Dr. John Bailar Interview

Office of NIH History
Oral History Program

Interviewer: Maya Ponte
Interviewee: John Bailar

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John Bailar: …extremely limited. 10 years later, maybe a little more, say '93/'94, there was some talk about doing an update of that study, and the decision was to not do that, nothing had changed. Now it's come up for a third time. Whether there will be such testing -- such a survey of the testing that's been done, I don't know.

Interviewer: So what you did with this committee was a survey of the known literature on all of the -- anything, and like you said, there was only a small fraction that had been properly tested, but you surveyed the entire --

JJB: We drew actual random samples of these 25 -- of these 65,000 chemicals that relate in substantial qualities, how many have an LD50? It's the most simple, most basic test of toxicity. The answer was something like 4 or 5%. Yeah, it's scary.

Interviewer: At this meeting was it at all discussed what form the proper toxicity testing should take, or proper risk assessment?

JB: Oh yeah. Actually, it was probably a dozen meetings over a period of three years. We did look into it very thoroughly and did a lot of work between meetings. And the committee came up -- not our committee, which was responsible for the sampling and the statistical analysis -- with a toxicity site, a separate committee -- let me back up. There were three committees working together, dealing with different aspects of this. The committee that was mainly toxicology came up with a list of something over 30 tests that they thought would be reasonable things to look for in different classes of chemicals. You wouldn't need every test in every chemical, but there was -- first the LD50 which, as I recall, they thought always should be done. And then there would be a lot of more specialized tests, like is it a carcinogen? Does it have reproductive effects? And there are scores, literally, of reproductive effects, from failure to conceive to malformations to failure to nurse, to blah-blah-blah-blah-blah. And then the effects on the male of the species. So neurologic tests. So they came up with something over 30 of these and then we started going through our samples to see how many had been done.

Interviewer: So it was on your committee where you then went and took the samples?

JB: Right.

Interviewer: Okay.

JB: Pesticides and food additives were fairly well tested. By fairly well I mean up to something like 25-40% of these tests, but that still isn't very much considering that the pesticides -- I'm sorry, I should have said pesticides and drugs. Those two are deliberately selected because they have biologic effects. So you might think for that reason alone they ought to get more testing than the average, and they do, but it isn't as high as we thought it should be. If you're interested in this they probably have a copy of it right downstairs at the National Academy Press office down there, or you can get it over the web. The National Academy Press has every report they've ever issued on the web.

Interviewer: Yeah, no that's always a [inaudible]. But, so being --

JB: But that's way off your topic.

Interviewer: It is off my topic but it is related because what we're talking about are, I mean a different -- I mean we're talking about chemicals, rather than biological -- how you classify prion. [laughter] It's very complicated.

JB: It's sort of in between.

Interviewer: It's sort of in between, but it is related -- I mean, because we're talking about ways of measuring -- with the toxicology, ways of measuring the effects of these chemicals, and then what you're talking about in sampling is how adequately are these things being studied. And what have you learned from that that you've taken to the TSE Advisory Committee when you've been reviewing the studies that are done on, let's say, web transfusion possibilities or whatever other surgical transmission -- other possibilities that are presented?

JB: It's hard to say, specifically. Maybe you're beginning to get a sense of why my kids laugh and say, "Dad can't hold a job," because I've bounced around among so many different things, but the net effect of that has been to give me a broad education in how to ask the big questions, which I think most of the people on that FDA committee don't do. Sidwolf [spelled phonetically] does.

Interviewer: How to ask the big questions.

JB: Right. They'll ask, "Is this the right test? Is this particular case of prion disease likely to have been transmitted by blood? And those are important things to know. But they aren't used to asking questions like, "How much testing should we be doing?" "How does testing fit into the operations of USDA or FDA?" "How is this going to affect our exports?" They're aware of these issues but they haven't been thinking about them.

Interviewer: And do you think it's necessary to think about these big picture issues when you're on an advisory committee that is charged with dealing with a very small piece of it?

JB: I think somebody has to?

Interviewer: And why? What does that give you? Because here you are, you're supposedly talking about medicinal products, mostly, right?

JB: Right. What it gives you, I think, is a better sense of what is going to be [inaudible]. A better sense for the need to balance risks with costs. I was much aware of that during this recent FDA meeting, talking about a very expensive testing program, and it's not clear how much or whether there is going to be another case. My guess is there will, but what is the risk? How much is it worth in testing costs to prevent one case of prion disease? The answer is millions. How many millions, I don't know. But I can come to that figure of millions on the basis of what I know about a lot of other safety programs that we spend -- we spend about $100,000 on highway safety for each death prevented, but for chemical hazards it's on the order of $2 to $5 million. To prevent the death of an astronaut, we spend $100 million. But I think somehow somebody should be thinking about this.

Interviewer: Do you feel that you're allowed, in that context, to think about cost and benefits?

JB: I don't much think about what's allowed. [laughter] I go ahead and say it.

Interviewer: [laughs] Right, well for instance, I'm thinking about in particular when it comes to the issue of blood transfusion, it seems to me that when -- I've looked back on some of the old meetings, and that when decisions were being made about how much of the -- or whether or not it's appropriate to have these deferrals for blood donation, they were considered on some level a cost-benefit analysis. Not so much monetary cost, but in terms of the cost to loss of blood supply.

JB: Right. But that occurred only because there were several people there from the Red Cross and from the independent blood banks, who kept pounding on the committee to give that adequate consideration. I think if these outsiders hadn't been there, the committee would have been much more restrictive. I have personal consideration -- concern about all of that because I twice had to have massive blood transfusions.

Interviewer: So you understand [laughs] how important it is.

JB: I know how important it is.

Interviewer: Right, right. So that's something that even personally you can recognize the importance of that.

JB: Resonate to that.

Interviewer: Right, because they certainly come, and I've only been to a few meetings but I see at least one representative from the blood industry at each meeting making a presentation about --

JB: They've learned that this is a critical matter for them, so they turn up every time.

Interviewer: Do you feel that the issue of blood donation has been handled appropriately in light of the new knowledge that we have?

JB: I think so. Remember I asked in this recent meeting, how many times have we run out?

Interviewer: Right, yes.

JB: And the answer was, when you strip away the garbage, never.

Interviewer: Never, yeah.

JB: So they're managing somehow, and that to me means that we're not overly restricted. Maybe it would be good to ease up a little bit, but that wasn't on the table. I think the pressure to ease up on the restrictions is probably minimal that you can get by.

Interviewer: How much did you know about prion diseases before you were elected to serve on the committee?

JB: Zero.

Interviewer: [laughs] So how did you end up serving on the committee, again? Were you approached by someone?

JB: We have, well by the Executive Secretary, Bill Freas. As you know, FDA wants a statistician on every committee. The one who had been there before recommended me.

Interviewer: Oh okay.

JB: I don't know why.

Interviewer: Who was the previous one?

JB: A fellow named David Hoel, H-O-E-L.

Interviewer: And he recommended you, and so then Bill Freas contacted you --

JB: Hoel asked if I'd be interested, and we talked about it for a while, and I said, "Oh sure, why not?"

