knowing how often in the occurrence of Lyme Disease, OspA is actually encountered. Certainly as a construct for the vaccine.

I think this is a very unique vaccine and I think a lot of thought went into the design and I think it was very clever. But what is the rate of human encounter with OspA and when.

We certainly heard about the issue of it being -- well at least some immune response to it being produced later in the course of illness. But I'd certainly want to know more information about that.

The whole issue of basic research on OspA I think is very important given what we now are learning more about regarding the whole issue of autoimmunity. And then the issue of enrollment in the Phase IV Study.

One question I would have would be: What can be done to enhance the enrollment without compromising the quality of data? Do you have to go to smaller HMO's that have smaller databases but nonetheless have high quality data? Would that be the type of data that would be needed?

You have to balance that with the HMO's that may have the appropriate quality data may have

been asked to participate in a lot of other studies because of the very nature of the quality of their data. So, clearly, there is a dichotomy here but perhaps one that should be explored a bit further.

And then the other issue I think that I had some questions about is the whole issue of reactivation. Some of the Western Blot patterns certainly presented in a bit anecdotal way in the information that we had to read are very interesting and I'd want to know more about that.

CHAIR DAUM: Thank you. Dr. Coyle?

DR. COYLE: Well, I was here two years ago, and the safety profile has changed, and it has changed for one real reason. Although the information presented on the 8,000 or so that have had the vaccine suggests this seem to be safe in the majority of individuals.

There is now, which wasn't a few years ago, the suggestion that in a minority of individuals, a few of those this vaccine can produce a devastating, a generalized chronic pain syndrome that really disrupts lives. And there was not a hint of that at all.

And the only data for that are the testimonies that I've heard. Because it's not

captured anywhere else. So I think that's of concern. That wasn't raised two years ago in my opinion and that indicates that there's a subset of individuals in whom it's a bad thing to get the vaccine. That it can be potentially a very devastating thing.

I think that the Cohort Study -- the reality is it sounds that they're not going to get 25,000 patients in a reasonable time frame. So something has to be done, something has to be done to increase the numbers because it just doesn't sound like they are going to get it.

Secondly, I think we need to learn more about the sorts of patient testimonials that we heard or heard about from letter. We know very -- we know nothing about these patients.

So let's get a registry of these patients to try to figure out what seems to be the background to try to cull out a group that may be at risk where you don't want to give this vaccine.

Finally, the preliminary, very sketchy, I mean 30 pregnant patients, and we have data on a minority of them and the data that we have available is very bothersome. I think we need to get some real pregnancy data. That should be a real push. That's disturbing.

And finally, I think something does need to be added to the patient insert -- to the package insert here. Even if we don't have clear cut data, the fact that it's now been raised that in, granted perhaps a very small minority, but in a small minority, this can be a bad thing to take, potentially.

It needs to be put in somehow that this has been raised as a question and investigations are ongoing, etcetera, so that people can know about it; and physicians.

DR. LUFT: I'll just make a couple of comments because I've commented enough today. If you look at the sponsor's data, there's no difference. I think that that's what they've stated and they showed us the data. There's no significant difference.

What's the problem? The problem is -- it's a problem of perception and a problem of confidence. And I think that that's a really big problem.

I think that everybody in this room whose involved with vaccine design or administration realize that that's a very large problem. It's a problem of perhaps why this vaccine has such poor uptake within the community.

And it goes on both sides now. My feeling is I was here two years ago. There were certain suggestions that were made. My expectation is that the company, that the sponsor, would have been very vigorous in doing it. Actually they got a gift.

They were approved for a vaccine for this disease which was really very unique in many ways. It's mode of action was unique. It was the first lipoprotein that was licensed, that was given an indication.

It was a new -- it was all new -- and you would have expected -- and it was done in record time if I remember. It was really done in a very short time.

And I'm disappointed today. Because I hear some information here and I hear some information there. And I don't hear good data. We really are sitting in a situation in a sea of just what we feel. Because no one is giving us data.

And the same thing could be said on the science part of it. Two years ago the group described the issue of the whole LFA. DR4 was something that was there. It's now being talked about as if it's gospel.

There was nothing that came out, or very

little that I know of that's come out since that time. There hasn't been anybody that has really come out and validated that work. That has looked at this patient population, etcetera, etcetera.

My greatest fear is that this is a big disease. When we talked about, I think Dixie was talking about that his perception was that there were a lot of people that were suffering. And I can attest to the fact that in our community, that Lyme disease was and is a very big issue.

It's not that there is no need for a vaccine. What I think there is a need for is a vaccine that people have confidence in. There's a need for a vaccine that, once it's given its license or indication that there will be ongoing research and surveillance, that will meet the privilege of being out there and the public being administered to -- to patients. I just don't think that's being done.

So I know there have been a number of suggestions that have been made as to how we can more vigorously and actively get to the answer as to whether adverse events are actually occurring or not actually occurring.

And I support that wholeheartedly. I support much smarter people than me making those

suggestions on how those types of studies should be done.

But at the end of a short time we should be able to come back here and get real information and not feel that we're on a ship that's sort of in the middle of a storm.

DR. RAY: I want to I want to comment briefly from an epidemiologic perspective. First, I think there is a real basis for safety concern with this vaccine. Back of the napkin calculations suggest that 5 to 6% of current VAERS reports are reports for this vaccine which seems large given that its uptake is less than expected.

So I think there is a basis for safety concerns.

Second, I don't think that the post-marketing studies that are planned are going to achieve their power objectives. And for that reason, I think studies with greater precision are needed be they Cohort studies or a variety of methods or case control studies.

