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Interviewee Information. Please list an address where we can contact you.

Full name: Aristides A.N. Patrinos Date of interview: 9-1-2011
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Interviewer Information.

Full name(s): _____
Affiliations(s): _____

I, the undersigned, have read the above, and I **AGREE** to release my interview materials, subject to any restrictions listed below:

(A) I place **no restrictions** on my interview materials.

OR

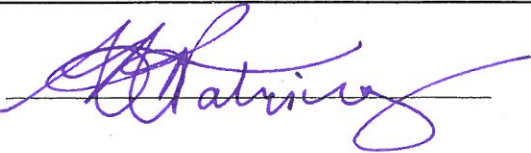
(B) My interview materials may be reviewed, used, and quoted by the researchers affiliated with the Center for Public Genomics, Duke University; *and in addition* (check all that apply):

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Posting interview materials to public digital archives: In spite of any restrictions listed above, I give permission for my interview materials to be made publicly available on the Internet by deposit in an institutionally affiliated archive:

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Date: 10-19-2011

Informed consent for: “The ethos and effects of data-sharing rules: Examining the history of the ‘Bermuda principles’ and their effects on 21st century science”

**University of Adelaide
Duke University**

Researchers at the University of Adelaide, Australia, and the IGSP Center for Genome Ethics, Law & Policy, Duke University, are engaged in research on the **Bermuda Principles** for sharing DNA sequence data from high-volume sequencing centers. You have been selected for an interview because we believe that the recollections you may have of your experiences with the International Strategy Meetings for Human Genome Sequencing (1996-1998) will be interesting and helpful for our project.

We expect that interviews will last from 30 minutes to much longer, but you may stop your interview at any time. Your participation is strictly voluntary, and you do not have to answer every question asked.

Your interview is being recorded and we may take written notes during the interview. After your interview, we may prepare a typed transcript of the interview. If we prepare a transcript, you will have an opportunity to review it and to make deletions and corrections.

Unless you indicate otherwise, the *information* that you provide in this interview will be “on the record”—that is, it can be attributed to you in the various articles and chapters that we plan to write, and thus could become public through these channels. If, however, at some point in the interview you want to provide us with information that might be useful for us to know, but which you do not want to have attributed to you, you should tell us that you wish to go “off the record” and we will stop the recording. We will, however, take notes for our own use. When you are ready to go back “on the record,” we will resume recording. Anything you say while “off the record” will not be on the audio recording and therefore will not appear in the transcript.

All *materials* from your interview (audio recording; transcript; interviewer's notes) will be available only to members of the research team affiliated with this project, unless you consent to their wider use, as described in the paragraph below. The digital materials will be maintained in a secure, HIPPA-compliant drive at Duke University. The paper materials will be stored in a locked cabinet.

In addition to the scholarly articles and chapters that we plan to write, we also hope to create a resource for other scholars and members of the public. We plan to post some of our research data to online digital archives. While we will use your “on the record” comments to inform and write our articles, we will not post your interview transcript or audio recording online unless you give us permission to do so, in a separate agreement. At the time we send your transcript to you for review, we will also provide a consent form asking your permission to post your interview transcript and/or audio recording online. The form will provide you with different options for how, when, and with whom the materials may be shared. You will, of course, also have the option not to share the materials beyond the Duke and Adelaide researchers.

One risk of this study is that you may voluntarily disclose identifiable information that later could be requested for legal proceedings, or otherwise be used against you. Please take this into consideration when you are speaking. There may be other risks associated with your “on the record” views being made publicly available, such as having your views mischaracterized or misunderstood.

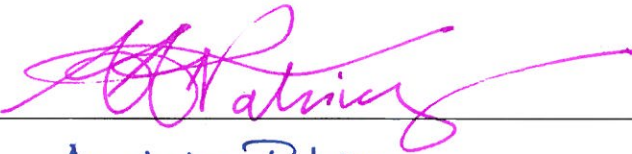
The main benefit of participating in this study is ensuring that your side of the story is properly portrayed in this history of the Bermuda Principles, which have become a model for open and collaborative research in genomics and other fields.

To help us protect the privacy of those parts of your interview that are not public, we have obtained a Certificate of Confidentiality from the U.S. National Institutes of Health. With this Certificate, we investigators cannot be forced to disclose information that may identify you, even by a court subpoena, in any U.S. federal, state, or local civil, criminal, administrative, legislative, or other proceedings. We researchers can use the Certificate to resist any demands for information that would identify you.

The Certificate cannot be used, however, to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person or institution obtains your written consent to receive research information, the researchers may not use the Certificate to withhold that information.

Signature



Printed Name

Aristides Patrinos

Date

Aug 31, 2011

If you have read this form in its entirety and agree to the interview and its terms, please sign and date above.

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*If you have any questions about your rights as a research subject, you may contact the **Duke University Institutional Review Board** at 919-684-3030 or ors-info@duke.edu.*

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Interviewers: Kathryn Maxson, Robert Cook-Deegan

BCD: Kat has joined me...and just to let you know, with your permission, the tape is going.

APatrinos: Absolutely.

BCD: And I won't read that whole elaborate informed consent document.

APatrinos: You don't have to.

BCD: Yeah, I just wanted to put on tape that in fact you've got it, you're signing it and you're going to send it back to us either digitally or...I guess probably physically.

APatrinos: You mean I haven't done it yet? Oh. Do I have it?

KM: So I sent it to your assistant.

APatrinos: Isi?

KM: Yeah, Isi, and she...I don't know if she sent it along to you. I think I also e-mailed a copy to you.

APatrinos: Hold on just a second. Let me check. Isi just told me that I signed it and she's already sent it to you.

KM: Oh, so she ...

APatrinos: She's going to PDF it to you right now also.

BCD: Okay, terrific. I just wanted to get that out of the way so we've got that on the record. And what we're trying to do, just to give you a little bit of background, is we're trying to reconstruct some of the history of why the Bermuda meetings happened in the first place, the principles that came out of them and interpret why people in retrospect seem to be attributing importance to the principles.

APatrinos: The lore.

BCD: Yes. So if you could let me just ask the first open-ended question about how you fit into that picture. You might give a little bit of your background of how you came to the DOE position and how that related to the Bermuda meetings. And then we'll just go from there. We've got a series of questions that we want to make sure that we cover, but my guess is we'll cover many of them by just letting you talk through the history.

