AW: Telefon interview

Ursula Hurtenbach <kontakt@scieconomics.com> November 7, 2012 8:54 AM
Hide Details
To: Kathryn Maxson <kat.maxson@duke.edu>
Cc: Laplace, Frank /614 <Frank.Laplace@bmbf.bund.de> (Frank.Laplace@bmbf.bund.de) <Frank.Laplace@bmbf.bund.de> , Andreas Weller <andreas.weller@dlr.de> , Bob Cook-Deegan <bob.cd@duke.edu>
AW: Telefon interview

1 Attachment, 53 KB Save Quick Look

Dear Kathryn,

please find attached the document with your questions and our answers. We have tried to give you a broad overview on the genesis and the handling of the German Human Genome Project. The corrections marked in red in question 3b on pages 3 and 4 reflect the correct name of one of the participants (M-L. Yaspo) and the correct affiliation of U. Hurtenbach.
If you have any further questions beyond the present information, we will be happy to answer them. Please understand, that we always prefer to answer questions in written form, in particular those with a political background, since we like to have the agreement of the Ministry when talking about political issues. If you wish a telephone interview beyond that, we prefer to discuss your questions 'off the record'.

I apologize for taking this long time to respond to your query.

With kind regards and my very best wishes for you personally and for your work,

Ursula

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AW: Permission to post our correspondence in a public archive

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Dear Mrs Maxson,

please accept my sincere apologies for this very late reply to your email of May 19,2013. I do hope that you can still complete your project including the deposition in the public database before your move to Princeton.

As to your question regarding IP:

a) Are you aware of the types of patents, specifically, that were desired by the industry consortium, especially with regards to genetic material? For instance, would you say that the privileged reading policy was driven largely by desire for patents of the like held by Myriad Genetics, on BRCA1/BRCA2 genes themselves and diagnostic methods for these genes? Or on genes for therapeutic proteins, like erythropoietin (Epo), as well as for the proteins themselves in purified form (of the likes held by Amgen)? Or both of these things as well as other inventions? In summary, I am interested in your sense of the major intellectual property motivators for this policy.
b) I am also interested in the IP that came out of the policy during the two-year period (1995-1997) it was in effect. I imagine that the patents would have been held by the companies in the consortium themselves. Are you aware of any major, profitable IP that resulted from the policy? If not, do you know how I might find this information?

a) We do not recall that the members of the Förderverein Humangenomforschung (industry consortium) had a focused interest in any specific type of patents. The types of patents you mentioned certainly were not excluded from the range of results that the industry consortium had been striving for. The major motivator for the rules was the expectation that the privileged reading access would lead to subsequent co-operations between academic research groups and German industry on particular results that had been generated by the academic groups.

b) No IP applications arose from the privileged reading access of the industry consortium to the Primary Database at the Resource Center. (We would like to add that any patents that could have resulted would have been owned by the groups that had generated the invention.)

Both Dr. Laplace on behalf of BMBF and I on behalf of the Projektträger DLR consent to making publicly accessible the PDF document you had been sent in November last year. You are welcome to also include the answer to your question in this email.

Please do not hesitate to contact me with any further question that may arise.

All the best to you and
kind regards

Andreas Weller

Dr. Andreas Weller

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Von: Kathryn Maxson [mailto:kat.maxson@duke.edu]
Gesendet: Freitag, 5. Juli 2013 02:49
An: Laplace, Frank /614 (Frank.Laplace@bmbf.bund.de); Weller, Andreas
Betreff: Permission to post our correspondence in a public archive

Dear Drs. Laplace and Weller,

I hope that you are both well.
I am working on our public archive of research materials for the Bermuda Principles project, which will be housed here: http://dukespace.lib.duke.edu/dspace/handle/10161/7407.

On that note, I am wondering if you have made any progress on my queries from May of this year. My questions were the following:

1) Are you aware of any notable intellectual property that arose from the privileged reading period the industry consortium had for the DHGP Primary Database from 1995-1997?
2) Are you willing to have the PDF version of your answers to my questions (attached), which you sent to me via email, archived in our public database? I would also include any answers you might be able to provide to question (1) above. We believe your answers are of great relevance to scholars of the Human Genome Project. Email consent would be all we would need. You could also provide a time embargo on the materials, so that they would become publicly available via the archive at some point in the future. (None of the materials will become available before 1 July 2014.)

