

1 those probably wouldn't.

2 CHAIRMAN BROWN: Would the Committee like
3 to just take five or ten seconds to see whether
4 they're prepared to take a yes or no vote on at least
5 one of the two questions, probably both, because
6 they're similar, although they have one significant
7 difference?

8 If the Committee is ready to vote, we can
9 take votes or we can continue discussing, you know,
10 things that we would recommend.

11 Yes, Barbara.

12 MS. HARRELL: I am very unclear as to
13 whether or not we're talking about bringing in live
14 animals.

15 CHAIRMAN BROWN: No.

16 MS. HARRELL: No, we're not talking about
17 that. Just the --

18 CHAIRMAN BROWN: Products.

19 MS. HARRELL: Just the products? Okay.
20 Already processed products, is that what we're talking
21 about?

22 CHAIRMAN BROWN: I think, if I'm not
23 mistaken, it could be, for example, it could be an
24 intermediate to a finished product, or it could be a
25 finished product. It's certainly not walking on four

1 legs.

2 MS. HARRELL: Okay, and so the other part
3 of that is what I think Lisa -- is that your name?

4 CHAIRMAN BROWN: Larry.

5 MS. HARRELL: -- has said, you know. She
6 said that the casings and all of that is prohibited by
7 USDA. Then that's something that we really could not
8 even vote on because it couldn't get through because
9 of USDA regulations. Right?

10 CHAIRMAN BROWN: Well, that's what they
11 say, but there's no reason we can't put up a second
12 wall if you choose to.

13 MS. HARRELL: So we could allow it even
14 though it couldn't happen. Is that what you're
15 saying?

16 CHAIRMAN BROWN: Well, that wouldn't
17 happen. We're not saying we allow it necessarily.
18 We're saying that if you did that, you would say that
19 the FDA doesn't need to take any pro or con position
20 on it in part because the USDA already has sufficient
21 safeguards.

22 In other words, you could say -- you could
23 say no. That is to say the FDA needs no further
24 guidance, needs not to guide, and the result would be,
25 if the product was already covered or the material was

1 already covered by a USDA exclusion, it would be
2 excluded.

3 If it wasn't or were not covered by a USDA
4 ~~ex~~clusion, then it would continue to come in as it has
5 always in the past.

6 MS. HARRELL: Okay. Lastly, I would like
7 for the Chair to summarize his feelings about this.

8 CHAIRMAN BROWN: I'm sorry. Feelings
9 about?

10 MS. HARRELL: About Question No. 1, our
11 recommendation, as you did yesterday.

12 CHAIRMAN BROWN: Hmm.

13 (Laughter.)

14 CHAIRMAN BROWN: I don't know, Barbara, if
15 it's really appropriate for the Chair to do that. I
16 can give you my own opinions. I would actually --

17 MS. HARRELL: You do that all the time.

18 (Laughter.)

19 CHAIRMAN BROWN: Touché.

20 (Laughter.)

21 CHAIRMAN BROWN: Well, you know, as I
22 said, you get me as the Chair; you get the whole
23 package.

24 (Laughter.)

25 CHAIRMAN BROWN: So I can do that very

1 quickly. I think -- I think -- I think that scrapie
2 per se remains a non-problem. I don't anticipate
3 scrapie to be a problem as long as it stays scrapie.
4 That's taking maybe a minimal risk because you never
5 know what can happen, but historically scrapie simply
6 is not responsible for CJD.

7 Therefore, I am not concerned about
8 scrapie in any shape, form, or manner, even as an
9 injectable.

10 With respect to the possibility that BSE
11 may have already been or may be reintroduced into
12 sheep, that concerns me a little more, and like the
13 blood issue yesterday, there is absolutely no way at
14 this time to know whether this has happened or whether
15 it's going to happen, but I think it is an issue that
16 is arguably dangerous, and so I would consider these
17 two questions legitimately separately, and I would
18 vote accordingly.

19 Robert.

20 DR. ROHWER: I think this first question
21 is limited not to the U.S. situation, but simply to
22 the import situation, and there I'd like more guidance
23 from the USDA themselves. Do they feel comfortable
24 with the restrictions and the surveillance that they
25 have in place and their ability to monitor that they

1 can actually cover this situation where they can
2 prevent the import of products like this that might
3 make their way into biologicals for parenteral use
4 ~~ju~~st by virtue of APHIS essentially? I mean, the
5 barrier is APHIS here.

6 And I guess the other question that's not
7 clear to me is that because manufacturers have to
8 reveal to the FDA what they use in their products,
9 isn't that something that the FDA already has, is a
10 tool for monitoring this and controlling it? I mean
11 do they need anything else?

12 Do we need to tell -- does the FDA want us
13 to tell them that, indeed, we don't want manufacturers
14 using sheep and goat products in parenterals derived
15 from BSE countries? Do we need to say that
16 explicitly? I would just assume that that's -- I
17 would just presume that that's already de facto the
18 case, that they can eliminate that without us telling
19 them that.

20 DR. ASHER: I think it would be helpful.

21 CHAIRMAN BROWN: Stan?

22 DR. PRUSINER: I'm sorry, Kiki, to say
23 that I think this is really unnecessarily convoluted,
24 this question. I mean it's --

25 CHAIRMAN BROWN: It's Proustian.

1 (Laughter.)

