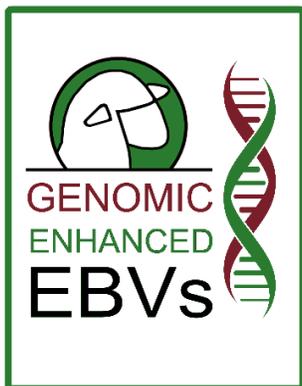


Framework for Obtaining Genomic-enhanced EBVs



In 2021, NSIP Katahdin breeders will be the first sheep producers in the U.S. to have access to Genomic-enhanced Estimated Breeding Values (GEBVs). From 2017 to 2019, a research project led by Dr. Joan Burke and her team laid the groundwork for this effort. During that 3-year period, Dr. Burke enlisted a group of 20 cooperating producers to submit DNA samples resulting in a genetic database of over 5,000 lambs. This formed the genomic reference population for the Katahdin breed. Building upon this research, Dr. Ron Lewis and his Australian colleagues used that genomic reference population to develop the first GEBVs for sheep in the U.S. Currently, the research phase is wrapping up, allowing NSIP to begin to bring this technology to all sheep producers. A grant, awarded to Katahdin Hair Sheep

International (KHSI) from the National Sheep Industry Improvement Center (NSIIC), will help NSIP to commercialize this technology for the U.S. Sheep Industry. Many KHSI volunteers have stepped forward to help with education and delivery of this exciting tool to NSIP Katahdin breeders this year. The NSIP Genomics Ad Hoc Committee has developed a roll-out plan for obtaining GEBVs for U.S. sheep producers beginning with Katahdins. Along with GEBVs, producers will receive reports on genomic-confirmed parentage and genetic conditions for all genotyped animals. Importantly, flocks submitting DNA samples and a minimum level of phenotypic data (Birth Date, Birth Type, Rear Type and 60-day weights) are expected to see slight changes to their animal's breeding values plus small to moderate increases in accuracy of their GEBVs further improving their ability to identify superior breeding stock.

How it will Work

The process of obtaining GEBVs for sheep in the U.S. entails some additional steps above and beyond the standard approach of simply submitting phenotypic data (weights, etc.) to Sheep Genetics and receiving EBVs. The primary contact for U.S. producers will be NSIP for all sample submission, reporting of parentage and genetic conditions, interpretation of results, and any questions that arise. The initial steps focus on collecting tissue samples and submitting those with a simple spreadsheet inventory (NSIP Genomics Sheep Submission Form – *see below under batching*), together with payment, to NSIP. Samples and supporting spreadsheet will be compiled by NSIP and forwarded to our partner laboratory, Neogen, for DNA analysis (genotyping). Also, because genomic-based parentage is critical to building the genomic pedigree and ultimately generating GEBVs, NSIP will work with the Animal Genetics Breeding Unit (AGBU) in Australia to conduct the parentage analysis. Figure 1 shows the steps involved in the process described below:

Stage I - DNA Sample Submission and Genotyping

1. Producer submits DNA samples, spreadsheet submission form, and payment (\$30 per sample) to NSIP for batch coordination prior to genotyping.
2. NSIP combines individual flock submission forms into a single file, pools all DNA samples into a single batch, and forwards all samples and combined submission form to Neogen for DNA testing.
3. Neogen genotypes all samples received by batch deadline and forwards results to AGBU.
4. AGBU conducts parentage analysis and determines genetic conditions based on genotype.

Stage II - Reporting of Parentage and Genetic Conditions to Producer

1. AGBU sends report on parentage and genetic conditions from full batch to NSIP for distribution.
2. NSIP sends flock-specific reports on parentage and genetic conditions to producers for final review and validation.
3. Producer reviews results of parentage analysis and makes any corrections necessary to flock data in Pedigree Master.

Stage III - Standard Submission of Phenotypes with Correct Parentage

1. Following the normal protocol for data submission, producer submits phenotypic data (e.g., Birth Weights, 60-d wts, Birth Type, etc.) including correct genomic-based parentage to Sheep Genetics for evaluation. For any lamb with a 60-d wt, NSIP invoices producer for data fee at \$3.50 per lamb.
2. Sheep Genetics (i.e., Stephen Field) runs the bimonthly genetic evaluation.

