time, is it related to the severity? If the patient has a severe illness of another kind, and then they also are complaining about these lyme symptoms, or whatever, would that be recorded?

And do you have any substudies to asses this sort of thing, so that you could characterize your reporting mechanisms?

DR. PLATT: It is the nature of these claims files that they can report up to three diagnosis at a visit.

CHAIR DAUM: I have Dr. Davis, Griffin, and Luft. Dr. Davis?

DR. DAVIS: Thank you. My question has to do with the consistency of using codes, since you are going to be bringing on two more HMOs. Do you have a method of assessing the consistency of the use of codes across the HMOs?

DR. PLATT: We can look at the frequency distribution of use of codes and stratify that by age and sex, that would give us the best sense of that.

We have done several other collaborative studies with these HMOs, and have found it could be, the data to be reasonably homogenous across the HMOs for the kinds of exposure outcomes that have been of interest in other pharmacoepidimiology studies.

CHAIR DAUM: Dr. Griffin, please.

DR. GRIFFIN: I am really following up on the question that Dr. Stephens asked, because I'm interested in the enrollment problems, and how much that is going to continue to hinder this study.

Because I think it is really an important study to get the kind of information that the committee, and probably everybody else is interested in.

So you had many fewer patients that enrolled sort of in the second, or two six months than you did in the first six months, which is maybe what you would expect with a new vaccine, you have sort of a buildup of people who wanted it.

So I have two questions. One is, is there any just sort of general idea of why the vaccine has had a much lower uptake than one would have, perhaps, what you anticipated, obviously in this HMO.

And, second, is there any idea, ballpark idea, of how many doses have been given in the two other HMOs that you are bringing on line?

DR. PLATT: I honestly don't have an expert explanation for the rate of use of the vaccine. The other two HMOs, when we have the data from those other two HMOs, we expect to have between two and

three times the total that we have now.

Which would mean a total of somewhere between 7,000 and 9,000 through two years of follow up.

DR. GRIFFIN: There is probably no reason to think in the third year that that will dramatically increase in frequency, that there will be an incremental additive number of individuals. It sounds like you are going to have a hard time getting 25,000, I guess.

DR. PLATT: We can predict equally well. There is really no information on that.

CHAIR DAUM: I have Dr. Luft, Dr. Kohl, Dr. O'Fallen. Dr. Luft, please.

DR. LUFT: Conceptually I love this approach because it uses computers, it is a lot of data that you can go through.

But I think one of the issues, you know, coming from the point of view of the department chair of ICB-9 codes as to what is the purpose of those codes from the physician's point of view, and that is for billing.

This is the way, and what you do is you try to -- you look at diagnosis and you put in as complex of the issues as possible in order to be able

to get as high of a level of care, and that is the incentive.

So the incentive from the physician's point of view is a financial thing that they have to represent, it is not to look for subtleties.

And I think that there may be a problem in what your readout is, as a result of that, especially you try to get three diagnosis. If I have someone who comes in with congestive heart failure, renal disease, diabetes, and joint pain, you will see where the first three, the complex disease will be first, and then joint pain will, myalgia or whatever, won't ever make it up there.

The other thing that most of these -- because I'm constantly dealing with my docs regarding billing to get them to fill out their billing sheets, is that they do what is easiest.

They are not going to look at the long list, they do what they have some facility at knowing. So, for instance, if they single out hypertensives, etcetera, and they could quickly write down those ICD-9 codes, they just do that.

It is not even that they will go in and look for the subtle diagnosis, or the things that are out of -- and I think those are two, you know, I'm

just kind of -- in some ways I just love this stuff, because it is just, like I said, it is reams of data, and you are able to compare it.

But I'm not sure what the acquisition of the data is as accurate as you want. And that is basically it.

CHAIR DAUM: Thank you.

DR. PLATT: I agree with all of the above, and that is why I would never publish a result, or suggest to the committee that it make conclusions on the basis of ICD-9 codes alone.

We use the ICD-9 codes as a very rough strainer to find the records. Among the thousands of people who are participants in the study, we need to find the hundreds whose charts need to be reviewed. And that is the purpose of using the ICD-9 codes.

And we trust the clinicians to get at least the right body system, organ system in their diagnosis codes. And if they don't do that then we will have missed these outcomes.

CHAIR DAUM: We are going to take questions or comments from Drs. Kohl, O'Fallen, and Diaz, and then we are going to ask Dr. Kahn to wrap up the sponsor's presentation. Dr. Kohl?

DR. KOHL: I took my Ginko Balboa so that

I can't remember my questions. I have two questions.

CHAIR DAUM: I was going to make a comment, and I decided that we have been friends for a long time.

DR. KOHL: In the summary we received as handout material labeled Synopsis of LYMErix Phase IV Observational Study, it states: While no obvious patterns are present, and I'm paraphrasing here, data suggests a higher incidence of rheumanological conditions among vacinees than non-vaccinees.

Was that referring to the 8.5 versus 7.5 percent, or are there other higher --

DR. PLATT: I'm sorry, I don't know. I'm aware of no other data that suggests that there is a higher rate of assignment of these codes.

DR. KOHL: Because you said they were similar, about 8 percent, and the handout says there is a higher --

DR. PLATT: One is eight and a half percent and the other is, I think, 7.8 percent.

DR. KOHL: Okay, and that is what you are referring to, okay. Because you modified your conclusion a little bit.

The second question gets back to what I think is a concern among committee members. And I'm

going to push you a little harder, and that is recruitment of vacinees.

It seems very slow, and if what Dr. Griffin said is true, it seems that possibly there was a bulk of people who wanted a vaccine, and now there is a fall off, although it is possible there were documents who didn't want to use the new vaccine to begin with, and now there will be an increased utilization as they feel more comfortable.

And it is possible that a hearing like this will make people less comfortable, and docs less comfortable, and there will be a gigantic fall off.

Do you have any idea what is going on? Because I'm concerned, where a year and a half or so, post-licensure, having mandated this kind of study, and it doesn't look like we are getting it very quickly.

And if there is a real problem out there, this is a question that needs to be answered with some timeliness. So give us a feeling for how quickly this is going.

DR. PLATT: I can't give you a sense of what the recruitment will be. I do think that by the end of this year, with the addition of the data from the new HMOs, we will likely be at two to three times

the number of individuals, and at that point my view is we will have real information about the relative risk of these outcomes.

The tyranny of power calculations is such that very large increases of numbers buy you a relatively small increase in precision. So a study that is half the size, in fact, will have pretty good power to exclude a relative risk of three, as opposed to a relative risk of two that we are talking about.

I'm not suggesting that the study be scaled back. But, in fact, even though -- I won't use the word recruitment, is slower than we expected, in fact there will be substantial information available, I think, by the end of the year.

DR. KOHL: But we have been told, so far, that this is a very rare condition. So rare that we don't even have an incidence number for treatment resistant lyme arthritis. And I'm concerned that the study is not going to be powerful enough, maybe even at 25,000, but if you scale it back further, that is a real concern.

CHAIR DAUM: Dr. Kohl, what I think we should do here is not push Dr. Platt further on this point, but rather raise this important issue when we have more general discussion with the sponsor, and

with our FDA colleagues, because they have a lot of input as to how the study is conducted.

And Dr. Platt may have a limit to what he can accomplish within the context of his one, two, or even three HMOs in terms of enrollment.

And I'm going to suggest that we use the word enrollment rather than recruitment, because I think we are getting some unnecessary juice here in response to the word recruitment.

Enrollment is what you are doing, really, at least as I understand it.

We had Dr. O'Fallen, and Dr. Diaz. And then we will move on.

DR. O'FALLEN: My primary point was very eloquently expressed by Dr. Kohl. I think we have a serious problem of enrollment. And I agree that is the proper word.

You all anticipated, obviously, 25,000 in two years. You are optimistically telling us that the addition of, let's pick on Minnesota, where the disease is not as endemic as it is in Massachusetts, I can't believe that the enrollment is likely to be as big there as you are anticipating, either.

And then we have the potential bias, if you can only list three ICD-8 codes that the doctors

who gave the vaccine will be more likely to list those codes, than we will find in the controls.

And so we will have to be trying to sort a lot of that out, too. So I'm seriously concerned about the study as well.

CHAIR DAUM: Thank you. Dr. Diaz, please.

DR. DIAZ: I think I'm the third or fourth in line with very similar question, and it has to do with this question about enrollment. And this question could be answered now, or later during the discussion.

But I think if the study is designed to look at safety as it is used in the general population, then we will, at some point, need to have some information about what the practices are of physicians who are giving the vaccine to these individuals, ie, are they offering the vaccine to everyone equally, or are they selectively offering the vaccine based upon subsets of patients and concerns about safety issues?

CHAIR DAUM: Do you want to respond to that? Or I think you already have.

DR. DIAZ: I'm curious if anyone has -- I guess the question is, then, does anyone, either you or the sponsor, have information about physician

practices with this vaccine, currently?

DR. PLATT: There are, so far, there are approximately 250 practices that have immunized someone who is included in the results that I've shown you. And they have, we guess, a couple of thousand providers.

The HMO communicates to those providers in a very general sort of way, providing the CDC guidelines for use of vaccine. That is the information that has officially moved back and forth in this provider group.

CHAIR DAUM: Thank you very much, Dr. Platt.

Now, can I get a sense, from the sponsor, of how much more time they need? I thought we were down to our final speaker. How long does Dr. Hoet need?

DR. HOET: I have seven slides, and then there will --

CHAIR DAUM: I think we can handle that. Let's go as quickly as we can through this, if you would, please.

DR. HOET: Thank you. Thank you, Dr. Platt.

The vaccine is now on the market since two

years, and 1.4 million doses have been distributed. And to date 984 adverse events have been reported to the company, until November 30th.

And what has been observed is that the only reactogenicity profile that had been reported during the clinical development, and that is presenting information of LYMErix occurred to -- it is confirmed.

And that some of the symptoms that are reported in prescribing information of LYMErix appear to occur concomitantly with an early onset after vaccination. Also hypersensitivity have been reported very rarely.

The slide here compares the adverse event reported during the post-marketing surveillance with the adverse events that were reported during the clinical development.

And in the left column here you see the adverse events that have been reported during the efficacy study to occur statistically significantly more frequently in the vaccinated group, as compared to the placebo group.

And on the right side you see the ten most frequently reported adverse event in the passive post-marketing report. And these adverse events reported

through the post-marketing surveillance are very similar to those reported on the label.

Next slide, please. In view of the theoretical concern faced regarding the risk of inducing autoimmune arthritis after lyme disease, all the cases of arthritis or rheumatoid arthritis have been analyzed.

