DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Cancer Institute

Memorandum

ADMINISTRATIVE CONFIDENTIAL

Date August 27, 1985

From Peter Fischinger, M.D., Ph.D.
Associate Director, NCI

Subject Patent and Related Claims of Institut Pasteur Concerning the Inventions Dealing with the Causative Virus of AIDS and the Resulting Testing Technology

To Lowell Harmison, Ph.D.
Science Advisor, OASH
Through: Director, NCI____
Director, NIH____
Office of the General Counsel____

I. INTRODUCTORY COMMENTS:

Following the August 6 meeting with representatives of the Institut Pasteur and their U.S. licensee, Genetic Systems, NCI was asked by Dr. Lowell Harmison to determine whether there is any factual support for their verbal claims that Dr. R. Gallo and his group either knowingly or mistakenly appropriated an invention claimed by Dr. L. Montagnier of the Institut Pasteur. Further, Dr. Harmison asked that the Patent Branch and members of the August 6 meeting assist NCI in this task.

Following conversations with Dr. Gallo and members of his group, and an initial review of the pertinent records from Dr. Gallo's laboratory, a review of the patent applications and scientific publications of the French and Dr. Gallo, as well as material provided HHS by Dr. Dedonder in support of the Institut Pasteur's position, NCI, Office of the Director, NIH, and the Patent Branch, concluded that there is no substantive support for the French claims of purported primacy of inventorship or of HHS' derivation of inventions from other sources.

A summary of findings and a discussion of the legal considerations raised by the French at the August 6 meeting were compiled as requested by Dr. Harmison and discussed at a progress meeting on August 21. Each allegation was discussed in detail.

These compressed assessments, which sequentially address the issues raised, were compiled from a relatively complex background information source, which in turn was abstracted from raw laboratory data, correspondence and other sources. The accuracy and the interpretation of the scientific content has been attested to by Dr. Gallo himself.

II. SALIENT POINTS OF INVENTORSHIP

It is now known that AIDS is caused by a newly recognized retrovirus. In terms of correctly attributing inventorship, based upon who first conceived the invention, the following questions must be addressed:

1. Who first had the idea that AIDS is caused by a retrovirus?

   It is unequivocal that Gallo proposed that a retrovirus may be the causative agent of AIDS in May 1982, at the Cold Spring Harbor Symposium on RNA Tumor Viruses, and is quoted in the medical lay press to that effect in August 1982.

2. Who first isolated the virus in AIDS patients?

   The examination of data from Gallo's laboratory showed that in mid-December 1982, the first two HTLV-III-type isolates had been identified from AIDS patients. A letter from J. C. Chermann, Institut Pasteur, to R. Gallo indicated that the first positive French data

were obtained in January 1983. Subsequently, in response to the French request to Dr. Gallo for virus-typing reagents, which he provided to them in March of 1983, the French isolated a virus, which they called lymphadenopathy-associated virus (LAV) from a single lymphadenopathy patient, and published their findings in Science, May 1983. Further, the French could not develop an effective diagnostic test until more than one year after this publication, and after Gallo's discovery as defined in the U.S. patent application # 602,946.

3. Who first linked the correct virus unequivocally to human AIDS? Scientists from Gallo's laboratory published in Science, May 1984, solid, unequivocal evidence that the causative agent of AIDS is HTLV-III. Subsequently, in Science, July 1984, a joint manuscript from the CDC and the Pasteur groups, stated a similar conclusion, using LAV for their tests.

4. Were any other laboratory's material used in the American invention? There is no evidence that material from any outside laboratory including the French, was used in generating the HTLV III_B virus. Based on the examination of raw data from Gallo's laboratory between June 1983 and September 1983, it can be unequivocally stated that they had ample isolates of typical HTLV-III for use as prototype infectious agents.

It is acknowledged that Dr. Gallo reviewed the French, May 1983, manuscript, and supported its publication, and that Dr. Popovic received the LAV isolate and signed the appropriate forms. However, because none of the above information or material was used in the generation of the U.S. inventions, the above acknowledgements are not germane to primacy of inventorship.