Stage IV - Standard Reporting with Genomic-enhanced Breeding Values

1. Following the normal protocol for reporting, Sheep Genetics sends reports via email directly to producer along with link to download their updated database.

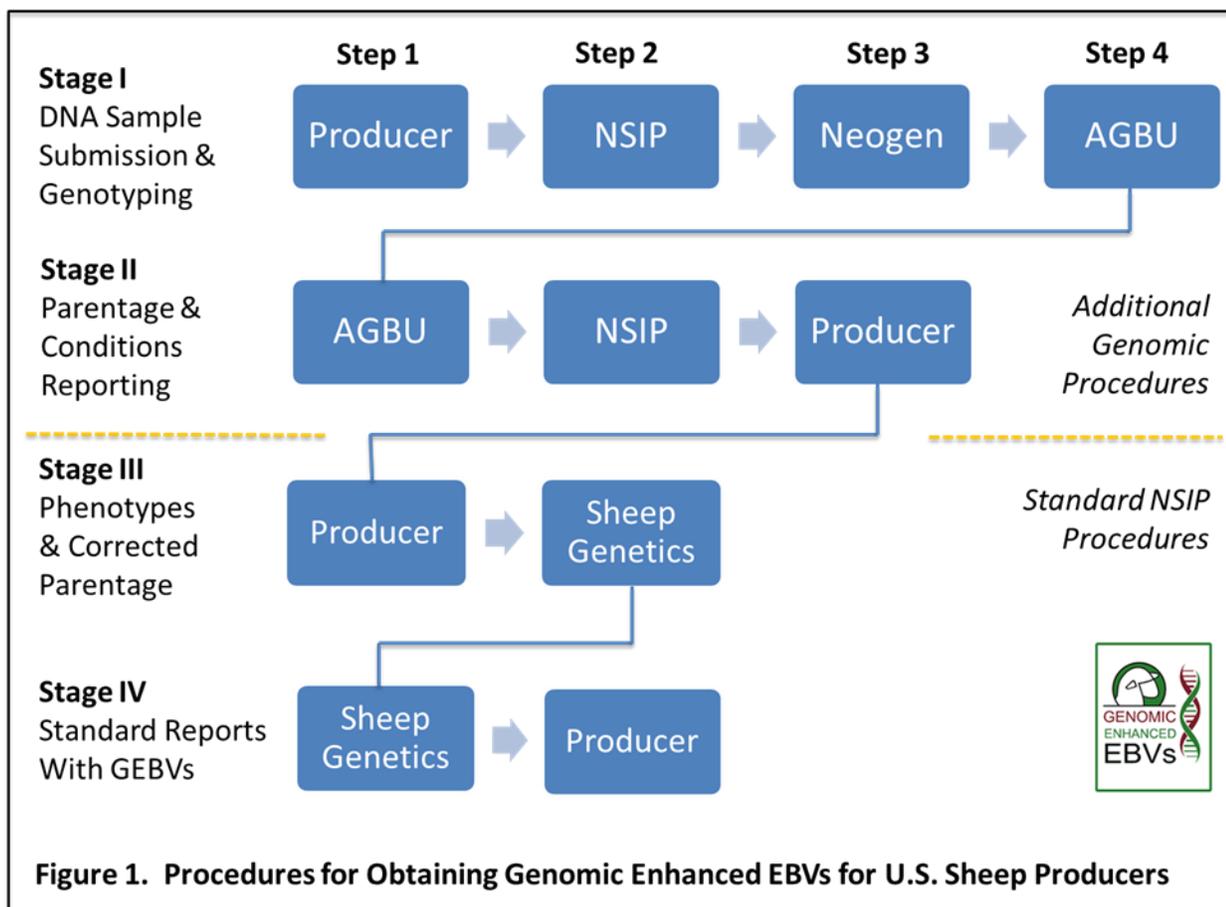


Figure 1. Procedures for Obtaining Genomic Enhanced EBVs for U.S. Sheep Producers

OPP susceptibility (TMEM154). We hope to add more genetic conditions over time. Many producers are already testing for one or more of these conditions. The current costs for independent testing for just 2 of these conditions is significantly less when testing is conducted as part of genotyping for GEBVs. Guidelines to help producers interpret the parentage and genetic conditions reports are under development and will be available at: <http://NSIP.org/genomic-enhanced-ebvs/>.

