From Science to Reality

With predictions of marker-assisted selection available to cattlemen within a year, BIF speakers challenged commercial entities to make them available to cattlemen within the EPD framework.

by Kindra Gordon, Meghan Richey & Troy Smith

Upon the heels of the U.S. Department of Agriculture (USDA) announcement of the completion of the bovine genome sequence, the 2009 Beef Improvement Federation (BIF) Annual Meeting and Research Symposium offered a forum to discuss current progress toward genomic selection of beef cattle. Speakers addressed opportunities, cautions, validation and options available.

Presented here are summaries to a select few of the presentations at the April 30-May 3 symposium. Angus Productions Inc. (API) provided complete coverage of the event at *www.bifconference.com*. Visit the "Newsroom" of the site to access summaries of all of the presentations, as well as accompanying audio and PowerPoint submissions. Visit the "Symposium Papers" page to read abstracts and proceedings papers provided by the speakers.

The *www.bifconference.com* site is made possible through sponsorship by Biozyme Inc. and the cooperation of BIF, the California Beef Cattlemen's Improvement Association (CBCIA) and the California Cattlemen's Association (CCA), who hosted this year's event.

Using DNA in selection

Keynote speaker Mike Goddard set the stage for a symposium focused primarily on using DNA analysis in beef cattle selection. Speaking during the May 1 opening general session in Sacramento, Calif., the University of Melbourne (Australia) geneticist said the gradual unlocking of the beef cattle genome promises greater opportunity for breeders to manipulate genetic variation.

DNA testing has already made it easier to select for or against some genetic traits, because they are known to be controlled by single genes. However, Goddard explained that most economically important traits are influenced by many different genes and the environment.

The genetic architecture for many traits remains a mystery. According to Goddard,

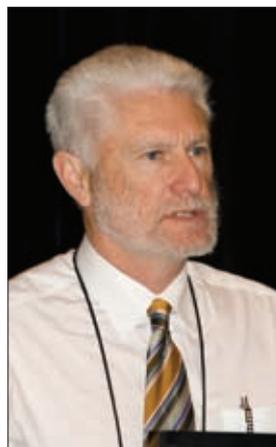▶ Mike Goddard, chief scientist, Beef CRC, Australia

results of human genome studies show that one gene marker, or single nucleotide polymorphism (SNP), may explain only 0.1% to 0.4% of the variation for a certain trait.

"That's a tiny amount of influence," Goddard explained. "And hundreds or thousands of SNPs might be needed to explain all of the variation expressed for just one trait."

Recently, Goddard said, panels of 50,000 SNPs have become available, offering greater opportunity to select for traits beef cattle breeders want to improve. To use these SNPs, their potential effect on important traits must be estimated. From a reference population, cattle are genotyped for the SNPs and measured for the associated traits. Then a prediction equation is derived to estimate a breeding value for each particular trait. The prediction equation is then applied to a different population

Feedlot marker-assisted management

▶ Bill Kolath, Cargill Meat Solutions

During the 2009 Beef Improvement Federation (BIF) symposium, speaker Bill Kolath told the general session audience how DNA technology is being applied by the cattle-feeding sector. Kolath, who oversees production research for Cargill Meat Solutions, said feedlot managers are using DNA gene marker panels to sort cattle into outcome groups.

"What we're going after," Kolath said, "is the ability to optimize not just the genetic potential, but the economic capability of each feedlot animal."

According to Kolath, challenges to improving production efficiency and carcass end-point management include various environmental and genetic factors contributing to diversity in the feedlot population. Cargill's approach to managing such diversity is to base decisions on both live animal evaluation and genetic information.

Marker panels help sort individually identified and genotyped animals into four outcome groups requiring different management strategies. Management strategies for each group differ, including length of feeding period and application of technologies, such as growth promotants, in order to take animals in each group toward an optimum marketing end point.

