

1 CHAIRMAN BROWN: So we have two plus-
2 minuses. Oh, I'm sorry. Don, your vote doesn't
3 count.

4 DR. SCHONBERGER: Let me pass for a
5 second.

6 CHAIRMAN BROWN: You mean you want to
7 come back to it after the committee makes its
8 decision? Put it on the line, Larry.

9 DR. SCHONBERGER: All right, I'll put it
10 on the line.

11 DR. LURIE: Larry, just a moment. Just
12 let me clarify. A no vote means no change. Is that
13 correct? Let's be clear on that.

14 CHAIRMAN BROWN: No, exactly. I think
15 that's a good point. We don't want to vote opposite
16 to what we think we do. Right?

17 DR. LURIE: I think that would be better,
18 yes.

19 CHAIRMAN BROWN: The FDA has a habit of
20 using double negatives in our questions. Does the
21 available scientific information justify a change in
22 the current FDA guidelines that bovine source
23 materials for the rendering of tallow should not come
24 from BSE or BSE unknown status countries?

25 In other words, a yes vote is a vote for

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1 the possibility of change. A no vote leaves the
2 current FDA policy intact. Larry?

3 DR. SCHONBERGER: Okay. Part of my
4 hesitation was that I wasn't -- All the possibilities
5 hadn't suddenly gone before my mind, and there might
6 well be something that I would say, oh, well, that
7 risk is so low, yeah, we could change it; but as a
8 general -- Since I don't have that in my mind right
9 now, I'm going to vote no.

10 I want to know that, if somebody brings up
11 something that I'm not thinking about that says that
12 there's a use or a certain product that really the
13 exposure is negligible, then I'm right at the border
14 line on that there being any risk at all here.

15 So I'm going to say no. Just leave it
16 alone.

17 CHAIRMAN BROWN: So you believe that the
18 scientific evidence does not constitute reason for a
19 change in the current policy?

20 DR. SCHONBERGER: No change.

21 CHAIRMAN BROWN: No change. Okay. You
22 understand that a no vote closes the discussion,
23 therefore. So you --

24 DR. SCHONBERGER: That's why I made my
25 comments.

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1 CHAIRMAN BROWN: You won't hear anything,
2 huh? Leon?

3 MR. FAITEK: I vote no for the following
4 reasons. One is that I don't see that any change that
5 we could make in the context of this discussion would
6 make the products that use tallow any safer than they
7 are now. Probably quite to the contrary.

8 I wouldn't try to put a number to that
9 increased risk factor, but I think that there is an
10 increased risk factor there.

11 Number two, unlike dura mater where if you
12 have a contaminated sample, one person may get sick,
13 which is not to minimize that -- one person getting
14 sick is bad -- but if you're using a pooled product
15 and, although again the possibilities are small of
16 anything untoward happening, the consequences could be
17 large.

18 Third of all, and this is an area where
19 the statement before says we probably shouldn't be
20 getting into, I would think that the industry would
21 want this added safety for their benefit. God forbid
22 that there's a BSE cow found in this state, and we
23 wind up with a mass of regulations that we heard
24 explained today from the European community.

25 I think that any change in this regard

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1 would be, I dare to say, which is counter to my
2 heritage -- My view is conservative in this regard --
3 would be unwise and certainly at the very least
4 premature.

5 CHAIRMAN BROWN: Ray?

6 DR. ROOS: I'll vote no. I think there is
7 clearly a very low risk for reasons that people have
8 noted regarding tallow, no obvious infectivity in the
9 studies that we have, small amounts of protein, heat
10 steps in the processing, species to species barrier,
11 etcetera. Still, the negative studies don't rule out
12 the possibility of infectivity and risk here.

13 We have presently guidelines from the FDA,
14 and I haven't heard sufficient evidence to change the
15 present guidelines, at least from my perspective.

16 An issue is whether one should deal with
17 this umbrella guideline or whether one should break
18 things away into different categories. At the moment
19 I'm just concerned about dealing with all of those
20 different little pieces, and I'm worried that it's
21 going to be a bit of a regulatory nightmare and a lot
22 of details that, as you described, Paul, look a little
23 bit like an IRS form with different schedules.

24 So at this point in time, I think I'd like
25 to deal with it as an umbrella with that umbrella, no.

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1 CHAIRMAN BROWN: Bill?

2 DR. HUESTON: I vote yes. I believe that
3 having this umbrella and this absolute approach to say
4 absolutely no really in the long run is
5 disadvantageous. The reasons are this: One, I think
6 it ignores the science. It ignores the fact that we
7 have opportunities to reduce the risk and to manage
8 the risk that may be present.

9 I think, secondly, it essentially labels
10 countries for having identified BSE and may further
11 preclude or minimize or damage the encouragement that
12 we're making globally for countries to report the
13 occurrence of disease, and this may in fact encourage
14 countries to pursue policies of hiding disease, an
15 that we are more likely to get high risk materials
16 into the United States as a result of a blanket policy
17 than we would be by having a reasonable -- what I
18 would consider a rational approach which says -- which
19 lays out here are the risks, here are the benefits or
20 the approaches that we can use in processing to
21 minimize or to inactivate the agent, here are the uses
22 which represent very low exposure to individuals.

23 I think, by that strategy of looking at
24 sourcing, processing and use, one could come up with
25 a very scientifically sound policy that would allow

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1 countries to see a way in which they might be able to
2 market their extremely low risk material in an
3 appropriate manner and might further our, I believe,
4 common and shared goal of global public health.

5 CHAIRMAN BROWN: Thank you. Linda.

6 DR. DETWILER: I vote yes also for the
7 same reasons Will did. Approaching this from a
8 scientific base is something that appears to have low
9 -- you know, negligible, if any, risk to begin with,
10 and then taking precautions.