Interviewer: So how has your education about prion diseases gradually taken place?

JB: I had missed a couple of meetings because of prior commitments -- you know, my schedule filled up a year ahead, but it took me at least three meetings to begin to understand how the committee works, what the issues are, I didn't even know the difference between CJB and ECD. Or between either of those and the other prion diseases. So I have very quiet in the beginning. Two meetings back I began to make myself known. I could ask the right kinds of questions. But again, the kinds of questions other people weren't thinking about. For example, we were hearing a great deal about how difficult it is to eliminate prion disease, prions from things like surgical instruments, stainless steel. And I asked two questions that I hope are going to have some effect on what research industry does on them. They would -- they tried sterilization, and it takes incredible amounts of heat for a long period of time to really inactivate the prions. And I asked, "Why is that?" It sounds like prions are getting into the bits and fissures of stainless steel, which I happened to know about -- one of the reports I had reviewed for the academies here. Apparently they hadn't thought about that [inaudible]. Well as soon as you know that prions are lurking below the surface in these microscopic defects, you might begin to have some sense of how you can tackle these successfully [inaudible]. The other had to do with the fact that they would grow back after extended periods of 300-400 degrees Centigrade, and I asked, "Is that a heritable property? If you recover the prion and pass it through another [inaudible] or whatever, do the [unintelligible] of that prion carry a greater resistance to heat?" Well nobody had ever looked at that.

Interviewer: Wow, that does seem like a really interesting question.

JB: Well, the response from the people who were presenting seemed to be that, "No, that couldn't happen." But it seemed to be a very simple, straightforward kind of thing, and somebody ought to look at it.

Interviewer: Right, it could have a -- you never know there could be a surprising result, or maybe not.

JB: It may be that there's a common variant that is resistant. And again, that might affect how you go after these things.

Interviewer: During your time on the committee, to you what seemed like the most important issues that you could tackle?

JB: One is the issue of tissues for transplantation, another thing I didn't know about, but it turns out that if a fresh body is donated for tissue transplant purposes they can take out some [inaudible] tissues. We don't know about [inaudible] either for transplant or for whole bone or [inaudible] and on and on and on -- bits of skin, everything. And [inaudible], which did come up in a recent meeting.

Interviewer: It did, yeah.

JB: So there were a lot of questions about how to protect the public against the possibility of transmitting prion diseases and I think that especially is very useful, and locked into place the notion that tissues should never be [inaudible]. I think it also gave additional emphasis [inaudible]. There are adequate substitutes and the risk would just be high.

Interviewer: When you're considering, within the context of committee meetings, relative risk of transmitting new variant CJD via whole blood or red blood cells versus plasma products, how do you weigh those risks? And the reason I'm asking is because you have two kind of different scenarios: on the one hand you have blood donations that it would be from one person to another, like it would be all the product from one person; in the other case you'd have pool product, but it also goes through a series of steps where supposedly amounts of affectivity are diluted. So how do you weigh those? I find that an interesting sort of --

JB: Well, they aren't easy to weigh. First, we don't know enough about where the prions are in [inaudible] in the blood. Are they in the red cells? The plasma? The platelets? The white cells? My guess is they are largely, maybe entirely in the white cells and not just the white cells but in the [inaudible]. And if you could get that out of there, all of it, there might be nothing left to worry about. The problem, of course, is getting it all out. You can sort of separate white cells from the red, but [inaudible] separation. Whether there are prions in plasma at low levels I don't know -- it might depend on whether some of the white cells are disrupted in the process of getting the plasma. We know they're mixed in with red cells. The red cells are not really the problem in the same sense, because those are not pooled -- somebody either [inaudible] red cells or they don't.

Interviewer: Exactly, yeah.

JB: Platelets, I don't know enough about the process to say.

Interviewer: Yeah, I'm not sure about platelets either. But I guess I mean with plasma products like factor VIII or things like that, where we know that it's pooled and it goes through a series of steps -- in various columns, you know, precipitations, whatnot, before you get to the product, but in the end it's pooled so how do you look at those kinds of products, like factor VIII, albumin and those kinds of things?

JB: First I wondered how much I had to discount the estimates from [inaudible]. They have a vested interested in overstating the safety of the supply and then I expect -- I imagine they're expecting all of the committee members to downplay that, but how much to downplay that I don't know. There are two kinds of issues. One is, what happens if everything goes exactly according to plan -- what's the residual risk? And then you have to ask on top of that what's the risk of some kind of a failure? If somebody is sufficiently careless, a little bit of the whole blood gets into the plasma at the wrong time or whatever -- they don't want to think about that kind of thing. But the fact is, as a committee member I think I have to think about it because the world does not always go according to plan.

Interviewer: So you have to think of the potential areas where things could go wrong, and this does kind of relate back to what we were talking about before, sort of getting a way of approaching these risk assessments or the data that's collected to look at all the ways in which things can go wrong in the entire process. So I see what you're saying. When you approach this data you're approaching it with the mindset of sort of examining it carefully.

JB: Yeah. Now, I have some complaints about the committee process at FDA because it doesn't allow for very much time for this. To come back to your primary concern, committees, I've been on a huge number of committees here which work in quite a different way. Having the committees at FDA and all other federal agencies complete open has some evident advantages. The public knows that there's nothing going on -- well, they swear that there's nothing going on behind the scenes. But it alters the committee dynamics in major ways. It's much harder to really explore an issue until everybody has a common understanding, so that right here, with that kind of in-depth discussion, committees almost always come out [inaudible] and that does not happen in the votes at FDA. I voted on some of the things there, for this committee, not a recent one but an earlier one, but I really [inaudible] I was casting the right vote.

Interviewer: Is that an issue of openness or is that an issue of not having time to really work with the data and discuss it?

JB: It's a combination.

Interviewer: It's a combination.

JB: Yeah. For one thing, I don't know how much you looked at the history of this committee but now and then they've cancelled a meeting because there wasn't enough for the agenda.

Interviewer: Yes, I know that.

JB: And I think that's a mistake. For one thing, I don't know if the next one is going to be cancelled so I'm a little bit reluctant to protect that time if something else is coming along that I think I really should be involved in.

Interviewer: Mmm-hmm [affirmative].

JB: The second is that when we do have the meeting it is so full -- you know, there's a whole lot of different things we talk about. You don't have time and the energy and the background to explore it the way you ought to be.

Interviewer: So would it be better if there were more meetings where fewer topics were discussed so that you could meet more often, have better familiarity with each others' concerns and expertise and, at the same time, be able to focus?

JB: Right. Now FDA has some problems with that because they're limited in the number of committees that they can have and in the number of meetings. There is a deep suspicion on the part of the executive branch about relying so much on outside advisors. So FDA is in a box almost. Maybe what they do is the best that's feasible politically, but it doesn't do any good.

Interviewer: They're kind of in a straight jacket. There's not a lot of room for them to really maneuver or change the format. Whereas at IOM they can do a very different structure?