III. LEGAL CONSIDERATIONS

The Institut Pasteur filed its patent application on the LAV virus in the European Patent Office on September 16, 1983, and in the United States Patent Office during December, 1983. No patent has yet been issued to Pasteur either in Europe or the United States. The two HHS patent applications involving the HTLV-III virus were filed on April 23, 1984. A patent on one of these applications, No. 4,520,113, was issued to the Department on May 28, 1985. That patent encompasses the identification of HTLV-III as the causative agent of AIDS and a 41,000 molecular weight envelope protein as the major viral component useful for diagnosing AIDS and pre-AIDS, and describes a process and test kit for utilizing HTLV-III extracts and/or subcomponents for diagnosing AIDS and pre-AIDS.

Patent applications are examined independently and in secrecy in the U.S. Patent and Trademark Office, an agency of the Department of Commerce, and we have no knowledge, nor any way to determine why the Examiner chose to issue our application, but not the Institut Pasteur application. No patent has yet been issued on the HHS application

involving the key process for growing the AIDS virus using an established T-cell line (H-9).

On the basis of its claim that Dr. Gallo and his group either knowingly or mistakenly appropriated Dr. Montagnier's invention, Institut Pasteur has demanded or threatened the following actions.

A. Actions in the U.S. Patent Office

1. Reissue of the Already Issued HHS Patent:

The Institut Pasteur has demanded that the Department surrender to the U.S. Patent and Trademark Office the patent that has issued to it, call the Examiner's attention to newly found information and request a reissuance under 35 USC 251-252, which would list Dr. Montagnier and the Institut Pasteur as the inventors or, at least, joint inventors with Dr. Gallo's group. Based on the information relating to the actual conception of the invention for which the Department has obtained a patent, we believe the claims of the Institut Pasteur lack merit and recommend against agreeing to the demand for reissuance.

2. Re-examination Request under 35 USC 302 by the Institut Pasteur:

The Institut Pasteur can on its own initiative call the attention of the Examiner in the U.S. Patent Office to pertinent prior acts and any other relevant information, and request that our issued patent be re-examined in the light of the new information being made available to the Patent Office. In

this proceeding, we would not be asked to surrender the patent, as in #1 supra, and would be able to present such pertinent evidence to the Examiner, as we choose.

3. Interference Proceeding (35 USC 135):

The Institut Pasteur would initiate this action by presenting its claim of an earlier conception of the invention patented by HHS, which Pasteur diligently reduced to practice. Pasteur would have to present detailed evidence in support of this claim and HHS would have an opportunity to present contrary evidence. We anticipate that this would be a protracted proceeding and that it would be extremely difficult for Pasteur to make any claim to the envelope protein of the virus, with a 41,000 molecular weight, since they have explicitly disclaimed it in their European Patent Office application. It is now scientifically certain that the antibody in man which is pathognomonic (i.e., key evidence) is solely and uniquely directed against the 41,000 molecular protein. We assume that their U.S. application reads the same, since it was filed three monehs after their European application, although we have not seen it, since the application is held in secrecy in the U.S. Patent Office until its issuance.

B. Actions in the Court of Claims

The possible causes of action in the Court of Claims against the Government were listed by the Institut Pasteur's attorney as:

1. Breach of contract
2. Conversion of the LAV virus
3. Unjust enrichment
4. Class action by affected organizations
5. Fraud by the U.S. Government's counsel in the Patent Office
6. Derivation by Dr. Gallo of the invention, resulting in an invalid patent.

These appear to be illusory causes of action. Although Pasteur could initiate an action in the Court of Claims, with the attendant publicity, we see no basis for this relief against the Federal Government, given the facts presented in this memorandum. In the event more detailed information is received from the Institut Pasteur regarding these charges, these conclusions would, of course, be re-examined.