11 I look at it just like I wouldn't want the
12 government coming and telling me I can't drive an
13 automobile because there's a risk of getting in an
14 accident versus they can tell me I must wear a
15 seatbelt or not drive with alcohol impairment.

16 CHAIRMAN BROWN: I vote yes, simply
17 because I think the level of infectivity likely to
18 occur in tallow is close to zero, and that being the
19 case, I think that oral products and cosmetics could
20 be easily and safely excluded from this restriction.

21 Donald?

22 DR. BURKE: I vote no. I'm not impressed
23 that the risk is zero, and I see little benefit in
24 changing the current policy.

25 CHAIRMAN BROWN: Barbara?

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1 DR. HARRELL: I vote no, because I'm not
2 impressed with the data, the available science that
3 has been presented today, and also I consider that,
4 even though we should not expect a zero risk, that we
5 are not in -- we are in a position where we don't have
6 to take any risk at all.

7 CHAIRMAN BROWN: Thank you. Peter.

8 DR. LURIE: I vote no as well. The risk
9 is so small as to be almost impossible to quantify.
10 Yet as pointed out, it can be reduced to even closer
11 to zero with no detrimental effect upon the American
12 public health that I can see. Therefore, I vote no.

13 CHAIRMAN BROWN: Doris?

14 DR. OLANDER: I vote yes for the
15 particular reason that we would drive reporting of the
16 disease underground in other countries.

17 CHAIRMAN BROWN: Beth?

18 DR. WILLIAMS: I vote yes. I think that
19 the evidence that's been presented suggests that
20 there's an insignificant risk, but especially I
21 believe that having a blanket policy isn't going to
22 serve the public. So I think we would need to
23 reevaluate some of the uses of these products.

24 CHAIRMAN BROWN: Well, the nos have it,
25 six to five, which eliminates question 2.

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1 Question 3: Same question with respect to
2 tallow derivatives. The tallow derivatives, you
3 recall, pass through or we can stipulate that they
4 pass through, if there's any question, just to be sure
5 that no opening is left, that we can specify that
6 tallow derivatives are processed through the minimum
7 heat/pressure conditions that are known to inactivate
8 the agent.

9 I think we were presented with information
10 which indicated that this was 100 percent the case,
11 but I think I would like to be assured that that is
12 100 percent the case. That is, every tallow
13 derivative has gone through a temperature of at least
14 132 degrees Centigrade under three bars of pressure
15 for at least 20 minutes.

16 DR. OLANDER: Question. How many strains
17 of these agents have been tested at 133 20 mins 3bars?

18 CHAIRMAN BROWN: Quite a few. The BSE --
19 Apparently, there is only one strain, but many strains
20 of scrapie, many strains of CJD, transmissible mink
21 encephalopathy and kuru. I think everything has been
22 -- if not 3bars, everything has been checked through
23 at least 121 to 134 degrees in an autoclave situation.

24 It's been found that 121 has sometimes
25 complete activity, occasionally incomplete activity,

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1 but that 134 at 3bars for 20 minutes -- and David, you
2 may now think that an hour would be better, but at
3 least 20 minutes. I think most of the processes we've
4 seen go at least an hour anyway and two and three
5 hours and sometimes longer.

6 DR. OLANDER: I was just wondering where
7 we -- how we could get scientific to set a benchmark.

8 CHAIRMAN BROWN: This is a -- Probably if
9 there is any consensus about the inactivation of these
10 agents, it's that the best known inactivation to date,
11 and it is virtually 100 percent without failure is
12 this method of steam under pressure heat.

13 DR. SCHONBERGER: Let me preface my
14 comment, now that I'm on the derivatives. I'm leaning
15 on the other side of having the FDA regulations
16 changed to loosen it, because I was impressed with the
17 procedure, the harsh procedure this has gone under and
18 the inactivation that would result, and that we're
19 dealing with a very insignificant risk. But at the
20 same time, Paul, I think it was you that mentioned
21 that the inactivation procedure was under a dry
22 condition and that that was somehow different from the
23 studies that have really been done to show the effect
24 of heat on the agent.

25 CHAIRMAN BROWN: Yes. The derivatives, I

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1 think, don't quality for that. That is, they are
2 under pressure as a liquid with that heat applied to
3 them as a liquid under pressure.

4 DR. SCHONBERGER: Good.

5 CHAIRMAN BROWN: Larry, your vote?

6 DR. SCHONBERGER: You want to clarify what
7 the meaning of the yes and no is, so we --

8 DR. GREEN: The one thing I would say on
9 derivatives, I know of nowhere you can make
10 derivatives without exceeding the minimum of the three
11 bars 133 degrees C. in 20 minutes.

12 CHAIRMAN BROWN: Right. In other words,
13 what we're talking about is, if you had to design an
14 experiment to inactivate these agents, you would
15 design a derivative process.

16 DR. SCHONBERGER: Do you want to clarify
17 what the meaning of the yes and no is?

18 CHAIRMAN BROWN: Again, it's the same
19 thing. No means we leave everything intact and leave
20 this rigorous exclusion of BSE or BSE status unknown
21 countries as verboten. A yes means that we recommend
22 that the FDA change their posture and relax it.

23 DR. SCHONBERGER: Okay. Well, unlike the
24 plain tallow, I think that the tallow derivatives have
25 an insignificant risk and, therefore, I vote yes.

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1 CHAIRMAN BROWN: Leon?

2 MR. FAITEK: This is a little tougher
3 question, and I agree that this is a relatively safe
4 product. All these products are relatively safe.