2 DR. ASHER: A camel is a horse designed by
3 a committee; is that right?

4 DR. PRUSINER: Is it not -- let me try to
5 state this in another way, a simple way. I mean,
6 isn't the first question asking us if we think that
7 the FDA should argue that you can import sheep and
8 goat products from countries where there has BSE been
9 reported?

10 DR. HELLMAN: Yes, that's exactly right.
11 Can we import sheep and goat derived material from BSE
12 countries or can we -- can we use sheep and goat
13 derived material from BSE countries for injectable or
14 implantable products or not?

15 DR. PRUSINER: Right. So can't we vote on
16 this now? This is -- this makes it a little bit more
17 straightforward

18 CHAIRMAN BROWN: That's a nice
19 clarification.

20 DR. HELLMAN: yes.

21 CHAIRMAN BROWN: I think we can.

22 DR. PRUSINER: Before we lose the thought.

23 DR. HELLMAN: Yes.

24 (Laughter.)

25 DR. DETWILER: Amendment, amendment,

1 though. BSE affected countries, do you want to
2 broaden it to "high risk" to keep concurrent with your
3 cattle definition or keep it to those that just
4 reported it?

5 CHAIRMAN BROWN: High risk.

6 DR. ASHER: BSE countries and status
7 unknown countries.

8 CHAIRMAN BROWN: Okay. Is that clear?
9 The question has become: Should the FDA allow
10 importation of products or sources of products from
11 sheep and goats residing in countries either with BSE
12 or of uncertain status?

13 Larry?

14 DR. SCHONBERGER: Part of the issue here,
15 as well, was that was the question I was just asking
16 the Department of Agriculture, and they said at the
17 present time this would not happen. So part of the
18 issue here is almost interagency coordination, is it
19 not; as to how -- right now the state of affairs is
20 that this is not going to happen.

21 CHAIRMAN BROWN: At least for the products
22 which the USDA current has a policy for.

23 DR. SCHONBERGER: Right.

24 CHAIRMAN BROWN: Which could change.

25 DR. SCHONBERGER: So part of our

1 recommendation to them would be perhaps, yes, let's
2 say, I don't want that to happen, but they need to
3 coordinate --

4 CHAIRMAN BROWN: Well, I think we --

5 DR. SCHONBERGER: -- their efforts.

6 CHAIRMAN BROWN: Yes. Well, you heard
7 yesterday blood. We've got three committees working
8 on blood and CJD.

9 DR. SCHONBERGER: That's right.

10 CHAIRMAN BROWN: Two, you know, is a
11 bargain. So why don't we go ahead and vote?

12 DR. SCHONBERGER: Yes, that's fine.

13 CHAIRMAN BROWN: I mean, I agree part of
14 it is coordination. We can discuss that later.

15 David?

16 DR. BOLTON: I was with you right up until
17 the change in the question.

18 CHAIRMAN BROWN: Okay.

19 (Laughter.)

20 DR. BOLTON: I thought I understood the
21 original question.

22 CHAIRMAN BROWN: Okay.

23 DR. BOLTON: Now I'm not so sure I
24 understand the second question.

25 CHAIRMAN BROWN: Stan, rephrase the

1 question for us.

2 DR. BOLTON: Well, let me try to rephrase
3 the first question. I thought that the original
4 question was asking whether FDA should change their
5 current policy --

6 CHAIRMAN BROWN: Right.

7 DR. BOLTON: -- without any specification
8 one way or the other, and my understanding is the
9 current policy really is no policy.

10 So now the question is are we adding an
11 exclusion, "don't do this," or are we saying, "Now
12 you're free to make a decision to do something," but
13 not specifying what that something is?

14 CHAIRMAN BROWN: I suppose I should
15 exercise direction, but I really don't feel like it.
16 Why don't you --

17 (Laughter.)

18 CHAIRMAN BROWN: Why don't -- I mean
19 Stan's rephrasing was a good one. It was nodded to by
20 our FDA people. Why don't you again state it and see
21 if everybody understands it?

22 DR. PRUSINER: I forgot what I said.
23 Okay. So my understanding of this at this time is
24 that FDA is asking us whether we think that there are
25 products made from sheep and goats, where these

1 animals originate in BSE countries, either known BSE
2 or high risk for BSE, that these products should be
3 imported into the United States.

4 DR. BOLTON: And a yes answer means they
5 should be imported or a yes answer means they should
6 not be imported?

7 CHAIRMAN BROWN: I think we can sort of
8 say should the FDA be allowed to, and if you say
9 yes --

10 DR. BOLTON: Import.

11 CHAIRMAN BROWN: Yes.

12 DR. PRUSINER: Yes, it's import; no, you
13 don't want them to import it.

14 CHAIRMAN BROWN: That's right.

15 DR. ALMOND: But the confusion here --

16 CHAIRMAN BROWN: I think my executive is
17 trying to write this down so we can -- he's not making
18 any progress.

19 (Laughter.)

20 CHAIRMAN BROWN: Jeff?

21 DR. ALMOND: Isn't the confusion here
22 arising from the fact that if the FDA were to -- or
23 you were to say the FDA were to decide, yes, they
24 could allow things in from sheep and goats in BSE
25 countries, they would be in violation of USDA rules

1 anyway so they couldn't do it.