JB: That's right. IOM committees hold three meetings every year. Over a period of months, two or three years, with a lot of staff working going on in between, and committee work, too. They have a first meeting to get an idea of the problem, to talk to the sponsor of the study, to hear some background presentations, and then they'll meet in closed session to talk about what they really need to do. So the second meeting, then, will have a lot to build on. The staff will have been hard at work in the meantime; committee members will have been doing a lot of reading, generally not any writing at that point, though some of them do. By the time they get to the third meeting they'll have a much better understanding of what they

need to do and begin to think about what should go into a report and so forth, and they end up with very substantial reports like this one.

Interviewer: Wow. That's huge.

JB: And it's very narrow. Insecticides and solvents.

Interviewer: Yes.

JB: I was actually the Chair of the first committee here on the Gulf War Syndrome.

Interviewer: Wow.

JB: And our report was smaller than this one. This is another one which they've kindly included in disc.

Interviewer: Oh, that's great.

JB: But it was probably about two-thirds the size of that, only because I insisted that the work be extremely short.

Interviewer: So it was more readable?

JB: Right. The shorter it is, the bigger the number of people who will read it.

Interviewer: Right. [laughs] That's definitely true.

JB: We wanted a lot of people to read that report.

Interviewer: Right. But it sounds like this whole process with the IOMs and various -- it's an iterative process.

JB: Yes. You come back and back and back. And then if there's a follow up committee, months or years later, they'll generally try to get somebody from the original committee who has some institutional history about it who can then serve on the new committee and make sure that -- I won't say seamless, but that it flows naturally from what was done before. That doesn't mean the committees don't come to different conclusions, they certainly do, [laughter] now with the accumulation of knowledge.

Interviewer: Exactly, exactly.

JB: Not in this instance. [laughter] Harder they look they still can't find any physical entity that they can call the Gulf War Syndrome. It's quite a different kind of beast.

Interviewer: Do you get the feeling -- with the FDA committee do you feel like there is that sort of historical or institutional knowledge or do you feel that that gets lost a bit.

JB: Well, there's some of it. They ask committee members, many of them, to come back another time or two because four years is so short in that context. Most of the committee members have been dealing with these issues for a long time so it doesn't take them very long to get up to speed. In the case of the committee you were at, the committee members all know each other already -- most of them -- because they have been working in the same rather narrow field. And all that helps the process along -- it didn't help me, but it does help the committee as a whole.

Interviewer: Right, I see. So we were talking a little bit about blood, getting back to blood. What are the studies or what are the reasons why you think that most of the activity is probably in the white blood cells?

JB: Well because people have tested the fractions and that's where it seems to be. I don't know how good the fractionation is. Are there still some white cells in the plasma? We know there are white cells -- red cells in the fraction. I don't know how sensitive the tests are. Just the whole field is beyond my knowledge.

Interviewer: What about -- so at the most recent meeting Robert Rower [spelled phonetically] gave a presentation where he was saying that with leukoreduction of whole blood they were able to get what he measured to be -- and this is only in hamsters, you know it was a model system -- but it measured a 50% reduction in the infectious units present in that sample. There was some discussion at the meeting about what that could mean for a reduction of risk, and how would you characterize that sort of the relationship between that data and any potential conclusions about risk reduction?

JB: We don't know enough about infected dose for me to answer. My guess is that if the unit of blood has a lot of infected units in it, and the infected dose is 1, then cutting the number of infected units 50% isn't going to do anything. It's hard to imagine that it could cut the risk by anything more than 50%. If the number of infected units is close to the infected dose you can imagine a linear risk such that cutting the dose by X%, you cut the risk by X%. But that's linear and my guess is that the dose response relationship is super-linear. Now we're getting back to things I've learned in other contexts. This is exactly the situation with respect to a lot of carcinogens. Not many other kinds of drugs, chemicals or outcomes, but for carcinogens it's pretty clear that the risk per unit of dose goes up considerably more steeply at low doses than it does when you get the

higher doses and I would guess the same sort of thing holds for prions, partly because of the variation which I think must hold -- variation in sensitivity, that there's a fraction of the population out there that will react badly to a very small number of prions and you might protect the non-sensitive part of the population better by cutting exposure 50%, 90%, whatever, but unless you get right down to almost zero, you aren't going to do anything for the ones who are sensitive, which are the group you have to care about.

Interviewer: How did you initially -- before you knew anything about TSEs, I'm sure that you had heard about prions before.

JB: Yes.

Interviewer: Before you were on the committee how did you think about the risk from prion disease and how has that changed, or has that changed, since you've been on the committee in relation to other risks?

JB: Well I haven't really thought about it much. I've thought about this as a problem in England. I go to England for a week every Spring for a meeting, but I haven't thought about it much. It never impressed me as anything that I'd have to deal with.

Interviewer: Right.

JB: Well, then I was asked to join the committee and I could see why people here do have to deal with it. At that time there hadn't even been a case in the US. Not a case [inaudible] in the US. But I began to see immediately why there were reasons to do things that way. And some concern about the possibility of importing.

Interviewer: And what impressed that upon you? What was the data or what were the things that you saw that made you feel like, "Oh, this is something that we need to be proactive about"? What kind of changed or enlightened your sort of thinking along these lines?

JB: Well, at this point I'm not sure I can recapture that. I know I was thinking about the ordinary CJD, which seems to arise spontaneously, and I'm wondering why. Do the proteins just, you know, once in a while fold themselves in the wrong way which would --if you regarded proteins as a microbiologic unit that would be spontaneous generation, which we've all been told is a no-no. Where did the bCJD come from? Apparently it was never recognized before it had arised as a variant from something. I don't know. But I think it was that kind of thinking that made me think, "We'd better find out more about this and see what we can do to prevent the introduction of this brand new bCJD in the US."

Interviewer: What is the sort of model of the organism -- What is the sort of model of the infectious agent that you sort of use in your mind when you're thinking about these diseases?

JB: Oh, it varies. Sometimes I think about microbes, specifically bacteria. Sometimes I think about chemical hazards I know. Sometimes I think these aren't really either one of those, they're something new and I have to think about it as a different sort of nature. It's generally sort of by analogy for me. I know that chemicals do this; maybe the prions do it. I know that microbes of one or another sort do that; maybe prions do that.

Interviewer: So you'll apply different models in order to try to think through what potential -- like you were saying, potential dose response relationships, potential problems with inactivation or removal -- all of that stuff, you might have multiple models running through your mind?

JB: Yes.

Interviewer: That's interesting. So you don't limit yourself?

JB: I don't limit myself. On the other hand, I don't have any prescription for how to think about A, B, C, D, E, just sort of try to cast back to whatever I know that might be relevant. If it seems to fit I use it.

Interviewer: Yeah. It sounds like a logical, practical way to approach the issue. With risk assessment as a tool, what do you think are the major things -- so when you're presented with a risk assessment what are the major things that you can use it for? Like, what are its major uses?