5 I will, nevertheless, vote no, because I
6 don't want to get into these other issues.

7 CHAIRMAN BROWN: Mean logic? Ray?

8 DR. ROOS: I vote yes. I think the
9 inactivation step here is a very important one. So
10 that, assuming we are dealing with infectious material
11 or some breakdown in processing or some -- you know,
12 if the BSE curve begins to go up rather than down, I
13 feel confident that the risk here is smaller than in
14 the first situation because of the inactivation step.
15 So I vote yes.

16 CHAIRMAN BROWN: Bill?

17 DR. HUESTON: Yes.

18 CHAIRMAN BROWN: Linda?

19 DR. DETWILER: Yes.

20 CHAIRMAN BROWN: I vote yes. Don?

21 DR. BURKE: I vote yes as well, but I
22 think it is a little more complicated, that there are
23 many different types of derivatives that are not all
24 necessarily, as I understand it, through the high
25 temperature and pressure, and we do need to consider

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1 them one by one.

2 CHAIRMAN BROWN: Barbara?

3 DR. HARRELL: No.

4 CHAIRMAN BROWN: Peter.

5 DR. LURIE: I agree that the risk in the
6 previous question was small and that it is now
7 smaller, but I still fail to see the benefit of
8 changing the regulations or the guidance. So I vote
9 no.

10 CHAIRMAN BROWN: Doris?

11 DR. OLANDER: Yes.

12 CHAIRMAN BROWN: Beth?

13 DR. WILLIAMS: Yes.

14 CHAIRMAN BROWN: The yeses have it, the
15 tally being eight to three, which means that we have
16 to consider question 4. I would propose that the
17 committee, to make their life easier --

18 DR. HUESTON: To have the break before we
19 discuss it. Thank you.

20 CHAIRMAN BROWN: Exactly. So that way any
21 last minute lobbying can also occur. We will
22 reconvene at eleven sharp.

23 (Whereupon, the foregoing matter went off
24 the record at 10:42 a.m. and went back on the record
25 at 11:02 a.m.)

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1 DR. FREAS: Would you take your seats,
2 please. If there is a Dr. Mara Ricketts in the
3 audience, I have two urgent packages. They will be
4 out on the table outside the room, if there's a Dr.
5 Mara Ricketts here. These are two packets marked
6 "Urgent."

7 CHAIRMAN BROWN: The committee has opened
8 up a discussion of question 4 in which we are going to
9 recommend to the FDA to make one or more changes in
10 their current policy. I think the first thing I would
11 like for the committee to hear is just a very summary
12 recapitulation from Dr. Green, if he is here, on the
13 process or alternative processes for, first,
14 saponification and, second, derivatization; but the
15 first, saponification.

16 DR. GREEN: Well, in saponification you
17 use a minimum of 12 molar caustic. Actually, most
18 people use 50 percent caustic solution. That is a
19 standard commodity that's sold in industry, and the
20 less water you put in, the less water you take out.

21 So when you start saponification, you
22 normally use 50 percent caustic. There would be
23 possible some small formulators that might not want to
24 go to 50 percent, but the majority of the industry
25 always starts with 50 percent caustic, because it's

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1 standard in our plants for many, many reasons.

2 It's less water in. It's less water out.

3 It costs money to take water out of the finished
4 product. You're taking your saponification up.
5 Actually, the lowest temperatures in which you're
6 doing saponification for soap making, as I said
7 yesterday, there are no fatty acids produced in this
8 country from saponification; because you would have an
9 actual salt formed, and then you would have to add
10 either one of the three mineral acids, either
11 hydrochloric or sulfuric or phosphoric, to neutralize
12 off the alkali.

13 This would then require you to filter it.
14 You would lose 15-20 percent of your throughput. Then
15 you would never get below the five part per million of
16 requirement to have in a fatty acid -- no more than
17 five parts per million sodium ion, because in
18 derivatizing the fatty acid to other derivatives,
19 whether it's oxalkylation or what have you, the sodium
20 ion interferes with this reaction, and very few
21 customers -- that's respect to setting a standard --
22 they will not allow you to exceed five ptm.

23 So you cannot produce fatty acids via the
24 saponification. I know of no company that does it,
25 and I am familiar with every single manufacturer of

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1 fatty acids in the United States.

2 CHAIRMAN BROWN: And then the second part,
3 the derivatization always involves at least -- at
4 least 20 minutes of at least 3 bars of at least 132
5 degrees Centigrade.

6 DR. GREEN: Yes, they do. Then if you're
7 dealing with the fatty acid itself and your
8 derivatizing that, it will take you at least an hour,
9 and you will exceed the three bars, and you will
10 exceed the 135 degrees C. There's no way you can make
11 any of those derivatives, with the exception of the
12 calcium stearate, but that calcium stearate has gone
13 through two processes to get to the stearic acid that
14 went through over 250 degrees C and, as we said, over
15 700 psi to get there up the distillation tower.

16 CHAIRMAN BROWN: Right. Thank you. Is
17 the committee clear about that? Also, when we're
18 talking derivatives, we're talking --

19 DR. BURKE: I'm not quite clear yet. When
20 we talk about derivatives, that they can either go to
21 be saponified and then to be derivatized after that or
22 that they go one way or the other?

23 DR. GREEN: No. In derivatives -- The
24 only saponification that's really going right now is
25 soap manufacturing. All the derivatives are now

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1 produced by the free fatty acid, and there has been a
2 massive consolidation in this country in the past 20
3 years.

4 I know -- I was originally with a small
5 company many years that was bought by Witco, and Witco
6 had acquired a massive number of companies. There's
7 been 16 consolidations by our company alone. So I
8 know when I say nobody is doing it, and that's how
9 it's done.

