of capital grant. This 50:50 balance between shorter term service income and longer term industry good income is strategically important as it allows ICBF to keep a balanced focus on “here and now” issues, versus issues that will affect the industry in years to come.

In consultation with industry representatives, research requirements are prioritized annually at the beginning of the year. Research is then jointly undertaken between the ICBF and Teagasc thereby ensuring any research undertaken is immediately and seamlessly implementable; research topics outside the area of expertise of either group is out-sourced internationally, e.g., to AbacusBio (New Zealand), Wageningen UR (the Netherlands) and MTT (Finland). Importantly all research results are scientifically peer-reviewed and the results or systems developed are available to all (i.e., producers, breeding companies). Furthermore, Teagasc and ICBF have both an extension and education component which are educated on developments through regular in-service training. Because neither body has any vested interests the message is clear, simple, and unbiased. A simple and clear message (i.e., genomics is merely a tool to improve the accuracy of selection) is a key driver of rapid implementation.

Irish Dairy Genomics Research and Implementation Program

Genomic predictions for Holstein-Friesian animals were launched by the ICBF in February 2009 following joint ICBF-Teagasc research. The initial reference population consisted of 985 Holstein-Friesian AI bulls with domestic proofs. The reference population was indirectly funded by the Irish tax payer through competitive research grants secured by joint ICBF-Teagasc submissions as well as funding allocated directly by both ICBF and Teagasc. This point, although may appear trivial, ensured that no restrictions whatsoever were imposed on the implementation of genomic selection. The total cost (including personnel) of implementing a genomic selection program in Ireland for dairy cattle was €0.4m. Farmers, indigenous breeding companies, foreign breeding companies and/or herdbooks can submit a biological sample or genotype from a Holstein-Friesian male or female animal to ICBF and receive a genomic proof. Once a genotype or biological sample of an animal is submitted to obtain a genomic proof, the genotype becomes the property of the ICBF, for the purpose of publication and ongoing research and development (both National and International).

Whilst this may seem like a very open system, certain constraints are applied that help confer some competitive advantage to service users, without undermining the core principles of the program. For

example, when a user requests a genomic evaluation on an animal, the evaluation remains private to them for a period of 3 days, after which it is public on the ICBF website. In this way, the program promotes a high level of genotyping of Holstein-Friesian male calves, as AI companies, herdbooks and farmers seek to identify exceptional animals for the breeding program. For example, in 2013 the number of male calves genotyped as part of the Holstein Friesian breeding program was 9,036, of which 55% were genotyped by AI companies, 40% by the Irish Holstein-Friesian Association (as part of their routine pedigree registration service) and 5% by farmers.

Genotyping was originally undertaken using the Illumina Bovine50 beadchip by AROS in Denmark. In 2010 the Illumina 3K chip plus imputation (using Beagle) was used (genotyping by GeneSeek, USA) which was replaced in 2011 by the Illumina Low density (i.e, 7K) chip (genotyping by Weatherby's Ireland). Genotyping since 2012 has been undertaken by Weatherby's Ireland almost exclusively using the Irish custom built genotyping panel, the International Dairy Beef (IDB) 19k chip (Mullen et al., 2013).

The cost of acquiring a genomic proof for a male calf including hair sampling, DNA extraction, genotyping and generation of a genomic proof is currently €50, based on the use of the custom built IDB chip. However, the cost is lower for females (€30/animal), because of our desire to increase the number of females being genotyped for future training population work (the €30/animal being the break-even cost of the service). This is provided that the herd is prepared to genotype all female available. Indeed a very recent development has also seen us link this price offering with an additional research and development requirement, whereby in addition to genotyping all females, the farmer is prepared to accurately record important health and disease traits, including female fertility. Assuming that farmer agrees to this commitment, ICBF will offer him genomic evaluations for all females at €15/sample, with the remaining €15 from the overall cost of €30 originating from ICBF and Teagasc competitive research grants. Response to this latest offering has been considerable with 70 herds and 15,000 females due to be genotyped in Spring 2014 as part of this initiative. ICBF and Teagasc expect that this latest initiative will help us establish multi-breed genomic evaluations for other dairy breeds (most notably Jerseys and the Red breeds), as well as more accurate genomic evaluations for low heritability traits such as health, disease and female fertility.