C. Marketing Action by Pasteur's U.S. Licensee

Institut Pasteur requested that the Department agree not to take any legal action against Pasteur's U.S. licensee, Genetic Systems, if it marketed the diagnostic test for AIDS encompassed by the HHS patent. This request could be granted through an HHS license to Genetic Systems. However, if one considers the specific uniqueness of LAV as a different isolate, and the use of a different continuous cell line by Genetics Systems which is not covered by the U.S. Patent application, these factors could make their application for an HHS license unique.

IV. FINDINGS

On the basis of this review and supporting material, to our knowledge, we find that:

1. Dr. Gallo and his laboratory were the first to identify the virus and to describe the blood antibody test. Therefore, the oral statements on August 6, and supporting material provided by Dr. Dedonder on August 20, that Dr. Luc Montagnier of the Institut Pasteur is the true inventor are not substantiated;

2. The Institut Pasteur's and/or their licensee (Genetics Systems) is not entitled to share in past or future royalties from the sale of the HTLV-III tests;

3. No base of information exists for us to seek a reissue or reexamination of the issued patent or any pending patent.

Peter J. Fischinger, M.D., Ph.D.

CC: Dr. Harmison
Dr. Rose
Mr. Lanman
Mr. Randall
Mr. Ferris
Dr. Hampar

BACKGROUND INFORMATION

U.S. PATENT APPLICATIONS

Patent Application # 602,946

Issued Patent # 4,520,113

INTRODUCTION

The following sections comprise answers to the oral allegations raised by the Institut Pasteur/Genetics Systems groups at the August 6 meeting with departmental personnel. NCI requested specific documentation of data from Dr. Gallo's laboratory, and received about 100 pages of copies of laboratory notebooks, as well as abstracted summaries of these data. Although some of these data are cryptic and very difficult to follow, enough clarity emerged to make the enclosed comments.

The resulting document was compiled by my office. It was next sent to Dr. Gallo to determine that it was accurate in both its content and interpretation. (c.f., enclosed concurrence statement).

Peter J. Fischinger, M.D., Ph.D.

A. Who is the discoverer of the virus which causes AIDS:

The statement that Dr. L. Montagnier is the true discoveror of the AIDS causative virus and should be so publicly acknowledged was made by both Drs. Dedonder and Nowinski. This categorization implies that discovery of a causative agent of a disease is a single event. One could alternatively define discovery as a process and dissect its component contributions. The latter would pose a series of questions:

1. Who had this idea first? It is unequivocal that Dr. R. Gallo first proposed that an HTLV-type of retrovirus may be the causative agent of AIDS. He talked of this at the Cold Spring Harbor Symposium on RNA Tumor Viruses, May 26-30, 1983. He is quoted in Medical World News, August 16, 1982, that this virus is a reasonable candidate as the causative agent for AIDS. It is documentable that the French workers took this idea back to the Institut Pasteur, and had an interview on it in October 1982. Furthermore, members of the Institut Pasteur team admitted at a scientific meeting that the original idea came from Dr. Gallo.

2. Who developed the relevant technology to be able to grow and work with the T_4 lymphocyte target cell? Again Dr. Gallo's major discovery of the T cell growth factor (TCGF or IL-2) in 1976 was the basis for being able to grow T cells in the laboratory.

3. Who first published on the isolation of the correct virus? This contribution belongs to Dr. Montagnier's group based on the May 1983 Science article by Dr. Barre-Sinoussi et al. However, no effective action was taken by the French group to develop a meaningful diagnostic test. This point is further discussed below.

4. The only way by which the Institut Pasteur laboratory could have differentiated HTLV III/LAV agent from HTLV I which at times is known to coexist with HTLV III was to have used Dr. Gallo's antibody reagents prepared against internal viral proteins of HTLV I; i.e., the anti p19 and anti p24. These were sent to the Institut Pasteur in March 1983.