10 DR. BURKE: But when we talk about
11 derivatives, we're also -- The broader term here
12 includes the saponified materials, because that isn't
13 tallow.

14 DR. GREEN: Yes, it is tallow, and it is
15 saponified, but even if you -- in the soap making,
16 which is a multi-step process, it's not a single step.
17 IN the drying stage in removing of the moisture in the
18 soap, you actually exceed the 135 bars.

19 DR. BURKE: So my question to the Chair
20 then is are we including in this -- in our discussion
21 of derivatives, do we also include in this the
22 discussion of saponified tallow?

23 CHAIRMAN BROWN: Well, evidently. Soap is
24 not considered a derivative, according to the charts.
25 Soap and soap products are not under the aegis of

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1 derivatives.

2 DR. BURKE: so are we not going to discuss
3 the saponified at all?

4 DR. CHIU: Soap is not regulated by FDA.
5 But the glycerin generated upon saponification would
6 be regulated by FDA.

7 CHAIRMAN BROWN: But would that be
8 considered a derivative?

9 DR. CHIU: Glycerin is a derivative.

10 DR. GREEN: It would be considered a
11 derivative, but in the distillation of the glycerin
12 from crude glycerin, as I showed yesterday, it's a
13 two-step distillation, and it far exceeds the
14 temperatures of the 133 degrees C and three bars,
15 although in distillation of glycerin you do it at
16 reduced pressure. Otherwise, you'll polymerize the
17 glycerin.

18 DR. BURKE: I think I understand. We are
19 not going to discuss soaps.

20 CHAIRMAN BROWN: Well, I don't know. Soap
21 is considered -- We're going to get some advice on the
22 FDA as to what they want to consider.

23 DR. HUESTON: It's not coming from the
24 FDA. It's not regulated.

25 CHAIRMAN BROWN: Oh, well, it's not

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1 regulated. Okay. So the entire soap industry is not
2 under the purview of the FDA.

3 DR. LAMBERT: Lark Lambert, Office of
4 Cosmetics and Colors. Soap as soap is not regulated,
5 but soap, if it has moisturizing or if it has a
6 cosmetic claim --

7 CHAIRMAN BROWN: Glycerin is regulated.

8 DR. LAMBERT: Right, but if you say on a
9 soap that it moisturizes, then it becomes a cosmetic.
10 If it's just soap, it's not regulated.

11 CHAIRMAN BROWN: Okay. Again, Dr. Green,
12 the distillation procedure that produces the glycerin
13 that goes into soap -- it's a two-step procedure?

14 DR. GREEN: Yes.

15 CHAIRMAN BROWN: And the temperature
16 exceeds 132?

17 DR. GREEN: Yes.

18 CHAIRMAN BROWN: But it's done under
19 negative pressure, is it not?

20 DR. GREEN: Well, it's done under negative
21 pressure, but the temperature is about 250C and not
22 133.

23 CHAIRMAN BROWN: Right. So we've got a
24 circumstance where the temperature is double what it
25 would be if under pressure, only it's not under

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1 pressure.

2 DR. GREEN: We do it under reduced
3 pressure, but you're taking the moisture out. So it
4 is not a dry heat. It is a wet heat.

5 CHAIRMAN BROWN: No, that's understood.
6 It's a wet heat, not under positive pressure at very
7 high temperatures. That's glycerin, and the
8 derivatives as such, which you see on the chart here,
9 are all subject to pressurized high temperatures for
10 length periods of time. Everybody clear about that?

11 We're not talking about soap at all, only
12 to the extent that it would contain glycerin or --
13 well, glycerin. Yes, Barbara?

14 DR. HARRELL: Is Dr. Green speaking for
15 the BSE countries or just for the United States
16 processes?

17 DR. GREEN: Strictly for the United States
18 processing, but I'm quite familiar with all the
19 processes, since we are a multi-national company, and
20 I deal with multi-national companies.

21 DR. HARRELL: So what you're saying is --
22 So it would include BSE countries?

23 DR. GREEN: Glycerin -- All glycerin
24 anywhere in the world is recovered the same way. You
25 have to distil it. You can't get it pure any other

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1 way. You can't get the water out.

2 DR. HARRELL: You would distil it, but
3 would you do it at the same temperatures? Would you
4 do it under the same pressure and time constraints?

5 DR. GREEN: You would do it under vacuum.
6 Otherwise, you lose the glycerin. It polymerizes very
7 easily, and we actually make product by polymerizing
8 glycerin. So we know how easy it is to polymerize it.

9 DR. HARRELL: But still, is it the same
10 temperatures, the same pressure?

11 DR. GREEN: All companies, regardless of
12 whether they do it within ten degrees, operate the
13 still the same way. You have slight design
14 differences in distilled, but they're plus or minus
15 ten degrees. They're around the same.

16 CHAIRMAN BROWN: Thank you, Dr. Green.

17 DR. OLANDER: One last question, Dr.
18 Green. On page 6 or 7 on your glycerin distillation,
19 you said just now that it was 250 degrees. It says
20 166 to 175.

21 DR. GREEN: Well, I'll correct that. I
22 didn't have my slides with me.

23 CHAIRMAN BROWN: Well, we have a number of
24 changes that we can consider. I'm not -- Maybe I can
25 again make an effort. Unless there is further

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1 discussion about the details of what we might wind up
2 doing eventually, I'll offer you a blank proposal for
3 your consideration and vote.

