

HOW TO USE COMMERCIALY AVAILABLE GENOMIC PREDICTIONS

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IMPLICATIONS

Genomic predictions for commercial cattle can be used to select replacement heifers, design mating strategies, and market calves. Presently, two companies (Igenity and Zoetis) offer genomic tests for commercial cattle. Like expected progeny differences (EPDs) on young bulls, these genomic tests do not perfectly predict genetic merit. However, these tests will be useful for identifying genetically superior and inferior animals for the traits tested. Some tests are useful only for predominantly Black Angus ($\geq 75\%$) cattle, while other tests can be used on all *Bos taurus* beef breeds and crossbreds. Further, some tests are designed specifically for producers who are retaining ownership or who are marketing their calves to feeder calf certification programs. Producers should choose a genomic test that includes traits that are economically relevant to their operation.

INTRODUCTION

Genomic science has already made important contributions to society. In clinical medicine, genomic science has discovered two mutations in BRCA1 and BRCA2 genes that increase risk for breast cancer¹, allowing women at higher risk for this cancer to be screened at more frequent intervals. Genomic techniques have discovered hundreds of mutations responsible for rare disorders linked to single genes². In crop production, genomics has resulted in creation of genetically engineered plant species³ as well as molecular breeding techniques⁴ that have increased yields and reduced losses due to disease. In livestock production, genomics discoveries are contributing to increasing yields and improving herd health. Genomics in the livestock industry has moved beyond simple selection against genetic abnormalities towards genomic prediction of genetic merit for complex traits such as calving ease, average daily gain, and carcass quality. Although many of these genomic predictions have been developed for the seedstock industry, genomic predictions have begun to be targeted increasingly to commercial producers, and the beef industry is no exception. This paper will explore the genomic predictions available to commercial beef producers and my opinion about how these predictions should be utilized.

WHAT ARE GENOMIC PREDICTIONS?

Genomic predictions are defined here as any DNA test that can predict genetic merit for a complex trait. A complex trait exists when expression of the trait is determined by many gene variants, each with small effect on trait expression, as well as environmental

factors. All traits with EPDs are complex traits and include fertility, survivability, maternal, growth, and carcass traits. In contrast, simply-inherited traits are affected by only one or a few gene variants and environmental factors play little to no role in trait expression. Examples of simply-inherited traits include genetic abnormalities and red/black coat color in Angus cattle.

Genomic predictions increase the accuracy of selection decisions^{5,6}. From this perspective, genomic predictions are performing the same function as EPDs. Genomic predictions are especially valuable for traits that are difficult or expensive to record, or that are measured late in an animal's life. Not coincidentally, these traits either don't have EPDs available or longer time is needed to achieve high EPD accuracies. Because genomic predictions can be theoretically obtained at birth, more accurate prediction of genetic merit can be achieved at an earlier age, allowing producers to make more accurate selection decisions sooner. Many commercially raised heifers lack EPDs, making genomic predictions a useful tool for selection of replacement heifers.

An important limitation to understand about genomic predictions is that these predictions are not perfect. The accuracy of genomic predictions is a function of the percent genetic variation for the trait that is explained by the genomic prediction. Recall that complex trait expression is affected by many gene variants. To explain the concept of percent genetic variation, let's assume that 100 gene variants affect trait expression, and each of these variants will be represented by either a red or blue marble in a jar of 100 marbles (one marble for each variant). A blue marble represents a genetic variant that is accounted for by the genomic prediction and a red marble represents a genetic variant that is not accounted for by the genomic prediction. If ten marbles are blue, then 10/100 or 10% of the genetic variance is explained by the genomic prediction. If 60 marbles are blue, then 60/100 or 60% of the genetic variance is explained by the genomic prediction. Obviously, the latter genomic prediction will be more accurate because more of the gene variants are accounted for in the genomic prediction. Although the accuracy of genomic predictions varies among DNA testing companies and traits, genomic predictions will not explain 100% of the genetic variance for any trait. Thus, genomic predictions cannot be 100% accurate. However, EPDs on young animals are far from perfect predictions of genetic merit, too, and genomic predictions can provide valuable information on genetic merit of calves.