2 CHAIRMAN BROWN: Jeff, this is not the
3 source of confusion. It's one source, but it's not
4 the source.

5 DR. HELLMAN: Well, if I may, that's
6 exactly right, and the original question had whether
7 the safeguards are sufficient. In other words, are
8 the safeguards sufficient to keep out sheep and goat
9 derived material from BSE countries or status unknown
10 countries? And those safeguards are primarily USDA,
11 or do we, the FDA, need something further?

12 CHAIRMAN BROWN: Before you --

13 DR. ALMOND: I think that's a very good
14 way of putting the question, Chairman. To me as an
15 outsider, that seems to encapsulate it. You have a
16 layer of rules in place. They do keep out most
17 things. Do you need an extra layer which is imposed
18 by the FDA?

19 My only response to that, again, as an
20 outsider, I think you do, and I think you can very
21 easily come to that decision, but I still have a
22 difficulty in concluding that you will be doing much
23 because it's clear that you can identify things like
24 sutures. It's clear that you can identify things like
25 blood serum derivatives that go into bacteriological

1 growth media that might then go into a manufacturing
2 process that produces a biological.

3 You don't gain anything from the second
4 ~~one~~ unless you also stop the importation of the
5 biologicals that were manufactured outside the country
6 that also used those materials in their biological
7 production process, and I'm not sure that you do.

8 So you have to be careful whether these
9 measures, even if you vote for them, have any teeth at
10 all.

11 DR. HELLMAN: Very good. Thank you.

12 CHAIRMAN BROWN: It occurs to me that you
13 could rephrase the whole question by saying: does the
14 FDA agree that the USDA precautions are satisfactory?

15 I mean if we're going to get into this
16 kind of an interagency dependency, one of the issues
17 here, I thought, was consistency, and that the FDA
18 wanted a policy that was consistent, and if you're
19 going to allow the USDA to be your umbrella of
20 consistency, it doesn't seem to me you've achieved the
21 goal you set out to do.

22 Bob?

23 DR. ROHWER: When I asked the question
24 explicitly, I feel the answer I got implied that the
25 FDA would like to have the ability to ask a

1 manufacturer what the source of their ovine tissues
2 is, and I think we should give them that ability.

3 CHAIRMAN BROWN: Did you want to say
4 something, Dave?

5 DR. ASHER: Yes, for biologicals, of
6 course, and I assume for devices, we have the ability
7 to ask now and sources of all material in all products
8 are disclosed, unless I'm mistaken, and finished
9 biologicals produced in a foreign country have to be
10 made to exactly the same standards as products in the
11 United States.

12 DR. ALMOND: So, therefore, you have all
13 the powers that you need already.

14 CHAIRMAN BROWN: Well, that's the --

15 DR. ASHER: But we don't have a policy on
16 whether the theoretical risk of scrapie in sheep and
17 goats constitutes an imminent danger.

18 CHAIRMAN BROWN: Well, that's Question 2.

19 DR. ASHER: BSE. We're not talking about
20 scrapie. That's Question 2.

21 CHAIRMAN BROWN: Dave?

22 DR. BOLTON: Yes, it seems to me that the
23 FDA and the USDA really serve different
24 constituencies, and that the needs, the regulatory
25 needs, may be divergent now or may diverge in the

1 future, and so it seems that it would be prudent to
2 have the FDA formulate their own policies on this just
3 in case.

4 Even in some cases where they may overlap
5 substantially and coordination obviously would be
6 good, it would seem to me that separate regulations or
7 policies would be worthwhile.

8 CHAIRMAN BROWN: Yes, Lisa.

9 DR. FERGUSON: Actually I would like to
10 build on that point, and I feel compelled to make this
11 statement.

12 We have already started somewhat of an
13 interagency process in relation to our regs, but let
14 me just clarify USDA APHIS regulations. Our authority
15 is limited to animal health, and sometimes it's kind
16 of stretching it in some of these products to say that
17 there's a possibility that these might get exposed to
18 the domestic animal population.

19 Now, we have never really been challenged
20 with that, and our regulations are very broad, but I
21 just want everybody to be aware of the fact that that
22 is the limitation of our authority, and that very well
23 could be challenged at some point in time in the
24 future.

25 CHAIRMAN BROWN: Ray.

1 DR. ROOS: It sounds like the Committee
2 agrees that we should not get products derived from
3 sheep and goats from BSE countries, and it sounds like
4 ~~we~~ want the FDA to have the powers that are necessary
5 to insure that that's carried out.

6 Maybe the FDA could guide us as to what
7 they would really like at the moment. You know, I get
8 the feeling that somehow you're dissatisfied with the
9 status quo or you're concerned about it, and maybe you
10 can guide us as to what you want, and that might help
11 with the wording here.

12 Because I have the feeling everybody
13 around the table has the same desires here, and it's
14 just a question of some agenda here and what programs
15 you would like to have implemented.

16 CHAIRMAN BROWN: Yes, I think the Chair --
17 just a second -- the Chair agrees. I think if we took
18 a vote right now, we would have a 100 percent
19 consensus if people understood what a yes meant and a
20 no meant, and this whole business about USDA looks to
21 me like a red herring. I think it has terribly
22 confused the issue. In a sense, it's punting the
23 issue. I really don't think it ought to be a
24 consideration.

