UNDERSTANDING THE NATIONAL GENETIC BASED FLOCK CLEAN-UP PLAN

How the Plan Works

• There are three basic steps in the genetic based plan:
  1. When an infected flock has been identified, the sheep are genotyped. The sheep’s genotype determines its risk for scrapie infection.
  2. Sheep with susceptible genotypes are either removed or their movement restricted.
  3. The flock is placed under surveillance for five years.

• Benefits of the Plan:
  In most cases, producers will be able to keep many more of their sheep with a genetic based plan. This plan allows owners to retain or sell without restrictions nearly all sheep that are AA RR, AA QR\(^2\) and most AV QR\(^2\) (Table II) from infected or source flocks once owners have met certain conditions.

It is estimated that, on average, 60 percent of a flock can be preserved when using a genetic based plan compared to 25 percent when using a traditional plan.

Requirements of the Plan

1. All exposed QQ ewes, exposed female goats, and female offspring of scrapie positive ewes will be removed or will be placed under movement restrictions.
2. The finding of a positive animal with a V at codon 136 in a flock indicates that exposed AV QR sheep in that flock or that originated from that flock may be infected with scrapie. In these flocks exposed AV QR ewes may be removed or have their movement restricted.
3. All animals in the flock must be officially identified and entered in USDA’s Scrapie National Generic Database by federal and/or state personnel.
4. Owners must have a post-exposure management and monitoring plan that includes:
   • Official identification of sexually intact animals that are sold or acquired and records of such transactions including basic information of the buyer/seller;
   • Reporting of deaths of any mature animals and submission of animals showing possible signs of scrapie for diagnostic testing;
   • Annual inspections of the flock for 5 years by state and/or federal officials;
   • Owners who elect to retain restricted female animals will have to meet additional requirements including testing and restrictions on offspring.

Other Aspects of the Plan

Owners whose animals are removed from the flock will receive indemnification from the federal government based on commercial market prices reported by the Agricultural Marketing Service. An additional premium will be paid for registered animals and may be paid for animals for which the owner can document a higher market value, such as some club lamb flocks.

Further, the federal government will provide testing and assistance with disposal costs. The producer is responsible for gathering and handling the sheep, applying identification, providing adequate handling facilities, cleaning and disinfecting, reporting suspect animals, and maintaining records such as sheep sales, purchases and lambing.

A FINAL WORD

These recommendations are intended for producers who:

• Have classical scrapie in their flock, or
• Have flocks that have been exposed to classical scrapie, or
• Have breeds that have a high prevalence of classical scrapie, in flocks that are not known to be free, or
• Purchase ewes of unknown status.

The selection of genetically resistant sheep is a highly effective method of minimizing the risk of classical scrapie infection; however, maintaining a closed ewe flock is the most effective preventative measure.

There is still much to be learned about scrapie genetic susceptibility in sheep and goats, so as research provides further information, the National Scrapie Eradication Program will be adjusted accordingly.

FOR MORE INFORMATION, CALL TOLL-FREE 1-866-873-2824

This number will put you in touch with animal health officials in the state you are calling from who are responsible for the scrapie eradication program.

The following websites provide additional information on scrapie genetics, genotyping and the National Scrapie Eradication Program:
http://www.aphis.usda.gov/animal_health/animal_diseases/scrapie
http://www.eradicatescrapie.org

This information brought to you by:

HOW ALL PRODUCERS BENEFIT – All producers can benefit from the National Genetic Based Flock Clean-up Plan in several ways. The plan allows resistant breeding stock to be preserved. Resistant sheep on average make up 60 percent of flocks. It protects other flocks from exposure by requiring the removal or permanent restriction of movement of animals that may spread scrapie. It permits affected producers to return to normal business practices more quickly than previous plans. The use of genetically-resistant RR rams will break the transmission of classical scrapie in newly exposed flocks, thus reducing the risk of them becoming infected or source flocks. Additionally, it encourages producers to limit their risk of acquiring scrapie by utilizing genetic testing and selection. All of this will help meet the goal of eradicating scrapie in the U.S. so that the nation can be recognized as “Classical Scrapie Free.”
GENETIC BASED FLOCK CLEAN-UP PLANS

The Flock Clean-up Plans based on genetic testing are an important aspect of the National Scourge Eradication Program. These plans apply only to classical scours infected, source* and exposed flocks. However, it is important that all producers are aware of how genetic resistance to classical scours can be used to (1) minimize the risks of acquiring the disease and (2) eliminate the disease from a sheep flock if it becomes infected.

* This plan does not address Nor98-like (non classical) scours. For more information on Nor98-like scours refer to the Veterinary Guide at http://www.erascatescours.org.

Due to their genetic makeup (see The ABCs of Genotyping in this leaflet) some sheep are more susceptible to classical scours and some are more resistant to the disease. The genes that control susceptibility/resistance can be identified by a blood test* known as genotyping or DNA testing. Prior to November 2003, with the exception of a few states with pilot projects, risk in flocks infected with scours was determined primarily by exposure to the disease. This resulted in a large percentage of exposed breeding animals being destroyed, prohibited from movement or sale, or restricted to movement by permit only.