Please let me know. My Duke credentials expire on 15 July as I am leaving to attend graduate school. I am hoping to attend to all of these archiving matters before I leave.
My kindest regards, and greatest thanks for your help on this project.
Kathryn Maxson

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Questions for Dr. Ursula Hurtenbach, Dr. Andreas Weller, and BMBF
September 11, 2012

1. **It is my understanding that the BMBF began formally funding German researchers as part of the international Human Genome Project in 1997. Federal grants for sequencing and analysis were then given to a consortium of three laboratories: the Department of Genome Analysis, IMB, Jena; the Max Planck Institute for Molecular Genetics, Berlin; and the German Research Centre for Biotechnology, Braunschweig.**

    a. **Is this information correct? If not, how am I mistaken?**

This is not entirely correct. There had not been a formal decision to participate in the international Human Genome Project with the aim to focus on the sequencing of the human genome.

Already two years earlier than 1997, on May 20, 1995, the German Federal Ministry for Education and Research (BMBF) together with the Deutsche Forschungsgemeinschaft (DFG) and the Max-Planck-Society had published a funding concept that aimed at the development and strengthening of the German scientific community in the area of human genome research at large. The primary goal was to establish a national research network (Deutsches Humangenomprojekt **DHGP**) for the identification of medically relevant genes and for the analysis of their structure, function, and regulation on the basis of an integrated systematic research approach. This concept included a tight cooperation of the national research with international activities in human genome research. A second and equally important goal for BMBF was to increase knowledge on the etiology and pathology of diseases with high socioeconomic relevance, and thereby to develop approaches for the causal treatment of such diseases. This included also the development of new products and services by the German pharmaceutical and biotech industry. Both motivations aimed at strengthening innovation and competitiveness in Germany.

The call which was published together with this funding concept comprised a very broad range of topics. Among many other topics the sequencing of the human genome was part of this call. In fact, a central element of the DHGP strategy was the provision and utilization of materials (nylon filters and later glass slides as forerunners of DNA chips) and resources (genomic and cDNA libraries) by the Resource Center (see more details below under answer 1b) in order to create a highly systematic and integrated national research network that is focused on the identification and analysis of disease factors. Thus, the participation of German research groups in the sequencing activities of the international Human Genome Project was certainly considered both possible and desirable by BMBF but was not the main focus of the DHGP. Thus, neither had there been a formal decision to participate in the international Human Genome Project, nor had there been a letter of intent to the Human Genome Organization HUGO announcing a participation.

During 1996 and early 1997, a peer review committee of national and international experts identified a number of research projects that subsequently were granted by BMBF. Approximately 60 grants were awarded, including those for the three research institutes involved

in sequencing of chromosome 21 and other regions (called the "Genomic DNA Sequencing Consortium"). All 60 grants together comprised the DHGP. Funding was awarded for a duration of 3 years.

b. What other bureaucratic information about the German Human Genome Project would enhance my understanding? For instance, was funding channeled through a particular project agency? How often were the grants renewed? What was the role of industrial funding in the overall funding for the German HGP?

DLR as a project management agency on behalf of BMBF:
BMBF is supported by so called "Projektträger" (project management agencies) in its project funding activities. Legally speaking, the "Projektträger im DLR" acted as the granting institution on behalf of BMBF. The Projektträger im DLR has been in charge of this function for the entire duration of the DHGP. The Projektträger im DLR is part of the Helmholtz Research Center DLR (Deutsches Zentrum für Luft- und Raumfahrt - German Aerospace Centre).

Renewal of grants within DHGP:
In August 1998, BMBF published a second call for applications as part of the DHGP. This call was open for the same range of possible research topics as the first call. It was also open to research groups not yet funded within DHGP. Among many other projects that had been funded during the first round, also the Genomic DNA Sequencing Consortium successfully reapplied for continuation of funding and was awarded follow-up grants.