25 Yes, I think, Dean, you had a --

1 DR. CLIVER: Okay, but the amended wording
2 we took down during the most recent presentation asks
3 whether any changes in current practices are needed,
4 ~~at~~ cetera, et cetera. I think that's the essence of
5 the question. If we're not satisfied with the status
6 quo, then the answer to that question is yes.

7 CHAIRMAN BROWN: Right. It's all right
8 with me. I was satisfied with that from the
9 beginning. I know what it means, but if there is
10 confusion about what it means on the part of any
11 Committee member, speak now.

12 DR. EWENSTEIN: Well, I would suggest that
13 we take a stronger stance rather than just saying
14 something should be said because I think we're clearer
15 than that, and the wording that I would suggest, if
16 possible, would be that it is the advice of the
17 Committee that the FDA take appropriate steps to
18 insure that sheep and goats originating from or
19 residing in countries where BSE occurs or are high
20 risk are not acceptable sources of material for
21 manufacture of, and continue the resolution the way it
22 was.

23 And the appropriate steps then would be up
24 to you in terms of rules, regulations, coordination
25 with USDA or whatever else is necessary.

1 DR. HELLMAN: Yes, and in fact, I would
2 say with regard to implementation of the
3 recommendation, we have different means that we can
4 use than to implement that. What we would like from
5 the Committee is a clear articulation of your
6 recommendation. Then we can translate that into
7 appropriate policy and use implementation
8 appropriately.

9 CHAIRMAN BROWN: I'd tend to go back to
10 the original --

11 DR. HELLMAN: That's fine.

12 CHAIRMAN BROWN: -- question rather than
13 say they should not be imported from BSE countries
14 because there may be circumstances and precautions
15 that are achieved that would permit that, and so as a
16 total exclusion, I think it probably is more than some
17 of us would agree to, whereas I'm sure -- I'm almost
18 sure -- all of us would agree to the question as it is
19 currently written, that is, know what it means and
20 will vote one way or the other clearly.

21 So let me --

22 DR. ROOS: Well, the total exclusion is
23 not correct because there's tallow and there --

24 CHAIRMAN BROWN: In any case.

25 DR. ROOS: -- are some products, in fact,

1 that -- but I like the idea of the second part of the
2 suggestion, and that is -- and maybe you could read
3 that again -- that the FDA allow --

4 DR. EWENSTEIN: Well, the advice of the
5 Committee is that the FDA take appropriate steps to
6 insure without getting into whether -- you know, how
7 that would work, and then the rest of it just read as
8 the original question read.

9 But if you didn't want it to say specifically
10 that it's not acceptable as sources of material
11 because it's too exclusionary, that could -- that
12 piece could be changed to further take steps, take the
13 appropriate steps to clarify conditions under which
14 sheep and goats can be used as sources of materials.

15 CHAIRMAN BROWN: I'm going to interrupt
16 you for a second. I'm going to call a five-minute
17 recess, and I'd like Kiki to come back at us with a
18 new question, in view of what everybody, you know, has
19 said, and nobody can rephrase his own question twice
20 because it gets complicated and they forget the middle
21 part of the sentence.

22 DR. ALMOND: Can I just say one thing?
23 That I really would caution against and would be very
24 worried by a very positive statement that says, you
25 know, sheep and goat material from countries with BSE

1 are unacceptable sources.

2 CHAIRMAN BROWN: Right. We agree.

3 DR. ALMOND: You've got that. If you do
4 that, that will be taken as this Committee telling
5 Europe that it's got BSE in its sheep, and the
6 consequences of that in the media could be horrendous
7 over the next few days.

8 CHAIRMAN BROWN: Right.

9 DR. ALMOND: And we are not saying that.

10 CHAIRMAN BROWN: Yes, and we're not saying
11 it either, and that was the point of the last two
12 minutes, and that's fine.

13 So let's just wait for two or three
14 minutes and get a new question, phrasing, that is a
15 little simpler.

16 (Whereupon, the foregoing matter went off
17 the record at 2:35 p.m. and went back on
18 the record at 2:45 p.m.)

19 CHAIRMAN BROWN: Will the Committee
20 reassemble around the table, please?

21 Here is the suggested revised question,
22 and it is essentially the original question,
23 simplified a little bit.

24 After considering possible risks and
25 benefits, the Advisory Committee is asked to advise

1 the FDA as to whether the FDA should take measures to
2 insure that sheep and goats originating from or
3 residing in countries where BSE occurs are acceptable
4 sources of materials for manufacture of FDA regulated
5 products intended for injection or implantation, both
6 as components of the products and as manufacturing
7 process reagents.

8 All of the baggage of the last part of
9 this is simply specifying in more detail the kinds of
10 things that they're interested in. We could, for
11 purposes of comprehension, stop after "occurs." In
12 other words, we're asked whether the FDA should take
13 measures to insure that sheep and goats originating
14 from or residing in countries where BSE occurs are
15 acceptable sources of materials for manufacture of FDA
16 regulated products.

