where there are viruses, and the worry about any procedure that might contribute to virus, that might escape into the environment.

Any patient that goes in, probably the first 10 or 15 patients that are treated would see no transplantation, I think should know that there will be a chance that they may be quarantined. Their spouse should also sign informed consent, and the health care workers who work with them should sign the informed consent.

I think that they need to have a set period of time in the hospital, are they going to stay one week or are they going to stay three or four weeks, and they will be let out maybe when you find that there is no shedding of the virus.

These things have to be laid out. This has to be a very unique informed consent document.

DR. AUCHINCLOSS: My recollection is that you had some material about informed consent in the initial guidelines. Will this, in fact, be developed further in your new version?

DR. SIEGEL: I can't speak to what the new version will look like, but it is certainly an area that we have been addressing throughout, and I take Abbey's Meyers' comments very seriously. Those are all issues I think that are appropriately part of the process.

We also learned from Jeff Getty a lot of things he felt should have been part of the process.

DR. AUCHINCLOSS: Karen, did the specific answer to your question about the heterotopic--what I mostly got was a sense of, boy, somebody had better come in with a pretty clearly defined group of patients and a pretty clearly defined rationale, and then we would start thinking about it because it is not something that is currently much on our radar screen, is that too much of an overstatement of where you were there?

DR. SIEGEL: At the risk of making a lot of hungry people unhappy, I have a question that we haven't asked, but I would be interested in hearing the committee's thoughts on it.

It occurs to me that as we have discussed this issue of how much preclinical data we need to have a reasonable chance or presumption of a reasonable chance of success or perhaps a reasonable chance of benefit, and we have heard at least several say that has to be compared with the alternative, expected outcomes given currently available therapy to the target population, that maybe one of the things we should be collecting data on as we are approaching doing these experiments in the not too distant future would be collecting data on that latter point.

For example, one thing that could be done now--and

I wonder what people might think about that--would be to identify the criteria for any given type of transplantation experiment one wanted to do to identify whether it's hemodynamic criteria or size criteria or arrhythmia criteria or whatever, and then prospectively identify patients on waiting lists who achieve these criteria, and not intervene obviously because there is no clinical trial, but follow those patients and collect data on what outcomes are in 1999 with currently available therapy that potentially could be very useful when one then brought the protocol and said, well, our experience with this patient population is, in fact, a 50 percent mortality in 60 days or some such.

I wonder also, having heard--I haven't thought this through much--but having heard some of Dr. Vanderpool's comments, whether, in fact, one might also gain from discussing with this population their thoughts and attitudes about how they would react to the potential future availability of a xenotransplantation option with all of its attendant risks.

DR. AUCHINCLOSS: My recollection is that there is some data now in the literature that speaks to the point about how potential patients might feel about xenotransplants, and the correlation is pretty steep. The sicker they are, the more they think it is a good idea.

DR. SIEGEL: In terms of the idea of identifying a

specific prognosis, given a specific entry criteria, you could do that at the very hospitals that you were going to do the trial or similar hospitals.

DR. AUCHINCLOSS: I think you could, and it seems reasonable.

DR. SIEGEL: Other members of the committee, would you all find that data useful when we bring the protocol to you, and it is some number of months or years?

DR. AUCHINCLOSS: Well, I think that the point that you are basically making is that if you are offering, in particular, the bridge xenotransplant for a selected group of patients, however defined, you and we, the committee, will feel much more comfortable if we do have some data about that specific population that has been defined as to what would happen to them with current absence of therapy. That is what you are saying.

DR. SIEGEL: Right. I guess I heard from Dr. McGregor, for example, that we do have data about a population that will die in three to four days, but I have also heard some discussion, including from Dr. Michler, maybe that is not quite the best population to go into first, so whoever the population is, it would be nice to have.

DR. AUCHINCLOSS: Whatever the population is, it would be a good idea for a sponsor to be able to show us

some data about what happens to that population with today's therapy.

DR. VANDERPOOL: Don't you think we can agree on that? I think that is what we do need. We have talked a lot about general issues. Can we be specific, population specific and xenotransplant benefit and harm specific and try to start matching the benefits and harms of a regimen with a particular population, and that particular case around which we could do some specific ethical thinking.

At that point, then, you need to ask what Leroy Walters said, are these people going to be fully conscious, are they going to be able to hear and understand informed consent, and so on, but I think at this point we are looking at more specific possibilities with populations, with particular types of interventions, with the harms and benefits including both longevity and quality of life, and that is what I would want to hear in order to move forward, but not at this point. I am reluctant to move forward without that kind of specificity.

DR. PARADIS: I just wanted to address Dr. Siegel's question. We, about a year and a half ago, started exactly that kind of a study, looking at patients in heart failure who would be eligible for these types of studies.

We had gotten approximately 20 different centers in Europe and the U.S., and what happens is that as you

heard, these patients are actually quite rare, and the number of patients we were able to recruit over a year was such that we realized by the time we would have recruited enough patients for it to make sense, the types of therapies, especially medical therapy and LVADs, et cetera, would have changed so much that the data was not really valuable anymore.

So, this is the real problem with these types of studies where you have got a very, very limited number of patients.

DR. AUCHINCLOSS: Robert?

DR. MICHLER: I think additional information could be garnered from transplant centers and looking at those patients who are not candidates for allotransplantation, in other words, patients who were referred for transplantation, but for whatever criteria--that data is available from many centers, and I would be surprised that it would be that difficult.

We have looked at it when I was in New York at Columbia and published on it, and other centers have also published on it, so there is historical data. I am not quite sure where the inherent problem resides with trying to accumulate data on patients who were referred to a center and were excluded because we have to go through a formal evaluation process.

John, you may wish to comment on your center.

DR. CONTE: I also am a little surprised because there are significant numbers of patients. Out of the 100 or 200 patients a year we see referred for a transplant, I would say at least 25 to 30 percent of them are not candidates, and in that 25 to 30 percent, I would say there is probably going to be 10 percent who might be eligible for some type of alternative therapy.

DR. AUCHINCLOSS: Members of the FDA, I am beginning to move into a closing comments mode unless you signal me that you have some other things that you want us to address.

I did want to thank the members of the subcommittee who are here today. I think your expertise has been outstanding for these two days, and your counsel has been wise, and it has also been a lot of fun to interact with you and what I have found repeatedly, both with this subcommittee and the parent committee, to be honest and fair and thoughtful interactions that have really been a lot of fun.

I also want to thank the FDA that I think has put together a superb program, puts tough questions to us, and I think has been superb in being the defender of the public welfare in the very largest sense, and outstanding in leading the public debate on this xenotransplantation issue.

I also particularly want to thank Gail Dapolito, who when I get things right up here, it is usually because she has been telling me what to do , whispering in my ear, and she is also just a terrific "can do." If you call her up and say, Gail, can we do this, she always fixes it, and everything works out perfectly, so, Gail, thank you very much.

Thank you all very much, and that will conclude this session.

[Whereupon, at 1:14 p.m., the meeting was adjourned.]

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CERTIFICATE

I, **ALICE TOIGO,** the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

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