And up to September 25th of last year 70 cases have been reported. And an in-depth review of the data show that there is no evidence that incidence is higher than in the general population, no practical or clinical pattern was identified, and no clustering time to onset was observed.

We do not consider that the arthritis cases reported in the post-marketing surveillance are associated with vaccination. However, as part of our continuing effort to address the theoretical concerns, we are convening a panel of experts to independently review this data. And this is ongoing.

Now, since licensure of the vaccine several clinical studies have been performed, or initiated. Firstly in the older population where cohorts of the efficacy study have been followed up, and secondly in the pediatric population.

And I will now give you the available

safety data of these studies. In the blue box here you see the results that were available at the moment of licensure. First you have the Lyme-008 efficacy study that enrolled 10,936 individuals randomly allocated to placebo or vaccine.

And that lasted with a follow up of 20 months. This study, as explained earlier, was followed up by a safety follow-up of four months, and these are the data that are available in the file.

And then most of the vacinees of this study have been participating to a long-term follow-up for an additional year, and this is approximately 5,000 subjects, and 352 have participated to booster studies.

The majority of the placebo cohorts has also been included in further clinical studies, and have received the vaccine.

Approximately 4,400 out of them have received the vaccine according to the license schedule. And somewhat less than 1,000, according to alternative schedules.

And 550, 1,550 of those subjects have participated to further booster studies. Out of the 4,400 subjects having received the vaccine, according to the license schedule, 3, 578 participated to a

crossover part of the efficacy study, for which I will show you preliminary results in a moment.

Next slide. So this was an open label study with crossover vaccination of the placebo recipients of the Lyme-008. 3,578 subjects, the schedule was the one that is licensed for the moment.

And there was an unsolicited adverse event reporting by a safety postcard. Similar to the pivotal efficacy study the most frequently reported adverse events were injection site pain, myalgia, arthralgia, and influenza like symptoms.

So two alternative schedules have been studied, namely 0, 1, and 6 months that was compared to the classical 1, 1, 12 months in 400 subjects per group, and the 0, 1, 2 plus 12 months, versus a 0, 1, 12 month in 500 subjects.

In addition, approximately 3,800 subjects participated to booster studies, receiving up to six doses of vaccine in total. Regarding the pediatric population 4,000 subjects age 4 to 18 years participated in these studies, out of which 3,000 received LYMErix according to the 0, 1, 12 month schedule.

In all those studies the nature and the frequency of the adverse events were similar to the

pre-licensure clinical trial experience.

In addition to the more than 6,000 subjects that have been vaccinated before licensure of the vaccine, more than 8,000 subjects have received a vaccine in the course of clinical studies since licensure.

And so safety data has been collected, in controlled settings, on more than 14, 000 vacinees to which the number of the cohort studies can be added.

In conclusion of regarding the licensure commitments, the post-licensure commitments, the study on cellular immunity showed no evidence of association between vaccination and incidence of inflammatory arthropathy, no maternal or fetal reproductive toxicity was seen in rats, and the pregnancy registry has been established, and no unexpected observations were made.

And the cohort study to asses the safety of LYMErix show enrollment lower than expected due to the low vaccination rates of the search population. No difference was, however, observed in the event codes between vacinees and the control group.

The post-marketing data have shown that the most frequently reported adverse events involved reactogenicity with symptoms already described in the

product label.

These symptoms, these reports show that in certain individuals these symptoms are described as occurring concomitantly. Hypersensitivity has been reported very rarely in post-marketing surveillance, and the arthritis cases observed in the post-marketing surveillance are not considered to be associated with vaccination.

Clinical studies involving more than 8,000 vacinees confirm that the safety profile observed during the development of the vaccine is --

CHAIR DAUM: Thank you, Dr. Hoet.

DR. HOET: And now I will --

CHAIR DAUM: I think I will now ask Dr. Kahn to show her conclusion slide, and then I will take Dr. Hoet and Kahn's presentation together for a few questions.

DR. KAHN: Thank you. Just one conclusion slide, an overall conclusion.

In conclusion now we have shown you safety experience in excess of 18,000 subjects in a number of controlled settings. Again, 1.4 million doses have been distributed in the marketplace.

All of the data accrued since licensure concern the safety of profile defined at the time of

licensure, and in particular we should confirm here that there were no cases of TRLA in any of our control trials extensions or, indeed, in the post-marketing surveillance.

As for all vaccines GSK is committed to continuing the safety assessment in collaboration with the agency.

Thank you, that is the end of GSK.

CHAIR DAUM: Thank you to the sponsors for their presentation.

We have time for a couple of questions on Dr. Hoet and Dr. Kahn's last comments. Dr. Kohl, Dr. Griffin.

DR. KOHL: I appreciate the presentation by the manufacturers. I'm sure, due to shortage of time, we could not see specific data on some of the last studies presented.

My question is, does the FDA have that data for the post-licensure studies, in order to be able to scrutinize the specific side effects of the vaccine?

DR. KAHN: For many of these downstream indications, where we have clinical trials, there are supplements, indeed, under review. And for that reason we can allude to the them because we have the

empirical safety data to look at, but we can't really comment specifically, because they are -- it would be unwarranted at this time, otherwise.

DR. KOHL: Under review in the company, or under review at the FDA?

DR. KAHN: At the FDA.

CHAIR DAUM: Dr. Griffin, please.

DR. GRIFFIN: That may be the answer to my question, too, because I was wondering what you meant by hypersensitivity. If this is an immediate hypersensitivity, sort of a delayed type hypersensitivity, or --

CHAIR DAUM: Dr. Stephens, then Dr. Coyle, then -- I'm sorry.

DR. HOET: In the post-marketing settings some immediate hypersensitivity has been observed.

CHAIR DAUM: Thank you. Dr. Stephens?

DR. STEPHENS: Do you have experience with this, or related vaccine, in Europe?

DR. HOET: Well, we are currently working in analyzing the possibilities of developing lyme vaccines in Europe, also.

DR. STEPHENS: Do you have clinical trials ongoing in Europe?

DR. HOET: There are phase II trials

ongoing in Europe at the moment.

DR. STEPHENS: Phase II trials.

CHAIR DAUM: Dr. Estes, please.

DR. ESTES: You summarized that you had studies on cellular immunity, where there was no evidence of an association between vaccination and inflammatory reactions.

Did you show us that data, the cellular immunity studies? Because my recollection was that the summary from the FDA is that that data was limited, and that final conclusions could not be made.

Am I correct in that?

DR. KAHN: Perhaps I can call on Dr. Montagne to answer that question.

DR. MONTAGNE: Well, actually I'm from R&D, I'm not sure it is needed to go into the details of the data. But indeed, as has been presented by the FDA this morning, indeed this is a primary report, for which the first purpose was to see if there was some sort of to different peptides, to the OspA and to the different peptides.

And we can't conclude, because of the background, to any significant, both hemologically and statistically significant difference. However, what we just can see is that there is some lympho

proliferation against some peptides.

And, for example, we confirm that, indeed, some TDR4 allele are used to present some peptide, as expected, just as expected. I don't know if you want to see the real data.

DR. ESTES: I think that is okay, I just wanted to confirm that the conclusions that we heard from the FDA this morning, that the study was limited, was a little different than the conclusion on your slide.

DR. MONTAGNE: On top of that, on top of the immunological data, what is true is that there was no correlation between the clinical picture and those data. So those data are confirmed how some peptides can induce some proliferation in association with some DR allele, and especially with DR4.

But what is interesting is that, indeed, there was no correlation between these data, this lympho proliferation in individual patients, and some clinical picture.

CHAIR DAUM: Dr. Coyle, did you have your hand up before? Dr. Coyle, then Dr. O' Fallen, and then we need to move on.

DR. COYLE: I wanted to ask you about the concomitant symptoms that have been identified post-

marketing, which I think in the report have been about 183 patients, which would be about 20 percent.

Do you have, is there any data of those 183 or so, how long the symptoms are lasting? Because there was a comment on months, and months, and months.

Is there any data on those concomitant symptom group?

DR. HOET: Well, this is post-marketing data that have, effectively, elements on the post-marketing duration for certain of these symptoms.

The best way to analyze this data, the post-marketing setting, is -- the best way to analyze this long-term follow-up, it is always difficult, in post-marketing settings to have this follow-up, and to look at them.

So it is a good practice to go back to more standardized and controlled elements. And what we have been doing is looking back to these kinds of symptoms into the efficacy study. And when we have been doing such an analysis we have been found that a certain percentage of subjects effectively have long-term, long-lasting adverse event in the vaccine group.

But this was not statistically different from the placebo group. And so, effectively, some of these adverse events that have been reported, either

in the post-marketing surveillance, or in the clinical studies, last for a long time, but this is not longer than what is observed in the placebo group of the efficacy study.

CHAIR DAUM: We are going to take two more questions. Dr. O'Fallen, please, I'm sorry for butchering your name before.

DR. O'FALLEN: It is not the first time.

The pregnancy registry, and the comments that I've heard really disturb me. You've made it sound as though you find no consequences, and yet you summarize, in one situation, that you know the outcomes of only 13 of 30 pregnancies, and in 4 of those 13 pregnancies the outcome was an abortion.

I don't consider that to be showing no pattern of anything. I think you have very little data and those kinds of statements I think should be made much more reluctantly than you seem to be making them.

DR. WHEADON: I'm David Wheadon, Vice President of Regulatory Affairs at Glaxo Smith Kline. A pregnancy registry is certainly one of the things we standardly do with any newly introduced drug or vaccine.

I think the statement is that to date, in

terms of the pregnancies that have been reported to us, we've not seen anything that is unexpected.

So certainly spontaneous abortion, within the context of pregnancy, in an overall population, is not something that is unexpected. And I think that was, indeed, what was intended to be said by the conclusionary statement.

CHAIR DAUM: Do you want to follow up, briefly, very briefly?

DR. O'FALLEN: What is unexpected is the rate of abortions, 4 out of 13.

CHAIR DAUM: Dr. Ferrieri, please, and then we will move on.

DR. FERRIERI: Dr. Kahn, could you clarify for me if you have revised the package inserts since licensure, the language of change in the package insert, and the information prompting any changes, if such changes took place?

DR. KAHN: At this time we've just seen a review of the post-marketing experience. And the two categories that Dr. Hoet discussed.

I think what we are talking about, first and foremost, we have discussed with the FDA the possibility of this, there has been no submission on this, so we are not even at the point of saying that

one is warranted.

But certainly the post-marketing experience has allowed us to better describe or characterize the early onset, the early reactogenicity in terms of their concomitant reporting.

But I don't think we see it as different from what was reported in the package insert to date. The hypersensitivity reactions is another issue that we will be discussing.

CHAIR DAUM: Thank you very much. We will now conclude the sponsor's presentation, and move back to additional presentation from the FDA.