4 That is that tallow derivatives -- and now
5 we're talking about tallow derivatives, not glycerin -
6 - that tallow derivatives which we've heard all are
7 subject to high pressure, high temperature, long time
8 procedures which are currently not permitted to be
9 sourced in BSE countries, whether they be for
10 injectables, for oral products, for other drug
11 products or for cosmetics, all four of the items that
12 you see across the bottom row -- that they all be
13 allowed. They are presently not allowed.

14 I would suggest that the committee first
15 vote on whether or not to remove this restrictive
16 recommendation right across the board, in view of the
17 processing that all derivatives go through.

18 So I'm going to take a vote on that.

19 DR. BURKE: But your definition here of a
20 tallow derivative is some -- you want to give a more
21 distinctive definition?

22 CHAIRMAN BROWN: Yes. Whatever is shown
23 on these two charts in the box derivatives, and
24 they've all gone through this
25 temperature/pressure/time process, every one of them.

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1 So there's not an alternative here in terms of
2 processing. They've all gone through heat, pressure,
3 time that has been demonstrated to be an effective
4 sterilizer of this group of agents.

5 DR. HUESTON: You're excepting or
6 including glycerin? I'm sorry.

7 CHAIRMAN BROWN: No, not considering
8 glycerin now. Glycerin apart. We'll take up glycerin
9 next. Now to try and make our job a little easier,
10 I'm talking about only those products which have been
11 subject to high pressure, high time, high temperature.

12 DR. ROOS: Just so I understand, Paul,
13 maybe it's taken for granted. The source material is
14 not a neurologically ill animal?

15 CHAIRMAN BROWN: Yeah, I think that's
16 understood. That's implied.

17 DR. ROOS: And there are particular
18 slaughter house procedures that are in effect in BSE
19 countries that relate to removing brain and spinal
20 cord first. Is that right?

21 CHAIRMAN BROWN: Well, let's find out.
22 Would it be possible for spinal cords and brains to
23 be amongst the materials which would be saponified or
24 used in -- not saponified but used as derivatives --
25 as source material?

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1 DR. BRADLEY: Since there's no -- If we're
2 talking about European Community alone, since at this
3 present time there isn't a specified risk materials
4 ban, that ban is -- If it exists at all, it's related
5 to the specific governments.

6 As far as I'm aware, all the governments
7 of countries which have native born cases of BSE
8 operate such a ban. So that the ante mortem
9 inspection/post mortem inspection and removal of brain
10 or skulls and spinal cord actually takes place in most
11 countries, but not necessarily in the other countries
12 of the European Community which have not reported a
13 case of BSE.

14 CHAIRMAN BROWN: Right. So that they
15 would not be, according to the USDA, considered as BSE
16 positive countries.

17 DR. BRADLEY: Precisely.

18 CHAIRMAN BROWN: So again --

19 DR. DETWILER: We changed the policy. Now
20 all of Europe is actually treated equally.

21 CHAIRMAN BROWN: As BSE positive?

22 DR. DETWILER: As BSE risk until they
23 complete the risk assessments, but right now it's the
24 entire.

25 CHAIRMAN BROWN: Well, let me amend the

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1 proposal then, which I think would be along the lines,
2 Ray, that you suggested, and propose a blanket change
3 to yes and stipulate these conditions of the removal
4 of either the head and the brain or brain and spinal
5 cord and pre- and post-mortem inspection of the
6 animals.

7 In other words, with those conditions,
8 setting those conditions, then we allow European
9 source material to be used for derivatives. That's
10 the proposal on the table.

11 DR. HARRELL: Dr. Brown, would that be
12 implied that the spinal cord is intact?

13 CHAIRMAN BROWN: What do you mean, intact
14 -- what? Taken out. It's removed. It's gone. It's
15 not part of the material. The spinal cord and brain
16 are not part of the input carcass. Spinal column.
17 Spinal column and either brain or head, whichever they
18 choose to remove. I beg your pardon?

19 DR. HONSTEAD: The spinal column is the
20 bones, and the spinal cord is the nervous tissues. So
21 you want the spinal cord -- the spinal column, the
22 bones, including the cord or just -- The SRM ban is
23 the cord.

24 DR. BRADLEY: Yes.

25 DR. HONSTEAD: They're removing the spinal

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1 cord after they split it.

2 DR. SCHONBERGER: Right. Maybe Ray should
3 describe what the system is.

4 DR. BRADLEY: It could be helpful to use
5 one of the slides I used yesterday of the EU proposal.

6 At this point in time, there is no
7 European-wide specified risk materials ban in
8 operation, but there is a ban in operation, obviously,
9 in the UK and in all those countries that have
10 actually had cases of BSE in native born animals. But
11 there are countries in Europe which have neither a
12 ban, but they have had cases of BSE in imported
13 animals.

14 CHAIRMAN BROWN: Yes, I understand. I
15 think it would be too complicated -- I understand what
16 you're saying. Go ahead.

17 DR. BRADLEY: But on -- The list that was
18 proposed to be operative from July last year is on the
19 board. So it would be the skull, including brains and
20 eyes; tonsils and spinal cord from all cattle greater
21 than one year old; and from sheep and goats also over
22 one year old, plus the spleen from sheep and goats,
23 plus the vertebral column from those specific species
24 would be prohibited but only from making mechanically
25 recovered meat.

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1 In the present context, we're looking at
2 the top three items, but I repeat, this is not in
3 operation throughout the European Union; but a ban
4 such as that does operate in all the countries with
5 BSE in native born animals. The precision of that in
6 relation to what's written on the chart there has to
7 be clarified with the governments concerned.

8 As Linda pointed out, it is sometimes
9 difficult to be absolutely precise in how they apply
10 their ban. Until it is a Union-wide ban, I can't
11 really speak for each individual government.