APatrinos: Sure. So my name is [APatrinos]. In August of 1993 I became the Acting Director of the Office of Biological and Environmental Research (BER) in the Office of

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Science in the Department of Energy (DOE). As a result of this new role, which I ended up getting permanently in March of '95, I had responsibility for the biological and environmental research efforts, including the human genome project (HGP). The HGP was launched by one of my predecessors, Charles DeLisi and had been ably continued by my immediate predecessor, David Galas. With me managing the DOE part of the human genome project were David Smith, who was the Director of the Life Sciences Division within BER, and Marv Frazier, who was also in that division. So both of these individuals played a fairly prominent role in the DOE human genome project, including the events related to the Bermuda conferences. So that's how I became associated with the HGP starting in August of 1993.

BCD: So just to lay out what we think we know, but we actually don't know for sure because all we have is some of the documents that were used to help plan and were recorded at those meetings, we have you as having been there in 1997 and 1998, but not in 1996. Does that jive with what you recall?

APatrinos: Absolutely. As I said, I had assumed the BER directorship in March of 1995. At that time, David Smith was the Director of the Life Sciences Division. He retired within the next two year and I believe he attended the 96 Bermuda conference. And that's one thing that I don't have with me, but I can have a follow-up clarification because I have taken very careful notes of each and every day I spent in my job at the Department of Energy.

BCD: You're kidding me!

APatrinos: No, no, I have everything that happened blow by blow in many of the very important meetings. So that's one of the reasons I wanted to have this opportunity to give you some of those data. And I don't have those exact notes with me from '96, but I remember that it was sort of like a swan song for David Smith to go to Bermuda. But I need to confirm it. I know that I did not go in '96 and that I wanted David Smith to have one more hurrah because he had been so instrumental and so pivotal in the launching of the HGP. But as I say, I need to go back and confirm it because I am now in La Jolla and my notes are in the basement of my home in Rockville. But I have all the notes from '97 and '98. My recollection is that I did not attend the '96 meeting.

BCD: Yeah, and we're trying to figure out if we have a record of David. He's not on our list for '96, but we will call him and find out.

KM: He is on our list, '96 only.

BCD: Oh, okay. Okay, never mind, I got that wrong.

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KM: Yeah, '96 only, it's a confusing big Excel spreadsheet I have for all of the Bermuda delegates, and we have David Smith as only being there in 1996.

APatrinos: Again, I will confirm it because I want to be exact and accurate. He had already told me that he was retiring. I thought that it was the least I could do to give him this last opportunity to travel there and say goodbye to a lot of people that he wouldn't be seeing after he retired. And furthermore, he was certainly a lot more knowledgeable of all aspects of our HGP program than I was. I was getting up to speed on aspects of the program during those times.

BCD: So we'll get more detailed in a minute, but from your perspective, your kind of general perspective on the Bermuda meetings, could you give us your sense of what the purpose of the meetings was? Why were they held at that time? What were they trying to do? And how might that be the same or different from how you think about those meetings in retrospect?

APatrinos: Well of course those were the heady days of the human genome project. It was still in the early phases before things were accelerated with respect to sequencing and before we had the heart stopping experience with Celera, to be a little facetious here. And before we knew each other very well. I mean we all had the sense that this was a program that was going beyond individual agency or even individual government programs. It was catching fire with respect to attention. Nothing like what happened during the last two years of the HGP, but still, and there was a recognition that this was one of those cases where we needed to find out more about each other, and because there would be a significant need for coordination down the road, not necessarily initially. And there was also a jockeying for turf and influence on the part of both the program managers associated with this program, be they NIH or DOE, as well as at the Trust, the Wellcome Trust in the U.K., but also among the scientists who had already started to shine with their capabilities and their ambitions. I'm referring to the ones that are now "household" names like Eric Lander, Bob Waterston, David Cox, Richard Gibbs, John Sulston and Elbert Branscomb. So there was a recognition that more coordination was necessary and there would have been a way to do it through some sort of a workshop that was held halfway between the US and Europe, and of course a nice place was always desirable at the time. There were also the ambitions of the individual program managers within these agencies, like Michael Morgan, Francis Collins and myself.

BCD: So that gives us a really good context. What felt like the purpose? Why would those meetings have been organized at that time? The project is picking up steam. What were the questions that needed to be resolved by getting a bunch of people together at a neutral forum?

APatrinos: Well of course I can't speak for some of the other program managers and organizers but maybe I can speculate. It was my impression that Michael Morgan

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and certainly the Wellcome Trust wanted to play a bigger role in the HGP. And so in many ways the initiative was theirs. There was also the harsh reality of US public service compared to the Wellcome Trust. The Trust enjoyed a lot more freedom with respect to funding of workshops, whether they be in nice locations, and putting together more elaborate meetings. So I believe it was clearly the initiative of the Wellcome Trust and in many ways of Michael Morgan. I think he seized the moment, proposed something that would have been an attractive place to come together. And once he secured the okay of NIH and DOE, then a lot of the principal scientists would have found it irresistible to not show up. There was a lot at stake at the time and a lot of these meetings were attended by people who were very worried about their funding. They wanted to make sure that nothing was launched where they'd be left behind, with understandable reasons. As I said, the HGP was starting to be organized as a major program. It was clearly getting more and more attention and competition for funds was getting stiffer. It sounds like a contradiction because if it was becoming more prominent you would expect more funding. But along with more funding would come also a stiffer competition because it would attract many more competent people who wanted to have a piece of this action.

BCD: So there were...incidentally, we did get your form so we're all set on that front... the two reasons that several commentators have laid out in kind of general categories, one was to kind of shift into gear for the sequencing aspects and allocate...do an assessment of who could do what realistically on what timeframe and what they had produced already and how much they could produce in the next year and kind of also allocate the workflow, so kind of a logistical meeting. And then the other component that seems to have become more prominent in retrospect was the process by which the rules for sharing data before publication very rapidly were endorsed...formulated I guess in '96 and then endorsed again in '97.

APatrinos: The "religious issue," like I like to say, the religious issue.

BCD: So if you're looking back on this, what was the relative ... did you expect this to be something that would produce a statement on data sharing? Or was it mainly an organizational and let's get started meeting? Or did you expect both?