Group 1 includes early-maturing cattle, which fatten relatively easily. The management goal is to promote lean meat yield and prevent them from becoming too fat. Group 2 consists of cattle that exhibit average performance. Group 3 is characterized by smaller, immature cattle that typically require more days on feed to reach a mature weight, but produce large carcasses of acceptable grade and yield. Group 4 consists of genetically superior cattle that marble easily and produce high-quality carcasses. They would be managed without growth implants that might interfere with that marbling ability and jeopardize potential market premiums for high-Choice and Prime carcasses.

"The economic impact from marker-assisted management has been a two-to-one return on investment," Kolath explained, "but I expect that to improve to a three-to-one return as costs of DNA-testing cattle continue to go down."

— *by Troy Smith*

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of animals that have SNP genotypes but no phenotypic information to calculate a molecular breeding value (MBV). The MBV is combined with the traditional expected progeny difference (EPD) value, creating a new and more accurate genomic EPD (GEPD).

It should be more accurate, but Goddard said obtaining a prediction equation that accurately predicts breeding value from SNP genotypes has been difficult, because a prediction equation that works in one breed or herd may not work in other breeds and herds. The answer, he said, will likely come from estimating prediction equations from very large reference populations that include several breeds, and then testing or validating the prediction equations across large populations involving several breeds.

The industry is attempting to utilize the first generation of genomic EPDs. In years to come, Goddard expects many animals will have DNA genotypes, and the methods used to calculate EPDs will change drastically, with results offering improved accuracy.

"Genomic technology will keep getting better," Goddard added. "We should have 300,000 or more SNPs available to us in the near future, and costs will lessen. DNA profiles, I believe, will become very common and will be used directly in the calculation of EPDs."

— *by Troy Smith*

Genomic selection is here

Whole genome selection technology is here, University of Missouri animal genomics professor Jerry Taylor told BIF attendees. "By the end of this year, beef producers in this audience are going to be buying the tests."

During his presentation, Taylor gave an overview of the SNP technology that is making it possible for genome selection in bovines. SNPs are the DNA variants that occur and can identify the genetic variation for specifically identified traits such as growth, carcass, heifer pregnancy, feed efficiency, palatability, shear force, etc.

Presently, an assay with 50,000 SNPs has been developed, but it costs more than $200 per individual animal. Because that cost is not practical for the industry, additional research

and refinement has led to development of a test with 384 SNPs. Taylor explained that to develop this test, instead of using random SNPs researchers used a process they dubbed "forward selection" in which they selected specific SNPs that were most strongly associated with a trait value such as marbling.

Taylor says the resulting 384-SNP test appears more practical and affordable for the industry. "We can deliver this at a price point that makes the test worthwhile," he said.

Taylor explained that the first tests that will be made available will be breed-specific, because they've found in their validation tests that when jumping between breeds, the prediction model is not accurate. Currently, Merial is working to commercialize a genomic assay for the Angus breed built from Taylor's genomic work in Missouri and validated in commercial steers and registered Angus sires. Taylor reported that the Angus breed is working to make genomic EPDs available to cattlemen soon, as well. *(Editor's note: Update — Angus Genetics Inc. and Merial have entered into an agreement to provide Angus breeders with genomic-enhanced EPDs. See page 162 for more information.)*

As more DNA genotypes are collected for beef cattle across breeds, Taylor says across-breed tests could be developed within the next couple years. Taylor says in addition to Angus, a great deal of genotype information has also been collected from the Limousin, Charolais, Hereford and Simmental breeds — and that information is being used to start developing across-breed tests.

Looking forward, Taylor emphasized to BIF attendees and leadership the importance of building a DNA repository for beef cattle breeds in the very near future. "We are going to need DNA from thousands of animals of each breed to make this work right," he said.

Specifically, Taylor reported that the dairy industry has found that genotypes from 6,000 bulls are needed to get accuracies of about 70%. Thus, Taylor said, the beef industry will also likely need at least 6,000 animals with DNA and EPDs

> ## "By the end of this year, beef producers in this audience are going to be buying the tests."
> — *Jerry Taylor*

►**Jerry Taylor, University of Missouri**

for each breed. He suggested that ultimately a 1-million-SNP assay is what will be needed for thorough and accurate genomic information in the beef industry.