JB: Oh boy. You almost have to think about the question in reverse. Say, "I have a problem, is there some kind of risk assessment that can help me with it?" The proper risk assessment has to get into a lot of things. One is, in chemical terms the so-called "no adverse effect level". How much can you give before anything happens -- anything detectable happens? Well, all right, there you go, problem: what do you mean by "detectable"? So in practical terms it comes down to the "no observed adverse effect level" or the "least observed adverse effect level" which is the smallest dose you've tested where something turns up. The problem with that approach is that it depends on the extent and quality of the testing and if you don't know enough, you may miss risks. I was going to expand on that in several ways but I've lost track of your question.

Interviewer: I was asking about risk assessment as a tool and you said what you do is you have a problem and then you create a --

JB: Yeah. First you want to know is there a hazard, and if so, is there a guarantee range where nothing bad will happen? That leads into natural questions about the shape of the dose-response relationship, which has two aspects: one is whether something will occur, you get a cancer or you don't, a birth defect or you don't; the other is how much -- if it's a liver toxin how much liver damage is there or kidney damage or lung damage. Those have to be approached in quite different ways. Proper risk assessment will then go on into characterizing the risk in terms of such things as the dose schedule -- if it's a chemical, does it matter whether you get all of it at once or it's spread out over a period of hours or months or decades? Generally it does matter. It gets in the questions of individual susceptibility, gets into questions of interactions with other sorts of things. So if you're a risk assessor you have to think about all these matters and then you have to think about how to make your risk assessment credible, which means attaching considerable discussion of uncertainty; if you can, as well as quantitative assessment of uncertainty. You have to make sure that it will be understandable to the people it needs to get to. And then unfortunately sometimes you have to work to get it used.

Risk assessment -- I'm sorry, risk decisions in the federal government are commonly made by people who are not experts in risk analysis, and to some extent that is a good thing because they have to consider a lot of things besides risk: benefits of whatever it is, and are there substitutes? That was a major issue of the risk assessment of saccharin -- it was easy to ban saccharin because we have cyclomate, another non-nutritive sweetener. Cyclomates their own problems and in Canada it was the cyclomates that got banned because they had saccharin as a substitute. [laughter] Somehow those can't both be the right options. There are questions of cost, there are questions of political force and political will, legal authorities; there are a lot of considerations that a risk manager has to go through.

On the other hand, there are risk assessors, and this is quite evident in the so-called red book, who think that the risk analysis should be -- whatever they say in there, journalism, and tossed over the transient for the risk managers to read and use the way they think. But none of the other inputs do that. The lawyers are going to be right there at the table with the risk managers -- the economists and the industry and the consumer representatives, and as a result the risk analysis is kind of squeezed out, not taken as seriously as it should be. So I'm really an advocate of getting the risk assessors to the risk management table.

Interviewer: It's too separated right now.

JB: Right.

Interviewer: Because in a sense, risk assessment -- or risk analysis and risk management are two sides of the same coin, right?

JB: I don't think of them as two sides, I think of them as being in linear sequence. First you have the concern, then you have the risk assessment, then you have the risk management, then you have risk communication of trying to explain all of this to people who need to know.

Interviewer: And you see those as a linear, step-wise arrangement. In what ways can a risk assessor present the result of a risk assessment to a decision-maker in a way that they can understand it across the uncertainties involved?

JB: It isn't easy and I am convinced this has to be done in person. Write the risk assessment in a way that is as clear and easy to follow as possible, write a clear executive summary, give the risk manager a chance to go through these materials and then go and talk about it. Talk until either the risk manager says he doesn't have anymore time or it's pretty clear that further talk isn't going to be productive. A lot of people don't understand about risk assessment -- they want a nice hard number, a bright line, and that's virtually impossible in any kind of risk assessment.

So the first idea is to get across the notion of a range of possible risks, which means basically dealing with probability, which means statistics in a very simple, down to earth way. As you came in I was working on a review of proper proposals that EPA has had for truly huge studies with health effects of particulate air pollution. What EPA would like is some guidance about saying that pollution up to this level is okay and above that it's a no-no. The effects aren't going to be -- they aren't going to have a sudden breakpoint like that, and even if they did the risk analysis couldn't pin it down very well. So there's going to be a big fuzzy region and somebody has to make a decision in the face of uncertainty. Who was it -- one of our presidents said he was tired of dealing with two-handed scientists, he wanted to deal with scientists with one hand [laughter] -- and you know the rest of that. But that's the way that science is and if you're going to be honest about it you have to say, "On the one hand this and on the other hand that." A direct decision lies somewhere between these boundaries but it has to be made on grounds that are not scientific grounds.

Interviewer: Because science doesn't tend to give you a solid, immutable answer.

JB: Yeah.

Interviewer: Along those lines, we were talking a little bit on Friday about the Harvard report and the way in which numbers are presented such that you get like a .002 chance of having cases remain after 10 years. You were saying

something about how that level of precision in the numbers can be misleading?

JB: Yes. How do you know it's .002 instead of .001 or .003, .009 or something bigger? There's uncertainty there that was not expressed in what I saw. Now I have not read the whole Harvard Risk Assessment -- I haven't in fact seen it so I haven't read any of it. I saw the presentation and I heard people talk about it. But I've heard about so many things that imply major assumptions that I know there is a lot of uncertainty. Now whether they tend to overestimate or underestimate risk, I don't know. It could go either way.

Interviewer: But what would your suggestion then be? How would you personally want to see things expressed rather than these calculations --

JB: I would like to see an independent group go through the whole risk assessment and first write down every assumption of any magnitude, whatever -- how the two can extrapolate from mice to humans in this respect, or the dose response relationship is linear or whatever, and there will be dozens and dozens of them. And then I would like to see a thoughtful consideration of each one as to how much uncertainty it adds. It might be very little, it might be a lot; most of them, I expect, would not be much, at least not individually but they might add up to something to be concerned with. Then you need to think about how these uncertainties might be correlated. Even when people get this far they generally treat them independently and that could be a mistake. Think about the relationships of all the uncertainties and then think about this whole mass of information about uncertainty and try to come up with an assessment of how much that should be translated into the bounds that you might put on the estimate of risk and then you push the bounds out for all the uncertainty that you haven't thought about. Mathematically you can show that the bounds have to go out, they can never go inward, but how much you don't know. You should at least be telling readers that this is as much as we know now and there may be other things that will come up in the future.

Now it may also be that if it's a good model that it will stimulate research and some of those uncertainties can come down. That would be a very happy outcome for a risk assessment. Part of the values of a risk assessment -- well I've said in talks I've given the best way to think about risk assessment is a process rather than as a number, because it gets you to think very hard about the data sources: how they fit together, the expertise you need to evaluate them, where the uncertainties are, what research is needed. There's nothing like having a risk assessment done by an experienced person or team to tell you about these and a lot of other things. I think a risk assessment can be very valuable in a lot of ways

besides just giving you the risk number that people probably start by wanting. You might, in the end, come to the conclusion that you can't do a good quantitative risk assessment because you don't know enough -- well that in itself is worth knowing.

Interviewer: In cases such as those is it useful to do a qualitative risk assessment?