Figure 1 shows a) the genetic superiority of the used genomically selected bulls versus the bulls with daughters in Ireland and b) the proportion of semen from genomically selected bulls used since 2009. The use of genomically selected bulls is consistently increasing year-on-year; in 2013 60% of the semen used in Irish dairy herds was from genomically selected young bulls

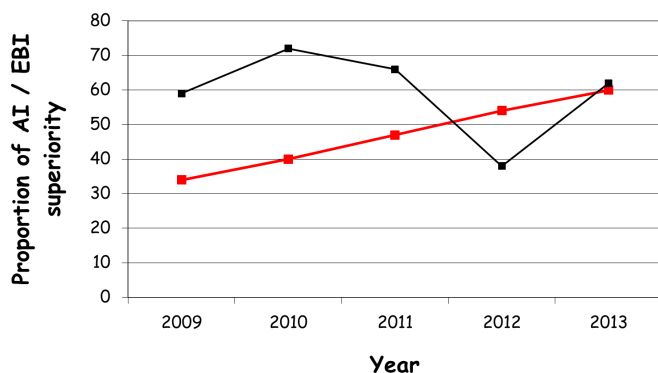


Figure 1. Superiority in the Irish national dairy breeding objective (EBI; €) of the used genomically selected bulls compared to the used Irish daughter proven bulls (red squares) as well as the proportion of semen used that originated from genomically selected young bulls (black squares).

Table 1. Mean (standard deviation in parenthesis) of the prediction bias between daughter-based PTA and parental average (PA), direct genomic values (DGV) and blended genomic values (GPTA)

	Milk (kg)	Fat (kg)	Protein (kg)
DGV	36(135)	-0.56(4.69)	0.62(3.65)
PA	67(135)	1.74(5.55)	2.37(4.40)
GPTA	54(127)	1.82(4.76)	2.16(3.69)

Table 2. Correlation between daughter-based PTA and PA, DGV and GPTA predictions for milk, fat and protein

	PA	DGV	GPTA
Milk	0.72	0.72	0.77
Fat	0.51	0.65	0.66
Protein	0.59	0.70	0.72

.Retrospective analysis of the 135 bulls genomically tested since 2009 that entered widespread AI usage and now have daughters are summarized in Tables 1 and 2. The correlation analysis suggests up to 29% improvement in prediction accuracy with the genomically enhanced PTAs compared to the parentage average PTA.

Little or no research funding has been invested in the Irish dairy genomics program since the initial investment in 2009. The exception was the genotyping of purebred Friesian AI and natural mating bulls to obtain more accurate genomic predictions in purebred Friesians. The increased training population size (now approximately 4,978 bulls) has been achieved through bilateral sharing of genotypes or from young genomic bulls eventually

receiving daughter proofs. Research funding is however going to be used in 2014 to part fund the implementation of an across breed genomic evaluation for dairying, as well as more accurate genomic evaluations for health and disease traits (as outlined earlier).

Irish Beef Genomics

Research and Implementation Program

A total of 4,233 Illumina high density genotypes on purebred beef male bulls (Table 3) have been procured through a combination of competitive research funding as well as funding provided by both ICBF and Teagasc. For socio-economic reasons, AI usage is relatively low in Irish beef herds (~17% of calves born on an annual basis). Therefore the number of high reliability AI sires is relatively low which is why high reliability natural mating bulls were also genotyped. Because (dairy and beef) across-breed evaluations exist for carcass traits, dairy sires can also provide information for genomic predictions of beef traits.