APatrinos: I expected both. I mean I had gotten wind of some of those notions, and interestingly enough, the initial hints I got were mostly against the Germans and the Japanese because they had ideas about release of data that were certainly different than those of the "true believers" at the Wellcome Trust, as I like to say, those of the British "socialists." [Laughter.]

BCD: So of course that would have been the case because you were at the 1997 meeting where this became quite a pointed issue for the Germans in particular, and the Japanese of course were watching very closely. So you would have basically

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entered the fray a year after this set of principles had been kind of piloted and the Germans were not...they were wobbling a bit I gather as they went into the 1997 meeting. And I gather there were some politics right at the meeting about what to do about that. Could you tell us a little bit about how that felt? What your role might have been in those discussions?

APatrinos: Sure. I am thinking of André Rosenthal...I don't know whether he's one of the people you're reaching out to.

BCD: We're going to.

APatrinos: He was the victim, so to speak, and was in some ways surprised. He thought that what the Germans were going ahead with was pretty sensible. And in a way he became the center of a controversy and was personally extremely upset. The Japanese were less so. I will get into those details, but I also wanted to conclude the thought that I started earlier. It started as an attack against the Germans and the Japanese, but ultimately, and especially in '98, the focus was against Craig Venter who was the big absent one at the '98 meeting. He had already dismissed our group of people as the "liars' club." And so in some ways the focus against the Germans and the Japanese shifted towards Craig Venter and Celera at the '98 meeting. Celera had already happened between the '97 and '98 meetings.

BCD: That's a really useful comment.

APatrinos: I'm going through my notes here. I can copy some pages, redact things that are irrelevant and send them to you.

BCD: That would be ...

APatrinos: I'm assuming you have the invitation, right? You don't want any of these things, right?

BCD: I don't think we have...we have seen the invitation, but I don't...so Michael Morgan is trying to abide by the privacy rules of British law, so he's been constrained in how much stuff...he's been trying to check with people about how much stuff he can share.

APatrinos: I don't think that I have that particular constraint, so I can send it to you. I have the invitation to me dated February 17, '97 from the Wellcome Trust. And then another letter from the Wellcome Trust January 30, '97, which gives you...but these are of course old invitations. If you want them I can certainly send. And I also have the revised delegates list.

BCD: Yeah, all those documents, even if you think we have them, we may or may not ...

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APatrinos: Okay, I will be glad to ...

BCD: ... and it would be really useful.

APatrinos: Okay. And then I have a 28 February of '97 note inviting me and others to dinner with Michael Morgan. If you don't have it, you'd probably be interested in this. Then there is a one-and-a-half page report on the international strategy meeting on human genome sequencing held at the Princess Hotel South Hampton Bermuda on 28th February 1996. And it has the aims of the meeting, and the summary conclusion that primary genomic sequence should be in the public domain and should be rapidly released. It also advocates increased coordination.

BCD: So we have that for the following year, but we do not have that for '96, so that would be an extremely valuable addition.

APatrinos: Okay. I also have what is a handwritten table from Francis that has as a heading: "human sequence production." In the left most column are the investigators and it goes: Sulston, Waterston, Lander, Hudson, Hawkins, Adams, Gibbs, Cox, Weisenbach, Maddock, Rosenthal, Bloecker, Olson, Chen, Sakaki, other Japanese efforts, Evans, Palazzolo (DOE) and Bruce Roe. The second column has the "cumulative finished sequence." And then, predicted finished sequence for March 1st '97 through 2/28/98, and March 1st '98 through 2/28/99. And there's an asterisk for this on the numbers, and it says in the footnote, "production dependent on funding decisions." Some centers, such as Lander's and Evans', give numbers based on anticipated...something (illegible), funding is not an obstacle. Others, Waterston, Adams, Gibbs, are more conservative. And he also notes for a couple of centers the principal scientist was not attending meeting and the data were reported by a colleague. So it looks like Waterston was not there? I guess not.

BCD: He was there at the first one, but I don't know about the second one.

APatrinos: I think he had a bout with cancer. I wonder whether it was around that time. Then I'm going to have to send you some of my scribbles that I took from all the various presentations.

BCD: That actually would be the single most useful thing.

KM: Something interesting is that we have Bob Waterston there at all of the meetings. And so he wasn't there at one of them?

APatrinos: No, no, no, I'm not saying that. So when you see this particular table, well Francis has predictions for 3/1/98 to 2/28/99 and he's got asterisks for sequence production dependent on funding decision. Some are optimistic; some are more

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pessimistic about the funding. And then he has some pluses as another footnote and he says, “not attending meeting reported by colleague.”

BCD: Yeah, it could be...we'll check with...Bob's going to be out here in about two months and we're going to do a joint interview with him and John Sulston when they're here. So we'll confirm some of this stuff. And actually, it would be useful for us now, we should add in advance to find out from him...just ask him explicitly if...we know he was supposed to be at all these meetings, but maybe something did come up at the last minute with his health.

APatrinos: Well let me look at the attendance list. This is the revised delegate list, so I'm assuming one that was...oh, he's listed as being there. It could have been that the person who gave the information may have been from his sequencing center, but it wasn't Bob.

BCD: We'll ask him, yeah.

APatrinos: A lot of my scribbles are basically just what the various speakers said, and at the time I jotted them down. Obviously, they're not complete or comprehensive. You probably can read most of my handwriting.

BCD: Yeah, and one thing that would be very useful as you're thinking about...this sounds wonderful and the documents would be extremely valuable to us...if you could also send us a CV, just as background on you, because you might not think of doing that, that would also be useful just as kind of background information. So back to the principles...and your perspective is especially valuable on this point in light of your role in being the mediator between Collins and Venter fast forward three or four years...tell us a little bit about the discussion about prepublication data access and how you were thinking about that, how DOE centers were thinking about that, and some of the politics and whether it was a good idea to do the Bermuda principles, what its impact was, just your general thoughts in those areas.