WHAT GENOMIC PREDICTIONS ARE AVAILABLE TO COMMERCIAL BEEF PRODUCERS?

Genomic predictions can be placed into one of two categories, based on whether the prediction is best used primarily by seedstock or commercial beef producers. Genomic predictions for the seedstock industry are breed-specific and the genomic prediction is incorporated into each animal's EPD. Expected progeny differences that include genomic predictions are called genomically-enhanced EPDs (geEPDs). Genomically-enhanced EPDs are interpreted the same as EPDs. The only difference is that geEPDs will be a more accurate prediction of genetic merit. The increase in accuracy is inversely proportional to the quantity of performance data that is available. In other words, genomic predictions will be more valuable for young bulls than for proven bulls.

Commercial beef producers may encounter geEPDs when purchasing bulls from seedstock producers who choose to utilize them. Commercial producers benefit because geEPDs will more accurately predict genetic merit, which decreases selection risk. Bull buyers take less risk when selecting bulls with geEPDs because a geEPD is a more accurate reflection of an animal's true genetic merit. However, the vast majority of commercial producers will not choose to use seedstock-specific genomic predictions on their cows, heifers, and calves.

Genomic predictions targeted to commercial producers are also available and options for genomic testing have increased in recent years. Because commercial cattle often don't have EPDs, the genomic prediction is reported directly to producers who purchase these products. These genomic predictions can be used to select for replacement heifers, market feeder calves, predict genetic merit for bulls that do not have EPDs, and make mating decisions. The industry is rapidly evolving, but as of this writing, two companies are providing genomic predictions to commercial cattle producers: 1) Igenity (Neogen) and 2) Zoetis.

Igenity offers two genomic predictions (GOLD and SILVER), and each of these genomic predictions are further stratified by breed: 1) Black Angus and 2) non-Black Angus *Bos taurus*, including crossbreds. The GOLD profile evaluates 13-15 traits depending on breed composition and the SILVER profile evaluates six traits (Table 1). Results are reported as 1-10 numerical scores, where higher scores reflect larger trait values. Thus, whether a score of 1 or 10 is desirable depends on the trait. For example, a score of 10 is desirable for heifer pregnancy rate because higher pregnancy rate is desirable, but a score of 1 is desirable for birth weight because lighter birth weights are preferred.

Igenity publishes a results key (Table 2) that allows producers to predict performance of an individual's progeny for each tested trait. To compare genomic predictions between two animals, first find the "molecular breeding value" associated with each animal's trait and numerical score from the results key. Second, take the difference between the two animals' molecular breeding values. The difference corresponds to the expected difference in performance of the progeny of each individual for the trait in question. For example, a calf with a score of 8 for stayability is expected to produce daughters that are 12.6% more likely to stay in the herd until at least six years of age relative to a calf with a score of 4 for stayability (Table 2). Although the numbers in the results key are called "molecular breeding values", these numbers are more similar to EPDs in how they should be interpreted. By themselves, these numbers are meaningless, but molecular breeding values can be used to compare expected performance of the progeny of two individuals, as shown above.

In addition to genomic predictions for individual traits, Igenity publishes a "production index", which is interpreted similarly to traditional selection indices published by breed associations (e.g., \$Beef, All-Purpose Index). This "production index" is based on genomic predictions for traits in the Igenity Profile. This index appropriately weights genomic predictions for each trait and then combines weighted genomic predictions into a single number that can be used to make selection decisions. The weights are based on economic assumptions about calf prices and costs. Separate production indices exist for Black Angus and non-Black Angus *Bos taurus* cattle (Figure 1). Producers can rank

animals using default weights assigned to each trait in the index (Figure 1) or customized weights chosen by each individual producer.