The role of the pharmaceutical industry:
By early 1995, it had become apparent that lack of awareness for IP protection prior to publication of research results by German academic researchers was a problem for industry to further develop the results into new products. In the context of its efforts in the development of the DHGP funding concept, BMBF had invited eight German pharmaceutical companies to participate in the DHGP initiative. BMBF together with this industry consortium (**"Förderverein Humangenomforschung"**) developed a concept that would improve the awareness for IP issues and support IP protection. The goal was to improve the transfer of scientific results into novel industrial applications. Central element was a patenting and licencing agency (Patent- und Lizenzagentur, PLA) that supported the academic researchers within the DHGP in issues such as IP protection, material transfer agreements and licensing negotiations. In response to the financing of this PLA by the Förderverein, the Förderverein members had been offered a privileged reading access to data in the **Primary Database** located at the **Resource Center (RZPD)** of the DHGP. The RZPD was financed by BMBF as part of the DHGP and run by the Max-Planck-Institute for Molecular Genetics at Berlin (under the leadership of Prof. Hans Lehrach) and the German Cancer Research Center DKFZ at Heidelberg (under the leadership of the late Prof. Annemarie Poustka). All research groups funded by BMBF within the DHGP were obliged to file the data which had been generated by utilizing materials and services of the RZPD into the Primary Database. The owners of the data could request confidentiality of these data for a maximum of six months after deposition of the data into the Primary Database. After this, a privileged reading access of three months was given to the members of the Förderverein, followed by open access to all researchers worldwide. Thus the privileged reading access meant

a head start of three months in data access for the members of the Förderverein in comparison to other research groups and companies world-wide. This reading access did not affect the status of ownership of the data but offered options for bilateral co-operations with the DHGP research groups or for licensing negotiations with the owners of the data. Also, this reading access related to all data within the Primary Database of all DHGP research groups.

c. What was the Ministry's understanding of the landscape of genomics research being conducted in Germany before the administration of BMBF grants?

The scientific community in Germany comprised many excellent research groups in human genetics, in molecular biology research including analysis of gene function and regulation. In addition, the scientific community also comprised a number of research groups in the emerging field of development and application of high throughput techniques, such as DNA sequencing. But the scientific community was considered severely lacking of sufficient capacity (both in personnel and resources) and nation-wide networking. With respect to aspects of technology transfer see above in answer 1b.

2. What factors motivated the Federal Ministry to become involved in the Human Genome Project? Along these lines, did any particular factors contribute to hesitation about BMBF participation in the Human Genome Project? (The project began in the United States in 1990, but BMBF participation came several years later.)

With respect to BMBF's motivation see answers to question 1. There had not been hesitation on the part of BMBF concerning participation in the international Human Genome Project. According to the German constitution, responsibility for academic research in general lies with the Federal Bundesländer (and the universities which are financed by them) and the German research institutions, such as the Max Planck Society or the Helmholtz Association of Research Centers. Apart from research conducted through these institutional funds, the Deutsche Forschungsgemeinschaft (DFG) is the main source for project funding of basic research in Germany. As in other countries, there had been a debate within the scientific community also in Germany concerning the international Human Genome Project and participation therein. In 1994, the DFG approached BMBF with the proposition of funding a German Human Genome Project. This was the starting point for BMBF for the development of the DHGP as described in answer 1a and b.

3. My research has shown that Germany sent the following (listed below) delegates to the three International Strategy Meetings on Human Genome Sequencing in Bermuda (1996-1998). Would you mind telling me if this is correct, to the best of your knowledge?

a. 1996: Hans Lehrach from MPI, Andre Rosenthal from IMB, and Frank Laplace from the Federal Ministry
b. 1997: Fiona Francis from MPI, Ursula Hurtenbach from Project Management Agency DLR on behalf of BMFB, and Andre Rosenthal from Jena

c. 1998: Marie-Laure Yaspo from MPI, Ursula Hurtenbach from Project Management Agency DLR, and Andre Rosenthal from Jena

Fiona Francis, Hans Lehrach, Andre Rosenthal, and Marie-Laure Yaspo had been invited by the organizers of the Strategy Meeting and participated as German scientists who had been pursuing large scale sequencing projects in co-ordination and cooperation with the international Human Genome Project. Frank Laplace and Ursula Hurtenbach (concerning her affilitation see above answer 1b) participated on behalf of BMBF as the funding institution of the DHGP.

4. Before the 1996 meeting, what was the Ministry's perception of what was to be discussed in Bermuda? Was there an expectation that data sharing procedures for the project were to be discussed? What was the reaction of the Ministry to the 1996 meeting, and how (if at all) did the meeting affect the decision of BMBF to formally enter the HGP the next year?