Before we call on Dr. Robert Ball, I would like to ask Dr. Karen Elkins to come up, who had a couple of remarks for us, that sounded like they might clarify some earlier confusion.

And once Dr. Elkins is done -- that would be fine, they will turn it around for you.

DR. ELKINS: Just to offer a few clarifications in return to the questions that were rattling around on the subject of animal models.

There is a long history of using both mice, hamsters, and dogs as animal models for lyme disease, and perhaps others that are familiar with this literature might want to comment as well.

In regards to the C3H HEGJ mice inbred strains of mice were surveyed about a decade ago, in a systematic way, by several investigators, including Eulick Shadley and Max Simon in Germany, with the finding that HEJs appear to be unusually susceptible to the development of arthritis after infection with borrelia.

There was some hint that there was an association with the H2 type of the mice, but there are certainly examples in which mice having the same HL, or H2 alleles, as HEJs, were not particularly susceptible to the development of arthritis.

They have been studied extensively for the pathogenesis, and I think it is fair to say that the mechanism of development of that arthritis is not well understood, there has been data presented that that suggests that it could be related to the development of both CD4 and CD8 positive t-cells that recognize OspA.

But it is, at this time, I think, an open question. The -- with regard to the question of whether vaccination with OspA has been studied in mice, instead of the HEJ model, I think this has been best examined in transgenic mice, in which the HLA 0401 allele, I believe, was introduced as a transgene

into mice.

And I think that it was initially on the 129 background, and then those were back-crossed on the B10s. And those were intended to be the model, if you will, for genetic control of development of arthritis in animals.

However, when those transgenic mice were infected, they did not develop fulminate arthritis, as I understand it. So that model has not been pursued, and I'm not aware of studies using recombinant OspA, or any recombinant proteins that have been studied in those mice, or at least reported publicly.

Now, the hamsters have also been used to study the development of arthritis following fulminate disease, and there has been one study reported looking at vaccination with recombinant OspA followed by infection.

And I believe that speaks to Dr. Griffin's question. These were an inbred strain of hamsters that I believe are LSH hamsters, and I know absolutely nothing about the HLA types of a relationship between the HLA types in the hamsters, and in humans.

But these hamsters, also, are fairly susceptible to the development of arthritis after infection alone.

One study from Ron Schmells in Wisconsin vaccinated mice with, I believe, 30, 60, or 120 micrograms of recombinant OspA, this was a home brew preparation of recombinant OspA that was absorbed to alum, but it was not the LYMErix product.

And the group reported that mice that were vaccinated with OspA did not get any observable hind paw swelling. But that when challenged with borrelia, 11 or 12 days, I believe, after vaccination, there was an increase in hind paw swelling, compared to those that were only challenged and not vaccinated.

There were a couple of features of that particular set of experiments that may or may not be relevant to the vaccination situation. First the time interval between vaccination and challenge with borrelia was very short, either 11 or 12 days.

There was sub-dose response data presented. The 120 microgram dose, I believe, showed less change with challenge than the 30 or the 60 microgram dose, which was a little peculiar.

And the other way around, that is, challenge followed by vaccination with purified protein was not reported.

CHAIR DAUM: Thank you, Dr. Elkins. Will you be around later in case people want to question

you further about that?

We will now introduce Dr. Ball to give us a report on the VAERS data from the FDA.

DR. BALL: Good afternoon. Today I will be speaking about adverse events reported to VAERS following LYMErix, and then briefly discuss our plans for follow-up studies to evaluate the safety to the vaccine.

Before I get into the details of the adverse events reported after LYMErix, I would like to give a brief introduction to the vaccine adverse event reporting system.

It is a national system for surveillance of adverse events after vaccination, and it receives about 11,000 reports per year. It is jointly managed by the FDA and the CDC.

Reports are received from health professionals, vaccine manufacturers, and the public. Anyone can submit a report about any event, and all reports are accepted into the data base.

This effort to cast a wide net results in both causal and coincidental events being captured. All death and serious reports, which are defined as events requiring hospitalization, prolongation of hospitalization, life-threatening illness, or

permanent disability as defined by the reporter, receive follow-up to obtain missing information, and when possible, detailed medical records.

Death and serious reports are reviewed by FDA medical officers upon receipt. VAERS is used to detect unrecognized adverse events, to monitor reactions, to identify possible risk factors for adverse events, and to conduct vaccine lot surveillance.

Surveillance systems such as VAERS are subject to many limitations. They include the fact that reported diagnosis are not verified if medical records are not included, or obtained in the follow-up.

There is lack of consistent diagnostic criteria applied to the reports. Reports are coded using a system called COSTART, which I will describe in a little more detail later.

There is a wide range in data quality. The reports range from brief descriptions to complete medical records. There is underreporting, although the amount of underreporting is unknown.

There is inadequate denominator data. We have information on doses distributed, not doses administered, and there is no data on the demographics

of vaccine recipients, in particular, age or gender.

And there is also no unvaccinated control group. So as a result it is usually not possible to asses whether a vaccine caused the reported adverse event.

I just want to show you the VAERS form, and I've highlighted the block 7. This is the block that is available for reports to describe events, and oftentimes this is the only information that we receive from reporters.

So given the limitations of VAERS, how do we use the system? We use it by describing characteristics, and looking for patterns to detect signals of adverse events that could be plausibly linked to a vaccine.

We do this by looking for unusual clustering by age, gender, time-to-onset, or dose. We examine positive rechallenge reports, which are defined as reports in an event after one dose, with the same event following subsequent doses.

And then we also examine symptom codes and clinical characteristics for unique or unusual patterns. We also evaluate the biological plausibility of a vaccine adverse event relationship, look at pre-existing conditions, and concomitant

illness and medication use that can also influence the adverse event.

But signals detected through the analysis of VAERS data almost always require confirmation through another type of study.

As I mentioned, there are no standardized case definitions in VAERS. And we use a system known as COSTART. We rely on coding of reports by non-physician nosologists using the system.

Within COSTART coding depends on the use of certain words or phrases in a report. For example, a report would be coded rheumatoid arthritis, and simply if that diagnosis is mentioned in the report without confirmation.

The report might be coded arthritis, if the report mentions the word arthritis, or arthritic, and a report would be coded as arthrosis if the report mentions joint swelling.

As a result, reports with different degrees of diagnostic precision may have the same coding term. And coding terms must be interpreted very cautiously.

I will shift gears to reviewing the adverse events reported after LYMErix. Again, the purpose is to describe the characteristics and look

for patterns to detect events that could be plausibly linked to the vaccine.

We reviewed all reports from December 21st, 1998, which is the date of licensure, through October 31st, 2000.

And I'm going to describe, today, selected adverse events, including the death and serious reports, hypersensitivity reports, because they are known to occur after many vaccines, reports of facial paralysis, and reports coded arthritis, or arthrosis, rheumatoid arthritis, because of the association between arthritis and lyme disease, and facial paralysis and lyme disease. Also reports mentioning lyme disease.

I am also going to discuss selected potential risk factors, including self-reported HLA types, and self reported history of lyme disease, because of the theoretical concerns of increased susceptibility to arthritis in these groups.

So from December '98 through October 31st, 2000, there were 1,048 reports in VAERS with approximately 1.4 million doses distributed. The vast majority of those reports occurred after lyme vaccine alone, there were no other simultaneously administered vaccines.

There were four deaths reported to VAERS, 85 serious reports, which were defined as hospitalization, prolongation of hospitalization, disability, or a life-threatening illness as defined by the reporter.

And of the selected adverse events there were 22 reports of hypersensitivity specifically urticaria, or urticaria with respiratory symptoms. There were 133 arthritis type reports, 13 reports official paralysis, 16 reports of lyme disease, and there are 19 reports of people reporting DR4 HLA type, 17 in people reporting other HLA types, and there were 76 people reporting history of lyme disease.

I just wanted to emphasize that these events have a temporal, not necessarily a causal relationship with the vaccine.

This map illustrates the fact that the vast majority of the reports are coming from the mid-Atlantic and New England region, where lyme disease is prevalent, and probably represents use of the vaccine, although we don't have data on state by state vaccine administration.

This figure shows the frequency distribution of all VAERS LYMErix reports by calendar quarter. The number of reports is on the Y axis, the

calendar quarter on the X axis. The white bars represent report numbers by date vaccinated, and the black bars represent report numbers by date reported.

You can see that most of the reporters were vaccinated in '99, in 1999, although about equal numbers were reported in 1999 and 2000. And this suggests some delay in reporting.

And it could be the result of stimulated reporting, from media coverage, of adverse events after LYMErix which began around the end of 1999. Delayed recognition of a connection between an adverse event and vaccination, or delayed onset of an adverse event.

This figure shows the frequency distribution of all VAERS LYMErix reports by age and onset. You can see most of the reports are in 40 to 50 year olds. There were 7 reports in people less than 15, 34 reports in people over 70, which are outside of the recommended age range for the vaccine. This could reflect off label use, or errors in the reported age.

We don't know the age distribution of vaccine recipients, so we can't say if age is a risk factor for adverse events. We also know that about 53 percent of the reports were for males, 47 percent for

females. And, again, we also don't know the gender distribution of vaccine recipients.

This figure shows the time to onset of adverse events after LYMErix. And as you can see most of the reports are on the day of vaccination, or in the next few days. This is a typical pattern of time to onset reported for most vaccines in VAERS.

You can also see that we have some reports many days after vaccination, and I think the longest is about 300 days.

This figure shows the previous distribution by dose, most of the reports are after the first dose. This table shows the ten most common coding terms reported to VAERS after LYMErix. And the italicized terms represent events that were associated with the vaccine in the trial.

So that you can see that most of the top ten events represent events that were reported in the trial. I would like to caution that the definitions used in VAERS for these events, the definitions in the trials, could be slightly different.

Also many of these events are non-specific, for example, flu syndrome, and that is commonly reported after many vaccines.

There were four deaths after LYMErix

reported to VAERS. They included two men who died from autopsy proven cardiovascular disease; a 43 year old man who developed arthritic and neurological symptoms, which he attributed, or which the report attributed to LYMErix, and that person committed suicide seven months after the second dose of the vaccine.

An autopsy was conducted and did not report any findings that could explain the symptoms, although it is not clear, from the report, what type of investigation was done.

The fourth death was in a 69 year old woman who developed anemia and thrombocytopenia seven months after the first dose, and died six months later, an unknown time after the third dose, the diagnosis of myelofibrosis, and no autopsy was conducted in that case.

And these deaths represent temporal, not necessarily causal, associations with the vaccine.

There were 85 serious reports, 44 reports of musculoskeletal events, which I will describe a little later. There were 24 reports of a variety of neurological events, including 5 reports of cerebral ischemia that included three cerebral vascular accidents, two transient Ischemic attacks.