Zoetis offers three genomic predictions for commercial producers. Two of these genomic predictions are targeted towards $\geq 75\%$ Black Angus cattle and the third genomic test is targeted towards *Bos taurus* cattle that are $< 75\%$ Black Angus. The two Angus-specific genomic predictions are GeneMax (GMX) Focus and GMX Advantage. GeneMax Focus targets two traits (Table 1) important to producers who are retaining ownership or marketing feeder calves to collect on premium prices. Genomic predictions for each trait are reported as 1-5 numerical scores (5 is always more desirable regardless of the trait) and a GMX Score (1-99) is also reported. The GMX Score is a molecular selection index based on genomic predictions of the two traits evaluated by GMX Focus. Higher GMX Scores are more desirable.

GeneMax Advantage reports three different economic indices similar in nature to Igenity's production index and GMX Focus: 1) Cow Advantage, 2) Feeder Advantage, and 3) Total Advantage. Each index weights genomic scores for each trait by its economic value to beef producers (Figure 1). Economic values are based on similar assumptions and data that are used for \$indices published for Black Angus cattle by the American Angus Association. The Cow Advantage index is targeted towards cow-calf producers who sell their calves at weaning. The Feeder Advantage index is targeted towards producers interested in improving feedlot and carcass performance of their calves or for marketing calves to a feeder calf certification program. The Total Advantage index combines traits from both of the above indices for producers interested in improving cow-calf, feedlot, and carcass traits. Like the GMX Focus Score, each of the above index scores can range from 1-100, where higher numbers are more desirable. GeneMax Advantage also includes "Smart Outlier" reporting, which identifies animals predicted to have poor genetic merit for tenderness, cow cost, docility, and marbling. "Smart Outlier" reporting also will identify animals predicted to have superior genetics for marbling. Default thresholds are cattle with genomic scores that correspond to the bottom 5% of the Zoetis reference Angus population for cow cost, tenderness, and docility as well as the bottom and top 25% of cattle for marbling. These thresholds can be customized by producers to better reflect traits economically important to a producer's operation.

The final commercial genomics test offered by Zoetis is PredicGEN, which is designed specifically for *Bos taurus* beef cattle that are $< 75\%$ Black Angus. PredicGEN predicts genetic merit for three carcass traits (Table 1). Results are reported on a 0 to 100 scale (same as the other Zoetis products) where larger numbers are more desirable. A "grid merit" index is also reported that accounts for only marbling and yield grade genomic predictions.

All of these genomic testing services offer sire parentage testing for no extra charge. Depending on the test, producers can leverage DNA samples collected previously by seedstock producers on registered Angus bulls in their herd or submit DNA samples from their bulls.

WHICH GENOMIC PREDICTION SHOULD I USE?

First, you need to identify the economically relevant traits in your herd. The economically relevant traits are those traits directly related to profit (income and costs) and may differ among producers depending on how calves are marketed and conditions where calves are raised. For example, producers who sell their calves at weaning based on calf weight are less likely to benefit from using genomic predictions focused on performance in the feedlot or the packing plant. Producers should choose genomic predictions that are well-aligned with their economically relevant traits.

Second, the breed composition of your calves needs to be considered. Some genomic tests are designed for cattle that are $\geq 75\%$ Black Angus. Producers should use genomic predictions that are non-breed specific when calves are $< 75\%$ Black Angus. Genomic predictions for commercial US cattle are not currently being marketed for *Bos indicus* or *Bos indicus* cross calves.

After considering your economically relevant traits and breed composition of your herd, you may be left with more than one viable option. Unfortunately, no data is available in the scientific literature that would help you choose a specific genomic prediction. Genomic predictions are proprietary and validation is completed within house. Zoetis and Igenity have not worked with independent scientists to publish the efficacy of their genomic predictions prior to releasing them to the general public. Although independent scientists can attempt to validate these genomic predictions after their release, funding for these validation studies is not readily available. Further, because of the rapidly evolving nature of the livestock genomics industry, by the time a genomic prediction is validated, the prediction may be obsolete or the DNA markers included in the genomic prediction may have changed. The percent genetic variation explained by each prediction is sometimes reported by DNA testing companies, but when reported may take the form of an “average” value across all traits, which is less informative than reporting on an individual trait basis.