Table 3. Number of Illumina high density genotypes per breed

Breed	Genotypes
AA	492
BB	314
CH	944
HE	352
HF	772
LM	978
SI	381
TOTAL	4233

An initial genomic prediction analysis of these data was undertaken to evaluate the genomic prediction accuracy achievable on a multi-breed group of the youngest high reliability sires. The correlation between genomic predictions and progeny-based EBVs of high reliability sires for three carcass traits when undertaken within breed (with either high density genotypes or the subset of genotypes on the Illumina Bovine50 beadchip) or across breed are in Table 4. The correlations were relatively weak; an average correlation of 0.38 for the across-breed evaluations and 0.41 for the within breed evaluation using the high density genotype panel. Moreover, the results were very variable across breeds and traits.

Table 5 summarizes, using the same population, the accuracy of genomic predictions in a validation population of just one breed where that breed was not included in the calibration dataset. Little or no benefit (and in some cases an unfavorable association) was obtained when genomically predicting animals of a given breed not represented in the calibration dataset. Moreover, these analyses were undertaken on carcass traits which are highly heritable and phenotypic data are available on all animals slaughtered in Ireland thus reliability of genetic evaluations of the sires used in the analysis was very high. Few sires have high reliability for maternal traits (e.g., fertility and maternal weaning weight) which are the traits that could benefit most from exploiting genomic evaluations.

Table 4. Correlation between genomically predicted and progeny based EBVs for a range of different breeds* genotyped for either the Illumina Bovine50 Beadchip (50K) or high density (HD) and the genomic predictions undertaken within each breed separately or a combined multibreed population (n=2,532)

Breed	Carcass weight			Carcass conformation			Carcass fat		
	Across 50k	Across HD	Within HD	Across 50k	Across HD	Within HD	Across 50k	Across HD	Within HD
AA	0.37	0.41	0.51	0.21	0.24	0.32	0.26	0.29	0.19
BB	0.33	0.44	0.36	0.47	0.49	0.31	0.40	0.40	0.48
CH	0.30	0.3	0.35	0.32	0.33	0.53	0.49	0.50	0.38
HE	0.29	0.25	0.20	0.33	0.33	0.41	0.35	0.35	0.29
HF	0.57	0.57	0.59	0.66	0.66	0.60	0.58	0.56	0.72
LM	0.26	0.29	0.31	0.25	0.27	0.55	0.49	0.52	0.29
SI	0.21	0.19	0.26	0.28	0.04	0.59	0.54	0.46	0.42

* Breeds are; AA – Aberdeen Angus, BB – Belgian Blue, CH – Charolais, HE – Hereford, HF – Holstein Friesian, LM – Limousin and SI – Simmental.

These results, in conjunction with the deterministic calculations of the reference population size needed for accurate genomic predictions (Figure 2), prompted two national schemes. In 2013 a jointly funded venture by ICBF, Teagasc and DAFM began where 75% of the cost of genotyping a pedigree male animal would be equally covered by the three aforementioned. The remaining 25% would have to be paid by either the breed society or the farmer. Other than being an investment in more accurate genomic predictions once the animals had phenotypes, the initiative also begun the transition from parentage testing using microsatellites to SNP-based. The IDB custom developed SNP chip was used which facilitated imputation from SNPs to microsatellites (McClure et al., 2012) thereby removing the necessity to re-genotype back-pedigree for SNPs. Most of the breed societies covered the remaining 25% (i.e., €10) with some splitting the cost between the breed society and producer. In 2012, 6000 pedigree male beef animals were genotyped as part of this scheme.