17 DR. CLIVER: Could that be phrased in the
18 form of a question?

19 CHAIRMAN BROWN: Okay.

20 DR. CLIVER: If we skip after
21 "considering" and so on?

22 CHAIRMAN BROWN: Okay, okay. So we could
23 say "should"?

24 DR. CLIVER: Yes, something that ends with
25 a question mark.

1 CHAIRMAN BROWN: Okay, Yes. That's fine.
2 Yes, it is. I can tell you that.

3 DR. ALMOND: Do you mean should have the
4 power or should have a policy to decide on such
5 things? Is that --

6 DR. PRUSINER: No, it's the meaning of
7 "is."

8 (Laughter.)

9 DR. CLIVER: It's the meaning of
10 "assures."

11 CHAIRMAN BROWN: Yes, we've heard that
12 recently.

13 Should the FDA take measures to insure
14 that sheep and goats originating from countries where
15 BSE occurs are acceptable sources of materials for
16 manufacture of FDA regulated products?

17 It's understood that this is for injection
18 or implantation and that they're products or
19 manufacturing process reagents. That's baggage for
20 specifics, but the sense is: should the FDA take
21 measures to insure that sheep and goats residing in
22 countries where BSE occurs are acceptable sources of
23 materials for manufacture of regulated products?

24 For "acceptable" you could substitute the
25 word "safe." It might be even better.

1 DR. BOLTON: Is it just residing in or
2 residing and or originating from?

3 CHAIRMAN BROWN: Originating from or
4 ~~residing~~ in. In other words, the source.

5 (Laughter.)

6 DR. ASHER: It's language that we have to
7 use so that it doesn't include just those animals born
8 there, animals transported through. It's language
9 that we have to use.

10 CHAIRMAN BROWN: Yes. Should the FDA take
11 measures to insure that sheep and goats originating
12 from or residing in countries where BSE occurs are
13 safe sources of materials for the manufacture of FDA
14 regulated products?

15 DR. DETWILER: Or high risk countries.

16 CHAIRMAN BROWN: Where BSE occurs.

17 DR. EWENSTEIN: And stated that way, that
18 would actually cover drugs that were manufactured
19 outside and brought in, correct? So that's even
20 better. Okay.

21 CHAIRMAN BROWN: Something that's not
22 grammatically correct about this, but I'm not sure
23 what it is. I think it's probably the reversal of
24 we're advising the FDA to insure that the sheep and
25 goats are safe rather than the products are safe.

1 Again, we understand perfectly well what the damned
2 thing means, but I think we're really saying to insure
3 that the sources of materials, that sheep and goat
4 ~~sources~~ of materials for the manufacture of FDA
5 products are safe.

6 Again, these are rephrasing. We still
7 haven't got it perfect, and it might be that we're
8 going to wind up with my saying: does the Committee
9 understand what we're talking about?

10 We are talking about the FDA taking
11 measures that will enhance the safety of products
12 derived from sheep and goats in BSE countries.
13 Stripped of all its baggage, that's what we're voting
14 on, and if the Committee is prepared to vote on that,
15 we'll go ahead and vote now.

16 Okay. Larry, we start with you.

17 DR. SCHONBERGER: Yes.

18 CHAIRMAN BROWN: Stan.

19 DR. PRUSINER: Yes.

20 CHAIRMAN BROWN: Raymond.

21 DR. ROOS: Yes.

22 CHAIRMAN BROWN: Ermias.

23 DR. BELAY: Yes.

24 CHAIRMAN BROWN: Peter.

25 DR. LURIE: Yes.

1 CHAIRMAN BROWN: Dr. Hoel?
2 DR. HOEL: Yes.
3 CHAIRMAN BROWN: David?
4 DR. BOLTON: Yes.
5 CHAIRMAN BROWN: McCullough voted yes.
6 I vote yes.
7 Dr. Ewenstein?
8 DR. EWENSTEIN: Yes.
9 CHAIRMAN BROWN: Dr. Detwiler?
10 DR. DETWILER: Yes.
11 CHAIRMAN BROWN: Mrs. Williams?
12 DR. WILLIAMS: Yes.
13 CHAIRMAN BROWN: Or Dr. Williams.
14 Ms. Harrell.
15 MS. HARRELL: Yes.
16 CHAIRMAN BROWN: Dr. Cliver?
17 DR. CLIVER: Yes.
18 CHAIRMAN BROWN: Fourteen of 14.
19 We're on a roll. Let's go to Question No.
20 2, or I really -- I think we can. If you, on the
21 other hand, would like to have a little more
22 discussion before we vote on Question 2, which is
23 fundamentally exactly the same question, but we're now
24 talking about countries that do not have BSE. We are
25 talking about non-BSE countries.

1 And the question as phrased is whether the
2 FDA -- should the FDA take any safeguards to insure
3 that sheep and goats originating from or residing in
4 countries where scrapie occurs are scrapie free and
5 acceptable sources of materials for the manufacture of
6 FDA regulated products, again, with the extra baggage
7 about injection, implantation, products and
8 manufacturing process reagents?

9 So here we are not concerned with the risk
10 of BSE. The concern here is about a hypothetical risk
11 from scrapie itself. Here we're asked to decide
12 whether such safeguards should be taken to protect us
13 from the potential danger of being exposed to scrapie.