APatrinos: I think the general concept was a reasonable one. I was a little turned off by what I call “the religious issue” primarily because I don't particularly like what could be seen as socialism and it seemed to me that it was such a clear influence of the Brits, and especially John Sulston. John is a wonderful scientist, but I don't agree with his political views. He wears some of those political views on his sleeve and I don't think they necessarily have a place in the scientific enterprise. I believe that the private sector and capitalism do extremely well with science, and we shouldn't try to constrain them. So I'm a little bit too candid, but that's the way I feel. And in some way, even though I signed onto the Bermuda principles, I thought it was a good idea to share information, as soon as we could make it reasonably available, but I was not hung up about this notion of doing it the same day the data were produced. I never thought it really made much difference

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anyway. And I also quite frankly thought that there should have been more consideration in the way the Germans and Japanese were treated. They were practically ambushed. The Japanese frankly were more like “deer in the headlights.” But Andre was, I think in my view, traumatized for a long time, without being necessarily responsible for his government’s decision. He was in a sense trying to defend a policy that was set up by the German government, but he took it personally and he felt as if we all ganged up on him. And that was something I have a bitter recollection of. It could have been done much, much better. He could have been alerted well ahead of time so that he was not embarrassed. There was no reason to take the “holier than thou” attitude frankly that mostly Michael, but also Francis, assumed at the meeting. And as you may know, if you’ve looked at the history of the human genome project, we at DOE always looked for opportunities of partnering more substantively with the private sector. We didn’t see necessarily something there that couldn’t be worked out if sensible people, reasonable people, wanted to make it happen. So there was that aspect that smacked of “religious fanaticism” that I don’t remember fondly.

But there were also good parts about the Bermuda meetings because my opportunity to interact with some of the wonderful scientists, some of the top scientists in the field, even ones that I may have disagreed with on this issue. And just seeing the strength of the intellect, in many ways the synergism among them contributing to very many good ideas that came up for how different problems could be attacked, how different collaborations would flourish were the bright side of things. And also a lot of these excellent scientists were also very interesting human beings and just the opportunity to socialize with them after the business meetings was a great memory. I remember ... this is an aside ... David Cox and I smoked some terrific cigars in the evenings at the Princess Hotel and had some very philosophical discussions after having imbibed quite a bit of wine. So those are my good and the not so good memories.

BCD: So play up a little bit how you said you thought that some things could have been handled better. So let me break that apart into a couple of separate questions. What do you think needed to be included in the principles? And what do you think could have been left out or softened or changed that might have changed the outcome, without getting in the way of the overarching objective of getting folks to share information into a collective information resource?

APatrinos: Well first of all I would have preferred if it the data policy weren’t presented as some sort of a manifesto. I mean this comes across, it’s a page-and-a-half and it’s like, the following principles were endorsed by all participants and these included officers and scientists supported by such and such and it was agreed, etc. This could have been softened. They could have been made as desirable outcomes as opposed to something that was just universally agreed upon. I mean it almost reads like a declaration of war, an attack against individuals or groups that for whatever reason could not endorse something like this because their governments

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had different notions. So there was something too absolute in my point of view. This was after all still a scientific enterprise, scientific effort, and anybody who gets involved in science knows that there is nothing absolute. Everything could have another side and everything could also be proven to be not the right approach or sometimes actually downright incorrect.

KM: So this is really interesting, particularly for me. One of the things I'm going to start getting into more headfirst now is looking at the policy background, not just in the United States and Great Britain, but in the other nations that were represented. So you mentioned how other governments may have felt a bit affronted because they had different views on how scientists should be sharing data and comporting themselves. Who would you say are some people that I would really need to talk to if I were going to conduct a few interviews with international people on this topic that we might not have flagged as needing to talk to right away, if you have any insight on that?

APatrinos: Well certainly André is one person you need to speak to. Another one is Sakaki of Japan. I'm not entirely sure that Sakaki was at Bermuda or that he had a different position on the data sharing policy.

KM: I had both of them flagged. Is there...thank you so much for that ... is there anyone else that you think? They'd probably be two good key informants because they're Germany and Japan.

APatrinos: I think those two are probably the most appropriate (to speak to). I think you should also at some point speak to Elbert Branscomb and to Marv Frazier, because, as you may know, we (DOE) tried to do this collaboration with Celera and much of the hassle was associated with the data sharing policy. So speaking to those two is also what I would recommend. I'm going to think about it and if any other name comes to mind, I will send it to you.

BCD: Great. So would you say on balance that this whole process helped, hurt, or a little bit of both? And in what ways?

APatrinos: Oh, I think it was definitely a help. I mean it was the beginning of at least getting to know each other. And it was fairly central to the ultimate success of completing the draft on time and putting up a reasonable challenge to Craig's effort. Had we not done these things years ahead, starting in '96, it would have been a lot more difficult to coordinate this program around the world. So on balance, it was a positive thing. I think there are scientific collaborations that started back then that are still flourishing. A lot of people benefited by being a part of a larger community. So on balance it's okay, but along with that come the other things such the ganging up on the Germans and the Japanese at Bermuda '97 and later on with Craig at Bermuda '98 and later on with Marv and me because of our

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efforts to do something other than what the big boys of the human genome project wanted to do. But on balance it's generally very positive.

BCD: And so let me just shift gears slightly. You have this set of principles that are agreed to in '96 and then corroborated again or confirmed in '97. And there are a statement of ... it's kind of a combination of here are the ... it's almost like rules. But what were the enforcement mechanisms and how were people thinking about that? What happens if you don't do this or what happens if you do it but you aren't producing as much data as you said you were? Or how were you all thinking about that part?

APatrinos: Well there is some typical schoolyard bullying. No scientist wants to be ganged up on.

BCD: Gang?

APatrinos: Yeah, it was more a case of embarrassing the people that weren't doing it, that would not be adhering to the data policy because in some way they would not be "pure." I think this whole notion was propagated mostly by the Brits that the genome sequence belongs to everybody, there shouldn't be any "dirty" profit-making associated with this. And the way you can guarantee that is by making all these data available immediately. So nobody has an inside track, so nobody can necessarily jump the gun and make any money out of it.

BCD: So one of the other dynamics of these meetings was the politics of big labs that had big budgets and were consuming enormous resources by the standards of biology of the day compared to little labs. And how much was that driving the discussion compared to the general sense of, we're creating a public resource? Or was it impossible to tell which of those things was doing most of the work in these arguments?

APatrinos: That's a good question, but let me complete the answer to your previous question, about how it would have been enforced. So one was a case of just exposing people that were not willing to go along and embarrassing them scientifically and publicly. There may have been also this other implicit threat never openly stated that in some way that the funding agencies had enough influence and ability to do more than just embarrass individuals who weren't going to be complying with the data policy, in a sense affecting their grants. As I said, it was never quite explicitly stated, but there were some hints about, well if a government wasn't going to go along or if the representative of the government wasn't going to go along, then we had ways through our foreign office or our state department to get to those governments at a higher level, influence them and therefore come down hard on their representatives at these meetings.