The median age in the people who had those events was 62, and events of this nature are common in that age group. There were also 5 reports of demyelinating events, two reports of optic neuritis, one 131 days after the vaccine, the other an unknown number of days after the vaccine.

Two reports of transverse myelitis, 10 and 13 days after the vaccine. And there was one non-specific demyelinating condition diagnosed 208 days after vaccination.

The remainder of the neurological events didn't fall into any single diagnostic category. There were also three hypersensitivity events, which I will discuss a little bit later, as well.

The remainder of the adverse events fell into a miscellaneous category with no clear pattern. This figure show the time to onset for the 24 hypersensitivity events, defined as either urticaria, or urticaria with respiratory symptoms after the vaccine.

And the two reports that are lacking represent a 39 year old woman who developed a red face, itching, and had the sensation her throat was closing within one hour of the second dose.

The second report was in a 39 year old

woman who experienced itching, hives, chills, myalgia, labored breathing, nine hours after the first dose. Both of these patients were treated with epinephrin and steroids, and recovered.

And the close temporal relationship in the specific clinical symptoms and signs in these reports, and the other, or some of the other urticaria reports, makes a causal relationship with the vaccine plausible.

The next exam reports coded arthritis, arthrosis, or rheumatoid arthritis, because of the link between lyme disease and arthritis, and the theoretical concerns that have been discussed.

Here we see the reports of thirty conditions by calendar quarter vaccinated in the white bars, and calendar quarter reported in the black bars. While most people who reported these conditions were vaccinated in 1999, more than reported in the year 2000, again suggesting delayed reporting, which could reflect either against stimulated reporting, delayed recognition of a connection between an arthritic condition, and the vaccine, or delayed onset of the adverse event.

As a remainder, in the pre-licensure trial there was on difference in the rate of arthritis in

the vaccine and placebo recipients. In the VAERS reports of arthritis or arthrosis, and rheumatoid arthritis, we looked for patterns by age, gender, and dose.

There is no substantial difference in age among the arthritis reports, but we did note two patterns that are illustrated on this slide. For arthrosis reports, which are reports of joint swelling, you can see a male predominance. When a female predominance would be expected based on the female predominance for the diagnosis of arthritis in the general population.

However, you will see that when we total all three of the coding terms, the gender is approximately equal between the two groups. We also found that for the coding terms arthritis and rheumatoid arthritis there was a predominance of these events occurring after the second dose, which persisted although slightly less for all the three coding terms.

And, again, this is not what would be expected based on the fact that most reports of adverse events after LYMErix were after the first dose.

So we further examined this dose trend by

looking at time to onset by dose for the rheumatoid arthritis, and arthritis coding terms.

And we did this because if the vaccine is causing arthritis through a common immune mechanism we might expect clustering of time to onset.

This slide illustrates the time to onset for the rheumatoid arthritis reports, the first dose report is in white, and the second dose report is in grey. And as you can see there is a wide range in time to onset with no particular clustering.

Similarly for the reports coded arthritis we see the first dose in white, second dose in grey, and third dose in black, we see a wide distribution of time to onset, with some clustering in the first week, but this is what we would normally expect for reports to VAERS.

And we also see some reports with delay onset, and those reports also did not cluster and range from 11 to 39 weeks after vaccination.

We wanted to address this issue further, so we tried to characterize the clinical symptoms and signs in the reports that were coded arthritis, arthrosis or rheumatoid arthritis, and see if they mentioned any of the five factors, joint pain, limited motion, joint tenderness, joint warmth or joint

swelling that is typically used for the diagnosis of an inflammatory arthritis, with joint swelling being the most suggestive.

So we see there that there are 58 reports that specifically mention joint swelling. And we further examined their time to onset by dose stratification and, again, see no unexpected patterns with a wide distribution of times to onset.

We also looked at reports of facial paralysis because of the association with lyme disease and facial paralysis. In the pre-licensure trial there was no difference in the rate of facial paralysis between the vaccine and placebo recipients.

In VAERS there were 13 reports. There was one unexpected pattern in that there were ten men and two women when we would expect approximately equal distribution based on the natural history of the disease.

Although, again, we don't know the distribution of vaccine recipients by gender.

We conducted a follow-up survey of the 12 people who had reported as of October 2000 to further assess these cases. We were able to contact 7, 5 were lost to follow-up.

Four of the seven had concomitant illness,

including two with hypertension, one with hypertension and diabetes, and one with multiple cranial nerve palsies of undetermined ediology. That patient had headaches prior to vaccination which might have represented the onset of that disorder. Five of the seven have completely recovered.

We also looked at the time-to-onset of these reports and, again, we see a wide range of time-to-onset with a slight peak at four weeks.

Because of the theoretical concern of the association of the DR4 HLA type and treatment resistant lyme arthritis we further examined reports that included this information.

There were 19 reports that included the DR4 HLA type and 17 reports of other HLA types. The coding terms arthritis and arthrosis were more common on people who reported any HLA type, but the clinical characteristics and coding terms were similar in the two groups, and there was not a predominance of arthritic conditions in the DR4 group.

There were more reports after the second dose for both of these groups, but the time-to-onset was reported to occur over a wide range.

We also looked at the 76 people with the self-reported history of lyme disease, and here you

can see their coding terms. We compared that with the ten most common coding terms for all reports, and what you can see is that there is some shifting in the order in which these coding terms occur, but the overall pattern is similar between the two groups, suggesting that people with a self-reported history of lyme disease report similar events, as others after LYMErix.

There are also 16 reports of people who reported they developed lyme disease after vaccination. The clinical characteristics in coding terms were consistent with lyme disease in this group.

Fourteen of these people developed lyme disease after their first or second dose, before completion of the vaccine series, and may not have achieved adequate immune response, possibly resulting in acquiring natural lyme disease.

A few of the reporters were concerned that the lyme vaccine had reactivated a previous lyme disease, or somehow influenced the course of lyme disease. But it is not possible, from the reports that we have, to evaluate this.

So, in summary of the VAERS analysis, VAERS has limited ability to asses the causal relationship of adverse events in vaccines. However,

hypersensitivity reactions reported to VAERS are common, but can be plausibly linked to LYMErix because of their specific timing, shortly after vaccination, and their clinical features, specifically urticaria and allergic respiratory symptoms.

The question of the association of arthritis with LYMErix cannot be resolved with VAERS data alone, although the reports of arthritic events reported to date do not provide clear evidence of a causal association.

We are attempting to gather additional information on people who report joint problems following LYMErix by conducting a telephone survey. We are looking at events that have been coded as arthritis, arthrosis, rheumatoid arthritis, joint disease, or arthralgia, in order to obtain detailed information about the events including medical records.

We intend to look for patterns of unusual disease or laboratory values in these reports. We also want to confirm the diagnosis of arthritis for a case control study, which I will discuss in a moment.

And as of last week we have completed 35 of approximately 200 planned interviews.

We want to further study this question by

conducting a case control study based in VAERS. We will use arthritis cases confirmed by the survey, and compare them with two control groups, also identified through VAERS, that would include arthritis cases reported following other vaccines, and events other than arthritis reported following LYMErix.

Our intent at this time is to conduct high resolution HLA typing in all three groups, and test for t-cell reactivity to OspA and LFA1.

Probably only a very strong risk will be detectable in this study, because of the relatively small numbers of arthritis reports in VAERS. But if the results are suggestive of an association additional studies will be conducted as needed.

At present the protocol for this study is still in development.

So, finally, our plans for continued safety evaluation of LYMErix include continual monitoring of VAERS reports, conducting a VAERS based telephone survey, a planned case control study to further evaluate joint problems following LYMErix.

And, of course, the results of the maintenance sponsored phase IV study will be very important to help evaluate safety concerns.

I would just like to acknowledge the

others at the FDA and CDC who helped to analyze this data. Thank you.

CHAIR DAUM: Thank you very much, Dr. Ball. We have a few moments for questions regarding Dr. Ball's presentation on the VAERS data. Ms. Fisher.

MS. FISHER: Dr. Ball, you stated that it does not provide clear evidence for an association with arthritis, but it must be enough of a concern for you that you are doing further studies, I see.

Is there any plans, in the one control group, arthritis cases reported after other vaccines, are you going to be looking at the genetic profile of those individuals to see if, since 30 percent, I think the DR4 allele, is there going to be an attempt to look at whether or not there is some sort of an association?

DR. BALL: The idea behind the case control study is to look at HL type in both the cases who develop arthritis after lyme vaccine, as well as the two control groups. So we will try to address that.

CHAIR DAUM: Questions, comments?

(No response.)

CHAIR DAUM: Okay. Well, the -- you must

be hungry. Thank you, Nancy, for reminding us of basic biology here.

It is now 12:28, coming up on 12:30. We will take a break for lunch and reconvene in one hour, at 1:30

(Whereupon, at 12:30 p.m. the above-entitled matter was recessed for lunch.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:35 p.m.)

CHAIR DAUM: Good afternoon, we are back in session. Committee members needing a jolt of caffeine will be pleased to know that a new pot of coffee will be forthcoming in a few moments, we hope.

We turn now to the -- everybody sort of settle down, please. We turn now to the open public hearing portion of today's session. As of last count we have 17 people who have indicated a wish to speak.

We are going to have to move on a strict schedule because we need to have time for the committee to digest, deliberate, and then discuss all of the data that they've heard today.

So I'm going to be a little more ruthless than usual about asking people to adhere to the time limits that we've all agreed to, and mentioned before.

What I'm going to do is to call three speakers names in a row, and asking one to begin, and the other two to sort of get ready. The options are to use the microphone that is just behind the committee tables, near the cameras, or to use the podium. Either is fine, but the same time limit applies, and I would appreciate your cooperation in that regard.

So the first speaker is going to be Karen Vanderhouf Forschner, who I know is up here already. The second is Stephen A. Sheller, I hope I'm not butchering anybody's names, I apologize if I am. And the third one is Jenny Marra.

So let's begin with Ms. Forschner, please.

MS. FORSCHNER: Good afternoon, and thank you for having me here. I'm with the Lyme Disease Foundation, which is the only national lyme disease group meeting federal standards as national.

I have a disclosure to make. We have always supported vaccines, throughout the Foundation's history, funding vaccines, and encouraging their development. We have testified at FDA and CDC meetings for this.

We also received, this year, a grant of 120,000 from SmithKline Beecham, which is part of a matching grant challenge from 1999, and there will be additional donations for the year 2000.

We have, I'm the mother of a child who had lyme disease, who died of lyme disease, and I have not taken the vaccine, though I was willing to enter the trials.

And my daughter, who was born subsequently, is healthy, and we were going to have

her on the trials, too, though she was sick.