12 In the UK we've got tougher rules than
13 that. We take heads out, as an example, rather than
14 just the skull.

15 CHAIRMAN BROWN: But the committee can
16 stipulate that the European Union that -- that this
17 restriction would apply not on a country by country
18 basis, but as a blanket basis. That is that we will
19 accept this material if SRM are not a part of the
20 input rendered material.

21 DR. DETWILER: May I suggest one
22 modification, if we do stipulate, if we would do like
23 either skull or brain and spinal cord, but not tonsil,
24 because it's -- To my understanding, in cattle there's
25 been no evidence of infectivity in tonsil. Is that

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1 correct?

2 DR. BRADLEY: That is correct.

3 DR. DETWILER: And I can tell you only
4 from somebody who has taken out now about 1,000
5 tonsils, it's no easy task.

6 CHAIRMAN BROWN: Would it be acceptable
7 then to ask for this blanket change and simply say
8 from cattle in BSE positive countries that have had
9 their brains and spinal cords removed?

10 DR. BRADLEY: Mr. Chairman, may I suggest
11 that you include the eyes as well, because we do
12 notice infectivity in the retina.

13 CHAIRMAN BROWN: Okay.

14 DR. BURKE: The issue of cord versus
15 column -- my understanding was that there is, not a
16 substantial, but at least relatively high amount of
17 infectivity in the dorsal root ganglia which are not
18 pulled when you do a spinal cord, and that was the
19 rationale for including the column. Is that correct?

20 DR. BRADLEY: Yes.

21 DR. BURKE: So there is some additional
22 tissue, and it's a call as to whether or not that
23 extra few grams of tissue makes a difference.

24 CHAIRMAN BROWN: Any feeling from the
25 committee as to whether vertical column or spinal

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1 column --

2 DR. HUESTON: Can I ask a more basic
3 science question? Are we hence saying that from the
4 science we believe that this proteinaceous agent can
5 survive distillation and cracking? That's where we're
6 headed.

7 I mean, I thought maybe you were going to
8 go stepwise toward that point, but isn't there a
9 question first as to whether or not this agent can
10 survive? What we're talking about are pretty darn
11 extreme processes.

12 CHAIRMAN BROWN: Yes. We have, as far as
13 I know -- and again, Bob can tell me if I'm wrong. I
14 know of no published or unpublished report of this
15 agent surviving this treatment.

16 DR. ROHWER: Bob Rohwer, VA Medical
17 Center, Baltimore.

18 I would agree with you, and especially
19 when alkali is involved. It seems very unlikely that
20 these agents could survive this. We have been
21 surprised in the past, and there is one element of
22 this that does bother me.

23 That is that there is one other ingredient
24 in this triad of temperature, pressure and time, and
25 that is water. There is some evidence, both from

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1 David Taylor's work and some of the things that I've
2 done and you've done, actually, Paul, that dry heat is
3 very ineffective in killing these agents.

4 So I wonder if, under these anhydrous --
5 just how anhydrous these conditions are, and whether
6 in the end it shouldn't -- It seems very unlikely that
7 things would survive, but I'd feel a lot more
8 comfortable to actually see it validated as a
9 consequence of that.

10 It's a condition that could be included,
11 I suppose, in these recommendations. But in terms of
12 aqueous conditions, indeed, I don't know of any
13 situation in which this stuff would survive.

14 DR. HUESTON: Well, I'd love to have a
15 flow chart that shows this, but if we talk about fatty
16 acid splitting, what it starts with is tallow and
17 steam, if I followed the presentation correctly. So
18 you're taking three to four hours at 248-271 C. at
19 pressure of 710-730 psi, with steam, with live --
20 That's wet heat, isn't it?

21 DR. ROHWER: I think that it would be nice
22 to have Dr. Green clarify that.

23 CHAIRMAN BROWN: He's right behind you.

24 DR. ROHWER: Yes. Okay. The other thing
25 that wasn't clear to me in his earlier presentation is

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1 I'd still like it stated in a totally unambiguous way
2 that everything that goes to derivatives has gone
3 through the saponification process first.

4 DR. HUESTON: Yeah, and if that's not
5 true, but --

6 DR. ROHWER: That's what the chart says up
7 here.

8 CHAIRMAN BROWN: No, but not for the
9 edible. The edible doesn't show saponification as a
10 first step.

11 DR. HUESTON: I think it would be ideal if
12 the chart was -- we took it one step further and just
13 made that flow, because I think we're losing some
14 people as to which goes where.

15 CHAIRMAN BROWN: Right. Dr. Green.

16 DR. GREEN: The conditions apply both for
17 edible and nonedible. They go through -- and when
18 we're talking about steam, there's three types of
19 steam. There's low pressure steam. There's mid
20 pressure steam, and there's high pressure steam.

21 This is high pressure steam. You actually
22 counterflow the tallow. Counterflow is against high
23 pressure steam. When we talk about water in there,
24 that's -- water comes out with the glycerin, but when
25 the two are intimately contacted in the reaction, it's

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1 high pressure steam at those temperatures, and that's
2 why it's expressed that way.

3 There isn't any fatty acid produced in
4 this country via saponification. All of it is
5 produced either by transesterification or by the
6 splitting or what we call hydrolysis. That is the
7 only two methods that any tallow fatty acid is
8 produced in the United States today, period.

9 DR. HUESTON: And this countercurrent
10 steam process at the beginning of it, there's a lot of
11 water there.

12 DR. GREEN: Well, yes, but --

13 DR. HUESTON: At the beginning.

14 DR. GREEN: -- what I'm saying is that we
15 inject steam at the top, and we inject the fatty acid
16 at the bottom of the reactor tube, and they pass each
17 other; and, yes, it is condensed down to water as the
18 steam reacts with it, but the temperature is still
19 maintained at the temperature and pressures I
20 presented in the chart.