JB: I wouldn't want to say no. A qualitative risk assessment is generally considerably less useful than a quantitative risk assessment.

Interviewer: Why?

JB: Why? Because if the qualitative assessment is "yes there is a risk" you may not know what to do about that. If you're talking about a new product or a new process or whatever, that may be adequate reason to delay introduction until you know more. But if it's something that's already [inaudible], widely used, it would be very hard to say, "Whoops, there may be a problem there, we don't know but you have to stop it." Which brings me to the general topic of the precautionary principle, which -- oh it's another thing I've heard about.

Interviewer: No, I would love to hear what you have to say about that, that's all very related to everything that we're doing here [unintelligible].

JB: The precautionary principle I find very hard to fault, but it's widely misunderstood. The risk goes from here to here -- I'm sorry, if the possible range of risk goes from there to there and you're pretty sure it's part of this region, where do you regulate? The pressures, generally, are to regulate on something toward the lower end of the possible risk -- pressures from manufacturers, pressures from users and so forth. Now if there's clear evidence of risk at some level they will accept that -- beautiful illustration of that was vinyl chloride, where there was a very sudden exposing of information about human hazards. Within two years vinyl chloride was off the market, voluntarily. The regulation came later but the manufacturers accepted the evidence and said, "We've got to do something."

On the other hand, the precautionary principle says you don't know way out to that end. You move the decision point closer toward the upper end of plausible range of risk. In other words, you should be more cautious about introducing things where there may be something going on that you don't know about. There have been a lot of examples studied in some depth by a group -- supported by the World Health Organization, showing that we found out later about hazards that we just didn't appreciate at the time something was brought into widespread use. A nice example of that is asbestos, where the potential risks were identified many, many decades

ago and there was great resistance to doing anything about it and actual suppression of information by the industry. But then I think we probably went too far in the other direction -- the hazards are not as great as some people think they are. They're there -- the stuff is not safe, but the hazards have been overstated and the benefits of removing asbestos have been seriously overstated because the act of removal stirs up so much.

Interviewer: Right, I see what you're saying. So the precautionary principle, the way it is used nowadays, what do you think its effect is on this whole --

JB: Well it's been used more widely, at least explicitly, in Europe than it has in this country. There are people who start frothing at the mouth if you mention the precautionary principle because they think that's an extreme environmentalist position. I don't know how much of that reaction is genuine -- do they really think it's an extreme position -- and how much of it is just defensive against having to change the way they do business. A great way to argue is to overstate some position that your opponent appears to take and then attack that overstatement -- that isn't what people are saying. So I don't know, I haven't really tried to sort that out, there's probably a range of answers to it.

Interviewer: I don't know if you're aware of this at all but I was listening to a Senate hearing on the BSE case in the US and one of the senators was sort of talking about the whole -- he brought up the precautionary principle and he brought up the idea of higher level trade talks that are occurring in the World Trade Organization between European countries and the US where the US has set a position that they're referring to as a science-based approach and attacking the Europeans for being precautionary, using the precautionary principle. In that case, what are they really talking about? I guess one of the things I'm a little bit confused about right now is what the term "science-based" is supposed to mean. To me, science-based could mean either way -- it could mean either having potential evidence of a risk and acting on it or waiting until you have definite evidence of a risk.

JB: I don't know about that but my guess is the term "science-based" is not being used in a way that either you or I would recognize. It's probably being used as a political word -- "It sounds good so I'll throw it in."

[change of tapes]

…we looked at it and it turned out that the benefit comes after the age of 50. And you find something at age 42, say, but they -- if there is a benefit, you find it in reduced mortality after 50 or 55. But this all remains highly controversial.

Interviewer: Oh I know. I've been to meetings, actually, on Capitol Hill and whatnot, briefings where they discuss the various sides of the issue so I do know that it's still controversial. And when you say as a result they lowered the doses do you mean as a result of the committees before? As a result of what?

JB: As a result over the controversy about it. They went to a completely new technology. They started with [unintelligible] industrial film, because you get very good images that way. It's much better than the standard medical x-rays. And after that they went lower doses with a technique that's related to Xerox copying. And then that still wasn't low enough so they went back to film, but with a new kind of film. Now, there was a fair amount of reluctance to do all of this, because each change of equipment was expensive -- $100,000-$200,000 for each radiologist. But they did that, and I'm no longer so much concerned about the radiation doses. I continue to be concerned about the lack of evidence.

Interviewer: This is getting out of step a little bit but are there things that you have learned from this experience that have affected your approach to risk assessment and to this sort of broad picture since then, and in relation to TSBs?

JB: We haven't talked about it at all but over the years I've done medicine, I've done biostatistics, most of my friends think I'm an epidemiologist. I've had a major interest in medical publication as a result of my term [inaudible] -- my six-year -- at JNCI, and I'll come back to that; I've had a substantial interest over a period of years in research conduct, or research misconduct, and a bunch of other things. And I've learned some things about shifting gears like this, one of which is that it's scary. The first time you wonder, "Am I making the right change, the right decisions?" The second is that nothing is ever lost. Everything I've learned doing any one of these has applications in what I do next, way down the road. And the third thing is that nothing's ever finished. [laughter] And I still get echoes of work I was doing 40 years ago. I just wrote a letter to the editor about a paper I published in the early '60s. I don't know if you read the newspapers, there's a lot of concern now about risks from the [inaudible] reactor in Washington, and in '63 or '64 I published a paper with one of my colleagues about the risks that somebody had claimed were associated with living downstream. They used immense amounts of water to cool the nuclear reactors, and we weren't able to find anything. Well, the issue has come back, and there's now a group that's done a very weak study -- they recognize it as weak -- based on voluntary submission of survey forms they handed out [inaudible], the editor saying, "It is weak. It's been done right, and here's a reference." So they said nothing's ever changed. But this is getting away from your question about how these things together --

Interviewer: Oh it's all related. It is related though because each time you deal with one of these episodes it gives you insight into how this process works, both scientifically and politically. So if we -- okay --

JB: I've been involved in a couple of other major controversies, one over the treatment of cancer of the prostate. Going way back, but we -- I was basically a statistician for a very large clinical trial run within the DA system, having to do with treatment of cancer of the prostate with a daily dose of 5 mg of [unintelligible]. And we were very puzzled because we didn't seem to find any survival benefit. Relief from symptoms, patients seemed to be better, but when I looked into it they weren't living any longer, but they were dying [inaudible]. So there's an elevation of mortality from cardiovascular diseases related to the [inaudible]. So once we had that pinned down they started a new study with 1 mg of EPS. We seemed to preserve most of the benefit without the risk, but we in particular got a lot of flak about this from radiologists, who simply couldn't believe they were doing anything [inaudible] -- give their patients fatal doses in a field unrelated to the treatment -- what they thought was unrelated.

Interviewer: Right, that there would be cardiovascular outcomes from --

JB: Everybody knows that EPS is safe. Women have all kinds of estrogens running around, and they live longer than men, and you know, one thing or another -- they didn't want to believe it, but that then became the standard treatment.