We have concern over the scientific evidence and criteria being not completely scrutinized and published. We are concerned about the closed loop and difficulty of other opinions and scientists getting into these government discussions and looking at the data.

We are concerned about conflict of interest. We know that there were HLA studies done, from what we understand, in phase II, we haven't seen it. There is significant amount of research that has been done, much to SmithKline Beecham's credit, that hasn't been published, unfortunately.

We are concerned about informed consents to patients, both with prior lyme, and on the HAL issues. There has been data compiled for adverse outcomes. We are concerned that the data that was captured before is still the same data that you are capturing now, and may not actually represent what is actually happening to the patients out in the real world.

We are concerned about the definitions used for vaccine failures. We are concerned about definitive lyme, and probable lyme, probable lyme I haven't seen anything up here on the screen.

We are concerned about the misuse of the vaccine in people that are older, and people under current treatment for lyme disease. We have concern about patients not being able to get into the VAERS system, which we have been hearing for years, for adverse events.

Doctors and investigators not reporting their patients as having problems, and fear of patients getting the vaccine from family practitioners, that they don't want to go ahead and say that they've had problems, it might affect their relationship long term.

As you know the science in the vaccine, and I'm giving the committee a tape, is 36 percent of the patients in the trials remain zero negative. Those were the ones that were culture and PCR positive, which means there are some people that will be zero negative, and may fall through the cracks.

We are concerned that only 60 to 70 percent of those people had EM rashes. I have four exhibits to show you. I think you can still hear me as I move over here.

As you know, in '93, there was -- and this material is just the front page of the material provided to the members here. In '93 there was an

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As you know, in '93, there was -- and this material is just the front page of the material provided to the members here. In '93 there was an

was published in '97 that showed that the vaccine may cause a state of partial immunity. I'm not saying that this is actually happening. I'm saying that this was in the scientific literature, and it was in the debate at the time. Did this translate to informed consent to the public?

What is happening out in the real world, even today, is patients are not getting into the system, they are having trouble reporting to their doctors, and they are having trouble. So there is an example of a letter that went in that my doctor would not report me as an adverse event in the trials.

And finally one that was, second to last, one that was more recent, and more home for me, since it is in my own home town, this patient had a doctor who gave him the LYMErix vaccine in the second week of treatment for lyme disease.

Three doctors in the practice had said it was perfectly safe to take it while you have active lyme disease, and actually gave it to the patient. In other conversations with the doctors, separate from this, they had indicated that they felt under pressure since they had invested so much in the LYMErix vaccine to actually use it, and get it off the shelf.

Finally, there is an issue of cost

effectiveness of the vaccine. The letter to the editor said, maybe instead of treating everybody in a large region to prevent it with a vaccine, with risks that still indeed continue to be questioned, maybe it would be better to treat just that small population that had a tick bite, and treat the tick bite with 15 dollars worth of antibiotics.

Right now I weigh the question about the vaccine myself, since I lost my son, and I would like a vaccine. I'm done. What I'm concerned is that right now I protect her with tweezers, and if she actually were ever to need it, I would ask for antibiotics. But right now I do tick checks, and I use tweezers.

And I'm afraid that this is a vaccine that may be a very good vaccine, worthy of all of our support, that has a bad reputation, or a vaccine that may have actually slid through the system on science that didn't quite build it up, and may not be worthy of being there.

And I think it is owed its due to get the answers verified.

CHAIR DAUM: Thank you very much, Ms. Forschner. And we will next call on Mr. Sheller, then Ms. Jenny Marra, and Dr. Sidney Wolfe. Mr. Sheller

represents, or is associated with the law offices of Sheller, Ludwig, and Bodey.

MR. SHELLER: Thank you. You know, sometimes I feel you are like a jury here, that is going to only hear one side of the situation. My recommendation to you is that for your next meeting you invite some speakers who can portray to you additional information.

For example, Dr. Rose from the Dupont Children's Hospital. You might even consider inviting the chief surgeon from the hospital, who was knocked out of surgery because he participated in a trial and got arthritis from it.

So what I'm suggesting to you is let's consider this committee having the full kind of flavor, instead of just five minute talks by a bunch of people, from at least some scientists that they can portray, give very good questions, you've asked tremendous questions, and I appreciate the effort you are making.

But let's have a trial where you get to hear the whole case. In any case I'm here to urge this committee to recommend the moratorium, if not withdrawal of LYMErix, or at the very least recommend substantially enhanced warnings for the vaccine.

With spring quickly approaching the time for action is now. People who started the vaccine schedule last year are coming due for their third shots, and additional people may start the vaccine schedule with their first and second shots very soon.

Therefore the committee has a chance now to save some people. And you can do your job by doing it right away. And I will give you some examples, but you are going to hear a bunch of people testify, and I prepared a document which you have, which outlines a bunch of papers, and materials, and I hope that you read it.

We put a lot of time and effort into it, and we try to bring you some expert testimony, but unfortunately we were not able to get the people to come, who had information, because they said for five minutes I can't just come here and do this.

Now, keep in mind this. And this is something I'm adding. I heard Dr. Ball talk about the study he is doing. I appreciate he is doing a study, I'm disturbed that the FDA waited all this time to get around to doing it.

But most importantly the numbers, and I think there is a chinese fortune cookie that says, when all else fails, manipulate the numbers. But

apart from that, I don't mean to joke, this is very serious.

But what I want you to do is keep in mind that there are 1,076 adverse events as of October 31st. There were, supposedly, 1,450,000 doses distributed.

I don't know what the word distributed to me is, but I know from doctors who have the vaccine, it is sitting on their shelves in a lot of cases. So my guess is that there are a lot of doses distributed that haven't been injected into any patient.

Equally important, the adverse event reporting system only captures a very small percentage of adverse events. And this has all been said, and there has been delayed reporting of a number of adverse events.

So you have 1,076 events -- and remember, most people get three shots, some as many as five. My guess is those -- you may have 100 to 150,000 people, at most, vaccinated. We have found that the real problem seems to occur after the second shot.

We have also found that a reaction on the first shot, and I've gotten calls from over 200 people, we don't advertise, we don't solicit, these are clients that I represent, some of them extremely

seriously ill.

And I'm just saying to you, if they have 1,076 adverse events as of October 31st, do some quick numbers in your mind, multiply it by 10, at least 10. That is 10,000.

Assume that may be 100,000, 150,000, build it up if you want, but just do some quick numbers, add some lag time to that, you've got an awful lot of adverse events being reported here, an awful lot.

And you ought to take a real close look, because the system for collecting adverse events doesn't really tell you much. In fact that is what I heard about the studies being done by SmithKline. They draw conclusions without revealing how many shots were administered, which is key, I'm telling you, it is after the second and third shot that people really get -- and you will hear that today.

What else you will hear is that there are studies that are being done. And not only by SmithKline, and you need to invite these people to speak to you.

I'm trying to get all this in, in five minutes. One of the worse things we've seen is physicians are failing to recognize adverse reactions to those first and second shots, very serious problem.

We have some poor client in the -- and what they do is they then get the third shot, even though they are suffering some adverse event, and then they are wiped out.

But, for example, we have seen people being -- we have one client from Peoria, Illinois, who was told that he needed his coccyx bone removed, and he had a reaction to the vaccine. The doctor had no inkling that is what was going on. He was operated on, developed osteomyelitis, and he is finished.

We have other clients who have gotten carpal tunnel syndrome diagnosis, and had operations on their hands. The doctors aren't being given information in the labels, they are not being able to properly be warned.

You can't get a -- you know how labels work. Most doctors say they read it, but they look at the warning section, and then they stop. And if these things aren't in black boxes, this HLA situation for example, I think is key.

And I see what SmithKline said, basically today, and I see you -- the HLA situation has not been adequately studied. Dr. Steere is studying some of it, but I refer to a case in our papers, where Dr. Steere does some peptide blood work, but he says in

his studies, you are supposed to do synodal fluid to find out about that.

And I mentioned that. Now, why? And you will hear one of these patients talk about their synovial fluid, even though swelling was never tested. And they were diagnosed as having an event, by their treating physician, relating to the vaccine that is extremely serious for them.

Thank you.

CHAIR DAUM: Mr. Sheller, thank you. We next call on Ms. Jenny Marra, followed by Dr. Sidney Wolfe, and Ms. Kathleen Dickson. Ms. Marra?

MS. MARRA: My name is Jenny Marra, I'm a hospice nurse from New Jersey. I'm also a LYMErix vaccine victim. I have been living with severe joint and muscle pain since getting the vaccine in early 1999. I'm also HLA DR4 positive.

I would like to start by quoting the chairperson at the FDA committee that approved LYMErix, Patricia Ferrieri. "I might comment that this is fairly rare for a vaccine to be voted on with such ambivalence and a stack of provisos."

The entire panel had concerns about the long term outcome of this vaccine due to the fact that it had only been studied for 20 months. They were

also concerned about the theoretical possibility that this vaccine, made from the OspA protein, could cause an untreatable, incurable form of arthritis in 30 percent of the populations.

In fact, the head of the clinical studies, Allen Steere had said: "This is an issue of concern, on-going surveillance will be important."

Steere had published an article in Science Magazine on this topic five months prior to the approval of LYMErix. The article is in the vaccine victims packet I've given you.

SmithKline was so concerned with this issue that they had study participants sign a paper indicating the theoretical possibility existed that vaccine, that the vaccine might cause arthritis in certain genetically susceptible individuals.

Yet SmithKline did not include this information in the product labeling, or inform the health care providers of this concern. Had I known this I personally would not have taken the vaccine.

I have obtained the VAERS reports up to May 8, 2000. They are a little different than what I heard today. During this time there were 467 reports. Out of those there were 146 reports of joint pain and/or swelling.

I have studied these for over a month, and going by the wording of the complaints, noted pain in the joints, joint pain, swelling, arthritis, and that is all that I included, I didn't even include most that he did.

And as most of us are aware, 90 percent of the adverse reactions are not reported. So there are many more people that are suffering from this vaccine that we don't even know about.

SmithKline knowing this theoretical possibility, even went ahead and tested it on children before knowing the long term outcomes on the adults. To me this is outrageous. This just shows the heartless disregard that SmithKline has for the children and adults of this country.

This is pure profit motivation. It is the only way to explain the total lack of concern for the public. I have done TV and newspaper interviews to educate the public of the devastating effects of this vaccine.

From this I am contacted daily by people harmed by this LYMErix, some of which are here today. Others cannot make it because of the illness they have gotten from this vaccine.

I have been told by some that they have

tried to contact SmithKline about the reactions. They are put on hold until they give up and they just hang up the phone.