14 Larry.

15 DR. SCHONBERGER: Yes.

16 DR. BOLTON: Stan?

17 DR. PRUSINER: Yes.

18 CHAIRMAN BROWN: Ray?

19 DR. ROOS: Yes.

20 CHAIRMAN BROWN: Ermias?

21 DR. BELAY: Yes.

22 CHAIRMAN BROWN: Peter?

23 DR. LURIE: Yes.

24 CHAIRMAN BROWN: Dr. Hoel?

25 DR. HOEL: Yes.

1 CHAIRMAN BROWN: Dave?

2 DR. BOLTON: Yes.

3 CHAIRMAN BROWN: Dr. McCullough also voted
4 yes.

5 I vote no.

6 Dr. Ewenstein?

7 DR. EWENSTEIN: Yes.

8 CHAIRMAN BROWN: Dr. Detwiler?

9 DR. DETWILER: Yes.

10 CHAIRMAN BROWN: Dr. Williams?

11 DR. WILLIAMS: Yes.

12 CHAIRMAN BROWN: Ms. Harrell?

13 MS. HARRELL: Yes.

14 CHAIRMAN BROWN: Dr. Cliver?

15 DR. CLIVER: Yes.

16 CHAIRMAN BROWN: Damn. Okay.

17 (Laughter.)

18 CHAIRMAN BROWN: Well, it's good to be
19 different once in a while.

20 Okay. So you have your two votes now,
21 FDA, and we can now just discuss at will any issues
22 that you'd like to discuss before the meeting ends.
23 Is there anybody on the Committee that, you know,
24 would like to express opinions or recommend ways in
25 which or recommend measures that the FDA might be

1 particularly recommended to look at?

2 David.

3 DR. BOLTON: Well, I'd just like to echo
4 Bob Rohwer's statement about trying to encourage the
5 use of closed herds and certified flocks as much as
6 possible.

7 DR. ALMOND: Could I just?

8 CHAIRMAN BROWN: Yes. Kiki?

9 DR. HELLMAN: We have heard the term
10 "closed herds," but would someone venture a definition
11 of what would constitute a closed herd?

12 CHAIRMAN BROWN: Probably Linda would be
13 the best one to answer that.

14 DR. DETWILER: There are actually
15 variabilities in what you consider closed. You can
16 have it closed to the movement of live animals. That
17 would be just sheep and goats.

18 You can have it closed to all livestock
19 and poultry, depending on what disease you're trying
20 to keep out.

21 Dr. Rohwer had mentioned something, too,
22 he would recommend: no cervids, no bovids. I don't
23 know if there's any kind of scientific information
24 just on lateral contact, but you could require that,
25 and if you wanted a totally closed flock-herd, you

1 could even go to the extreme of preventing an
2 introduction of germ plasm, although that's very
3 difficult for even a pharmaceutical if you're going to
4 maintain genetics because you're going to introduce
5 hereditary problems in that. So you might not want to
6 totally close it to germ plasm introduction.

7 And you could close to even the outside
8 environment, again, not for a TSE issue, but for other
9 pathogens in the PSP.

10 So there's really broad definitions of
11 closed.

12 CHAIRMAN BROWN: Other Committee comments?
13 Bob.

14 DR. ROHWER: But I would like to emphasize
15 that one of the most important things to close it to
16 us feed routes of contamination. So feed should be
17 carefully regulated, and the easiest way to do that is
18 make sure they only get vegetable feed.

19 And in terms of genetic isolation, I don't
20 think you have to go that far, but because you can
21 maintain and improve the genetics through semen, but
22 I think it is very important to make sure that these
23 animals don't have direct animal contact with other
24 sheep, and the idea of bringing in animals themselves
25 to improve the or maintain, you know, genetic health

1 of the flock I think is a very bad idea.

2 CHAIRMAN BROWN: As another strategy that
3 was already mentioned, FDA probably ought to be
4 encouraged to themselves encourage alternative
5 products to natural base products whenever they can be
6 used. For example, the vascular grafts from goats,
7 presumably -- it was goats, wasn't it? Goat vascular
8 grafts or was it sheep? Sheep?

9 Probably in the next year or two or five,
10 they'll disappear as technology improves, but always
11 be alert to the possibility of using a substitute if
12 it's nearly or just as good.

13 DR. EWENSTEIN: Yes, I was going to say in
14 a similar vein that I see more use of these transgenic
15 animals. Already there are some products that you
16 have listed as transgenic products, especially in
17 goats, and that that would be of particular interest
18 because I see that as in a lot of people's minds the
19 escape route out of a lot of the infectious problems
20 in the biologics. So it would be important to make
21 sure that the sources of those transgenic products
22 were free of the pathogens that we're trying to get
23 away from in the human sources.

24 CHAIRMAN BROWN: Ray?

25 DR. ROOS: A couple of things with respect

1 to the transgenics. It would be good to target the
2 transgenics to have some resistance genes as well. So
3 that might be valuable with respect to the sourcing.

4 I'm all for promoting flocks that are
5 certified as scrapie free because I think, you know,
6 it's a valuable goal in this country to try to get
7 scrapie free sheep. I just don't know how realistic
8 that is. Maybe you can comment, Linda.

9 And the idea that pastures can remain a
10 source for the agent for years or at least that's what
11 one reads, and if that's the case, then one should get
12 an infected sheep in one of these certified flocks.
13 It's a worry of mine that there's a continuous nidus
14 for contamination.