BCD: Was this in the public session ... excuse me.

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APatrinos: This was a case of the dictatorship of the majority. I've always had a problem with bullies. In this case there was a certain amount of bullying there and that just stuck in my craw several times.

BCD: So these statements about what you're describing is kind of veiled threats that are only semi-explicit. Were those over wine and beer, or were those in the public sessions, or both?

APatrinos: It was probably over wine and beer. And, again, it was never explicitly stated. There was a hint of that, but you can just sense sometimes, especially with bureaucrats as they speak about the different machinations and the deliberations of their political masters. So there was never any doubt in my mind that that was certainly on our minds. And that's sort-of standard practice in many ways if you're fighting in the bureaucratic world and this is something that you try and do, because if you don't, you're always going to lose. You have to practice some of those techniques that are not always pure and commendable. Politics is the art of the possible.

With respect to the question that you posed that I didn't immediately answer about big labs versus small labs, big science versus small science, we were just starting to see some of that tension, but it was still too early. There were other meetings in subsequent years that were mostly NIH-led where some of the bloodletting was pretty vivid when the small labs realized after a certain point that there were not going to be 14 or 15 sequencing centers, and that there was only going to be a handful. And some of them, however prominent they may have been, or however hard they thought they were working on genome sequencing they were going to get cut off because they simply didn't have enough critical mass to be one of the major centers. But at the Bermuda meetings, even though there were hints of that, it was not something that was front and center.

BCD: So drawing you out on two things that are actually not on our script, but just they're related to it, one is you alluded to alternative frameworks other than a formal statement of principles and kind of almost a voting process that happened. I presume you have models in mind from other things in Department of Energy practice or in your personal experience or somewhere. Could you just give us...do you have some examples in mind of similar problems solved by different means?

APatrinos: Of course. I was very privileged in my career in government to be associated with the human genome project, but as it turned out I joined the federal government to become involved in another large scale both interagency and international program, which was known as the U.S. Global Change Research Program (USGCRP). The USGCRP was launched in 1989, during the first Bush administration. And it was in response to the realization that the rising greenhouse gas concentrations in the atmosphere were changing the climate. I don't know whether you remember that the summer of '88 was very hot and Jim Hansen, a

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famous NASA scientist, declared that climate change was upon us. Jim was arrested in front of the White House yesterday for protesting against the Keystone pipeline...that's a different story. The USGCRP is a major program that involves 13 agencies of the federal government and also has a larger than the human genome project international participation. The U.S. piece of the international program is about \$2 billion per year. The big-ticket item are the NASA satellites referred to as the Mission to Planet Earth, a set of very serious "birds" up there that make environmental measurements. And with the USGRP there are, interestingly enough, similar efforts to make sure that all the data acquired by satellites, ships, ground-based sites, etc. around the world as well as numerical models that are used to predict climate change, were shared widely. However, we never were extremely fanatical about how quickly the data should be shared. There was a sense that before you shared data you had to make sure you "quality assured" them, so that you wouldn't share "garbage." Therefore there was latitude given to individual data takers in terms of disseminating or sharing their data so that they would get an opportunity first of all to publish those data and get the scientific credit for their hard work, as well as also making sure that whatever was shared was of good quality. So I always felt that that policy was very sensible.

We encountered some opposition by several countries for a variety of reasons. I seem to recall that India was one of them, and maybe continues to be. I think that they consider all environmental data to be national security data. So they may have been reluctant to share those data with other countries. However, through the work of international agencies like the United Nations Environment Program and the World Meteorological Organization we made a lot of progress towards universal sharing of environmental data. And in fact, I had used that example when I had discussed it with Francis and Michael Morgan. But they didn't really see the relevance or the connection. And they thought this was entirely different because who would use those data to make money? I don't think that's true because climate data are used by Wall Street in the futures markets. I thought our USGCRP data policies were sensible. They didn't have those "religious" aspects to them.

BCD: So let me ask two questions to get at a couple of other things. One is, what happens if there are no Bermuda meetings? And what happens if there are no Bermuda principles? Do a kind of a counter-factual. How do you think things might have played out without the meetings at all and without the principles that came out of the meetings?

APatrinos: In many respects my answer is tied to the emergence of Celera and Craig Venter. So if Bermuda had not happened, it would have been invented subsequently when Craig posed the threat that he posed to the publicly funded program. The reason was that the data sharing policy could have been the one thing that would have distinguished the public program from the private effort because Craig would

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have been beholden to his corporate masters who did not agree to anything as harsh as releasing data within 24 hours.

BCD: And what about spillover to subsequent meetings in slightly different technical areas, like the Miami, the Toronto meetings, the Fort Lauderdale agreements, the other places where people have talked about sharing data, other than DNA sequence data? Did you participate in any ...

APatrinos: Well it was one of those cases where the more the principles were discussed and the more people agreed to them, the more united they became, the more they saw this as a way to become members of a smaller club and feel a lot more virtuous than the rest. And also to put more substance to what were principles in terms of application. I don't mean to be critical of Francis. Francis had both the vision and also had the strength and the inspiration and the energy to coordinate all these disparate groups. He also had incredible patience in managing all of these big egos. So in a sense, Bermuda prepared the ground for what were much easier subsequent negotiations, e.g. to divvy up the genome sequencing job and the data quality criteria. I repeat myself when I say that, on balance, the Bermuda meetings were very useful because they prepared the community that became the human genome project to undertake something under the gun, in the public view, and with reasonable success, I would say. And had those meetings not happened, we would not have been as prepared to meet the Celera challenge as we were.

BCD: So now shifting gears again, were there any discussions ... and the answer to this may be no ... but were there any discussions about people who should or should not be invited that would give us insights into how things were being thought about in the meetings that you were involved in planning? And what would be most interesting is if there were explicit decisions to not invite certain factions because of one reason or another.