A few of the people were in the clinical studies. I have been told by them that they would go to SmithKline with different problems that were happening to them, and SmithKline would not document the reactions they were having.

One study participant, Lewis Ball, wrote a letter to respond in an article in the New London newspaper that states: "I am part of the original test group that got the vaccine mentioned in this article. On two different occasions I contacted Dr. Sisken with health problems that I wanted to be part of the record on the study, into the heading of possible side effects."

"I was told, on both occasions, that there was no column to file these health problems in, because they weren't expected. One involved sudden memory loss, and the other was much more involved."

In the VAERS report I have there is a 43 year old gentleman that you heard of earlier, that committed suicide seven months after getting this vaccine because the pain is so severe, and from being unable to get relief from 14 doctors he had seen.

I can relate to this man's pain, as can most of the 75 people I have spoken to, that have been hurt by this vaccine. Most of us agree that if it was not for the support of our families we would not -- we would have done the same as this vaccine victim.

This is how severe this pain is we are living with every day. We have all seen several doctors looking for help. Our health care providers are turning us away with statements like "I don't want to get involved".

That is what a rheumatologist told me and my husband a few months ago. This is the attitude a lot of the health care providers, these people hurt by the vaccine are dealing with.

This vaccine is not causing just some minor joint pain, it is destroying lives. It is destroying the lives of our most healthiest population. These people being vaccinated are healthy outdoor people.

They thought they were protecting themselves from a horrible disease. Instead they've gotten an even worse disease, one that cannot be treated or cured.

We all would have been better off getting lyme disease. SmithKline wants this vaccine approved

for children. I know a few children that were in the studies that have already been severely hurt.

From what I can gather, from the study participants I have spoken to, SmithKline's adult studies were tainted. How can we trust the children's study results?

I ask this panel today to recommend that this vaccine be stopped immediately. If you cannot pull it, at least put it on hold until the studies that you are talking about today are done.

It may be too late for us vaccinated, but it is not too late to stop the destruction of more lives. Thank you.

CHAIR DAUM: Ms. Marra, thank you. The next speaker is Dr. Sidney Wolfe, followed by Ms. Kathleen Dixon, and Ms. Kay Lyon.

DR. WOLFE: Thank you. This is the first time in more than 20 years --

CHAIR DAUM: Can you speak right into the microphone, Dr. Wolfe. Do you want us to help you adjust it?

DR. WOLFE: This is only the second time in the almost 30 years since I left NIH to start this group, that we have become involved in some vaccination or vaccine issue.

The first was the swine flu. And although there are a number of differences, such as the high mortality disease influenza was more meritorious generally, not the swine flu, but of having immunization.

But there are also a lot of frightful similarities. One is that in the case of swine flu, the vaccine caused an autoimmune disease called Guiembre.

Secondly, there was a gross overselling of the vaccine for what amounted to a few cases in Fort Dix, New Jersey, there was a recommendation for nation-wide immunization.

So those similarities are where I would like to start, and just simply say that when, and you all know this, when you evaluate a vaccine you have to look at the benefits, which are a function of what the risk of the infection is for someone, which in this case varies enormously around the country, and the effectiveness of the vaccine.

You have to look, obviously, at short term and long term effects of the vaccine. And, finally, in combination you have to look at the benefit risk ratio.

But equally important, and this was the

tragic lesson of the swine flu vaccine, one has to look, when one sees a very questionable immunization campaign such as this going on, about the implication and the negative effect on public health, generally, and on vaccinations in specific.

I mean, a huge setback was dealt by the really ill-conceived swine flu vaccine, and I'm afraid that already, and it may even be worse later on, with what is going on with this campaign, it will deal another setback.

As several people have mentioned, you voiced some concerns when this was discussed for approval in May of 1998. There is some new information since then.

If you go to a website called LYMErix.com, you see some extraordinarily reckless promotion of this vaccine. The first page shows backyard fun, golfing, gardening, pet owner outdoor sportsman, don't let lyme disease interfere with these activities.

You then can go on to another page and see that lyme disease, if you check the backyard for grilling, may be as close as your backyard. And there is a little cartoon movie there that shows someone in the backyard grilling, getting bitten with a tick.

You later get on to see a map of the

United States. We have complained about this ad, which is what it is, and hopefully -- the FDA has actually agreed to look into it.

Another problem related to the gross overuse, even if there were any appropriate use for this, is the failure right now for the labeling, and certainly the promotion to fall in line with the ACIP recommendations of 1999.

The ACIP recommendations stressed, very clearly, that it is a combination of where you live, and the kinds of activities you are engaged in. So that, for example, persons who live in a high or moderate risk area, it is not recommended that they get vaccinated if their exposure to tick infested habitat is minimal or none.

Anyone, regardless of what kind of activity they are engaging in, is not recommended as having a lyme vaccination if they live in the low to no, or very little tick kinds of areas.

Related to this is the labeling. And I think that one thing, aside from whether or not you believe a moratorium should be put forth, which I think a reasonable argument could be made for, the current labeling, outside from the advertising, is really off the wall.

Nowhere in the indications section is there any mention of geography. That is mentioned in a separate section on epidemiology. It simply says individuals most at risk may be those who live or work in borrelia burgdorferi infected, tick infected grassy or woody areas, landscaping, brush clearing, forestry, and so forth.

And it doesn't really get into the geography. Obviously you have to combine both. This label really needs to be changed.

Other new information is this very interesting study published in 2000, an animal model in hamsters showing that vaccinating them with this antigen, the OspA antigen, and then subsequently exposing them to the bacteria, the spirochete, developed destructive arthritis.

And in the conclusion of their paper they said OspA vaccine should be modified to eliminate epitopes of OspA, outer surface protein antigen responsible for the induction of arthritis. These are people from the state hygiene lab in Wisconsin.

There also have been thoughtful studies by the CDC, by Dr. Melsorn, an economist there, and by the IOM, raising serious questions about the benefit risk ratio on this. The IOM placed this whole idea in

what they call their less favorable category, the lowest ranking in priorities of vaccine development, just because of the fact that A, the vaccine is not extraordinarily effective; B, it is not preventing a life threatening disease; and C for most people a successful antibacterial intervention can occur not when you have a tick, but when you have some clinical symptoms that are suggestive of actually beginning to have lyme disease.

What recommendations would I make? Well, I think that the idea of surfing for a safer vaccine, if one is going to go ahead with vaccination to prevent this disease, certainly is a good one.

We have seen enough other instances, in the history of vaccines, where one comes up with an idea of a safer vaccine, and a safer vaccine is always better, particularly when the benefits of this are so questionable.

And, secondly, as I mentioned before, immediately require changes in the labeling, not just with respect to the indications, which are flawed, and missing entirely anything about geography, but also the warnings.

I think that the labeling should include a lot of information that is missing now, such as this

very, very worrisome animal study model for developing arthritis.

Secondly more information about the fact that HLA D4 has clearly been linked, in the case of post-lyme disease arthritis, as a risk factor, and it is reasonably likely that the same will occur here.

And, also, I think that in the labeling needs to be some explanation about some of the very well documented post-vaccine cases that you will hear about today, and which I think are clearly there. These are documented cases of arthritis in people shortly after they took it.

I think the company should be forced to send a letter out to all physicians reflecting the change in labeling that I hope you will recommend.

In conclusion, one sentence and I'm done, I think it is highly likely that the majority of people in this country who have been vaccinated with the LYMErix vaccine have had an unfavorable benefit risk ratio when they were vaccinated.

As a matter of public health policy it is important to do everything to minimize the damage that may be done from the use of this highly questionable vaccine.

CHAIR DAUM: Thank you very much, Dr.

Wolfe. We would like to request, again, one of our operating rules here is that there is no flash photography, please. I hope you will all respect that.

In an arrangement with Ms. Cherry, Ms. Dixon has been accorded seven minutes, two extra minutes.

MS. DIXON: My name is Kathleen Dixon and I am an analytical chemist from southeastern Connecticut. I would like to talk about the validity of the LYMErix adult trial, specifically the validity of the serological standard used, and how that standard affected the vaccine trial results.

The problem is the deer borne IgG standard. One of the testing procedures used in the trial, the western blot, looks for antibodies to specific antigens expressed by borrelia burgdorferi.

The limitation of the western blot is that it qualifies the body's reactions to the infection, but does not actually quantify, or identify the infectious agent.

In lyme disease patients produce variable antibodies over time. I want to point out the IgG response in these patients appear in a characteristic sequential pattern over months to years, to as many as

11 spirochetal antigens, the appearance of new IgN response, and the expansion of IgG response, late in the illness, and the lack of such responses in patients with early lyme disease alone, suggests that borrelia burgdorferi is alive throughout the illness.

And, again, Steere reports that in the body of the Dressler report, which I included in the data package for the FDA, the specific immune response in lyme develops gradually over a period of months to years, to greater than or equal to ten spirochetal polipeptides.

I want to point out here, of the 237 patients presenting, this is from the Dressler-Steere report, 54 met Steere's criteria for lyme disease, and these showed IgG criteria 0 causivity to 72 percent.

The majority of these were lyme arthritis patients, and arthritis patients always have a higher antibody response, it is supported in all the literature.

Back in 1994, '93, the CDC decided that they wanted to establish a new zero diagnostic standard. We assume it is to facilitate these vaccine trials. In May of '94, this was prior to the Dearborne Conference. The Dearborne conference was in October of 1994, members of the CDC met and decided

that the Dressler-Steere standard criteria for IgG of five of ten bands, should be the zero diagnostic case definition to be used in the vaccine trial.

And this shows the data sets that they chose, that the studied in the Dressler report, and it shows the bands representative from the arthritis data set only, and just ignored neuro brulliosis.

So the problem with the IgG standard is that they calculated that there should be five of ten bands, and that would be a 99 percent specific for borrelia burgdorferi. That was not empirically derived, that was not based on any patient data set. They never showed that, characteristically, 80 or 90 percent of all patients with lyme disease have five of ten bands.

This data, from this Dressler report, was generated by borrelia burgdorferi strain G-39-40, a strain which Barbara Johnson of the CDC later, at the Dearborne meeting, recommended not using.

And it artificially represents a summary of what the arthritis only presenting patients showed over time.

Dressler and Steere report, in the Dressler report, that individual specific bands, such as OSP A, B, C, 1893, and 28, generated from a B

strain G-39-40, are specific markers of infection.

Confoundingly, OspA and OSPB were left out of the Dressler IgG Dearborn case criteria. And, therefore, the Dearborne case criteria using the LYMErix trial, excluded to Steere, major immunogenic outer surface proteins from the case criteria, OspA and OSPB.

So we really don't know what Dearborn case definition means. It doesn't mean -- we really don't know.