DR. DATTWYLER: Well, I was here two years ago and as a matter of fact I was sitting in this seat and I also had the last word at that time.

CHAIR DAUM: I have the last word.

DR. DATTWYLER: Oh you have the last word. I meant of the panel. You know I totally agree with what most of the people have said. I think that Dr. Snider's point of the atmosphere at that meeting versus the atmosphere in this meeting is very important to realize.

And ultimately physicians have to decide what's best for their patients. And to do that in an intelligent way you need to know the risks and the benefits.

And as I sit here, like everybody else, have no greater feeling for what are the risks of this vaccine than I did two years ago. And that's bad. And I totally agree with what Dr. Myers said and what Dr. Loft said and everybody else is that we need to get that data so we can plug that into a risk-benefit analysis and make an intelligent choice for our patients.

Vaccines and drugs, we know can have adverse reactions. If you know what the adverse reactions are and the incidence of those adverse reactions and then you know what the risk that your patient runs, then you can make an intelligent choice and right now we can't make an intelligent choice. So I agree that we need to, like everybody else, that we

need more data.

CHAIR DAUM: Dr. Ellenberg.

DR. ELLENBERG: Yes, I'm sorry. I just want to make a quick clarification on the back of the envelope calculation. I think we have somewhat over 1,000 reports, is that right, on Lyme Disease vaccine. We have well over 100,000 total reports in the database. We've been getting 10 to 12,000 reports a year. So it would be more like under one percent I think of the total.

DR. RAY: Well let's think it through though. You get about 10,000 a year, according to the documentation. And there have been 1,100 reports approximately in two years so that is 550 over 10,000.

DR. ELLENBERG: Okay. That's not what I --

DR. RAY: I would come up with about 5 percent of current reports or 5 to 6 percent are for this vaccine which seems to me high.

CHAIR DAUM: Well just to sort of anchor and to try and not be repetitive. I, of course, was here two years ago also and am grateful to Dixie and others for making the comment about how different the atmosphere was then.

But I still don't feel that it's

appropriate to apologize for that decision. I actually think it was a correct decision to go forward.

I'd like to, before I say anything, remind everybody that this meeting we had today was very unusual in that the FDA has called us together to talk about a licensed product -- to get our sense of where we think the safety data are. And I think that's a tribute to the agency's concern.

I'm also profoundly moved by the patients and families who took the time to come here and talk to us. But I had some concerns about the safety profile two years ago and some concerns about the efficacy two years ago and I believe I'm on the record as having articulated those.

I'm not sure whether I believe that there is convincing evidence of new safety concerns or not. And that may be a statement of where things are and perhaps should not be. I can't accept the notion that this study can't be done anywhere else.

The case control study is going forward so slowly because there are no other quality sites to do it and I am very disappointed that that hasn't gone forward more quickly.

I applaud Dr. Ball and colleagues for

taking VAERS reports which are very difficult to make head or tail out of, separate numerator data from denominator data and trying to nest a case control study within that to look at some important issues as well.

I'm disappointed that we're not further ahead I guess in understanding the safety issues of two years ago and remain unsure of whether we've deteriorated or behind or not. I didn't hear convincing evidence that there are major new concerns despite all the comments that were heard.

The package insert does need to be updated. At the very least reflect issues like hypersensitivity that have come to light since two years ago, but they appear to be relatively minor in the overall scheme of things.

I think the people who came to talk to us today from all over the country -- that their comments need to not go unheeded. And what I would suggest is to begin to see if what Dr. Lufts said is true. Are those reports not in any of the databases? Are they not in the manufacturers pre-licensure database? Are they not in the VAERS database?

I would like to really find out whether that's so. Because if your conclusion is correct that

they're really not, then something is wrong with our system. Something is really wrong with our system. And, once I've made that determination, I would then go forward designing studies to address some of the diverse complaints that the patients and their families had, which by themselves, need some thought as to how frequently they're occurring.

The information sheets takes a lesson out of the pediatric vaccine book and patients who take this vaccine or any vaccine have got to be informed of what they're getting into.

And so, I highly applaud that and believe that Dr. Manley's comments are difficult to implement because we can't standardize what patients are told in this country but nevertheless, having the sheet available like that, would go a long way to providing the framework for a physician or a provider to have dialogue with a patient.

So I think that we've really had a wonderful meeting here. We've heard lots of points of view. I think the call for Dr. Ferrieri and others that more basic science needs to be done to address the issues that are unknown about the pathophysiology of this disease are beyond the scope of dealing with just the vaccine -- but also intimately tied up with

it. They can't be neglected. But I'm not sure we can solve those problems in this room.

I want to thank everybody who took the time to share views with us and debate these issues with us. I think we've had a wonderfully informative day. Before we stop, Dr. Ellenberg will have the last word.

DR. ELLENBERG: Well, I just want to say that that certainly some, perhaps many, or even most of the stories that we've heard today, have been reported to VAERS and they are included in the summaries that Dr. Ball presented and I would certainly urge that anybody here who has not made those reports, do, because that's the only way we know what is happening if those are reported.

As Dr. Ball described, he is going to be following up on these reports to try to and have a better understanding and a grasp on all of these types of reports that we have received.

CHAIR DAUM: Thank you for clarifying that and this meeting is adjourned.

(Whereupon, at 5:25 p.m. the above-entitled matter was concluded.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: Vaccines and Related Biological Products Advisory Committee

Before: DHHS/FDA/PHS/CBER

Date: January 31, 2001

Place: Bethesda, MD

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