those folks who are technical experts aren't ready today. They will be ready in the future. Can you say it more elegantly?

DR. MacGREGOR: I would agree. And I guess the other aspect of looking to see if Dave Lester was still here, who spoke and had some other people come in at the last meeting. But Dave's feeling in discussing this internally was that he already has in place a small collaboration in that area that he feels will essentially occupy our resources for the present time. And for all the reasons that Jerry presented, we felt that PET was probably a way to go through this committee at this particular time.

CHAIRMAN DOULL: Yes, Jack?

DR. DEAN: Could I also endorse -- I also endorse Jerry's position. Because at least from an industrial perspective, PET gives us a lot more flexibility in looking both at receptor ligand interaction and looking at metabolism. It offers, I think, a lot of opportunity. So I would strongly support that. I would even make a motion if you would like a motion.

CHAIRMAN DOULL: Yes, I think so. It is the same argument we had for biomarkers. You know, do you want a narrow recommendation or a broad one, which would be for imaging. And what they are recommending is the narrow one.

DR. DEAN: So I would move that we form a working group on PET imaging.

CHAIRMAN DOULL: Okay.

DR. CAVAGNARO: Second.

CHAIRMAN DOULL: Gloria, that is your area.

DR. ANDERSON: It's not clear to me how we came to decide on PET imaging, but if we are going to at some point take a look at the others, then I don't have any objection to this. Maybe I am tired.

CHAIRMAN DOULL: The Subcommittee is agreeable that -- a focus group.

DR. ANDERSON: There is a very real drawback to PET imaging. I wonder if the committee is going to look at that. And that is getting the materials that you need in order to make it worthwhile. What we saw on the mini one or micro or

whatever it was called, that was one class of compounds and they were all used in mice whatever. The larger question, I think, is how useful will it be if we cannot get the radio-labeled compounds that we need. That is one question. The second question is in terms of humans particularly, how much do we know about the effects of the kind of gamma radiation on individuals, particularly if it is incorporated into the system of the individual. I am not asking for answers, but I think those are some things that any group would want to explore.

CHAIRMAN DOULL: Yes. I guess in order to do PET scanning in people, you need a cyclotron close by in order to do the isotopes. Is it the same isotopes that we are talking about for animals?

DR. CHERRY: Maybe I will just quickly address those two questions. The first one related to the label compounds. And you are right that in most of the large PET centers right now, they have their own cyclotron. But with the growth of clinical PET, we are seeing a lot of distribution centers being set up of fluorine 18 labeled compounds now. So in a lot of

urban areas, you can buy these compounds from a third party. And that is only going to continue to grow. The other thing that is happening, and this comes also out of some of the NCI initiatives, is that people are looking at some of the longer-lived radio isotopes that can either be generator produced or have long enough half-lives that you can ship them across the country. I think we are going to see a lot of chemistry being developed around those isotopes. And then the issue of having the on-site cyclotron goes away.

The second question was about the radiation dose to the mice, and that is very insignificant. That is not an issue. It is much smaller than the dose we are giving normal humans in studies.

DR. ANDERSON: I am not as optimistic as you are about the fluorine compound. I am a fluorine chemist, and fluorine is the hardest halogen to put in a molecule.

DR. CHERRY: Oh, no, I understand. But there are already hundreds of fluorine 18 labeled

compounds that have been synthesized.

DR. ANDERSON: But basically they are all in the same class. So they all do the same thing.

DR. DEAN: John, Joy asked me an interesting question. And since I made the motion and still stick by the motion, I think it is fair to get an answer. What will be the outcome from this focus group? I mean, what do we hope to have in the future by having this kind of a focus group around PET? Maybe Jerry can answer that.

DR. COLLINS: I think the potential benefits are in two areas. Right now, there is a series of independent investigations going on in which each group follows their own favorite flavor of thymidine. And there is no effort at all underway to do a comparative evaluation of the relative benefits of one versus another. I think if we could get a consensus from an expert working group on the design of the ideal experiment -- and it could be done -- that particular question could be done in people -- a comparative evaluation of the probes that are out there -- that would help enormously. The sooner --

you know, you want an opportunity to look broadly at first and to get as many molecular structures as you can. But after a certain point, you want to hone in on one because you won't have the resources to do all the others.

The second thing I think in terms of the preclinical or nonclinical evaluation, there is actually not as much data as their are for homosapians. And I think in terms of other applications outside of direct cancer treatment -- applications of looking at this as a probe of tissue injury -- we don't have a data base to say what the resolution is in that context. And with this particular fortuitous timing of more small animal imagers being available, this expert working group could be charged with designing an experiment of inducing an injury and then looking to see time -- again, since these are non-invasive, you can do serial measurements in the same animals that Dr. Cherry showed. I think those are the two kinds of areas that might be most profitable.

CHAIRMAN DOULL: We talked last time a

little about how does the resolution compare with radio-autography, and clearly it is not quite as good. But on the other hand, you can't do radio-autographs repeatedly in the same animal. Any other concerns? Okay. So the motion, Jack, would be that we should create a focus group that would explore the use of PET/SCAN as a means for enhancing -- I guess both toxicity evaluation and clinical evaluation -- preclinical evaluation of new drugs.

DR. CAVAGNARO: But Jerry also said something very specific. Because I think that is a piece of this particular committee. Because everybody is doing it. But I think that was very important what you said, Jerry. Because we just heard NIH has a huge initiative and how does this group -- you know, what is the distinctions or what are the -- I mean, will there be collaborations? I am sure there will be some collaborations. But I think if we are going to set up a separate working group, then I think the goal is -- so I would refine it to include what Jerry had stated, those two specific aspects of it. And that is to better identify the thymidine. And then you will get

that as an endproduct, and that will be the product for this particular working group, I think.

CHAIRMAN DOULL: We could probably also mention the utilization for that purpose. We could probably also mention -- if we put that in the announcement, that will ensure that NIH will get a rash of requests. Jim?

DR. MacGREGOR: I think one of the values in defining if you do want to stick with some of the specific focus such as replication markers, is that you also have some other questions to think about in addition to the imaging I think. For example, Jerry presented the proposition that you should be able to image replication in conjunction with certain pathology. So a question is how tightly linked is compensatory cell replication with various pathologies. You might want to include someone to address that and to ask is it useful in that context. It is clearly useful in imaging tumors. But how broad are the applications?

CHAIRMAN DOULL: And last time you all talked about distribution and the power of it for

doing the usual sort of things that we used to do with radio-autography and the fact that you can do those repeatedly in the same animal. The mechanism part is the new part, and hopefully the committee would get into using this technique to look at mechanistic kinds of things. Okay. So we will do both of those things. We will put together an announcement. And I guess, Jim, we could then circulate that amongst the committee and see how that goes. And then we would go through the process which will mean it will take it a while for that announcement to actually appear in the Federal Register. But in the meanwhile, we would encourage people to contact one another and begin to line up candidates for this committee.

Is there any other business that we need to do?

DR. ANDERSON: The minutes?

CHAIRMAN DOULL: Oh, yes. Did you all get a chance to look through those minutes from the last meeting? It would be nice, I think, if we could have a motion and approval. Could you make that motion?

DR. ANDERSON: So moved.

CHAIRMAN DOULL: So moved. Okay. And if there are any corrections at all, Kimberly said that if you will write them on there, she will fix them. Okay, we are adjourned.

(Whereupon, at 3:38 p.m., the meeting was adjourned.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: MEETING

Before: ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE

Date: MARCH 9, 2000

Place: ROCKVILLE, MARYLAND

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

Rebecca Davis