15 So although I think these are good goals
16 and all, I'm just maybe a little bit pessimistic about
17 how successful we're going to be nationwide.

18 DR. DETWILER: I think you can do it, and
19 I think there are companies already that have done it
20 for sourcing, as well as private owners that have done
21 it.

22 One, the best scenario would be to start
23 where you've never had sheep and goats housed before,
24 and that's what a number of either people have done or
25 companies have done to do that.

1 The other thing if you wanted to go right
2 to the top is bring in animals from Australia and New
3 Zealand, or start with known especially breeds here.
4 There are breeds here that we have not diagnosed
5 scrapie. To get those as source and start them from
6 the bottom and bring them up.

7 And the other thing is to constantly
8 monitor your deaths loss in there, and then I think
9 with precautions, and you know, Bob pointed out
10 something that is really important, that we have
11 certain guidelines for our program in the country, and
12 in some respects, we have to keep those broad or else
13 we would totally not have participation because you
14 can't start up a program in this country and preclude
15 your genetics altogether, genetic improvement on other
16 things.

17 But for sourcing of injectables and
18 biologics, the FDA can definitely put more -- build
19 more, you know, stringent requirements into that basic
20 thing and require that as well. So I think there's
21 even more things you can build in.

22 CHAIRMAN BROWN: Dr. Hourrigan, all of
23 this must seem like deja vu, and I wondered if you
24 would like the opportunity to say 30 seconds' worth or
25 five minutes' worth of your own thoughts and give us

1 a little historical perspective.

2 I don't mean to put you on the spot, but
3 if you'd like to, we'd love to hear you.

4 - Could you come to the microphone, please?

5 DR. HOURRIGAN: It's nice to be here and
6 not to have to vote yes or no on any of the questions.

7 (Laughter.)

8 DR. HOURRIGAN: A problem has always been
9 in situations of this kind that whatever work we do is
10 going to be reviewed by the Monday morning
11 quarterbacks, and there are very severe critics
12 usually, and sometimes we're put out with them, but
13 often we can't wait until Monday morning.

14 We have to vote today, and perhaps if we
15 could wait until Monday morning, we might vote
16 differently, but that's not the way it goes.

17 And perhaps it's well that we do have
18 Monday morning quarterbacks so we can do even better
19 than our best to try to come to the best answer we can
20 for our various problems.

21 And I have been involved in scrapie for a
22 number of years, and these same questions come up, and
23 you certainly have a lot more answers now than we had
24 then, and most of the things you're talking about we
25 hadn't even heard of when we first started into the

1 scrapie program, but some things haven't changed all
2 that much either.

3 And it's nice to be here, and godspeed.

4 CHAIRMAN BROWN: Did you want -- have you
5 got any thoughts for us about achieving a scrapie free
6 U.S. based on your vast 30, 40 years of trying?

7 DR. HOURRIGAN: Well, I had a boss at one
8 time that was always bugging me on when are we going
9 to get rid of scrapie, and he'd do that about twice a
10 day.

11 (Laughter.)

12 DR. HOURRIGAN: And I said, "Well, yes, if
13 we do everything just right."

14 And he said, "What would that be?"

15 I said, "Kill all of the Suffolk sheep."

16 Well, he said he didn't think that was
17 feasible, which obviously it wasn't, and it's going to
18 be a hard row to hoe, and we used to say and we used
19 to hope instead of -- we always sat on the fence. On
20 one side we said that it's an infectious disease
21 spread laterally. On the other side of the fence we
22 said it's a genetic disease, and we seemed to have to
23 do that, and it was a very uncomfortable seat to sit
24 on, but it seemed to be one that we had to occupy.

25 But we thought that if it ever did become

1 genetic, perhaps we could get out of it. That would
2 solve all of our problems, and we see that scrapie is
3 considered more genetic in many respects and so are
4 most other disease and conditions than they were years
5 ago, and we find that even though this partial goal of
6 looking at the genetics of scrapie is more a reality
7 than it used to be, it still hasn't answered all of
8 our questions. Perhaps it never will.

9 And we used to argue if you could get rid
10 of scrapie in one flock, you can in all of the flocks
11 in the county, and if you can do it in the county, you
12 can do it in the state, and so on and on.

13 With a number of diseases that does work,
14 and in the case of Australia and New Zealand, they
15 really didn't have the intrinsic disease problem that
16 we have with scrapie and many other countries. They
17 could do that because they weren't really infected,
18 except through imports, and then only recently.

19 I would hope that it would be successful,
20 but it won't be seen in my time, and I hope it will be
21 perhaps in some of your times.

22 CHAIRMAN BROWN: Well, we rather hope it
23 might be seen in your time as well, Dr. Hourrigan,
24 from both our points of view.

25 Stan.

1 DR. PRUSINER: I'm just sitting here
2 trying to think if I'm a sheep farmer and I want to
3 create a flock and I want to be able to supply the
4 most possible scrapie free products for injection or
5 implantation.

6 So how I would begin -- I'll just be very
7 brief -- is I would go out, and I would need some
8 advice on the number of animals that I would collect
9 sperm from that are RR 171, and then I would bank
10 these sperm, and I would bioassay these sperm, and I
11 would also immunoassay some portion of these sperm.