HOW SHOULD I USE GENOMIC PREDICTIONS?

Towards the end of this paper is data reproduced from a field study published on Zoetis’s website on the GMX Focus prediction which evaluates genetic merit for marbling score and average daily gain (ADG; Table 3)⁵. Data was collected on high percentage Black Angus steers ($n=173$) in a feedlot in Kansas. Steers were harvested at a packing plant in Dodge City, KS. Steers were placed into one of four groups based on their GMX Focus prediction and mean marbling and ADG for each group was recorded (Table 3). First, note that steers in the “high” GMX Focus score category had significantly higher marbling scores than steers in the “mid-low” and “low” categories ($P < 0.05$). However, marbling scores were not significantly different between “high” and “mid-high” or “mid-low” and “low” GMX Focus categories, although a numerical difference in marbling score was observed. No significant differences among GMX Focus scores were found for post-weaning ADG. In fact the “mid-high” group had a slightly higher mean ADG than the “high” group, although numerically steers with higher GMX Focus scores also tended to have higher ADG.

Taken together, this data supports a two-tiered strategy for using genomic predictions for making selection decisions. First, genomic predictions can be used to identify animals with superior and inferior genetic merit for traits of economic importance to your operation. For GMX Focus, individuals with GMX scores <40 and >79 likely had inferior and superior genetic merit for marbling and ADG, which led to higher marbling scores and ADG phenotypes. Depending on the economic value of the trait (or the traits in the index) to your operation, acceptable genomic prediction scores may be only those individuals with superior genetic merit or all individuals except those predicted to have poor genetic merit. After selecting which animals had acceptable genomic prediction scores for traits of interest, producers could use additional selection criteria (e.g., conformation, soundness, performance) to make final selection decisions on which heifers will be kept as replacements. Simply ranking heifers and setting a threshold based on their genomic prediction score to select replacements is not recommended at this time. Less evidence exists that individuals with small differences in genomic prediction scores (e.g., “70” vs. “75” or “7” vs. “8”) are truly genetically different for the traits evaluated (Table 3). Focusing solely on the genomic prediction ignores other potentially valuable selection criteria and the fact that these genomic predictions are not perfect predictors of genetic merit.

One limitation of my interpretation of the available data is that the data have not been published in a peer-reviewed scientific journal. The available data has been culled from promotional literature and technical summaries published on a company website. Further, the data used to make these recommendations is based on the GMX Focus prediction because very little data was available on other genomic predictions. Keep in mind that even if a genomic prediction explained 100% of the genetic variance for a trait, we would not expect the genomic prediction to perfectly predict ADG and marbling score. Diet, management, health status, and stress will also affect these traits. Also, the GMX Focus score may have predicted marbling score better than ADG because the GMX Focus score may place more emphasis on the marbling genomic prediction.

In addition to making selection decisions, genomic predictions may also be used for making mating decisions. For example, heifers with low genomic scores for marbling may be kept as replacements but mated to a bull with superior genetics for marbling. Although progeny may not be genetically superior for marbling, they are also less likely to have poor marbling scores when slaughtered because of the contribution of the bull's genetics. Genomic predictions may additionally help producers market their calves. For example, Black Angus calves may qualify for the Top Dollar Angus certification program in part based on the GeneMax Focus prediction of their dams or the calf itself.

HOW CAN I GET STARTED?