Interviewer: At the 1mg dose or the higher dose? The 1mg dose.

JB: The 1mg dose. Yeah, the 5 had been standard --

Interviewer: So it was decreased as a result of this study?

JB: Right. Then in '86 I published a paper making me even more unpopular [laughter] showing that the cancer mortality rate had been going up steadily for years, despite all the claims of great success. I published an update on that in, I guess, '97, in which we showed it had reached the peak in 1991-92, and the data through '94 looked like it was going down.

Interviewer: Oh really?

JB: And I am now working on a third paper showing that it did in fact go down by about 10% over the period of 10 years.

Interviewer: Wow, that sounds like a lot.

JB: Well, figure how long it would take to wipe out cancer at that rate.

Interviewer: [laughs] Not too long.

JB: Another hundred years will do it.

Interviewer: Right, that's great.

JB: But unfortunately, the last three years, it looks like the decline has flapped out.

Interviewer: Okay. So it might have been at one time --

JB: Which I expected, because much of that decline came from the big drop in deaths from lung cancer in men, which of course had nothing to do with treatment. A lot of men gave up smoking 30/35 years ago and it's showing up now in the mortality rate. Lung cancer in women is still going up, because so many of them took up smoking [inaudible]. And I feel very bad every time I see girls and young women smoking because I think it's going to be very bad for them in the long run. But anyway, I have not been any stranger to controversy.

Interviewer: And what about controversy or debate over the way that biostatistics is done. Have there been any times that you've been involved in larger discussions about --

JB: Oh yeah, but nothing much seems to happen.

Interviewer: And can you explain your concerns about some of the way that biostatistics is done?

JB: I think we have a serious problem [inaudible] because it is taught primarily as a mathematical discipline. It's taught in a lot of different kinds of departments at schools, but the approach is always mathematical and it shouldn't be. Statistics should be seen as a way to educate your common sense and to sharpen your skills in a fairly straightforward analysis. So I've been advocating -- I've been advocating for years now that departments of statistics, specifically graduate programs, should try to recruit students with an interest in applications, and they don't. That's rarely a consideration, that they should have a different kind of practical experience, particularly in their dissertation and a substantial fraction of them should take at least six months off and go work as an intern in some operating statistical agency and learn what the real problems are. You know, how do people have to deal with [inaudible]. But I'm not having much success in this.

Interviewer: What are the practical issues? Like when you say -- there are a couple of things like key words that you seem to be saying, like straightforward analysis, and a familiarity with the practical use of these things. And how would you describe those?

JB: Well, I'll give you some examples. Our federal assistance supports a very large statistical enterprise. There's the Census Bureau, the Bureau of Labor Statistics, the Bureau of Education Statistics. There's one in transportation and justice. We have the National Center for Health Statistics. I have heard people at the head of all of these complaining about how recent graduates in statistics don't know what they need to know. One of my friends is now the chief statistician of the United States, with responsibilities [inaudible] her role is in [inaudible] budget. She was not trained as a statistician, she's an economist, but she's had to learned these things on her own that a statistician would do. And at one point I talked to her about this, she had a list of 32 federal statistical agencies. 30 of them were headed by people who were not statisticians, which to me indicates that there's a very serious failing.

Interviewer: Definitely. But can you be a little bit more specific about what it is that they need to know that they don't know? You said kind of common sense, but in terms of approach to the data in the analysis.

JB: A new graduate in statistics might come to work for a statistical agency with responsibility for some specific area. And this new graduate's first question will be, "Which of the tools in my lovely new toolbox can I use?" And that's the wrong place to start. So they end up doing very sophisticated analysis [inaudible].

Interviewer: Where should they start?

JB: They should start by learning about the --

Interviewer: And how should they do that?

JB: Well, I think the first thing is to [inaudible] how the data has been collected, the definitions that have been used, and then you talk with people who have been using the data to learn about all the things that are known to have gone wrong. Think pretty hard about what else could go wrong and look at simple tabulations, simple measures like proportions, rates, averages -- rather than jump right into analysis because you often find that you can learn more from what you [inaudible] that way, and other times you find that there are problems you didn't expect and a straightforward analysis is going to be wrong. Plus [inaudible].

Interviewer: But basically what I'm hearing you saying is that to be a good statistician one first has to be sort of be -- first be at ground level to see sort of how the data's being collected, or at least talk to the people who are actually collecting the data and find out how they did it.

JB: I'd go further and if you can have this new graduate go out and collect some data. Go do some interviews. Go to the manufacturers, if you're dealing with data on manufacturer's inventories or costs. But get involved in data collection. You get a whole new perception of things that way.

Interviewer: There's been a little bit -- I mean from my perspective, when I look at the literature on the statistics related to TSE's, there's sort of a movement it looks like to me of sort of more and more complex models, computer programs, where you can simulate multiple runs and create, try to -- like multivariable analyses where you try to see which is the variable that has the most effect on the outcome and -- do you have any idea what I'm talking about?

JB: I do.

Interviewer: What do you think about that sort of movement and those sorts of studies?

JB: I'm very skeptical. I looked at that Harvard model [inaudible] and it's quite intricate. What they have done, basically, is to replace the few broad assumptions in a straightforward analysis with [inaudible], and I'm not sure they made any progress that way because there's so many more things now that can go wrong. It's hard to point to it and say, "They made a mistake here, here and here." I didn't have that problem with the guy from the FDA, who was presenting their model.

Interviewer: Steve Anderson?

JB: Was it Anderson?

Interviewer: I think so. He presented twice. Are you talking about the most recent meeting?

JB: Right.

Interviewer: Yes, that was Steve Anderson. So you're saying when you saw Steve Anderson present you felt like you were readily able to pick apart the model?

JB: Right, because he assumed that whatever risk gets -- whatever infectious agents get into the food supplies are evenly distributed over the population, and they're not. [inaudible] because one mad cow will all go

into the processing chain at one place at one time and come out as a small number of packages -- and have all the risk and nobody else is affected. Well, what you have to have is a model that assumes a small number of people get big doses rather than everybody gets little doses. And this can make a big difference if there is a thresholder. And we don't know about the infectious dose. It's pretty clear that one prion isn't going to do it. 1,000 prions. 5,000-10,000, the risk begins to go up. I think an appropriate risk model ought to consider that. I don't know if that's in the Harvard model. I didn't look at it hard enough to see.

Interviewer: You mean a threshold dose or any kind of --

JB: Right.

Interviewer: They assume -- I think they assume a species barrier of 1 to 1,000 for cattle human, and so that would then -- and then they assume an infectious dose for cattle so therefore there is an assumed infectious dose for humans. And in one part of the model they have a worst case scenario where they double the -- I think they double the infectious dose or the possibility -- or not double, I mean they double the potential amount of infectious material that could be in a cow, leaving the assumption of what the infectious dose is and calculate that, but all they do is double it and I don't know really know the infectious dose to that sort of accuracy.