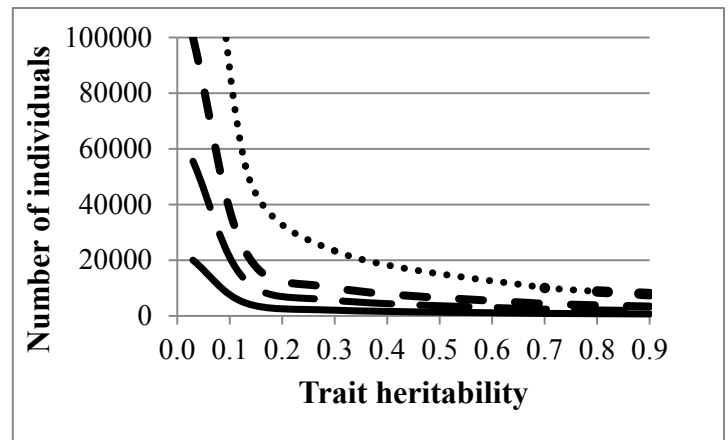


Figure 2. Required number of animals in a reference population to achieve a reliability of 70, 60, 50, or 30% (line dashes getting larger with declining reliability) as a function of trait heritability (Calus et al., 2013)

Table 5. Correlation between genomically predicted and progeny EBVs for a range of different breeds* genotyped on the Illumina Bovine50 Beadchip (50K) or high density (HD) and the genomics predictions undertaken using a multibreed population (n~2,532) excluding the breed of animal being predicted

Breed	Carcass weight		Carcass Conformation		Carcass Fat	
	HD	50k	HD	50k	HD	50k
AA	0.03	0.00	0.07	0.05	-0.00	-0.00
BB	0.1	0.06	-0.10	-0.14	0.20	0.25
CH	0.02	0.02	0.03	0.03	0.05	0.03
HE	-0.1	-0.10	0.09	0.01	-0.00	-0.10
HF	0.16	0.09	-0.00	-0.06	0.27	0.31
LM	0.00	0.04	0.06	0.13	0.07	0.04
SI	0.08	0.05	0.00	0.02	0.08	0.04

* Breeds are; AA – Aberdeen Angus, BB – Belgian Blue, CH – Charolais, HE – Hereford, HF – Holstein Friesian, LM – Limousin and SI – Simmental.

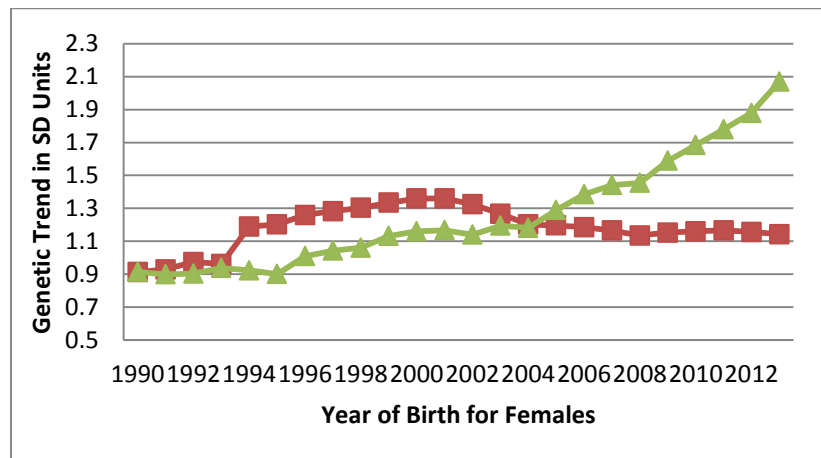


Figure 3. Annual genetic trends in Ireland for maternal replacement index value for beef females (€; red squares) and the equivalent dairy cow breeding objective, the Economic Breeding Index, for dairy females(€; green triangles).