Efforts on the table in Missouri right now would help in getting a beef breeds DNA repository effort started, but additional support is still needed from the industry to provide semen samples on AI bulls to stock such a repository.

Taylor told those in the beef industry to be thinking about what traits are really important that can be applied to this genomic technology. As examples, Taylor pointed out disease resistance and meat palatability. In closing, he said now that genomic selection is here, the industry has the opportunity to produce genomic EPDs for traits such as these that were previously too expensive and difficult to predict.

— *by Kindra Gordon*

Where are we with whole-genome analysis?

Understanding the beef genome offers tremendous potential value in improving genetic selection for economically relevant traits (ERTs) for which EPDs don't exist or are of low accuracy. Dorian Garrick, who holds the Lush Chair in animal breeding and genetics at Iowa State University, presented an overview of current activities and progress being made in whole-genome analyses.

Garrick first explained that genomics evaluation consists of three phases:

1. training, also called discovery, in which you analyze either individual SNPs or analyze the entire genome looking for markers of value;

2. validation, in which you confirm whether or not those markers are in fact valuable; and

3. commercialization of those validated markers.

Garrick said there are two primary training populations currently available, both of which are dominated by Angus genetics. These include a dataset at the University of Missouri from Angus AI (artificial insemination) bulls that have published EPDs, and a multi-breed dataset developed by the U.S. Meat Animal Research Center (USMARC) at Clay Center, Neb. Numerous universities across the country are also working to collect data for specific goals such as detecting markers for carcass and meat attributes, including beef

healthfulness, feedlot health, performance data and female fertility.

"Collectively, these projects represent major intellectual and economic investments in beef cattle improvements through funding by Pfizer Animal Genetics, Merial, land-grant universities and the U.S. Department of Agriculture," Garrick said, noting that these investments will deliver improved selection tools to the U.S. beef industry and answer important questions we have in understanding the beef genome.

Specifically, he said three questions may be answered within the next 12 months:

1. What is the upper limit for predictive ability using a high-density genomic panel with 50,000 markers?

2. How is that predictive ability influenced by genetic distance?

3. Can a sample of just a few hundred markers offer similar predictive ability for

► Dorian Garrick, Lush Chair in animal breeding and genetics, Iowa State University

substantially less cost?

These questions are the current focus of whole-genome analyses in U.S. beef cattle based on the Bovine Illumina™ 50K Panel, a panel of 50,000 SNP markers that was developed using federal funds and made commercially available by Illumina in January 2008.

The 50K panels have also been used to make predictions for both the breed they were based on and other breeds. The most extensively analyzed dataset has again been those of Angus AI bulls, and correlation between discovered markers and existing EPDs have been calculated at 0.5-0.7. This correlation rate is equivalent to genomic predictions that account for between 25% and 50% of genetic variance.

"When you put that in perspective, that means that the 50K genomic prediction is equivalent to about six to 16 offspring in a progeny test if that trait had a heritability of 25%," Garrick said. However, he said that

when genomic predictions are made across breeds the information is far less reliable, often equal to observations based on only one progeny.

The 50K panels have also been analyzed to determine if fewer markers can be used without sacrificing predictive ability. Garrick said that for within breed predictions a sample of the best 600 SNPs taken from the 50K panel may actually offer information that is "almost as good" as the more expensive, larger panel.

— by Meghan Richey

Enhancing EPDs through genomics

"The beef seedstock business is entering a new era of animal evaluation. Breakthroughs in genomics technology now offer the potential to increase the accuracy of existing EPDs, as well as select for traits not previously evaluated," said U.S. Beef Breeds Council representative Kent Andersen.

Genome analysis has already yielded sizable panels of markers and led to the development of MBVs. Andersen said that for this information to most effectively influence seedstock selection decisions, it

DNA companies share vision for whole-genome future

"This is really an exciting time in animal breeding with the new technology coming available," Mark Allan of Pfizer Animal Genetics told attendees at the annual Beef Improvement Federation (BIF) Symposium April 30-May 3 in Sacramento, Calif.