21 CHAIRMAN BROWN: What I'm getting at is
22 trying to answer Bob's question about the aqueous.

23 DR. GREEN: Yes, it is water.

24 CHAIRMAN BROWN: At the beginning, it's
25 aqueous. So live steam is going through a solution

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1 that could be considered aqueous. At the end, it's
2 less aqueous.

3 DR. ROHWER: Probably the most relevant
4 thing is it's hydrolytic, and that's probably the
5 crucial feature of the chemistry in terms of
6 inactivating these agents.

7 DR. HUESTON: So those tallow derivatives
8 that flow from the initial process of hydrolysis would
9 go through this wet heat treatment initially, and then
10 go to further cracking on down the line.

11 DR. GREEN: That's right.

12 DR. HUESTON: Now how about those
13 derivatives that go through transesterification? You
14 talked about time and temperature. Is there -- Help
15 me understand. From raw tallow through
16 transesterification to tallow derivatives, is there a
17 wet heat treatment there?

18 DR. GREEN: Yes, there is some wet heat in
19 that. It is not to the extent that you do, but you
20 have methyl alcohol in there, and you're forming a
21 direct transesterification with methanol and replacing
22 the glycerin with methanol at those temperatures and
23 pressures.

24 Then they further do that, but prior to
25 that there is a partial hydrogenation that is at

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1 rather high temperatures and a fair amount of time
2 involved there. You do have to do a partial
3 hydrogenation.

4 We -- The industry -- this is across the
5 board. There is a slight partial hydrogenation of raw
6 tallow before we ever go through the splitting
7 process. We do this because it makes the unit run
8 smoother, and you get a more efficient yield out of
9 your process.

10 DR. HUESTON: But that's just hydrogen,
11 not steam. Right?

12 DR. GREEN: Yes. That's just hydrogen,
13 but I'm making a point. You do a partial
14 hydrogenation prior to going to either one of these
15 reactions.

16 CHAIRMAN BROWN: Is the committee clear?
17 Okay. Now you wanted, Will -- Thank you, Dr. Green.
18 We may call you back.

19 Will, did you want to --

20 DR. HUESTON: I was just suggesting, for
21 those -- As an example, to sort of help us, for those
22 things that go through this process of hydrolysis,
23 fatty acid hydrolysis, the splitting, and then go to
24 the derivatives from that beyond that, I'm asking the
25 question: Is there anyone here that thinks, that

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1 believes that the agent can survive that; because if
2 not, then our discussion is moot. You follow me?

3 CHAIRMAN BROWN: Yes. No, I follow you
4 perfectly, and the implications of what we would be
5 voting on would be, no, this process is a 100 percent
6 killer, but just in case it isn't, we'll take the
7 spinal cord and brain out. I mean, that's the logic
8 of that particular vote.

9 Sometimes we vote without perfect logic,
10 actually.

11 DR. HUESTON: Let me ask, did anybody ever
12 take the BSE agent through from this beginning step
13 and look for what happened to infectivity?

14 CHAIRMAN BROWN: Validation through a
15 derivative?

16 DR. HUESTON: Yes.

17 CHAIRMAN BROWN: I don't think so. David,
18 there's been no validation studies on a derivative,
19 have there?

20 DR. TAYLOR: Certainly, not published, as
21 far as I'm aware.

22 DR. HUESTON: It's pretty -- Well, I was
23 going to say, it's pretty tough since you can't find
24 it in the tallow, to begin with. If you can't
25 identify it in the raw material going in, how are you

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1 going to identify it in the raw material coming out?

2 DR. ROOS: Let's spike the tallow going
3 into the derivative and --

4 CHAIRMAN BROWN: Yes, you can imagine all
5 kinds of validation tests, but I think Will's point is
6 well taken. If you can't find it in the input, to
7 begin with in reality, and then put it through a
8 process that is about as good as you can imagine to
9 kill it if it were in there, I'm not sure that anybody
10 would care to spend the time or money to try and
11 validate the procedure.

12 I mean, it's been validated so many times
13 in the laboratory, not using tallow, for sure, but
14 even so -- I mean, the temperatures, times and
15 pressures that are being used on all these derivatives
16 we don't achieve in the laboratory, and yet we get
17 total kills. So personally, I'm totally comfortable
18 with this procedure as a killer.

19 DR. ROOS: So that's been validated with
20 the BSE.

21 CHAIRMAN BROWN: Right.

22 DR. ROOS: This temperature or comparable
23 temperatures and pressure.

24 CHAIRMAN BROWN: David, you've done that.
25 BSE has been one of the agents used in an autoclave

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1 style experiment. Right?

2 DR. TAYLOR: Yes.

3 CHAIRMAN BROWN: No -- Yes?

4 DR. WALKER: Paul, I just wanted to point
5 out that in terms of the reaction sequence of making
6 various derivatives from fats, there was a flow sheet
7 that was provided to the Advisory Committee yesterday,
8 a one-pager, which provides that flow in terms of
9 reaction to form saponification or hydrolysis or
10 transesterification. So that should be in your paper
11 work that you have with you.

12 CHAIRMAN BROWN: It's just that it's been
13 growing by about two pounds an hour.

14 DR. WALKER: I understand.

15 CHAIRMAN BROWN: If you would like to come
16 up and find it -- Yes?

17 DR. ROOS: I guess another issue has to do
18 with regulation of this process itself and how
19 confident we are that, in fact, all of the processors
20 will follow these safety regulations in an appropriate
21 way.

