From Susan Ellenberg, interviewed by Suzanne Junod and John Swann, 7 December 2004:

SE: I eventually came to FDA. I was working at NIH, first in cancer research and then in AIDS research, and I was at the Division of AIDS at NIAID (National Institute of Allergies and Infectious Disease) starting in 1988, and I began to work much more closely with the FDA than I had ever had before because AIDS was so new and there was so much emotion and so much urgency about AIDS drug development. This was like nothing anybody had ever seen before. People were realizing the need to invent new ways to do research and new ways to regulate.

We worked very closely with -- when I say we, at NIAID, worked closely with FDA. Carl Peck was head of CDER then, and after Ellen Cooper, who'd been head of the antiviral group, left, Carl actually became Acting. So he was the Center Director, but he was also an Acting Division Director because he really wanted to make this go. We would have weekly meetings, the Division of AIDS staff, with the Antiviral Drugs staff at seven in the morning because that's the time Carl started his day, and that was the only time we could fit it in. We had weekly meetings from seven to eight over in the building on Nicholson Lane next to White Flint, which was where the Antiviral Division was at that time, to talk about what was going on with the AIDS Clinical Trials Group and what new studies were starting and what was going to get started, and to make sure that we were sharing enough information so that we wouldn't end up with delays in getting drugs approved or even getting initiated because there were some misunderstandings between the researchers and the FDA. The FDA needed to understand why the study was being designed in such a way or what the issues were so that they could avoid delays. That was

very exciting. And, of course, there was all the controversy with the AIDS activists.

And a statistician at CDER (Center for Drug Evaluation and Research) -- I think he's still here, Satya Dubey, suggested to me one time that we start an informal, regular meeting of statisticians interested in AIDS research to talk about some of the issues, because there were huge controversies as to how these studies were being done. If you remember, the activists were saying, oh, no placebos and no this, and you've got to have this and have it this way, and you have to have humane studies and all of this. Everybody agreed we have to have humane studies.

So we agreed with that, and we started a regular meeting, which ultimately the activists became involved in. It was just a wonderful period of a few years when I think I must have felt a little bit like physicians who go and work in Third World countries, where you have to sort of figure out what you're doing minute by minute and you're saving lives, and you feel like you're really doing something for the world. That's kind of how it was, where we had the Act Up people and statisticians from NIH and FDA, even people who weren't involved in AIDS research on a day-to-day basis, people of other parts of NIH who wanted to contribute.

And, of course, the statisticians who were part of the statistical centers for the AIDS groups, the Harvard group who had the statistical center for the AIDS Clinical Trials Group, and some of the Minnesota people who had the statistical center for the community clinical trials group. Some of the physicians who were more interested in study design, they would come.

We started off with a meeting of maybe twenty to twenty-five people. We met

four times a year in conjunction with the AIDS Clinical Trials Group meeting, and within a couple of meetings we had 100 to 120 people, and we had activists and clinicians and statisticians, and it was very lively. I would invite people, statisticians and others, who had interesting ideas about study designs to come and present. I asked some of the top people in research anywhere. Nobody ever said "no," they weren't going to come to this group.

SJ: Did you have a formal title for the group?

SE: We called it the Statistical Working Group, and it just was very informal. We had these meetings. They were going on for a year before the activists were welcome in the clinical trials meetings. So I think we were a little bit pioneers there.

I still haven't gotten to the point where I was leading to with all this. Your question was how I came to FDA, so at this time in AIDS when we were working so closely with the FDA and on development of new issues and how to get drugs approved fast, it was very motivating.

So when the new position in Biologics came up, and there were people there who asked me -- I had actually just agreed to serve on the Biological Response Modifiers Advisory Committee. But it was all because I'd become known to the FDA through the AIDS stuff, and I decided, well, it might be interesting to work on this side.

JS: You mentioned the challenge to statisticians in dealing with this unique problem

of crafting drug studies in a way that would be statistically sound yet responsive to the immediate clinical needs, as spoken to so forcefully by the AIDS community, Act Up and others.

SE: Yes.

JS: How do you broker those two, what seemed to be pretty difficult sides to bring together?

SE: Actually, it was not so difficult. That was what was so beautiful about it. I remember going to the international AIDS meeting in Montreal in 1989. It was my first interaction with the activists, and they were there dressed in their most provocative style handing out this brochure. It was called The Treatment Agenda for ACT UP, and it was a fifteen- or twenty-page Xeroxed document. I took one and I started reading it, and I found myself scribbling furiously. My notes were like, "You mean that's not how it's being done?" "You mean the studies aren't like that?" "Why can't . . ." Most of the things they said were very sensible, and you could do studies in the way they proposed. It was just not the traditional way that companies had done clinical trials, at least in infectious diseases. There were things that they weren't used to.

For example, it's pretty standard in a lot of the areas at FDA, when you do a clinical trial of a new drug, you don't want people taking other drugs at the same time because it might interfere with the action of the drug or there might be an adverse

reaction. If there's an adverse effect, you don't know which drug is causing it. And so companies like to keep things very clean and pure.

Well, when people have a life-threatening disease, you can't say to them, "You can't take anything else." In fact, you should question whether you would even want to do that, because you want to know -- it doesn't do you any good to know whether it works in one context if it's going to be used in this other context. You need to study it in a way that it's going to be used. And in cancer, while I was involved in cancer research for ten years before, we didn't have any such restrictions. People got the normal things that they got, and people didn't try and make it all tight. The question was, if you added new drug X to the standard regimen or everything else people might be taking, all in all, was it better?

Then there were things that were just non-standard and new. There were new drugs being developed for -- there were antivirals, and there were drugs to prevent or to treat opportunistic infections. Because the disease was so new, lots of the most promising treatments were not yet approved. They were in trials. But people wanted to be in more than one trial at the same time, and there was a lot of resistance to that because it wasn't the way things were done. The first instinct is, well, how are we going to sort things out?

But my feeling, and the feeling of a lot of other people, was that first you have to decide what's best for the patients. You have to make sure that you're treating everybody as effectively as you can treat them. Then you worry about how you're going to sort it out. You don't say somebody's going to get, or somebody is more likely to die

because you couldn't get the right statistical design. The people who were putting patients on trials are people who are treating those people for a life-threatening disease, so once you got into the mindset that first you have to make sure all the patients are fully treated . . .

I don't mean to suggest that there were people who really didn't think patients needed to be properly treated. It wasn't that way at all. It was just, it was a little bit like when I started working in cancer studies after I had been working more in the heart disease area, that was a culture shock, too, because in cancer studies, people were much more loose about a lot of things related to study design. There was a recognition that people were going to have their standard treatment and you were going to try this, but things weren't controlled as rigorously. There were different cultures. So the cardiovascular people thought that the cancer people were impossibly sloppy and couldn't figure out how they could ever learn anything about what they were doing, and the cancer people thought that the cardiovascular people were ridiculously restrained and were testing in situations that weren't generalizable. Neither of them was right. I mean, you have to test things different ways in different arenas.

One of the things I've learned over my career, working in different disease areas and also working, first working at NIH and now FDA, is that people develop truths based on their own experience, and find it sometimes very hard to see that what's absolutely true for them or what they believe to be absolutely the right way to do things may not apply in other areas. It's not an absolute truth. It may be a strong truth for this particular area.