Now, under the National Genetic Based Flock Clean-up Plan Individual sheep that are found to be genetically resistant to scours through genotyping, and whose owners have met various other conditions, can be moved and/or sold in a normal manner. Details of the plan appear in the reverse side.

The ABCs of Genotyping

A General information about genotyping

- The animal's genotype never changes, so it can be tested at any age.
- Under most circumstances one test during the animal's life is adequate to determine its genotype (susceptibility/resistance to scours). In the case of exposed sheep, the plan currently requires two tests to minimize any chance of error in sampling, labeling, or testing.
- The genotyping test measures only an animal's susceptibility/resistance to scours, not whether it has scours. The third eyelid or rectal biopsy test can be used to detect scours infection in some animals.

B Basic facts about sheep genetics and how genotyping is used to determine scours resistance/susceptibility

- Out of the many sheep genes scientists have identified, only one affects scours susceptibility as well as the disease's incubation time. That gene is known as PRNP, which stands for the PrP ProN protein.
- Each sheep has two copies of the PRNP gene, one derived from each parent.
- In uninfected sheep, the PRNP gene produces the normal cellular prion protein molecule known as PrP. In scours-infected sheep, the abnormal prion protein, PrPSc, or Prions, is found. Prions are closely associated with scours infectivity and are believed to be the causative agent.
- Genes are made up of codons. Each codon instructs the body cells to put a specific amino acid at a particular location when building a protein molecule.

- Since PrPSc is composed of 256 amino acids, these locations are numbered from 1 to 256.
- Two condons – 136 and 171 – are particularly important to classical scours susceptibility in the USA.
- Codon 171 can give instructions to insert the amino acid Histidine (H), Glutamine (Q), or Arginine (R) at a position 171 of PrP. The letter in parentheses is the single letter biochemical abbreviation for each amino acid. At codon 171, R is very important because it produces the greatest scours resistance.
- Codon 136 can give instructions for either Alanine (A) or Valine (V) to be the amino acid at 136 of PrP. The presence of V (Valine) at 136 makes AV QR sheep susceptible to certain scours strains.
- As previously stated, sheep have two copies of the PRNP gene, one from each parent that can produce one of four commonly occurring combinations of amino acids at codons 136 and 171 as shown in Table I.

C Producers need to be familiar with six genotypes and their corresponding amino acid combinations to understand genotyping for scours resistance.

When both copies of the PRNP gene are considered, a sheep can have one of six genotypes. Based on what is now known, the following genotypes at codons 136 and 171 (shown in Table II) are used to determine the scours susceptibility of sheep.

<table>
<thead>
<tr>
<th>TABLE II – Genotype Susceptibility/Resistance Combinations</th>
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<tbody>
<tr>
<td>1. AA RR – Sheep which are resistant</td>
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<tr>
<td>2. AA QR – Sheep which are rarely susceptible</td>
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<tr>
<td>3. AV QR – Sheep which are susceptible to some scours strains*</td>
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<td>4. AA QQ – Sheep which are highly susceptible</td>
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<td>5. AV QQ – Sheep which are highly susceptible</td>
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<td>6. VV QQ – Sheep which are highly susceptible</td>
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*These strains are believed to occur with low frequency in the U.S.

Table I – Amino Acid Combinations Indicating Susceptibility/Resistance

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<th>Codon 136</th>
<th>Codon 171</th>
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<tr>
<td>Location</td>
<td>Location</td>
</tr>
<tr>
<td>A</td>
<td>R</td>
</tr>
<tr>
<td>H</td>
<td></td>
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<td>Q</td>
<td>V</td>
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<td></td>
<td>Q</td>
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*H, or histidine, at codon 171 is considered to have the same susceptibility as Q. (glutamine) and is therefore represented as Q in all combinations discussed in this brochure.

*Rarely other amino acids may occur at codon 171 or 136 and are also treated as susceptible.

Full implementation of the National Scours Eradication Program began in 2001 by the U.S. Department of Agriculture’s (USDA) Animal and Plant Health Inspection Service (APHIS) Veterinary Services (VS). As a result of the Program, the percent of black face cull sheep that test positive for scours through slaughter surveillance has decreased by 80 percent since 2003.

Footnotes

1. A source flock is the flock of birth of a scours positive animal. If the scours positive animal is no longer in the flock, it must be under 72 months of age when tested for the birth flock to be considered a source flock.
2. The program utilizes a blood sample to determine the genotype of live animals, but other tissues can also determine genotype and are used in sheep that are necropsied.
3. In addition to 136 and 171, codon 154 is known to play a minor role in scours susceptibility and is not often tested for in the U.S.
4. These sheep are restricted only in rare cases when the animal is: (a) the female offspring of a female positive animal, (b) a clinical suspect, (c) from a flock with unusually high prevalence, (d) from a flock that has a history of recurrence, or (e) from a flock that included a positive sheep of a resistant genotype.
5. Any AV QR that is likely to have been exposed to a strain to which it is susceptible is restricted.