APatrinos: No, I think it was pretty "democratic." Michael Morgan and the Wellcome Trust did very well in terms of reaching out to the appropriate communities. We in DOE were already starting to feel left out. I mean we had the Rodney Dangerfield syndrome of not getting much respect. You probably heard it yourself that we felt we never got enough credit for having launched the human genome project. I always used to tell my colleagues: Okay, we launched it. Now what are we doing? [Laughter]. What have we done lately? So we were flattered quite frankly with the attention and the inclusiveness that Michael Morgan and the Wellcome Trust practiced. They could have very easily ignored us. I mean it was very clear that DOE was not going to play a very big role in the program. And even if we had protested, and we may have had some support by the U.S. government, they could have very easily ignored us. So the fact that they included us and even listened to us was fairly significant to us. As far as I know there were no groups that should have been there that were excluded.

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BCD: So let me ask, in kind of retrospect now looking back X years, are there groups that you would now think about including that you didn't think about, or that the organizers didn't think about including at the time? And I'm thinking of two categories of constituencies in particular. One would be companies, whether that would have made sense. And the other is did it feel like this was a guys' thing, or was there any discussion or any thought about gender balance? Or were there disciplines that were left out?

APatrinos: With respect to companies, it was very, very clear that with the Wellcome Trust in the driver's seat that would have been a non-starter. And I think Francis went along because one of the main questions would have been, which companies would have been invited and which would not have been invited as a result? And that would have been a huge problem to reconcile.

I don't think it was a guy thing. I've worked in various areas of science and I find that in biology there is less of a gender problem than in other disciplines. Now it could be because I have the offending Y chromosome and I didn't notice. [Laughter]. However, I believe that I am sensitive to these things.

In terms of disciplines, remember that the focus here was sequencing, genome sequencing. There was always the argument that we did not include practitioners, geneticists, ethicists or others because this was focused on the sequencing. And it was always the argument we used when somebody perhaps may have wanted to come and felt slighted for not having been invited. So there is an interesting corollary or relevant little vignette that speaks to the question you've raised. I don't know how much you know about this, but between '97 and '98, I got into some really hot water with NIH and with the Wellcome Trust because I commissioned the group JASON to do an HGP study. It was led by a good friend of mine, Steve Koonin, who is now the Under Secretary of Energy for Science in the DOE. He was the chairman of JASON for many years, also Provost at Caltech. I don't know whether you've heard of him or know of him, but he led our study that involved many of the principal players of the human genome project, including Francis and Eric who came to La Jolla and made presentations to JASON. But then JASON shocked Francis by issuing a report that got picked up by *Science Magazine*. I don't know whether you've seen that report. It was prepared in the summer of '97. And it made some statements that were both insightful as well as naïve, as would happen with a group dominated by physicists who after all are the smartest people in the world, but also the most arrogant. And I love them dearly and some of my best friends are physicists, as I like to say.

BCD: Well just a parenthesis, we had our students read the most recent JASON report on DNA sequencing for our class on Wednesday.

APatrinos: Biologists Jerry Joyce and Steve Block were members of the JASON team that took on this study. I see these guys occasionally and I very much respect what

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they do. And frankly, the reason why I did what I did was for exactly what I was accused of doing. I wanted to “upset the apple cart” and get a perspective different than the mainstream because I became frustrated by the self-imposed isolation of the genomicists who did not want to see scientists from other fields getting into their turf. They had been waiting for many, many years to finally get some adequate funding. So there was a certain amount of let’s say “it’s our turn, so back off, guys.” But anyway, as a result of this report I got into fairly heated arguments with Francis and he also had words with Steve Koonin who summarized the JASON report in *Science Magazine*. I don’t know whether you’ve seen it. Eliot Marshall wrote a piece on that as well for that same issue of *Science*.

KM: Yes, we have seen it I think. I think it’s in our records, yeah.

APatrinos: So as a result of that spat with Francis and because after all we were still friends, during a breakfast with Francis (Francis and I continued to have our breakfast meetings every few months since 1995) we decided it would be a good idea to invite Steve Koonin to the Bermuda meeting, which was how he came to the ’98 meeting. Along with him came Jeff Wadsworth, who was the Deputy Director of the Lawrence Livermore National Laboratory, currently the CEO of the Battelle Memorial Institute, who at the time had oversight on behalf of the three major DOE labs of the Joint Genome Institute. The JGI was just launched with Elbert Branscomb as the director. So these were two individuals that certainly didn’t come to Bermuda because of their research involvements, but because of these other reasons. In some ways it’s sort-of a rebuttal to what you said. There were other people at Bermuda invited for various reasons. And there is a group picture that I will try to find of the participants of the ’98 meeting, with Jim Watson at the very center with Steve Koonin and Jeff Wadsworth next to him. And I recall that in his introductory comments Jim Watson surprised Francis by welcoming Steve Koonin and urging him to continue to be provocative with respect of challenging the principal players of the HGP.

BCD: And what was the point of conflict? What were the points of disagreement?

APatrinos: Well the principal one was that there wasn’t enough done in the HGP in terms of technology development. And that stung Francis because he believed that he was funding just the right amount of technology development.

KM: Sequencing technology?

APatrinos: Yes. So I mean you can get your hands on that particular report. It’s probably buried in some of my files. I haven’t been able to find it. I think the ...

BCD: So it would have come out of MITRE?

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APatrinos: Perhaps the article in *Science Magazine* is all you need to read because Steve Koonin was the author and he summarized the conclusions of the report. Eliot Marshall also referred to these conclusions in his one-page piece. That was the principal criticism that JASON made.

BCD: And what about computation and informatics and infrastructure and storage and transfer of data?

APatrinos: There was that as well. And in fact I think you can appreciate this: I spoke to Steve just yesterday, and he okayed sharing with you a pretty candid memo to files that he wrote on March 2nd '98 about the genome meeting in Bermuda. In it he speaks about his experience and the fact that he was welcomed as well as gives many other details of the meeting. ***[KM: This memo is included in the packet of files also containing APatrinos' notes from the 1998 Bermuda meeting.]*** My copy of the memo is in a three-hole binder so some of those words are obscured but you'll be able to figure them out. For example, in terms of the JASON report, he says, "Despite the strom and drang from some in the sequencing community, private conversation shows that our report found an interested and favorable audience. Most were pleased to see physical scientists engaged in sequencing problems and many of our recommendations and observations kept coming up in the private discussions. Whether there is cause and effect here in either direction is an interesting but largely irrelevant question. Maybe people were just being polite, the tenor of all of the interactions was more gentile than in the norm in physics, but my sense that we got it right, at least in the large, was reinforced. I think I've managed to patch things up with Phil Green and Francis Collins." Phil Green was one of the ones that really "foamed at the mouth" about the report. Steve Koonin says, "Beyond some of the technical nitpicking and sensitivity to the unprecedented outside scrutiny, much of the problem here can be summarized by the reaction, "Of course! We've already thought of that. You just didn't hear about it because of the mostly DOE briefers you had. Indeed I could well have interpreted some of Francis' and Phil's public remarks as the unacknowledged echoes of our recommendations. Their future engagements with the human genome project need to be done with a bit more tact and forwardness involving the NIH and DOE as equals if NIH is amenable to that." Anyway, you'll find it interesting.