Allan remarked how advancements in genetic selection over the last four decades — such as performance data and expected progeny differences (EPDs) — have aided in improving beef cattle performance and adding value to the industry. With the addition of whole-genome selection, Allan said, "The industry is adding more tools for genetic prediction and accuracies."

Allan and Brent Woodward of Igenity shared remarks about their respective company's vision for implementation of whole-genome selection in the beef industry.

Igenity is presently working to commercialize a new breed-specific genome marker panel that will likely be available later this year. (See page 162 for more information.) Woodward explained that his company has been collaborating with university and government researchers, and even researchers on the human health side, to select SNPs to make the new panel of markers.

"From the 50,000 bovine SNP chip, Igenity has looked at numerous analytical methods to help pick out the best panel that is also most cost-effective for the beef industry," Woodward said.

In the future, he said, Igenity will make additional whole-genome marker panel tests available. He said he foresees different tests offering different SNP levels and price points, which he dubbed small, medium and large. Woorward explained that a 100-SNP panel, for instance, could be made available for a relatively inexpensive cost. Whereas, some breeders may seek a larger SNP panel that could explain more variation in traits, and that might be made available for a higher price.

Additionally, Woodward shared that Igenity has agreements in place with several breed associations and national cattle evaluation centers to assist in producing molecular breeding values (MBVs), or genomic EPDs. Igenity is also developing software tools available on their web site for producers to use to do custom sorts based on

their herd's genomic information from Igenity tests or to benchmark within a breed or the entire Igenity database.

Likewise, Allan reported that Pfizer Animal Genetics is developing a whole-genome selection product, using what he called their own "robust system with a novel approach" to select SNPs for their specific marker test. Allan emphasized that Pfizer is using different methodologies with checks and balances in place to ensure that the product will align with customer needs and expectations. He said Pfizer will make its whole-genome product available "when we are confident in the offering."

Looking forward, Allan said he, too, anticipates that a variety of whole-genome panels will be developed for specific traits, suites of traits and even specific markets. He foresees whole-genome tests for traditional cow herd and postweaning traits like fertility, growth and carcass, as well as for newer traits like feed efficiency and health.

Additionally, Allan said, this new technology should give way to some new evaluations for traits. As one example, he said he anticipates the creation of a SNP for a "healthfulness index," which would look at the healthy attributes of beef and ultimately help promote the consumption of beef.

Allan noted that the end goal of genomics-based tests is to be a useable resource that assists producers in their decision-making and allows for prediction of animal performance at a young age.

He emphasized that for whole-genome technology to advance and be credible, the industry must also continually invest. "It's going to take lots of phenotypes and lots of environments to make this happen," he said.

Allan said Pfizer is committed to this new era of genetic selection tools not only in providing products, but also investing in the education and implementation process.

"We're assembling a team of people to deliver a product with full service," he said. "Education is a huge part of the implementation of whole-genome selection, from scientists to producers."

— by Kindra Gordon

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should be integrated into existing breed association performance programs. This would require new business infrastructure to integrate the activities of breeders, breed associations, genomics companies and genetic evaluation service providers.

It is a worthwhile undertaking, he said, because substantial ambiguity and confusion could result if traits were instead evaluated separately by both traditional EPDs and by MBVs from multiple service providers.

"Integrating MBVs into existing EPDs would eliminate ambiguity, enhance accuracy and reduce the possible change, or error, associated with the predictions," Andersen said.

As an example, consider a weaning weight (WW) EPD with an accuracy of 0.20 yielding a possible change of ±12 pounds (lb.). If MBV information were integrated into that EPD, improving the accuracy from 0.20 to 0.60, the magnitude of possible change would be reduced by half. The possible change would then be just ±6 lb.

"With increased accuracy there is significantly more value in the information because there is less risk," Andersen said, noting that bulls with this enhanced data would likely be perceived as more valuable, too.

