FAWN CALF SYNDROME

-- An Update from Dr. Jonathan Beever and a Word from President Bill Davis --

On December 21, 2009, the Association posted an Update on Fawn Calf Syndrome that it had sought and received from Dr. Jonathan Beever, a Ph.D. in genetics at the University of Illinois and the individual responsible for developing the diagnostic tests for AM and NH. Nearly three months later, Dr. Beever has again agreed to respond to some of the questions that his December Update prompted and that are, on occasion, addressed to the officers, Board and professional staff members of the Association. The Association remains grateful to Dr. Beever for his tireless and ongoing efforts on behalf its members and its breeders.

In your Update on December 21, 2009, you indicated that you were working toward having a 100% accurate test for FCS. While noting that you had made significant progress, you also reported that you had encountered a few roadblocks. Where do you believe you are today in your efforts to have a 100% accurate test?

The status is relatively the same. We know what gene causes the mutation. In fact, we have known it for approximately eight months. We are actually dealing with a deletion of a significant segment of DNA (on the order of at least 38,000 base pairs at the moment). That is very similar to the size of the deletion we saw in AM. We know the DNA sequence on one side of this deletion but we are still trying to discover what it looks like on the other side. That is what we are focusing our time and effort on right now.

Your December 21 Update referred to the fact that you had succeeded in developing a genetic marker test, which performed well in allowing you to predict an individual animal's genotype for FCS. But you also cautioned against releasing any results you obtained from these marker "tests". You reasoned that because these markers are not the

specific mutation causing FCS, they cannot, by definition, be 100% accurate. Is that still your belief?

Absolutely, that continues to be my belief. There is a significant danger of misusing or misinterpreting these results. That is why we have never released them or otherwise made them known to the Association.

Until we know the DNA sequence on both sides of the deleted DNA segment, it is impossible to develop a diagnostic test that is 100% accurate. It is important to understand what we are talking about here: We currently have a single assay that is approximately 30,000 base pairs away from the end of the FCS mutation we've discovered. This assay can be used to predict whether an animal is free of the FCS mutation but, unfortunately, the same assay can – and does – also generate "false positives" in a number of pedigrees. A "false positive" means that the assay predicts that an animal is a carrier of the FCS mutation when, in fact, it is not.

The development of this test for the FCS mutation has been difficult but we are making real progress. It is true that we had a test fully-developed and in the marketplace for AM and NH in a lesser period of time. But we have also had more difficult issues to work through. In the case of another breed with whom we worked three or four years ago, we dealt with a deletion that encompassed approximately 430,000 base pairs. That took us some time to work out – but we ultimately got there. Here in the case of FCS, we currently estimate the size of the deletion to only be 38,000 pairs.

So, I believe a diagnostic test is still imminent and by that, I am not saying I believe it is one or two years away. We are at the point where we are pulling out all the stops and we are doing everything we can. We believe we will have something that will work very soon.

Several members have suggested that breeders would be better off utilizing a test that is less than 100% accurate, even if it meant providing the marketplace with false positives. Do you believe that the Association would be better off using the current marker "test", even with these limitations?

My answer to that question continues to be "no." I addressed that very issue in my December 21, 2009 Update but it is, in my opinion, worth discussing once again. Currently, I know that I can look at certain pedigrees and actually find false positives. If one were to publish such results, breeders would wrongly identify animals as carriers when, in fact, they were not. And breeders would simply stop using those incorrectly stigmatized animals. That is the opposite of what the AM and NH tests allowed breeders to do. I would not recommend the use of the current "test".

In the case of AM, members were provided the name of a historic bull even before there was a valid test available for use in labs approved by the Association. Why isn't that being done in the case of FCS?

At this stage, after looking for and locating the gene that causes the mutation, I believe that it would be counterproductive to start naming names. There are several reasons I say this. First, with the false positive findings, naming historic bulls could seriously prejudice some percentage of pedigrees that do not really have a FCS problem. Second, the frequency of this mutation is low when compared to AM and NH and it does not appear to be rising. By waiting for the 100% accurate test, I do not believe you are creating a bigger problem. That was not the case in 2008 where the frequency was high and appeared to be rising.

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Bill Davis, the President of the American Angus Association, also felt that it was important for the membership to know that FCS has – and remains – a topic of focus by the officers and the members of the Board.

Where is the Board of Directors on this issue and what, if anything, does the Board see as its primary objective at this point?

I want to provide some context for my answer to those questions. The Board learned of AM for the first time at its September 2008 meeting. At that meeting, the Board unanimously agreed that our approach to that issue would be marked by transparency and reliance on sound science. Since September of 2008, the officers and members of the Board have collectively spent literally hundreds of hours on the issues related to three defects. I look back with a sense of pride on what three successive Boards have done since the fall of 2008. I think we have acted appropriately and prudently under several difficult sets of circumstances. And we have had the invaluable assistance of two scientists, each preeminent in their respective fields: Dr. Jon Beever of the University of Illinois and Dr. David Steffen of the University of Nebraska.

I want to emphasize today that we are continuing to exercise the same high level of attention in our approach to FCS that we did in the cases of AM and NH. In February 2009, we posted a notice from Dr. Steffen asking members to notify him or the Association of FCS calves. In November 2009, we informed the membership that if, as expected, FCS was caused by a simple recessive gene, we would generally follow the same policy in place for AM and NH. In late December 2009, we posted a detailed report from Dr. Beever in which he laid out exactly where he stood on his efforts to develop a test that can, with complete certainty, identify those animals that are FCS carriers from those that are not. And today, Dr. Beever once again has reported on exactly where he is in that process, emphasizing the concerns associated with a

premature announcement of suspected carriers (that is, the presence of false positives in a number of pedigrees).

This delay in the development of a test has led to some frustration. That is only natural. It has also led to a series of questions, several of which Dr. Beever addressed on December 21, 2009 and again today. For me personally, I would estimate that the two questions most often posed to me are (1) does the Association have some list of animals on which Dr. Beever performed his marker test, and (2) why has the Association not at least acted upon the reported findings of Angus Australia? Dr. Beever has answered the first question today. He has never provided the Association with a list or the names of any animals on which he conducted his less-than-100% accurate test. And he has made clear why he has not chosen to do so: such a list could be misused and misinterpreted.

As for the second question, the answer is closely related. At this time, the Association intends to follow the advice of Dr. Beever and avoid identifying any animal by name as a FCS carrier – or as FCS-free – until there is a 100% accurate commercial test, available at labs approved by the Association. Interestingly, that appears to be similar to some degree to how Angus Australia is approaching the issue. Although FCS is recognized by that organization as a "genetic condition", it too has stopped short of displaying whether an animal is a carrier or free of FCS on their registration certificates – in the absence of a test. Its stated reasons for not marking their pedigrees: publishing the names would not be beneficial at this time and the frequency of FCS carriers will likely be considerably less than AM. Indeed, Angus Australia has stated that it too is cooperating with Dr. Beever and that it has suspended any further research into this mutation pending his development of a test.

I just wanted to assure each member that the officers and members of the Association's Board – your officers and your Board – are monitoring the FCS situation in a careful and prudent manner. We are optimistic that we will be able to announce an accurate test in the relatively near future.