BCD: Yeah, we've got the report in front of us here.

APatrinos: Oh, you have it, okay. Sorry, I shouldn't have read it.

KM: Well we found it online.

BCD: No, no, no, we don't have that memo.

APatrinos: Oh, okay.

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BCD: No, we don't have that memo. What we have is the JASON report. No, that memo is going to be incredibly valuable.

APatrinos: Yeah, Steve in the end notes, "in reading this and the official report of last year's meeting I was struck by a similarity of the two. Everyone seems to be so busy cranking out sequence that the issues and the suggestions discussed get short shrift. And also although the venue was charming, this wasn't the boondoggle it might seem. Rather I had two solid days of meetings without the chance to see anything of the island, which appeared to be a place worth going back to as a tourist. But overall a worthwhile trip." Anyway, you'll find that interesting.

BCD: So on the point of computational biology, one of the points that some people have raised in many venues, in many writings, is the relative amount of attention to sequencing and generating data compared to storing, transmitting and making it useable and thinking about how to interpret it and do computation based on it. In retrospect do you feel like you all had a pretty good balance? And were the Bermuda meetings at all about the computational aspects?

APatrinos: Oh, yes, there was quite a bit of that. I guess also when you say "computational biology" what do you mean? I distinguish computational biology from bioinformatics, so for me when you say "computational biology" I mostly think about such things as the inverse protein-folding problem whereas I think you refer to mostly as bioinformatics. Is that correct?

BCD: Well, yeah, bioinformatics certainly and even both ... each of those terms has lots and lots of definitions. But really what I was trying to get at is you're creating lots and lots of data and then you're going to try to make sense of it. And the making sense part is where you really can't do that without computers and algorithms and people who curate databases and all sorts of both infrastructure and intellectual activity that's different from the biology or the sequence generation. And I was just wondering whether in retrospect it felt like, yeah, we were paying enough attention to that, we had a pretty good idea what the problems were going to be down the road? Or does it feel like there were things that came back later that proved to be more important as the central problems that weren't fully considered at the time?

APatrinos: All right, so I've got my biases here and they're going to come through obviously, in how I respond. So could we have done things much better? Of course! Hindsight is always 20/20. There were many, many things that we did wrong. And I blame myself for that. We made some investments in things like GDB and GSDB that were frankly not particularly helpful or didn't really lead to anything. And I also found that bioinformaticists could be crybabies sometimes. They always want more attention; they always want more funding. They are the ones that usually complain the loudest, and maybe sometimes for good reasons, but not always. So I think given the fact that the scientists involved in the HGP were

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mostly biologists meant they were fairly unprepared and culturally not ready to do this large project. Physicists had 100 years on them with respect to working in large teams and collecting and processing and analyzing large amounts of data from all the accelerators and reactors and all these other big toys that physicists have had the luxury of enjoying for a century. This was biology's moon shot. So in some ways we were on virgin territory. I think the investment that was made and the attention that was paid to bioinformatics was just about right. I know David Lipman will kill me [Laughter] and Phil Green will continue to dislike me. And even my good friend and former deputy when I was in DOE, John Wooley, will disagree with me on this. So I thought we were just about right with respect to bioinformatics.

BCD: So, Kat, do you have any...I feel like, [APatrinos], you've covered an awful lot of the bases that we wanted to make sure that we've gone over, and you've been incredibly succinct and articulate. Can you think of anything ... this is always the hopelessly open-ended question at the back end ... but is there anything on the tip of your tongue that we should have asked you?

APatrinos: No. I think this last coverage with respect to JASON is fairly important because I think it had a fairly significant influence on us, on the public program, however much bad blood it caused. And it also in some way presaged the advent of the Celera threat. And that played out in some way at the '98 meeting in Bermuda. By that time of course, Craig had already declared us "the liars' club." And continued fairly publicly referring to us as people making outrageous and too ambitious statements about what we had accomplished so far, and what we were capable of producing in the next few years. So that was the only thing that comes to mind. Otherwise, again as I said in the beginning Bermuda on balance was a good thing for the HGP because it really prepared us for many of the battles that came subsequently and we would not have been as prepared had we not had those meetings. So in some ways, Michael deserves a lot of credit for thinking about that and pushing hard to make these meetings happen.

BCD: So now you have alluded umpteen times to Celera and the fights that came after May of '98 up until...well after actually the June 2000 announcement and the publications in February of 2001. We've got you on the line, and you were a truly pivotal figure in that story. Do you have any observations about that and how Bermuda colors that history?

APatrinos: Well it certainly was my 15 minutes of fame. [Laughter]. I think again that Bermuda was the first time that this community of people came together that was so central to what transpired subsequently, and what ended up as a good news story with respect to at least the appearance of comity and calling the race a tie in June of 2000. There is no question that during those heady times many of us thought back to the Bermuda meetings because that was the first time we had come together as a community and frankly, even had this vision of something that

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was much bigger than our individual involvements. That's the thought that comes to mind.

BCD: So who had the idea of the pizza meetings?

APatrinos: Well I was interviewed about this so I'm going to say what I've said all along, and that I was extremely privileged to know, work and be even considered a friend by these two very wonderful people, very different in so many respects, but yet so near and dear to my heart, and people that I also admire in terms of their capabilities, their dedication and above all, their passion. And that's Francis and Craig. So as 2000 was unwinding, and even before then, in '99, I was very distraught about what was coming across as a mudslinging fight that was distorting the image and the reputation of both of these men that I admired so much. So there was no question in my mind: I wanted to work as hard as I could to come up with some solution that avoided either one of them looking bad, because neither one of them deserved to look that way. I was lucky that I had the ear of both of them; there weren't very many people, frankly, that had that. I was also a neighbor of Francis. Sometimes some of the things that help are very simple. So I would see Francis quite often, especially during those days. And I was already pretty good friends with Craig and I would see him usually or speak to him on Sunday, and sometimes we would walk his dogs in one of the parks. So I said, Well why don't we do this? Why don't we meet off the record? In many respects both of them had been enveloped by their own cocoons. Now these cocoons, they made them themselves, but they may not have been very conscious of what had been happening to them. They were surrounded by people who were mostly keen or eager to see their own man be the victor. On that point both Francis and Craig were not well served by their immediate entourages. I wanted to see an outcome that was a win-win. In many respects I was also helped by the political masters at the time, especially Ernie Moniz, who was the Under Secretary of Energy. He's at MIT now. I don't know whether you know Ernie.