JB: We don't. Furthermore, the comprehensive model undoubtedly didn't count the fact that susceptibility varies. There are not [inaudible] susceptible. I don't know if immunologic defenses matter. This is not an immunologic -- it's not a microbiologic disease in the usual sense. It is in the growing organism, but I have no trouble at all imagining that some people are much more sensitive than others.

Interviewer: It certainly seems that way given what we've seen from the UK so far, that that must be the case.

JB: Young people would be more sensitive to [inaudible]. I don't know if we can go any further than that.

Interviewer: Right and the reasons for that aren't really well known yet either.

JB: They're not known at all.

Interviewer: So I guess also in terms of the format of the Harvard model is 5,000 simulations and they give sort of like a 25^{th} percentile -- they do percentiles -- 75^{th} percentile consider possible outcomes. What do you think of that format for analyzing data and representing that data.

JB: I think that part of it makes sense. I think if you have a lot more, if you have a whole distribution -- if you had a good model to crank in all the data, all the uncertainties and you will not come out with a single answer, you would come out with a range of possibilities with extremes, both high and low being very unlikely and all piled up in the middle, and I'd like to see that whole distribution. So I like that aspect of it.

Interviewer: So, you'd like to see a graph, almost, of what it could look like for potential distribution. Why do you think they haven't provided that in the [inaudible]?

JB: Well, I don't know. They might feel that people are addressing at the quantity, but I don't think it takes a whole lot of [inaudible] to understand that type of graph. To say, "We don't know what the risk is, but it's somewhere in here and we think this is about the place."

Interviewer: Right. And with something like the Harvard study, they didn't really do any of the on-the-ground data collection. They wrote to people who would then give them -- and then they would say, "Oh, we think that spinal cord gets lumped in this amount of times" or that this -- "Potentially there could be this much cross contamination on a feed line." And what do you think about using those sort of inputs for –

JB: I wonder if ever any of us have been in a slaughter house. See how it is, in fact, done.

Interviewer: Have you been in a slaughter house?

JB: I have.

Interviewer: What's it like?

JB: Three times. First I found all three of them were spotless. The public concern about a lot of unsanitary conditions just doesn't hold.

Interviewer: Mmm-hmm. So they were clean?

JB: They were clean. They were neat. Actually one of them wasn't a slaughter house, it was a sausage plant. So they got the meat from elsewhere and ground it, mixed it, stuffed it in casings. And then I saw two separate chicken establishments. The first three were primarily neat. The two chicken places, both were from big chains. One was Purdue and one was Spicy and they were not nearly as spotless because chickens there's just a lot messier, but on the whole I thought they did very well in controlling the spread of things with a couple of serious exceptions. The cooling bath where they just dumped all the chickens in and keep them

their long enough -- move slowly along. It's a huge tank, about 12 feet high and about 12 feet wide and 25 feet long. The chickens go in on one end and there's a bunch of paddles that just move along very slowly and they take them out at the other end and by then they're cold. I was little concerned about cross contaminations. Chickens have an awful lot of salmonella on them, on the outside, but fortunately most of the population doesn't have problems with salmonella, only small ones.

Interviewer: Are there people who are extra susceptible?

JB: This one really does go to people whose immune defenses are way down.

Interviewer: Okay.

JB: Inherited immunological deficiencies, AIDS patients, patients on some kind of drug treatments, cancer chemotherapy -- I think they're more susceptible. Anyway, on the whole I was really fairly well pleased with what I saw at both kinds of establishments.

Interviewer: So at the cattle slaughter house what where the exceptions that you saw there to -- or were there any exceptions that you saw to there -- you said by and large they do a good job controlling the spread but was there anything that you noticed that could have been an exception?

JB: I didn't -- I don't remember seeing anything that concerned me about that. My focus in doing this was on the meat and poultry inspection process.

Interviewer: The FDA meat and poultry -- or do you mean the USDA?

JB: No, the USDA.

Interviewer: The USDA meat and poultry inspection process.

JB: Correct.

Interviewer: FSIS?

JB: Right.

Interviewer: Okay.

JB: I was chair of the committee here -- first I was a member of the committee for the poultry inspection operation and then I chaired a committee that was looking specifically at the inspection of [unintelligible] chickens, and it was in that context, those two committees that I saw these things. Since then I have been on another committee where I went to inspect three or

four dairy farms. We were concerned in that one with -- again the different aspects of the operation. It had to do with the air emissions. There were lots of complaints about the enormous consolidation of the animal feed operation -- pigs, chickens, cattle. So I went to a couple of the dairy places and a couple of the meat places. I was not able to go on the trip where we inspected the swine or poultry operations, but I talked to committee members who did go, and again the process with respect to the product that it turned out really was very good. It's not to say that there aren't some nasty problems with the people who live close to these.

Interviewer: Right. So how do you think it benefited the people who did the Harvard risk assessment to have gone to some of these slaughter houses and witnessed this themselves?

Interviewer: I think they would have gotten a much better sense of how the data were wrong, because the focus is not on data collection, the focus is on producing clean product. I think they would have come away with an appreciation for the need for all of the samples to be chosen strictly at random, rather than convenience. They would have, I hope, seen one or two downer cows and understood the problems with getting those cows in and out of the slaughter house the problems for determining why they were downers. Is it an orthopedic injury or a general weakness or an infection or something else, an immunologic disease? I think they would have come up with a much more realistic model.

Interviewer: And we had talked a little bit earlier about -- or when we were talking on Friday you seem to have some very clear ideas about surveillance and the importance of sampling in particular ways. Can you explain a little bit about that, the importance of --

JB: Right now we have no idea whatever about the real frequency of prion disease is in our cattle population. Nobody has ever done much testing. I say we don't have a clear idea -- I'm sure that it's very low, but is it that one cow in Washington? Is it 1 in 1,000,000 -- basically 35 cows over the US? Is it 1 in 10,000 like in some of the European countries? We don't know. I am not sure that we need to sample -- that we need to test every cow. What I would like to see instead, for a bunch of reasons, is to have other connections to the national identification system that is used at the time of slaughter to determine which cows will be tested. I don't want it to be used ahead of time because that might affect which cows get sent to slaughter. But after the cow arrives at the slaughter house, read the tag and then take a sample of, I don't know, 1 in 1,000 or whatever it should be. Test them and use that information for positives if there are any. Go back to the place of origin. Where did that cow come from? What might have gone wrong? What are the other cows that were there at the time, and can they still be tested? To use the surveillance system as a way to

improve what goes into the slaughter houses. What we have now is carcass by carcass inspection, both the meat animals and poultry. So the defective product can be taken out of the food supply and that is a remarkably inefficient way to deal with the problem.

Interviewer: Why is it inefficient?

JB: Because you can learn so much more by taking a sample 1 in 100, 1 in 1,000 and trace back to fix the problem wholesale instead of looking at these things one by one. One of the things you learn from watching the inspectors is how fast they have to work. Inspection lines for poultry go by at 90 birds a minute, which means that the inspector has almost no time for any one bird. They have to use what's called organoleptic sampling, which means they look, they feel, they smell, give it a sniff and then they're off to the next bird.