- **Parentage Validation** – One key component in the improved accuracy of GEBVs is genomic-based parentage. Each producer will indicate on their submission form all possible sires and dams for each lamb with a DNA sample. These are referred to as “Nominated Sires” and “Nominated Dams”. Having genotypes of possible sires and dams “on file” with AGBU, greatly enhances the power of the genomic pedigree. Although we encourage all producers to genotype all their sires, not all dams will have been genotyped. AGBU will return a report to NSIP with the results of the parentage analysis for each animal genotyped in the batch. These are then subdivided by flock and forwarded by NSIP back to individual producers to be corrected, if necessary. Any errors discovered by AGBU during parentage validation should be corrected in the producer’s on-farm database in Pedigree Master prior to submitting phenotypic data (weights, etc.) to Sheep Genetics. As stated previously, producers must recognize that accurate recording of sire and dam and assigning a specific TSU number to an animal’s 16-digit ID number is critical for accurate parentage assignment. Again, if an animal needs to be re-genotyped due to an on-farm clerical error, the producer will be responsible for that additional expense.
- **Costs to Producers** – There are 3 costs to producers for obtaining GEBVs:
 1. Producers must first purchase TSUs and applicator. As described above, each TSU costs from \$2 to \$4. An applicator is approximately \$45 to \$50. Only one applicator is needed, but each animal sampled will need a separate TSU.
 2. Producers pay \$30 to NSIP at the time of DNA sample submission. This covers the costs of batching samples, genotyping, reporting genetic conditions, as well as parentage analysis and reporting.
 3. Producers pay a data fee of \$3.50 per lamb with a 60-day weight submission. This is not an additional charge, but rather the standard fee charged by NSIP for processing the genetic evaluation.
- **Genomic Certification** - To help producers add value in marketing any lambs that are genotyped, NSIP has developed an “NSIP Certified Genomic Tested” label. That label can be used to promote the enhanced reliability of an animal’s GEBVs. Individuals that have been successfully genotyped will be identified in summary reports from Sheep Genetics (e.g., Individual Listing Report) as well as in the NSIP Searchable Database. The logo at right is available for use by producers to promote genotyped individuals.



When to Sample

Producers should plan on at least a 60-day turnaround time from DNA sample submission to reported GEBVs (In future years, we anticipate this lead time will be reduced). If GEBVs will be an important part of your marketing plans, especially sale promotions, then pre-planning will be a necessity.

Things to consider when deciding on when to collect and submit DNA samples:

- Whether you lamb early or late.
- When you market your butcher lambs.
- When you market breeding stock or make decisions on replacement ewe lambs.
- Lamb handling logistics: when it's most practical to collect DNA samples.
- Your budget for TSUs and sample processing.
- When "batches" will be processed: 4 to 5 dates will likely be established throughout the year to accommodate the various breeding schedules of producers.

The following are example scenarios that should help producers establish sampling timelines for their flocks.

SUBMISSION TIMELINE EXAMPLE SCENARIOS			
	Scenario #1: Light Lamb Market	Scenario #2: Heavy Lamb Market	Scenario #3: Range/Pasture Lamb Operation
Birth	<ul style="list-style-type: none"> ▪ Sample DNA & submit top % based on pedigree EBVs 		<ul style="list-style-type: none"> ▪ Sample DNA from all lambs at birth, but do not submit
30 days			<ul style="list-style-type: none"> ▪ Submit top % based on pedigree EBVs plus visual appraisal/survival
60 days	<ul style="list-style-type: none"> ▪ Make parentage corrections as reported ▪ Submit 60-day weights 	<ul style="list-style-type: none"> ▪ Submit 60-day weights ▪ Sample DNA & submit top % based on EBVs plus visual appraisal 	<ul style="list-style-type: none"> ▪ Submit 60-day weights
90 days	<ul style="list-style-type: none"> ▪ GEBVs received before making slaughter/sell/keep decisions 		<ul style="list-style-type: none"> ▪ Make parentage corrections as reported ▪ GEBVs received before making slaughter/sell/keep decisions
120 days	<ul style="list-style-type: none"> ▪ Submit 120-day weights ▪ GEBVs updated 	<ul style="list-style-type: none"> ▪ Make parentage corrections as reported ▪ Submit 120-day weights ▪ GEBVs received before making slaughter/sell/keep decisions 	<ul style="list-style-type: none"> ▪ Submit 120-day weights ▪ GEBVs updated