To the best of our recollection, the perception of topics to be discussed in Bermuda related to all questions important for the successful realization of the very demanding international "big science project" of sequencing the human genome. These included aspects such as avoiding redundant sequencing, questions of data quality and data banking, and certainly also data sharing and data publication. The perception had been that the speed of publication of results was an important issue, but also that there was no consensus, yet, within the international scientific community in what time frame (and at what level of finalization) large scale sequencing projects would be expected to publish their sequencing results. The perception also included that the conditions of the German DHGP with respect to publication were not problematic as they in fact demanded the rapid publication of the data within the Primary Database of the Resource Center and that the privileged reading access of the members of the Förderverein of only 3 months were quite in line with the time frames discussed in the scientific community at that time. Thus, the discussions at the 1996 meeting did not in any way affect the finalization of the review process after the 1995 call for proposals and the formal decisions on the DHGP grants including those for the German DNA Sequencing Consortium (see also answer 1).

5. At the 1997 Bermuda meeting in particular, concerns about the BMBF policy on sharing genomic data were raised by American and British scientists. The following is a quote from the 1997 Bermuda meeting report, obtained from the U.S. NIH:

"The conditions imposed on data release in Germany were extensively discussed. The German genome sequencing initiative is partly funded by industry and partly via the BMBF. The BMBF funding is dependent on demonstrated benefits to industry. Raw data is not released but submitted to a private database for three months to which the industrial funders have exclusive access. At the end of this period, sequence which has generally been finished in this time is released into the public databases."

a. Is this an accurate representation of the BMBF policy, in terms of content only, about the release of genomic data in 1997?

No, this is not entirely correct.

All of the German DHGP and thus also the German Genomic DNA Sequencing Consortium was exclusively funded by BMBF; none of the scientific projects from the entire DHGP obtained industry funds. The sentence ***Raw data is not released but submitted to a private database for three months to which the industrial funders have exclusive access*** is correct with respect to the privileged reading access rules of the DHGP for the Förderverein members at that time. It is not correct in that the Primary Database of the Resource Center was a **public** database. The privileged reading access rules were changed for data of the German Genomic DNA Sequencing Consortium. This change was instantly initiated after the Bermuda II meeting (in March 1997).

b. Content aside, the tone of this quote (and the tone of other segments of the report on the same issue) is relatively harsh. What are your reactions to this tone?

The 1997 Bermuda meeting was characterized by intense discussions on data release policy. The emotional intensity was reflected to some degree in the wording of the report. The threat to exclude German scientist from the international human genome research community, however, was more severe and was taken very seriously by BMBF. In response to this threat, immediately after the Bermuda II meeting a 'Bermuda workshop' was organized to which all important players from the US and UK were invited. It was unfortunate from our point of view that none of them followed the invitation to the 'Bermuda workshop' where the issue of data exploitation and harmonization of the international regulations were to be discussed.

c. Could you please tell me about the history of, and reasons for, this policy? For instance, was this the policy for all scientific data generated by projects supported by BMBF, or did it apply only to HGP sequence information? What were the major factors motivating this policy, and how does it relate to the philosophy of BMBF towards federally funded research (in terms of disease treatment, drug development, improved public health, etc.)?

Most aspects of this question have been answered above (in particular answer 1b). The policy of a privileged reading access for pharmaceutical companies was a particular agreement in the context of the DHGP. It applied to all research project funded as part of the DHGP (except for the Genomic DNA Sequencing Consortium after March 1997), and it was limited to the duration of the DHGP (1995 until 2004). This policy was not relevant for any other research funding by BMBF before, during or after that time. It was established by BMBF in the DHGP concept with the goal of supporting the rapid transfer of research results from academic research groups into medical, pharmaceutical and biotech products and services through co-operations of industrial research groups with the academic groups.

d. Does this policy still exist (at least in some form) today? If so, how? If not, why not?

Since completion of funding of the DHGP (in 2004) after the second DHGP call for proposals, a privileged reading access to primary data for pharmaceutical or biotech enterprises has not been established again in any BMBF funding measure. In line with the very rapid developments in "omics" research, such a reading privilege has not been considered sufficiently important any

more. However, other aspects such as support of academic research groups in IP and technology transfer issues have been developed further and are still in place.

6. It is my understanding that by the 1998 Bermuda meeting, BMBF had changed its policy with regards to the release of DNA sequence data generated by high-throughput sequencing centers funded with public money. Here is a quote from the 1998 Bermuda meeting report, also obtained via the U.S. NIH:

"The Wellcome Trust reaffirmed its commitment, and that of the Sanger Centre, to early data release. Confirmation from the BMBF that the German genome sequence consortium could now fully adhere to the Bermuda Principles was warmly welcomed."

a. What factors influenced the decision within the Federal Ministry to change its data policy? For instance, did any individuals external to the Ministry exert pressure on Ministry representatives? (My research has shown that both Andre Rosenthal, and Michael Morgan/Francis Collins, did so in the form of both public statements and letters. Is this true?)