BCD: Yeah, I do.

APatrinos: Ernie at least had my back because I was doing things that were now getting into the political realm and there's always some danger of getting seriously hurt when you get to those levels. So anyway, the details have been ... I don't know whether you read any of the books.

BCD: Yeah, we've read them all.

APatrinos: I think Jamie Shreeve did a very good job describing what happened.

BCD: One thing I did want to get at though is one of the questions that's always lingered in the back of my mind, the story that comes out of most of those accounts, especially Jamie's, is this Clinton to Lane to Patrinos, it sounds like it was a top

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down decision. The way I've heard you just describe it, it sounds like this might have actually happened anyway. Bill Clinton might have ... certainly when the President says, "It would be nice if these guys stop yelling at each other in public," that would certainly intensify the energy going into solving that problem. But it sounds like you were already paying attention to this and distressed by it and prone to do something about it anyway.

APatrinos: So I don't have a very big ego, but I can understand how people with big egos want to make sure they take as much credit as they can. And I don't mean it in a derogatory way. So in some way people in the White House may have wanted to present this as this very powerful leader who just slammed his fist on the table and said, "Make this happen!" I never heard from Neal Lane, and Neal Lane himself, you can ask him, chuckled about it when we've discussed it. Also to be a little critical of Francis, even though I love him dearly, in his own book at some point he wanted to make it seem like he was the one who asked me to do this, which was also not true because I had been bugging him to do this for a very long time. He was very, very concerned and paranoid about what his brethren in the human genome project, for example Lander, Sulston, Waterston, and some of the other big boys on his side would say. So it was only until it got so obvious that things were going to go from bad to worse that he gave in and sort of reluctantly agreed to come in and have at least one of those meetings, never expecting that anything would come of it; the same way on the part of Craig. And it was one of these magical moments when they were by themselves, because I was frankly just a bystander that it clicked. It was the first time they had been together alone in a long time. I don't know, maybe it was the first time ever. So the chemistry happened very, very quickly. It was very, very obvious that they realized what had been happening to them with respect to their own individual cocoons that they themselves had created.

BCD: That's really helpful. And just to make sure that I understand, so it sounds like maybe some of grand political, that this was a puppet show from the top is a little bit of an urban myth. Is that a fair statement?

APatrinos: Yeah. I mean ... as you said yourself, Clinton may have in fact said something to that effect. But the first time people heard about this in the White House, at least the people that interacted with Neal Lane and Rachel Levinson was when this had already pretty much been cooked. We had already met three times and then we decided it was time that we tell our political masters, which is when I told Ernie Moniz who immediately said, Gee, this sounds like a great thing. I'll support you whatever you do, and keep up the good work, and just let me know what I can do to help. And then Francis told...at the time it was...oh, I forget her name, the one that passed...

BCD: Bernadine. Bernadine Healy.

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APatrinos: No, no, no, not Bernadine Healy. No, no, no. That was Varmus's deputy...what's her name? She was acting director of NIH.

BCD: Oh, oh, oh, Ruth Kirschstein?

APatrinos: Yeah, Ruth Kirschstein. And immediately when Neal Lane found out about it, he was very eager to make it happen. And one person you need to speak to is Jeff Smith. You know Jeff?

BCD: No, I don't. That's a new name.

APatrinos: Oh, gosh, Jeff Smith was Neal Lane's Chief of Staff. He is now in the White House. He is sort of the Senior Assistant to John Holdren.

BCD: Okay, so he's in OSTP.

APatrinos: Yeah, he is. When he found out and the White House found out about these negotiations, he was the person that I communicated with almost on a daily, sometimes hourly basis as we were trying to make sure that the fragile ceasefire and agreement were nurtured and maintained, because there were many, many threads to this. And as I said, the people in the "cocoon" may not have been thrilled with this rapprochement. Anyway, talk to Jeff Smith.

BCD: Yeah, that's an extremely helpful comment, so we will follow up on that. So I don't want to consume a whole bunch more of your time. So I hope that we can get back to you. And I would love to ... is your secretary going to be preparing a package, or do we need to come out there?

APatrinos: No, I'll ask Isi to make copies and then I'll redact some of the things that are personal. Whenever it's something personal it's usually in Greek. [Laughter]. There's that added security.

KM: What do you mean? I speak fluent ... [Laughter] ... really kidding.

BCD: All right, well [APatrinos], thank you so much for giving us so generously of your time. And also for organizing your documents. That's incredibly helpful to us. And we will keep you in the loop as we make progress on this.

KM: Yeah, thank you so much. And so we're going to make a transcript of this interview and as soon as we get it back, which will be the middle of next week, assuming I get it to the transcriptionist tomorrow, which I will, you will have the opportunity to edit and take anything out that you want and then send it back to us. And there's also going to be a permission form that we send along with the interview because we're thinking of making a database of research materials from

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this project and you can read about it on this form. But, Bob, is there anything else you want to say?

BCD: So there will be a form that basically stipulates when it can be released. And so your responsibilities at this point are to review the transcript, take out anything that you don't want made public. And there will be a set of choices about sharing it. It could be here through Duke, or we're also trying to ... our grant's going to expire in about four years and it can't be renewed ... that's a ground rule of the CEER grants, the ELSI grants. So we are also trying to build some bridges to permanent archival repositories for documents like this, so it could be Cold Spring Harbor, Wellcome, Duke University Libraries or wherever. We're trying to figure that stuff out, but we do want to make these public records.

APatrinos: Good luck to you guys.

BCD: Okay.

KM: Thank you so much.

BCD: Thank you.

APatrinos: A pleasure, bye-bye.

END OF RECORDING