Pros:	<ul style="list-style-type: none"> Lower labor as sampling when lambs are easier to handle 	<ul style="list-style-type: none"> Allows for more informed choice of which lambs to sample for genotyping 	<ul style="list-style-type: none"> Lower labor as sampling when lambs are easier to handle Avoid paying for genotyping on lambs lost from inventory Most options for submitting DNA at later times
Cons:	<ul style="list-style-type: none"> Sampling choices made on pedigree data alone May pay for genotyping on lambs which are later lost from inventory 	<ul style="list-style-type: none"> More handling labor to sample larger lambs May not have GEBVs in time for sale consignment deadlines. 	<ul style="list-style-type: none"> Increased cost of # TSUs used More TSUs to handle/store

Example Timeline: Flock follows Scenario #2

The following is an example, based on Scenario #2 above, of some possible dates for the steps to generate GEBVs. Subtle deviations are likely, especially in dates for weighing, sample processing and parentage reporting (especially in 2021). Please use this as a simple guide to the approximate timeline in year 1 of this effort.

Timeframe	Activity/ event
February	Lambing
~Apr 13	Collect 60-day weights and submit data to Sheep Genetics for the April 15 th run
~Apr 19	Producer receives EBVs from Sheep Genetics
Late April	Producer selects 15% of ram lambs and 45% of ewe lambs for genomic testing, collects DNA from selected lambs, and ships TSUs & form to NSIP for batching prior to May 1 st
Early May	Coordinator compiles submission forms, batches TSUs, and submits both to Neogen for genomic analysis
Late May	Neogen sends results to AGBU for determination of parentage & genetic conditions
Early June	Producer receives reports on parentage & genetic conditions, corrects any parentage errors in Pedigree Master
Late June	Producer collects 120-day weights and submits data with genomic-based parentage to Sheep Genetics for the June 30 th run
~July 4 th	Producer receives updated database and reports from Sheep Genetics including GEBVs

How Many to Sample

The number of individuals and which individuals to sample are important considerations for both cost effectiveness and creating detailed genomic pedigrees. Producers need not sample every individual in their flock. Also, because the Katahdin genomic reference population is believed to adequately represent the genetic diversity in the breed, no specific number of “bottom performing” lambs need to be sampled. A more thorough discussion of on-farm sampling considerations and recommendations will be available by late March at <http://NSIP.org/genomic-enhanced-ebvs/>. The following list summarizes those guidelines:

- Because rams play such a large role in flock genetics, we suggest sampling all sires and a portion of the lambs from each sire.
- Genotyping ewes is encouraged. Testing any potential replacement ewes should be a cost-effective strategy. Plus, the ewe lamb’s genomic data will be in the database for future parentage analyses.
- Producers need not sample every lamb. Instead, we recommend targeting at least 25-35% of your lamb crop according to the following guidelines:
 - Sample all of the lambs in a litter if you will keep replacement ewe lambs or stud prospects from that litter, if your flock:
 - Is genetically linked to multiple NSIP flocks,
 - Has many animals with multiple years of NSIP data, or
 - Is closely linked genetically to the genomic reference population
 - Sample 1 lamb per litter from as many litters as feasible, if your flock:
 - Lacks genetic connections to other NSIP flocks,
 - Has few or no animals with NSIP data,
 - Has submitted data to NSIP for only a few years, or
 - Has no or only remote genetic linkages to the breed’s genomic reference population

Reap the Benefits

Early adopters of the GEBV technology will have a marketing advantage for the sale of seedstock. They will benefit from increased accuracy in making data-driven decisions on replacement ewes and selection of herd sires. GEBVs will help producers make genetic progress in their flocks faster than ever before. Join in and help the Katahdin breed be the trendsetter for the U.S. sheep industry!

Making history, defining the future ★ Katahdins: a breed whose time has come