The major driving force for BMBF for cancelling the privileged reading access rules for data of the Genomic DNA Sequencing Consortium was to hold off distress from the German scientists and to keep them an equal member of the human genome research community. A voluntary moratorium of the reading access had been offered by the Förderverein already in March 1997 and was implemented immediately by the RZPD. This was communicated to the organizers of the Bermuda meeting (Wellcome Trust / Michael Morgan and NIH / Francis Collins), who had informed BMBF about the meeting by letter. Public statements and letters by third party persons just reiterating the Bermuda II events were not a decisive element.

b. With which individuals in the Ministry did the ultimate decision about this policy shift eventually lie? Were there any individuals who were particularly influential within the Ministry during this process?

The issue was discussed intensely at several levels within BMBF and with several external institutions including the Förderverein and the Scientific Steering Committee of the DHGP (representatives of the funded DHGP projects elected by the DHGP researchers; at that time: Profs. Rudi Balling, Hans Lehrach and Jens Reich). In addition, a 'Bermuda workshop' was organized (see answer 5b and below). The final decision of course was signed by one BMBF officer, however, this decision was consensual among all BMBF representatives involved.

c. **Could you describe the process of policy change between the 1997 and 1998 Bermuda meetings? For instance, were there particular formal discussions and meetings within the Ministry about this issue? Did American or British scientists play any role in negotiations, etc.?**

As already mentioned in answer 5b, a 'Bermuda workshop' was organized shortly after the 1997 meeting. The invitation list included renowned genome researchers from Germany and from

abroad (in particular from amongst the Bermuda participants), experts on patent law as well as representatives from the industry Förderverein. The workshop took place on May 26, 1997 at Bonn.
It was stressed at this workshop that impediments to co-operation and communication between German and international human genome researchers would be very detrimental to the German genome research community and that this should be avoided. However, it was also pointed out that rapid publication of sequence data may impede exploitation of the research results by impeding patent protection of inventions, an important prerequisite for the development of medical and industrial products. It was also pointed out that the patent law in Germany (and in all of Europe) due to its principle of "first to file" causes a disadvantage in comparison to the US patent law which is based on the principle of "first to invent" and which includes a "grace period" of six months after publication, during which patent applications can still be filed.

Final result of the discussion process was that the voluntary moratorium of the reading access implemented immediately after the 1997 Bermuda meeting became permanent. British or US representatives did not play important roles in this discussion process as none of them followed the invitation to this workshop.

d. Could you tell me a few more specifics about the new policy described above? For instance, in 1998 the Bermuda agreement was extended from just human sequence data produced in high-throughput centers, to data produced for all organisms. Did the new BMBF policy apply to all data, or just to human?

The abrogation of the privileged reading access for the members of the industry Förderverein which was implemented in March 1997, already then encompassed both human genomic as well as cDNA sequences. Therefore, an extension to large scale cDNA sequence data in response to the 1998 Bermuda meeting was not necessary.
To the best of our knowledge, there were no DHGP grants directly financing high throughput sequencing of model organisms. Other funding measures by BMBF such as the National Genome Research Network NGFN which commenced in 2001 and which eventually replaced the DHGP, did not involve any privileged reading access for third parties.

7. What was the German policy on patenting genetic material at the time of the Bermuda meetings (1996-1998)? (To add some context, these meetings were in the wake of the NIH/Venter cDNA patent applications of 1991 and 1992, and the breast cancer gene patent battle already beginning to brew in the United States and Britain.) The Bermuda agreement was explicitly (at least in part) intended to prevent patents on primary human genomic sequence. How did this agreement interact with the norms of patenting genetic material already present in Germany, especially in the midst of a worldwide trend towards biotechnology patents more generally?

The focus of this question lies outside the area of BMBF responsibility and goes beyond our expertise. We would propose to contact institutions such as the European Patent Office for details in the development of the patent law or of regulations specifying patenting procedures involving sequencing data during that time. However, it may be helpful to mention that Germany

as a member state of the European Union also signed a European convention on patent law. Thus, any changes in German patent law require prior negotiations at this European level.

8. **Do you have any comments that were not covered in your answers to the questions above? Furthermore, do you have any questions for me?**

No.