Whilst the objectives and uptake of this scheme were positive, it was quickly recognized by ICBF, Teagasc and the DAFM, that given the decline in numbers of the national suckler herd in Ireland (down 9.4% from 1,014,000 cows in 2012 to 919,000 cows in 2013) and the steady decline in genetic merit for maternal traits (Figure 3), that something more radical would have to be undertaken if the suckler beef herd was to remain as a viable entity for Irish cattle farmers. Comparing genetic trends with the dairy breeding program highlighted what could be achieved in beef through having access to large numbers of animals with accurate genetic/genomic evaluations for key profit traits. For example, whilst genetic merit in the beef program is currently declining (for maternal traits), genetic merit within the dairy program is increasing at a rate of 0.2 SD unit/year in terms of dairy breeding index (equivalent to some €750m in net profit to dairy farmers over the past 15 years). Whilst this rate of genetic gain seems quite remarkable, it should be acknowledged that only 10 years prior to this, rate of genetic gain in dairying was also close to zero (with gains in milk production traits being eroded by losses in female fertility performance). The establishment of the EBI in 2002, the GENE IRELAND dairy breeding program in 2005, and genomic selection in 2009 have been the catalyst in this turn-around, with genomics undoubtedly playing the largest role. For example, of the 75 bulls on the latest ICBF Active Bull List, 49 are domestically bred with 39 of these being young GS bulls (indeed 9 out of the top 10 bulls are Irish-bred GS bulls, with one NZ-bred GS bulls). This is a remarkable turn-around as only 10 years ago, there was no Irish bred bull on the ICBF Active Bull List, with the list being completely dominated by bulls from New Zealand, The Netherlands and North America. The fact that 26 bulls on the current list are still New Zealand bred (with 20 of these being GS bulls) also serves to highlight the benefits of bi-lateral sharing of genotypes for both the establishment of the training population but also identification of elite young bulls for Irish dairy farmers.

It was a consequence of this knowledge, that a much more radical and significant scheme was launched by DAFM in 2014. At its core, the program recognized that approximately 100,000 individual cow fertility records

(heritability of 0.03) would be required to achieve a reliability of 60% for this trait (Figure 2). This of course could be supplemented with higher effective heritability phenotypes based on EBVs for sires. Commercial farmers were financially incentivized to genotype at least 15% of their cows identified by the ICBF (some 120,000 cows across program participants); the vast majority of cows in Irish commercial herds are crossbred. In addition all natural service sires in these herd would also be genotyped (a further 30,000 sires). Farmers enrolled in the scheme on the basis that they would receive a direct payment of €60/cow, provided that they recorded accurate data on cows, calves and natural service sires (e.g., cow milk, cow docility, calf quality, calf docility, calf scour, calf pneumonia and stock bull functionality), with the cost of any genotyping then being netted off the per cow payment. Whilst the level of investment in the project would appear high (~€5m in 2014), the very strong view from our DAFM was that genomics was the one technology that had the potential to add significant additional profit to our National beef herd (based on experiences derived from dairying). Cows were selected on a combination of information content (i.e., number of parities) and phenotypic diversity for key traits including maternal weaning, calving interval, calving performance and carcass traits. Greater emphasis was given to maternal weaning weight and fertility. Priority was also given to minority beef breeds to achieve at least 2,000 purebred equivalent records. A selection of the cows were also first parity which would have minimal contribution to genomic predictions in the short term but would be necessary to minimize any selection bias or purging of unfavorable alleles in older parity cows. The objective is to have accurate multi-breed genomic predictions for Irish beef cattle in late 2014, with a service available to the beef cattle industry in 2015.

Custom Built Genotyping Platform

A plethora of genotyping platforms now exist in cattle. An Irish team of researchers (ICBF, Teagasc, Weatherby's) developed the international dairy and beef (IDB) genotyping chip in 2012. Information on the content of this chip is freely available from the author and details

are given in Mullen et al., (2012). The platform was developed to fulfill three purposes: (i) Accurate imputation to higher density, especially in beef cattle, (ii) Imputation from SNPs to microsatellites for parentage verification (McClure et al., 2012) and (iii) Screening of the population for known lethal recessives, congenital defects and genomic mutations of major effect. The IDB is built on the base of the Illumina LD and contains approximately 19,000 SNPs. If the sire of an animal is not SNP-genotyped then the microsatellite is imputed and compared to the microsatellite recorded in the database. If discordance exists then the animal is re-genotyped for the microsatellites. Microsatellites have been imputed for approximately 6,000 animals so far and the accuracy of microsatellite imputation is 96%. The IDB is under continual development as new structural variants affecting or associated with performance are identified. Version 2.1 of IDB was launched in April 2014.