The first step is to contact the company's regional sales representative. They will be more than willing to explain how to collect a DNA sample and how to interpret results. Each company has their own preferred method of collecting a tissue sample for DNA isolation. The three most common methods are a blood spot on a blood card, hair follicle sample from the tail switch, or an ear notch tissue sample. Your sales representative will help you procure all the supplies you need for collecting a tissue sample. If using a blood card, be sure not to oversaturate the card with blood; a few drops of blood are sufficient for DNA isolation. If using hair cards, make sure to collect about 20-30 hair

follicles; the hair shaft cannot be used because it does not contain DNA. None of these methods require special handling or storage of tissue samples. Room temperature storage and shipping is sufficient. However, ensure that each tissue sample is labeled with the correct animal identification or else genomic predictions will not be matched to the correct individual.

REFERENCES

¹ Bansal, A., G.C. Critchfield, T.S. Frank, J.E. Reid, A. Thomas, A.M. Deffenbaugh, and S.L. Neuhausen. 2000. The predictive value of BRCA1 and BRCA2 mutation testing. *Genetic Testing* 4(1): 45-8.

² Yang, Y., D.M. Muzny, F. Xia, Z. Niu, R. Person, Y. Ding, P. Ward, et al. 2014. Molecular findings among patients referred for clinical whole-exome sequencing. *JAMA* 312(18): 1870-9.

³ Prado, J.R., G. Segers, T. Voelker, D. Carson, R. Dobert, J. Phillips, K. Cook, et al. 2014. Genetically engineered crops: from idea to product. *Animal Review of Plant Biology* 65: 769-90.

⁴ Kole, C., M. Muthamilarasan, R. Henry, D. Edwards, R. Sharma, M. Abberton, J. Batley, et al. 2015. Application of genomics-assisted breeding for generation of climate resilient crops: progress and prospects. *Frontiers in Plant Science* 6: 563.

⁵ Van Eenennaam, A. 2010. DNA-based biotechnologies. *Beef Sire Selection Manual*, 2nd edition. National Beef Cattle Evaluation Consortium. http://www.nbcec.org/producers/sire_selection/chapter13.pdf Accessed 09/18/2015.

⁶ Spangler, M., and A. Van Eenennaam. 2010. Utilizing molecular information in beef cattle selection. *Beef Sire Selection Manual*, 2nd edition. National Beef Cattle Evaluation Consortium. http://www.nbcec.org/producers/sire_selection/chapter14.pdf Accessed 09/18/2015.

TABLE 2. Igenity results key for <75% Black Angus Bos taurus GOLD and SILVER genomic predictions (selected traits)^{1,2}

Igenity Scores	Heifer Pregnancy	Milk	Stayability
	%	lbs.	%
10	13.1	35.1	29.9
9	11.6	31.2	26.8
8	10.2	27.3	23.6
7	8.7	23.4	20.5
6	7.3	19.5	17.3
5	5.8	15.6	14.2
4	4.4	11.7	11.0
3	2.9	7.8	7.9
2	1.5	3.9	4.7
1	0	0	0

¹ Selected traits taken from results key in “Igenity Gold and Igenity Silver results key.” Neogen Corporation.

http://www.neogen.com/Genomics/pdf/AG160_IgenityGoldSilverResultsKey.pdf.

Accessed on 09/17/2015.

² Separate results key is used for Black Angus cattle.

TABLE 3. Relationship between GMX Focus prediction (Zoetis Animal Genetics) and marbling score and average daily gain in high percentage Black Angus steers (n=173)¹.