22 Now maybe there's no way to get this
23 processed tallow except by inactivating it. So I just
24 wonder whether I can have some assurance there. If in
25 fact, people say there's no way that this agent could

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1 survive, given this, sounds good to me; but I'm just
2 worried about the controls here.

3 CHAIRMAN BROWN: Yes. You're worried
4 about what they call good manufacturing processes.

5 DR. ROOS: That's why, you know, we've
6 always come back to the source material as being
7 important. Now maybe we don't want to be quite as
8 stringent as the original suggestion, but I still want
9 to return to the confidence that everything is going
10 to follow what everybody believes is going to be 100
11 percent inactivation.

12 CHAIRMAN BROWN: Yes. For this I turn to
13 the FDA proper. I assume that any recommendation you
14 make includes some stipulation that what you are
15 recommending is, in fact, carried out.

16 DR. CHIU: As Kiki mentioned earlier,
17 recommendations are different from regulations.
18 Recommendations is the best current thought of the
19 agency. We recommend to industry, and it's not
20 enforceable. It's not like regulations. Then it's
21 law. You have to follow.

22 CHAIRMAN BROWN: So there are no
23 guaranties, Ray, until it gets past the guidance --
24 them one, recommendation; two, guidance; three, law
25 phenomenon, but it is, I think, understood that good

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1 manufacturing practices become a part of this as it
2 goes through this procedure, and it's something that
3 we probably shouldn't concern ourselves with other
4 than to have it on the table that we think that this
5 is, obviously, a part of the whole package.

6 We could then vote on one of two things.
7 We could vote on the original proposal that I made,
8 which was unrestricted use of derivatives. That is,
9 unrestricted in terms of the source material,
10 including anything which went into the bin; or we
11 could vote on a proposal that is a little more
12 stringent, saying that this is okay as long as brains
13 and spinal cords have been taken out.

14 Would the committee like to vote on either
15 one, neither, both? Yes.

16 DR. OLANDER: Question. We have several
17 options when we get to the head. We have the whole
18 head, the skull and eyes or the brains and eyes.

19 CHAIRMAN BROWN: Yes. Well, the first
20 decision, I guess, is to whether or not -- Why don't
21 I just not ask the committee but ask the committee to
22 vote on the original proposal, which has nothing to do
23 with what tissues are going into the mix, simply these
24 derivatives may come from BSE positive countries or,
25 to rephrase it in terms of question 4 which was voted

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1 yes, that the alteration will be that derivatives may
2 be sourced from BSE positive -- from any country,
3 irrespective of BSE status. I think that's the
4 question on the table.

5 Derivatives, derivatized products made
6 from tallow may be sourced from any country,
7 irrespective of BSE status.

8 Larry?

9 DR. SCHONBERGER: I'm in agreement with
10 that.

11 CHAIRMAN BROWN: I'm sorry?

12 DR. SCHONBERGER: I'm in agreement.

13 CHAIRMAN BROWN: Okay. Leon?

14 MR. FAITEK: I vote no.

15 CHAIRMAN BROWN: All right. Ray?

16 DR. ROOS: I guess I have this continuing
17 problem with the source material being central nervous
18 system material from BSE address countries. I'm not
19 sure that I would get involved with all countries in
20 the European Union, but I do have a problem with that
21 source material. So I'm --

22 CHAIRMAN BROWN: Okay. The vote is?

23 DR. ROOS: So is that a no?

24 CHAIRMAN BROWN: No. Bill?

25 DR. HUESTON: Yes.

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1 CHAIRMAN BROWN: Linda?

2 DR. DETWILER: Yes.

3 CHAIRMAN BROWN: I vote yes. Don?

4 DR. BURKE: I vote no, because I see no
5 advantage of including known risk materials, and there
6 are several types of inactivation that we're talking
7 about here. I think it's still too early to wave a
8 blanket and say that they're all equally effective in
9 activating the agent. They include saponification,
10 transesterification, hydrolysis, and a number of
11 techniques, and unless I'm sure which process we're
12 talking about, I don't want to vote yes.

13 CHAIRMAN BROWN: We are talking about high
14 pressure, long time, high temperature, aqueous
15 solutions for the derivatives. You can forget about
16 saponification.

17 DR. HUESTON: We excluded saponification.

18 DR. BURKE: Well, there are still two
19 other major techniques, as was pointed out,
20 transesterification and hydrolysis, and I'm still not
21 sure that they all include a high water -- a high
22 proportion of water in the process; and if it's dry,
23 I'm not sure that that's inactivating. I'm sorry.
24 I'm still a little -- enough confused in the process.
25 I'm not sure that all of the products that we're

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1 talking about meet those characteristics.

2 CHAIRMAN BROWN: Barbara?

3 DR. HARRELL: No.

4 CHAIRMAN BROWN: Peter?

5 DR. LURIE: No.

6 CHAIRMAN BROWN: Doris?

7 DR. OLANDER: Yes.

8 CHAIRMAN BROWN: Beth?

9 DR. WILLIAMS: Yes.

10 CHAIRMAN BROWN: Yeses carry.

11 DR. SCHONBERGER: What was the vote?

12 CHAIRMAN BROWN: I'm sorry. The vote was
13 six to five. That concludes tallow. Thank you very
14 much, committee, a very tight deliberation.

15 Now we go on to the question of gelatin.

16 DR. ASHER: Good morning. You are to be
17 commended on your strength in being able to stay
18 engaged after this morning's difficult deliberations.

19 This is new-variant CJD, something that
20 all of us, regardless of our opinions on some of these
21 topics, would very much like to keep out of the United
22 States.

23 I'm David Asher from the Center for
24 Biologics Evaluation and Research, and I've been asked
25 to revisit with you the topic of an advisory committee

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