Genomics technology may also be applied to those ERTs that do not lend themselves to traditional EPD evaluation due to the time or expense needed to measure them, he said. This could include traits such as feed utilization, animal health, the healthfulness of beef products, palatability and adaptability to environmental stress.

Ultimately, Andersen said breeders'

►Kent Andersen, U.S. Beef Breeds Council Representative

abilities to realize value from MBVs depends on the degree to which breed associations, genomics companies and genetic evaluation providers effectively collaborate.

— *by Meghan Richey*

Is there gold in genomes?

Wrapping up the first general session of the symposium, Garrick said work to apply genomic selection in beef cattle is moving forward.

"We were at a crossroads a year or two ago," Garrick said, noting how there was uncertainty about how to move forward with DNA marker-assisted selection. There were questions about the respective roles of breed associations, DNA-testing companies and genomics companies. And there were questions about how to combine marker selection with EPD values.

Garrick said it is now understood that genomics companies will offer services that include computing MBVs to enhance EPDs. It is known that enhanced EPDs will increase the accuracy of predicted performance for young genotyped cattle, with accuracy increasing according to market panel size. It also appears that market-assisted management is viable, particularly as demonstrated for sorting feedlot cattle into outcome groups. However, Garrick said, some breeds are poorly represented in discovery populations.

"In the future we can expect some breed associations to incorporate molecular breeding values into their national cattle evaluations. And we can expect ongoing improvement in accuracy," Garrick stated. "And I expect the scope to expand to other breeds."

— *by Troy Smith*

Dairy industry steps ahead

During the 2009 BIF committee presentations addressing emerging technologies and advancements in selection decisions, University of Melbourne (Australia) veterinarian and geneticist Mike

Goddard explained that practical application of genomic evaluation is more advanced in the dairy industry, compared to the beef cattle industry. Goddard explained that all major dairy countries are applying selection based on a panel of genetic markers to establish estimated breeding values (EBV) or EPDs among animals.

This requires a reference population that has been genotyped for markers associated with economically important traits. In dairy cattle, Goddard said, this has usually consisted of progeny-tested bulls. However, Goddard says future reference populations will also include females.

The reference population is used to estimate a prediction equation for breeding value from marker genotypes. The prediction equation can then be applied to genotyped bulls and heifers that do not have individual records or progeny. With increased size of reference population, Goddard said, comes increased accuracy of the prediction equation. It is possible to predict an animals breeding value for milk yield, for example, almost as accurately using markers as with a progeny test.

"Applying intense selection for high-accuracy bulls and selection for the best females promises to double the rate of genetic improvement," Goddard said.

A potential consequence of whole-genome-based selection is an eventual decline in the use of artificial insemination (AI), he said. "Improvement in bulls raised for use naturally, might reduce the previous AI advantage."

— *by Troy Smith*

The 2,000-bull project

It's all well and good that geneticists have mapped the bovine genome, identifying 50,000 SNP markers. And knowing that certain DNA markers are associated with genes that control certain traits provides a new tool for genetic selection of beef cattle.

According to USMARC geneticist Mark Thallman, whole-genome selection represents a huge leap in technology. But to be most effective, Thallman says, this technology must be incorporated into the national cattle evaluation (NCE) system. In other words, DNA-marker selection must be combined with the calculation of EPD values currently used to guide genetic

►Mark Thallman, U.S. Meat Animal Research Center

> **Breeders' abilities to realize value from MBVs depends on the degree to which breed associations, genomics companies and genetic evaluation providers effectively collaborate.**
>
> — *Kent Andersen*

> **"The initial focus will be on weight traits, with carcass traits to follow. The loftier goal is to provide MBVs for hard-to-predict traits, including efficiency."**
> — *Mark Thallman*

selection to generate an enhanced genomic EPD.

During the 2009 BIF symposium, Thallman described the USMARC whole-genome selection project involving 2,000 beef cattle sires. The project was designed to collect genotypic data on a large number of influential sires. The population includes sires representing 16 breeds. Some sires had been part of the USMARC Germplasm Evaluation project, but most were selected by respective breed associations, which provided semen from which DNA samples could be taken. Many of those sires have relatively high-accuracy EPDs.