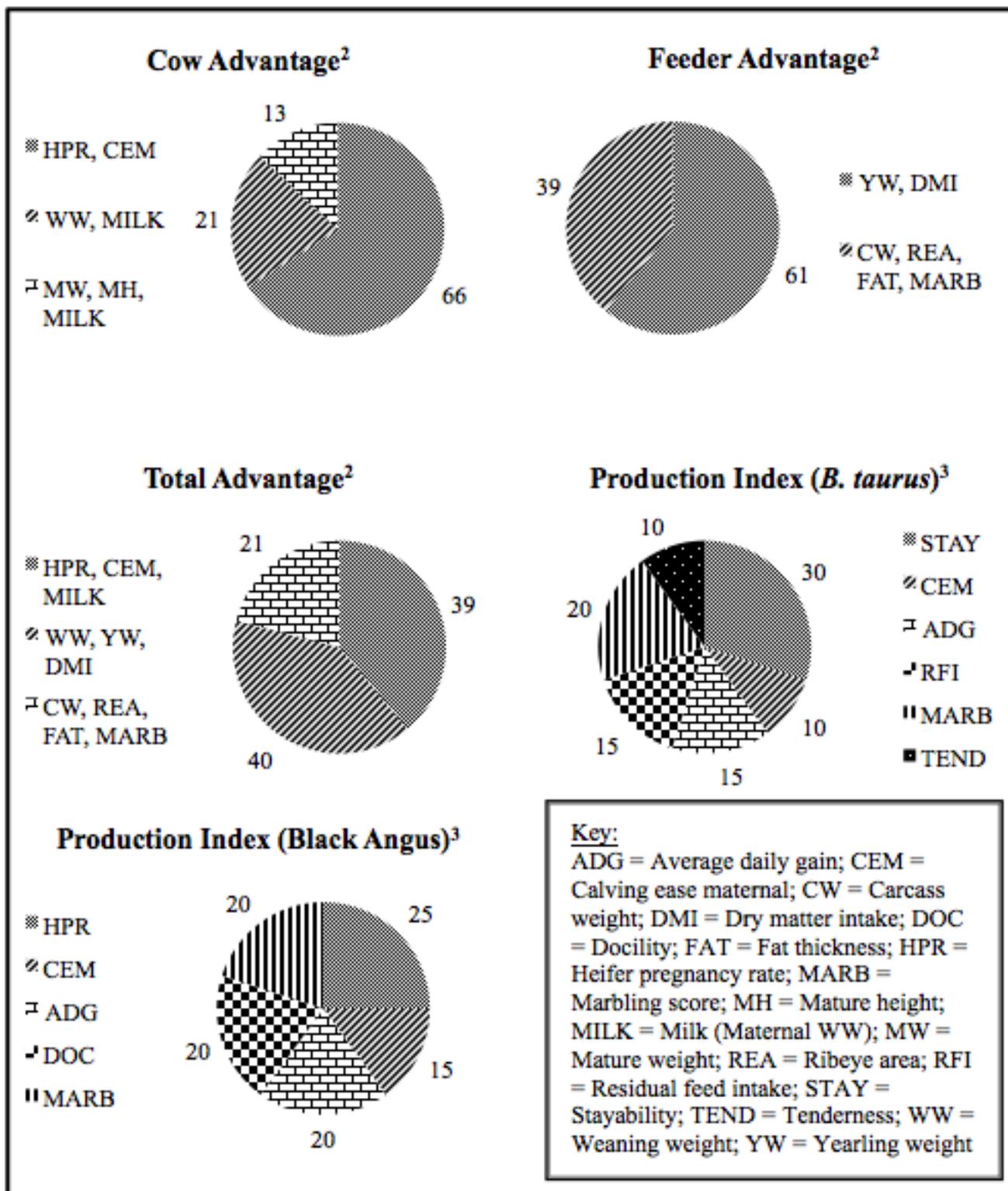
GMX Focus Score Category	Number	Marbling Score ²	Average Daily Gain
High (80-99)	83	538 ^a	4.33
Mid-High (60-79)	32	518 ^{ab}	4.36
Mid-Low (40-59)	30	479 ^b	4.27
Low (0-39)	28	466 ^b	4.22

¹ Data taken from “GeneMax™ Field Study Summary.” Certified Angus Beef.

<https://www.zoetisus.com/animal-genetics/media/documents/prattstudytechnicalreview.pdf>. Accessed on 09/15/2015.

² Means with different superscript letters are significantly different (P < 0.05).

FIGURE 1. Relative emphasis placed on traits for genomic prediction indices¹



¹ PredicGEN and GMX Focus are not included because data is not publically available.

² Zoetis Animal Genetics

³ Neogen Corporation (Igenity)