But what this has affected is that Dearborn case definition misses a lot of patients. Instead of weighing the specificity of an individual band, such as OSPC or P93, both highly specific alone, it will result in the patients lost opportunity for early and successful treatment.

This was the previous sera diagnostic standard, according to the CDC. The third one says, significant change in IgM or IgG antibody response to borrelia burgdorferi impaired and acute phase convalescent serum samples.

Although potential useful in confirming active lyme, neither cultural isolation or paired serum specimen testing has been used much for validating cases of routine lyme disease surveillance,

since the procedures are not often performed in a general medical setting.

That used to be the case definition, changing bands over time. You saw that Allan Steere said that earlier, this is a borrelia, borrelia have antigenic variation, you show different antibody profile over time.

So we believe what -- how does this apply to the vaccine trial? If few people have lyme disease, and this is Dressler Dearborne criteria will exclude most patients with lyme disease, the vaccine will not be shown to be a failure, or cause adverse events. And we believe that is exactly what happened in this trial.

This is the New England Journal of Medicine report of the 1998 LYMErix trial. Only 22 people got lyme disease in the vaccine group in the first year, while there were 515 unconfirmed lyme cases, compared to the placebo group, of 468.

. The following year is no significant difference, but there were ten percent unconfirmed lyme cases in the vaccine group than there were in the placebo group.

As Dr. Luft alluded to earlier this morning, the western blot serology from these

unconfirmed lyme cases will need to be reviewed for evidence of other BB specific bands, and compared to the placebo group by an independent group of analysts.

If there are any other specific bands besides OspA the case must be counted as lyme disease in the presence of symptoms. Note that there were only two asymptomatic cases in the first year of the vaccine group, versus 13 of the placebo group, and in the following year there were zero asymptomatic cases, and 15 asymptomatic cases in the placebo group.

We believe that these results do not show that the vaccine is effective at preventing asymptomatic lyme disease, but rather that it is turning asymptomatic lyme disease into symptomatic cases.

Continued follow-up on these unconfirmed patients should have been with further western blotting from one of the CDC recommended strains, and the original case definition, which would be to look for changing bands, or any other specific bands besides OspA.

Or maybe one of these newer antigens D complexing messenger has been developed at SUNY and by Leonard Siegel.

We already discussed this earlier. It was

mentioned earlier that an adverse vaccine event can't be distinguished from vaccine failure. An adverse vaccine event in a previously infected asymptomatic lyme patient.

An asymptomatic BB infected adverse LYMErix event case may never be detected until the patient is vaccinated and symptoms occur, which we think explains the majority of adverse events regarding LYMErix.

Many previously infected lyme cases report systemic symptoms after vaccination, and many find out they had lyme disease after being vaccinated, becoming ill, being tested for lyme disease, and finding other specific antibodies.

The FDA should, therefore, not be looking just for arthritis as a potential adverse event, but rather -- and not to the exclusion of systemic illness.

According to Allan Steere the rate of asymptomatic infection to symptomatic infection is one to one. So that for every person walking around with lyme disease that has symptoms, there is a person walking around with asymptomatic lyme disease. And we think those people are at the greatest risk.

Vaccine failure and exacerbation of

asymptomatic infection are identical according to the patient data collected and on the on line VAERS data base.

The Dressler Dearborne Steere standard is not a valid criteria for assessing lyme disease, the former CDC criteria of changing bands is more valid. Until there is an independent review of the western blot data from the SmithKline Beecham adult trial, we have no idea how safe this vaccine is, it all needs to be retabulated.

Am I done? Okay.

CHAIR DAUM: Thank you very kindly, Ms. Dixon. We have next Kay Lyon, followed by Emily Biegel, and Lynn Lane.

MS. LYON: Good afternoon. I'm Kay Lyon from Windham Massachussets, a highly lime endemic area. I'm a member of a group advocating for lyme patient rights, and lead a line information and support group in my community.

In the past few months members of our group have read through much of what has been written on LYMErix, especially the material provided by the CDC and FDA.

Today I would like to present what we see as two realities. The reality facing my community in

Essex County, Massachussets, where children play in the woods, and on sand dunes where deer and field mice abound, and the reality constructed by SmithKline Beecham.

It appears from our research that the children of Massachusetts and elsewhere have paid a high price to clear the way for the approval and marketing of this questionable product.

How can this be, you might ask, when our children haven't been vaccinated? As our group reviewed the material from the government these facts were clear.

In spring of 1994 to enable clinical trials for LYMErix, SmithKline Beecham, the CDC, and the FDA held a special meeting to agree on a case definition for lyme disease. We just heard Kathleen talk about the changes that they made, which included a stringent serological definition.

In October of 1994 at another meeting in Dearborne, Michigan, these stringent serological criteria were extended to cover all lyme disease studies and serve as the official buyer for doctors to determine what they report as lyme to the CDC.

The CDC agreed to these criteria to help analyze data and report. But the criteria were not to

be used by doctors to make the diagnosis of lyme disease.

The CDC maintained that lyme disease was to be diagnosed based on clinical review of symptoms, patient activity, and possible exposure to borrelia burgdorferi.

Despite this recommendation by the CDC when making a diagnosis most pediatricians and primary care doctors refer to the CDC criteria for reporting in an extremely rigid way.

As a result our children get lyme disease and are not diagnosed and treated in a timely fashion. Many of our kids get very ill before doctors are willing to treat them with antibiotics.

And even then the majority of doctors are not willing to treat a child if he or she does not meet the serological requirements for CDC reporting of lyme disease.

The CDC's 1999 initial report recommending the use of LYMErix stated OspA was not expressed in natural lyme disease infection in humans, a statement clearly refuted in the 1998 FDA Hearing on which those recommendations were based.

Further research shows the CDC retracted that assertion some three months later, stating that

OspA, the antigen used for this vaccine, is in fact expressed with increasing vigor as natural infection disseminates.

In light of this correction we must ask that the agency also revisit the recommendation for the use of the LYMErix vaccine. This vaccine is made of recombinant outer surface protein A.

Despite the fact that the antibody reactions to OspA and OSPB are highly specific for lyme disease these bands were removed from the CDC criteria for reporting lyme disease.

This is a disaster for the children of Essex County, Massachussets. Outer surface protein A is expressed with increasing frequency as untreated infection disseminates.

And in Massachussets we see that many of our sickest children end up showing this band on the western blot. However, because of the CDC strict serological criteria the laboratories and the doctors they report to do not consider this band diagnostically significant.

We are concerned about the phenomenon of sera positive asymptomatic infection, which Allan Steere has stated occurs as frequently as symptomatic lyme disease.

In the last FDA Hearing on LYMErix Pat Coyle called this form of infection smoldering. Many have expressed concern that the vaccine might be a trigger that turns this smoldering infection on, converting it almost instantly into late stage disseminated lyme disease.

We also note that in the vaccine trial those whose sera converted were treated with the antibiotic, whether they had symptoms or not. This was, of course, the humane way to treat study participants.

But it is absolutely not reflective of medical practice in the real world our children live in.

In summary I am presenting to you two very different worlds. In the world in which my family and friends live we have children who live at risk in an environment teeming with the lyme disease spirochete borrelia burgdorferi.

We have doctors who almost universally will not treat lyme disease unless it has been confirmed by the faulty criteria set by the CDC for reporting lyme disease, created initially to enable this vaccine.

We have children who get bitten and are

never treated because our doctors do not understand the CDC recommendation that lyme is a clinical diagnosis, not a serological one.

We have children who get bitten and infected but are asymptomatic, unlike their counterparts in the vaccine trials, they are not treated and as Pat Coyle said, they are left smoldering.

Because of all of the above it is impossible for us to know which of our children are infected, and which are not. It is therefore impossible to gauge the true safety or efficiency of this vaccine, efficacy of this vaccine in this population.

It is also impossible to know which of our children, when challenged by OspA might have a dormant or subclinical infection rev suddenly to late stage illness.

On the other hand in the world of SmithKline Beecham data we do find LYMErix, we have an experiment whose success is based, in part, on a set of criteria created to enable the success of the experiment.

This is the proverbial circular reasoning scientists are supposed to avoid. There is a

significant gap between the world my family, friends, and I inhabit, and the world shown in data defining the study of LYMErix.

In light of this for parents everywhere I stand before you to say the gap must be bridged before we consider, even remotely, the notion of vaccinating any of our children.

Also, most importantly, the CDC's strict serological guidelines must be changed. Thank you.

CHAIR DAUM: Thank you, Ms. Lyon, very much. The next speaker is Ms. Emily Biegel, followed by Ms. Lynn Lane, and Mr. John Hardy. Ms. Biegel, please, thank you.

MS. BIEGEL: I'm Emily Biegel but I'm here to talk about my husband John. Some of you may have seen him come in with a walker.

John is an active outdoorsman and so I had the bright idea, a year or so ago, that he should -- that we should both receive the lyme vaccine. He had lyme vaccine on April 13th and May 11th.

He was frequently exposed to tick bites in his leisure activities, and we thought this was good idea to protect him, although as an aside I should say that we have labradors and golden retrievers, and do not give our dogs lyme vaccine because Cornell doesn't

recommend it.

So we made a decision for ourselves that we spare our dogs from. In July he started neurological symptoms which were initially diagnosed and Guiambari syndrome, and subsequently in September, when he was not responding, but continuing to deteriorate as chronic inflammatory demyelinating polyneuropathy.

And this, really, has -- it was just like floodgates opening to a nightmare that has turned our lives, and the lives of our friends, family, and work colleagues, upside down.

Six months later he has had four hospitalizations, a lot of atrophy, insulin dependence, depression, yeast infections, compression fractures, edema, tremors, and 25 plasma for reeses treatments.

It is a bitter harvest that we've reaped. His neurologist has -- the neurologist, not we, has reported this to VAERS as a vaccine adverse event. John is now profoundly disabled. He spent 33 years training guide dogs for the blind, walking ten miles a day, doing all kinds of physical activities like gardening in his spare time.

Now he does physical therapy, and he sits

in a chair with his feet elevated. He bought a kayak a few weeks before he got sick, and every time I look out in that backyard, at that kayak he has never had a chance to use, it is an ugly reminder of how our lives have been changed by a decision to do something that we thought would be helpful.

If you tell me that LYMErix is statistically safe to take I will tell you to imagine, for a moment, that you are John, and your life, your work life, your social life, your driving, everything that is part of your day to day functioning is taken away from you.

And then you will know that this is a terrible place to be, and the worst of it is that it could have been avoided. Thank you.

CHAIR DAUM: Thank you, Ms. Beigel. While I appreciate the sincerity and the effort that it has taken every individual on the program to come and communicate their views to the committee, I would ask that everybody hold their applause, because I think it is important the committee hear and digest, and that we have as much time as available, as possible available for this.