Future Perspective

Genomic selection will be available for both dairy and beef cattle in 2014. It has already caused a paradigm shift in dairy cattle breeding (Figure 2) and the same is likely in beef. The largest most comprehensive sexed semen study was undertaken in Ireland in 2013 and based on the results from this study, sexed semen is now a viable option for Irish farmers. Uptake by dairy farmers in 2014 is likely to be very large; once sufficient dairy females have been generated for the expanding Irish dairy herd Irish farmers will want to use Y-sorted beef semen for short gestation, easy calving high reliability beef bulls. Genomic selection will help identify these genetically elite beef bulls.

Access to a large database of phenotypes and genotypes is the main limiting factor to achieving high accuracy of genomic predictions in dairy and beef cattle. Genomic selection reference populations in most dairy populations include MACE evaluations from INTERBULL because the information content of a high reliability bull is greater than that of a cow, especially for low heritability traits. INTERBEEF is therefore key to achieving high accuracy of genomic predictions in beef. ICBF play a key role within the INTERBEEF project, helping to build the required infra-structure to ensure more accurate genetic (and genomic) evaluations in the future (Venot, 2014). ICBF are also actively engaged with BreedPlan UK, sharing genetic evaluations for animals that move between

these two respective countries. Our goal is that this sharing will extend to many countries and genetic evaluations organizations in the future. Moreover, there is a growing interest in difficult to measure traits in beef (and dairy) including feed intake and efficiency, environmental footprint, meat quality, and animal health and disease. Successful international initiatives are already well underway in dairy cattle to develop international genetic and genomic evaluations for dry matter intake in cows (Berry et al., 2014; de Haas et al., 2014).

Conclusions.

The Irish experience of developing and implementing genomics within our dairy cattle breeding industry has been hugely positive. Furthermore, we expect to see similar opportunities and gains in beef cattle, but with the proviso that it will present additional challenges both in terms of technical difficulty (ie. multi-breed, pedigree, cross-bred, low levels of AI etc) and industry uptake (due to the low levels of profitability being generated from beef production). Nevertheless, we are absolutely committed to addressing these challenges and to implementing genomic selection in Irish beef cattle in 2014.

Literature Cited

- Berry, D.P., Coffey, M.P., Pryce, J.E., et al. (2014). *J. Dairy Sci.* (In press)
- Calus, M.P.L., Berry, D.P., Banos, G. et al. (2013). *Adv. Anim. Biosci.* 4: 618-625
- Connolly, S. Cromie, A.R., Berry, D.P., (2011). *Proc. 10th WCGALP. This Proceedings*
- Evans, R.D, Kearney, F, McCarthy, J, Cromie, A, Pabiou, T (2014). *Proc. 10th WCGALP. This Proceedings.*
- Evans, R.D., Berry, D.P. (2014). *J. Anim. Sci.* (In Press)
- de Haas, Y., Calus, M.P.L., Veerkamp, R.F. et al. (2014). *J. Dairy Sci.* (Submitted)
- McClure, M, Sonstegard, T.S., Wiggans, G.R. et al. (2013). *Frontiers in Genetics*, 4, 176.
- Mullen, M.P., McClure, M.C., Kearney, J.F., et al. (2013). *Interbull Bulletin NO. 47.*
- Venot, E. Pabiou, T, Hjerpe, E, Nilforooshan, M.A, Launay, A, Wickham, B. *Proc. 10th WCGALP. This Proceedings.*