That was appropriate 100 years ago, maybe even 50 years ago, when the primary concerns had to do with the general health of these animals. The concerns now are focused on hidden problems -- microbial contamination, chemical contamination and now prion disease in cattle, and you cannot see those, you can't smell them, you can't feel them. The inspection process doesn't pick them up. I mean, it's nuts. Whereas if you took a sample, took that cow out of the food supply temporarily long enough to do the testing for microbial contamination, for chemicals, for prions or whatever else and then release it 24 hours later or whatever it takes to do that on a small sample -- first we'd cut costs enormously and second we'd learn a whole lot more about the process and how the whole process can be improved.

Interviewer: So rather than inspecting every bird or every cow or every piece of meat, only sampling certain ones but inspecting them very carefully running all the tests and seeing if there is anything and being able to trace it back to the origin of where it came from and figuring out if you can find the cause of the problem that way?

JB: Exactly.

Interviewer: And then in terms of determining so it looks like you set a goal of 1 in a 1,000 for testing -- would it just be randomized 1 in a 1,000? So somehow the tags that you randomized so there would be some database or some computer system --

JB: You have a national file of all the cattle and as they go to the slaughter house the tags are read and the program says -- it generates random numbers and 1 out of 1,000 is marked -- independently of all the others, is marked for detailed testing.

Interviewer: So are you familiar with -- yeah?

JB: It's important it be independent. You don't want to take 1 out of every 1,000 because once you've got the cow who knows what will be slipped in behind it, all the ones that don't look so good. So you want to make sure that every cow has the same probability of coming into the sample, even if the one just ahead was picked.

Interviewer: You've worked with the USDA before it sounds like. Do you recall how long they've been discussing an animal identification system?

JB: At least 20 years.

Interviewer: Really?

JB: Yeah.

Interviewer: That's a long time.

JB: We pushed this idea in our report on poultry inspection and that was over 10 years ago when it was not in depth.

Interviewer: Do you remember what year that was?

JB: No, I don't.

Interviewer: Okay. But it was over a decade ago? And this was the project for which you were on the committee and you went around and visited all these different slaughter houses and poultry?

JB: Yeah.

Interviewer: So it was at least recommended by you then and I think it's probably been recommended by other committees also.

JB: Oh yes, before then and after then.

Interviewer: Why do you think it hasn't been acted upon?

JB: It would cost the industry a little bit.

Interviewer: Do you think it has a better chance of --

JB: There's a lot of political opposition to this, which is based on the industry.

Interviewer: What are they afraid of?

JB: I don't know, Maya. My guess is that they're thinking about this in the wrong way, that every producer thinks, "What happens if my cost goes up 1 cent a pound? I'd lose the competitive advantage." But that wouldn't happen -- everybody's cost would go up. This is why I asked the question in that meeting about the price elasticity -- do you know that term?

Interviewer: Yes.

JB: Okay.

Interviewer: You could explain it though, that would be helpful.

JB: It says if price goes up by 1% how much does demand go down, or if price goes down how much does demand go up? And in the region, a narrow region of change you can create it and it's pretty much linear. And my guess is that demand for beef is not terribly price sensitive within a narrow range. That is, raising the cost by 1 cent a pound or five cents a pound is not going to have much impact on how much beef is purchased.

Interviewer: Especially if it's -- so you're saying it's across the board so no one individual is at a competitive disadvantage?

JB: Right, it would affect everybody.

Interviewer: Right, and how much would the population actually change their eating habits?

JB: The population might in fact increase consumption if they have that extra assurance of safety. I doubt if that would happen. It might become a critical issue if there's a second cow. I don't think -- I think ahead of time you could have predicted that one cow imported from Canada wouldn't have much effect, but a second cow -- would say, "Look this is a real problem," and I think that by the end of the third cow we have a much bigger impact.

Interviewer: Do you think -- there was a lot of discussion at the meeting about whether or not the USDA's goal, testing 40,000 animals this year, is adequate, and do you think that if there is another cow that they would find it with the current testing regimes?

JB: Well what was the number? There's something like 35 million cows per year go to slaughter, so they're testing about 1 in a 1,000. Well there's kind of a rule of thumb. That should be adequate to determine whether there is a hazard as great as 1 in 12,000 with one big qualification, and that

is the sampling would have to be random and what they do now is not random. It's a convenient sample.

Interviewer: In order to do random samples would that require a mandatory testing program? Because right now all [inaudible] they do is voluntarily-based.

JB: No-no, the federal inspection is mandatory.

Interviewer: Right, but the BSE testing.

JB: Oh, the BSE testing is not mandatory.

Interviewer: Because you can't do random sampling unless you have everyone as part of the system, otherwise you're going to be --

JB: Well, that is quite true. You could institute a requirement for random sampling in every cow west of the Rockies, because that's where the problem was.

Interviewer: Sure, yeah, you could have --

JB: And for those pick 1 in 1,000 or 1 in 500 or 1 in 10,000. Pick whatever seems appropriate. That might be a useful thing to do, if you figure that anything further east is going to be safe. Or you could use a lower sampling fraction for cattle for further east. They don't have to be identical. 1 in 1,000 there and 1 in 10,000 here.

Interviewer: Right, right.

JB: That won't help consumers unless you have [inaudible] as the place of origin. Most beef is purchased not too far from the place of slaughter.

Interviewer: At least within a certain region. Okay, can we go back a little bit to -- okay so let's talk about some of the committees you served on in the past. You mentioned the USDA -- the SFIS committee that you served on. When were you inducted into the Institute of Medicine and when did you start serving on National Academy Committees?

JB: Well, it's not required that a person be a member on a committee or even to chair a committee. The first committee I was here -- I was on here, was actually not in IOM. It was in NAS. You know about the three institutes?

Interviewer: Can you explain?

JB: The National Academies are made up of the National Academy of Sciences, the Institute of Medicine, and the National Academy of

Engineering and membership is partly separate. Some people are members of more than one but they are very rare. I'm a member of the Institute of Medicine, but that committee was -- it was the 38, '81/'82, and I was chair of the committee, so I was never in any of these.

Interviewer: And what was the committee on?

JB: That was on toxicity testing. The National Institute of Environmental Health Sciences was very much -- which had the responsibility for this kind of thing, was very much interested in what we know about the toxicity of huge numbers of chemicals that are out there. There are by now 25 million chemicals that have been identified and put in the American Chemical Society database. There are about 65,000 of them that are produced in significant quantities, that is more than a 1,000 pounds per year. That is the general chemical history. We have probably 6,000 that are recognized as drugs, that are separately regulated by the Food and Drug. Probably about the same number of food additives -- a smaller number, maybe a couple of thousand that are covered under the Cosmetics Act. The FDA is food, drugs and cosmetics. And then there are the pesticides and what are called incipients, things that are used to make pesticides. They are used as solvents, carriers or otherwise added and there are several thousand of those. But we looked in all of these separate groups and the level of ignorance about toxicity is just appalling. Tiny fractions that had been adequately tested. Now most of them have a very long history --

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