12 Then I would have this bank. Then I would
13 use that to turn the -- and then I would have to be
14 very careful about how I selected the females that I
15 would impregnate with those sperm.

16 And then I would have to choose a piece of
17 land where there had been no history of scrapie. I'm
18 just reiterating a few things that have been said
19 already by several people.

20 The feed obviously is critical. Isolation
21 from all other farm animals I would believe is
22 critical, and I would autopsy every single animal that
23 dies or is sacrificed for scrapie.

24 I think those are really key ingredients,
25 and I think that the USDA and the FDA should get its

1 act together, and it should create this bank of sperm
2 that could be used then to breed these animals to
3 homozygosity for 171 because that's clearly a risk
4 factor, and it clearly renders animals quite
5 resistant.

6 It may not be 100 percent perfect, but
7 they're quite resistant to prions, and I think that's
8 something that government should do and then make it
9 available.

10 CHAIRMAN BROWN: Does anybody know what
11 the genotype of Dolly is?

12 (Laughter.)

13 CHAIRMAN BROWN: That's a few years down
14 the road, but it's an alternative.

15 DR. PRUSINER: Yes.

16 CHAIRMAN BROWN: Bob?

17 DR. PRUSINER: There are people trying to
18 make Dolly-like animals, in fact, I think at the same
19 Rosslyn Institute that are PrP null, and whether
20 that's going to work or not is unclear because one
21 doesn't know what the phenotype of those animals will
22 be a year or two or three or four out from birth.

23 CHAIRMAN BROWN: She was four when she was
24 born, so she is hitting the age of maximum
25 susceptibility or we can expect something to happen

1 soon or nothing at all.

2 Bob?

3 DR. ROHWER: I think another critical
4 element of a closed herd program is sentinels, but I
5 wouldn't create the sentinels by bringing them in from
6 the outside or by necessarily creating highly
7 susceptibles.

8 I think the way you go about this is that
9 you hold some proportion of your stock for their
10 lifetime, and so that they have an optimum opportunity
11 to develop the disease if it is in the population, and
12 you use the animals that you're breeding anyway.

13 I think one of the problems with the sperm
14 bank idea -- I'm not an expert on this, Stan, but my
15 understanding is that in breeding, you're breeding for
16 other traits besides scrapie susceptibility. In other
17 words, you're looking for animal health and vigor
18 traits, and you can't always get that from just one
19 particular sire. It's the mixture of sires that have
20 to go into that program.

21 DR. PRUSINER: Well, that's why I'm
22 suggesting that multiple animals be banked, not one.

23 CHAIRMAN BROWN: Yes, this is almost like
24 breeding tomatoes. You've got six different
25 characteristics that you like, and they're all on

1 different genes, and that's what the breeding, you
2 know, is all about.

3 Yes.

4 DR. ROHWER: There is one other thing
5 though that this breeding business brings up, breeding
6 for resistance instead of susceptibility, and that is
7 that I have heard it proposed by Katherine O'Rourke at
8 a meeting I attended recently that instead of
9 populating your flock with resistant animals, you
10 should populate it with susceptibles because you have
11 a higher probability of seeing the disease in a
12 susceptible.

13 This is completely counterintuitive from
14 my point of view, but it is seriously being proposed
15 by people in the USDA, and I think maybe that's
16 something we should weigh in on.

17 I'm not sure that's the way to go.

18 DR. DETWILER: Can we correct about the
19 USDA? That's a research arena, the USDA, not APHIS.
20 It's not, at least to my knowledge, not being
21 seriously proposed by APHIS.

22 CHAIRMAN BROWN: Yes, it sounds like a fun
23 research project, and that's fine.

24 One other thing, we're talking strategies.
25 Something that really hasn't been brought up or

1 emphasized very much -- I'm surprised that Bob hasn't
2 brought it up -- and that is don't overlook the
3 possibility of decontamination procedures, processing
4 steps for any individual product that could further
5 reduce risk even if the source is a little dicey.

6 Yes?

7 DR. HOURRIGAN: Some of you may recall
8 that Alan Dickinson attempted to select susceptible
9 and what he called short incubation sheep, and he was
10 highly successful. The incubation period got shorter
11 and shorter, and in his flock he was losing out on his
12 sheep that lived longer because they came down with
13 scrapie when they were about ten or 11 months old, and
14 eventually his flock died out because they didn't live
15 long enough to reproduce.

16 CHAIRMAN BROWN: Would any Committee
17 member like to express further comments or statements
18 or opinions?

19 (No response.)

20 CHAIRMAN BROWN: In that case, I hereby
21 terminate this two-day meeting and thank very much the
22 members of the Committee for their participation.

23 DR. FREAS: I would just like to thank our
24 Chair and everybody for participating in these public
25 discussions. We appreciate you taking your time to

1 come here to Washington, D.C. for these very important
2 meetings.

3 Thank you.

4 - (Whereupon, at 3:10 p.m., the meeting was
5 concluded.)

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C E R T I F I C A T E

This is to certify that the foregoing transcript in

the matter of: MEETING

Before: TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES
 ADVISORY COMMITTEE

Date: JUNE 3, 1999

Place: GAITHERSBURG, MD

represents the full and complete proceedings of the
aforementioned matter, as reported and reduced to
typewriting.