So if you would, please, listen and let's emote together, but let's hold the applause in between

speakers.

Ms. Lynn Lane is next, followed by John Hardy, and Pat Smith. Ms. Lane, please.

MS. LANE: Hello. I have handed out several copies of the original story about my lyme disease vaccine trial study experience. There are more available if anybody is interested.

I will go back a bit to tell you that I was doing okay managing my lyme disease, which I was unaware I had, until the shots began. Little lumps formed on my kneecaps, and dark discolored patchy rashes were visible on the inside of both knees.

Increased connective tissue pain radiated from all points along my spine in waves that migrated to different areas, mostly the left side of my body. Brain fog, paranoia, anxiety, heart pounding, slurred speech, heightened sensitivity to light and sound, visual overstimulation brought on migraines, nausea, vertigo, etcetera. My balance was off most of the time.

Grocery stores, malls, driving at night were all impossible to do without getting sick. Meanwhile, my children now ages 8, 15, and 17, and my husband, all with diagnosed chronic lyme disease are prone to waves of most all these symptoms and more.

Everyone of us has symptoms seemingly dependent on location of tick bite, and number of times bitten over the years.

If I were not directly aware of both sides of this vaccine issue, I would likely have had all my children vaccinated with LYMErix. Thankfully this will not be so.

My husband and I heard about the SmithKline Beecham lyme disease vaccine trial studies on a local radio station in 1995, offering 350 dollars to each participant. We never received any money, I don't recall why.

We unknowingly had been living with lyme disease for years. Tested western blot negative we received all three shots. The symptoms that followed from the second shot on has devastated our lives.

I sure would like to know if my husband is considered to be in the 78 percent effective group. He has managed to work over the last four plus years, but not without pain and suffering ever since the LD vaccinations.

SmithKline could not find his records. He works outside every day and is a living testimony as to why no one would choose the vaccine if they knew of his adverse event, especially outside workers.

I have brought all my symptoms to the attention of both the doctors of SmithKline Beecham, and the investigative doctors involved with the study. They denied my symptoms even existed, and broke their own rules, within the written consent form.

That was not their right. When considering money and reputation they have much to lose. I can only hope the truth will prevail. Please acknowledge what is happening to others who have now received the FDA approved vaccine.

Before approval my complaints about the lyme disease vaccine seemed not to represent enough people. Unfortunately, I'm sorry to say, that is no longer true. Thank goodness I found a lyme literate doctor, and more than enough up to date information and research on lyme disease than I could fathom would be available.

This has empowered me to go back to the fact that doctors only practice medicine. A good patient is someone who learns about the disease him or herself, and then helps the doctor.

The doctor must be willing to learn about the disease along with the patient. If not up on the latest information, then behind the times. This concerns both sides of the issue, not just the ones

with the most monetary values.

We live on Cape Cod in Massachussets, which is considered an area highly endemic for lyme disease. I personally believe it is an epidemic proportion now. Antibiotics have, undoubtedly, helped me to gain back some of my former self. But this continues to be a long, daily, and painfully difficult task.

I wish I were back to just living with lyme disease. This vaccine has already harmed many lives. Please do not do this to our children too.

I profoundly suggest complete termination of the LYMErix vaccine until further research can develop reliable tests, and better diagnostic tools.

Thank you for listening.

CHAIR DAUM: Thank you, Ms. Lane. We would like to next hear from Mr. John Hardy, then Pat Smith and Lori Gelbart. Mr. Hardy.

MR. HARDY: Good afternoon. I'm John Hardy, I'm 65 years of age, live in Georgetown, Delaware, and I'm retired from AT&T as a fuel engineer.

I've always been very active in playing golf, hunting, fishing, camping, traveling, and working in our garden, along with taking care of four

grandchildren ages four to nine.

I have been in excellent health until April of 2000. During my physical in 1999 a discussion with my physician about receiving a vaccine for lyme disease due to my outside activities, I received my first and second shots in April and May of 1999 with no side effects.

I received my third shot on April the 18th of 2000. The following week I couldn't get out bed with stiffness in my hips, neck, ankle, knees, and couldn't close my hands to make a fist.

I made an appointment with my physician, the doctor gave me some reflon, and sexlon, and sent me in for blood work. The lab work showed no lyme disease, showed a high segregate for rheumatoid arthritis.

I asked them about the vaccine I had received, and he said he never heard of any side effects. He referred me to a rheumatologist. The rheumatologist had more lab work done, and put me on solvrex, predazone, placmanil and flexarol.

My stiffness has slightly improved over the months, but I still have stiff joints, mainly in my knees, my ankles, my hands. My latest blood work has shown no inflammation in my system now, and I was

tested for genes HL4DR4 and DR2, which were negative.

I really believe that this vaccine is unsafe and should be tested further. SmithKline should also have some accountability with reversal of autoimmune arthritis.

If the FDA does not take this vaccine off of the market they need to have SmithKline relabel all packaging and educate all physicians with all the potential adverse reactions.

This vaccine should not be approved for children 15 and under until all further testing is completed. It is the first time in my life I've had to rely on, or take medication, in order to function in my daily living.

Being a better informed consumer is a right, not just a privilege. Thank you.

CHAIR DAUM: Thank you, Mr. Hardy. We call next on Pat Smith, who is up at the podium, to be followed by Lori Gelbart and Linda Scharf Lurie. Ms. Smith, welcome.

MS. SMITH: Thank you. Mr. Chairman and Committee Members. The Lyme Disease Association's mission is lyme disease education, prevention, and research funding.

So one might automatically assume were

favorable to a safe and effective vaccine for lyme disease. That is certainly a valid assumption.

The Association's board consists of patients, and families of patients, all of whose lives have been personally touched by this disease, and all who are dedicated to preventing others from experiencing the physical, mental, and emotional devastation lyme disease can produce.

To that end we fund national research projects, sponsor medical conferences, and continue to work with members of Congress, developing federal legislation, providing 125 million dollars for lyme disease research, physician education, and prevention.

I am here today because we do favor a safe and effective vaccine. But we are unsure as to whether an OspA based vaccine can meet those criteria. Since the inception of OspA vaccine trials we have heard from individuals experiencing difficulties after immunization.

The information was startling, not only because of the problems described, but also because of the parent doctors incomprehension of those problems.

At a vaccine meeting sponsored by the LDF where pharmaceutical reps were discussing how well the trials were going, I questioned, without satisfaction,

the issue of these trial patient complaints.

After vaccine approval LDA received inquiries about the vaccine. Many from individuals who had received all or some of the vaccination series. Most proceeded to talk about the symptoms they developed subsequent to receiving the vaccine.

When asked if they had reported this to the administering doctor, and if the doctor had reported the adverse event, the usual response was that the doctor did not take the complaint seriously, or did not think that these symptoms were related.

Sadly none were aware of the HLA DR4 situation. And several were in the midst of the immunization series, and did not know whether to continue taking the shots.

Some called to ask if they should get the shots if they had had lyme in the past, a question which appears to have no clear answer, particularly in light of the unreliable antibody response test used to determine who has, or who had lyme disease.

A few insisted they had gotten full blown lyme from the shots. And after further discussion indicated that they had had lyme disease in the past.

I want to share an email that I received on Monday, and this is a quote. I live in Wisconsin,

I received your name from person X who told me you may be able to give me some direction. I received two vaccines in the spring of 2000.

A couple of days within the first shot my neck and higher back stiffened up severely. In a month I went back for the second shot, and asked the nurse and doctor to check for side effects before I took the second. They informed me there were none.

I took the second dose and the problem with my neck and back worsened within a couple of days. My family doctor gave me anti-inflammatories, but they did nothing.

I have tried a chiropractor, but the only relief was for a couple of hours. Never tried one before but I'm getting desperate. Then I went to an orthopedic, and I am now on anti-inflammatories again, but not helping.

He told me I have a disk that is somewhat smaller than the others in my neck, and maybe the vaccine somehow aggravated it. Prior to the vaccine I have had zero neck or back problems. I am looking for treatment somehow, some way.

I called him, he is 39 years old, he asked me to help him, he wants treatment for whatever he has.

Today you are hearing about how this vaccine has physically impacted human lives. It appears that little can be done to stop whatever process triggers some of these reactions. Or if something can be done it remains, as yet, undiscovered.

I listened to the despair and bewilderment of those adversely impacted. How can this happen from a medicine to keep me from getting sick, who can help me get better?

I can only comfort them, as I do not have any answers, and I don't know of anyone who does.

This Committee has the authority to formulate recommendations that may prevent others from potentially suffering the same fate. You can revisit the original data and research which appears to show a link between OspA and adverse reactions, and view it in light of the adverse events you've now heard about.

You can recommend further studies, you can find out why many doctors who treat lyme disease are not giving the vaccine.

The Advisory Committee on Immunization Practices recommends, under future considerations in their report on the lyme disease vaccine, June 4th, 1999, in the MMWR, "Establish post-licensure

epidemiological studies of safety, efficacy, prevention effectiveness, cost effectiveness, and pattern of use."

We concur with that recommendation, and would like to see a moratorium on vaccine administration until those studies are completed, and the results critically analyzed.

Thank you very much for your time.

CHAIR DAUM: Thank you for your time, Ms. Smith, as well.

Ms. Lori Gelbart please, and then followed by Linda Scharf Lurie, and Terry Elias. I hope I'm saying that right. Ms. Gelbart, please.

MS. GELBART: I'm grateful to have the opportunity to address --

CHAIR DAUM: No, not well, sorry.

MS. GELBART: Am I okay now? Thank you.

I'm grateful to have the opportunity to address this committee, and devastated by the circumstances that bring me before you.

Since taking the LYMErix vaccine my life has changed dramatically. Let me explain. My family and I live in Chicago, I have been married for 29 years, have two children, and am a social worker.

Most importantly, until I took the LYMErix

vaccine I was a healthy and productive person. My family spends summers in southern Maine, in an area with high lyme incidence, where we are surrounded by woods and grasses, viewing deer in the yard nightly.

Already following recommended safety procedures we decided to further protect our health by having the LYMErix vaccine. We received our vaccinations at the travel clinic of Northwestern Memorial Hospital, a major teaching hospital.

Neither the staff, nor the manufacturer's literature handed to us cautioned us about the possibility of any long term ill effects. We were given no reason to believe that LYMErix warranted different consideration than any other immunization.

My husband, 15 year old son, and I had the first two injections in the spring of '99. On May 15, 2000, my husband and I received the third shot. The very next day I experienced body aches, and on May 17th I awakened with severe pain and swelling in my hands.

I was unable to bend my fingers closer than 90 degrees to my palms. I became incapable of performing activities such as basic personal care, brushing my teeth, cutting food.

Since early June I have been constantly