Thallman said the project requires a training population that consists of animals with genotypic and phenotypic data. Thereby, DNA-based selection can be tested against a population for which there is prior knowledge, with respect to various economically important traits. At USMARC, the primary training data is in progeny and grandprogeny (both steers and females) representing 22 sires of seven different breeds.

Practical application of the project results comes after prediction equations for various traits are calculated and validated through a separate cattle population. Once MBVs are derived from the genotypes of the 2,000 bulls, MBVs will be provided to breed associations for calculation of genomic EPDs. For the short term, genomic EPDs will be breed-specific.

"The initial focus will be on weight traits, with carcass traits to follow," Thallman said. "The loftier goal is to provide MBVs for hard-to-predict traits, including efficiency."
— *by Troy Smith*

Weight trait project

During discussion of advancements in genetic prediction at the 2009 BIF symposium, Cornell University geneticist John Pollak described the Weight Trait Project (WTP) — a collaborative effort of Cornell, USMARC and the University of Nebraska. Pollack said the project is designed to further implementation of DNA-based selection in conjunction with EPD values.

Pollack explained that through an association study of the 50,000 known SNPs of the bovine genome and weight traits collected on cattle at USMARC, DNA markers for birth weight, weaning weight and yearling weight have been identified. Through the project, researchers intend to concentrate on application of the most informative SNPs associated with early growth.

According to Pollack, breed associations have identified seedstock breeders in the region surrounding USMARC's Clay Center, Neb., facility that will provide DNA samples on 1,000 animals per each of seven breeds. Igenity® has agreed to serve as genetic service provider by genotyping all 7,000 animals.

Marker effects will be estimated using information collected from the seedstock producer in conjunction with USMARC data. Resulting MBVs will be validated using university herd records.
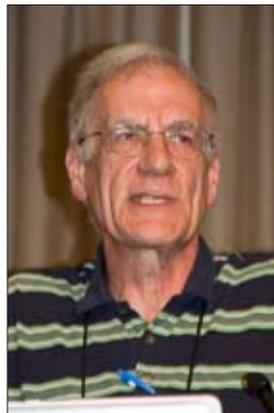
"To examine the impact of integration of MBVs into the calculations of EPDs, we will compute EPDs for animals in the herds providing DNA," Pollak explained. "Those results will be compared for improvement of accuracy in the evaluations of yearling bulls."

Pollak said that while there has been much discussion about the value of moving DNA information into genetic evaluation, there has been little preparation for it. The Weight Trait Project, he added, represents a unified effort among researchers, breed associations, seedstock producers and a DNA-testing company to improve the process of developing and validating DNA tests and to investigate the infrastructure necessary for the flow of information needed to deliver marker-assisted EPDs.

▶ John Pollak, Cornell University geneticist

"This project forces us to investigate issues we may have been ignoring over the last couple of years," Pollak stated.

In the future, he hopes to see the project replicated in different production environments and expanded to involve more breeds.
— *by Troy Smith*

What proportion of genetic variation is explained?

Cornell University geneticist Richard "Dick" Quaas said evaluation of commercial DNA tests has begun to shift from whether a certain test works to how well it works.

"Increasingly, we want to know what proportion of additive genetic variation [for a particular trait] is accounted for by a DNA test," Quaas said. "Is it some, most or very little?"

Quaas said the NBCEC statistical team has applied three different estimators of percentage of genetic variation explained. All estimators performed similarly, on average, and none were very precise for tests associated with traits with low heritability. However, Quaas said the team considers the squared genetic correlation between the observed trait and the molecular breeding value to be the best estimator.

"We consider the reporting of percentage of genetic variation accounted for by DNA test to be an integral part of the validation process,

▶ Richard Quaas, Cornell University geneticist

in the short term," Quaas concluded. This estimation will be required to incorporate DNA testing into the national cattle evaluation (NCE) system and, thus, for the beef industry to utilize this technology much more effectively and extensively than it is currently being utilized."
— *by Troy Smith*