5. Who first linked the correct virus unequivocally to human AIDS? Dr. Gallo's group had precedence in this area as well by more than two months. Their evidence was based on a solid and unequivocal relationship, whereas the subsequent joint manuscript from the Centers for Disease Control (CDC) and the Pasteur group was numerically much less firm. (Parenthetically, the first author of that paper was Dr. Kalyanaraman, who a short time earlier was part of the Gallo team, was hired by the CDC, and was rapidly sent to France to help set up diagnostic testing.)

The third point needs further subdivision: For example, how complete or convincing was the French data in May 1983? What was described was reverse transcriptase (RT) activity in a single lymphadenopathy patient, without p19 and p24 HTLV I cellular reactivity, and electron micrographs of budding particles from degenerating cells. The latter pictures were technically imperfect so that several of the world's experts in retrovirology questioned the morphological compatibility of the buds with retroviruses in oral and written presentations. Accordingly, one could say that although the inference by the French that this is the authentic AIDS virus was correct, it was based on very limited evidence. At that time, the French also considered their virus isolate to be a member of the HTLV family.

An ultimate criterion of primacy of isolation of the true AIDS virus would depend on actual laboratory notebook data. The sufficient criteria in this case would be correct reverse transcriptase detection, failure of reaction with p19 and/or p24 of HTLV I, and a failure of cell immortalization. When these criteria are applied, the examination of raw data from Dr. Gallo's laboratory showed that in mid-December 1982, two such isolates have been obtained from AIDS patients. A letter from J. C. Chermann to Dr. Gallo indicated that their first positive data were obtained in January, 1983. Although it is tempting to determine primacy from a comparative analysis of timing, it may be inappropriate to identify a subcomponent bit of evidence as the watershed of discovery. It is with that thought in mind that, in this instance, the alternative concept of the discovery, as the above outlined "process", seems the more relevant criterion.

B. Evidence that Dr. Gallo Had Numerous HTLV III Isolates Before Receiving HTLV III from France.

Based on the examination of raw and compiled data of Z. Salahuddin and P. Markham between June 1983 and September 1983, it can unequivocally be stated that the Gallo laboratory had more than ample isolates of typical HTLV III which could have been used as protoypte infectious agents.

For example, 17 different retrovirus isolates were obtained from AIDS patients during that time. These were characterized by having the correct and unequivocal reverse transcriptase activity, as well as being negative for HTLV I core antigens p19 and p24. Four of the above were further tested immunologically by ELISA and RIA for HTLV I and were again negative. Fourteen of these were transmitted to human cord-blood cells, peripheral leukocytes, or bone marrow

cells. None of these immortalized the cell cultures they infected. Aliquots of some of these virus samples are still available. Therefore, the above isolates had the same criteria as the infectious LAV subsequently received at the end of September 1983.

The receipt of the following materials from L. Montagnier is acknowledged by Gallo's laboratory:

1. 20 micrograms of "LAV proviral DNA" was received April 1983. No viral DNA was present, only cellular DNA.

2. Supernatant fluids of one patient's T cells, not with AIDS but with lymphadenopathy, were received in July 1983, which did not contain any infectious LAV virus.

3. In late September, a second sample supernate from T cells of the above patient was received and did contain the first infectious LAV. It was successfully transmitted only to normal T cells and a human cell line TI 7.4. Thus there was no logic for the motivation to use the Institut Pasteur derived LAV in any infection sequence for any purposes other than a comparative analysis.

C. <u>What virus(es) does the HTLV III$_B$ cell line contain:</u>

It is noteworthy that an innovative technique of pooling of several highly RT-positive samples was used to infect the H9 subclone. Although under normal circumstances, pooling of isolates would be considered unusual, up to that time no one had been able to stably infect a continuous T cell line with HTLV III despite repeated single isolate attempts. It was determined in Dr. Gallo's laboratory that a finite amount of reverse transcriptase activity is necessary

(c.a. 100,000 cpm) to effect an infection of H9 cells. However, in most patients, the amount of virus in available lymphocytes is on the order of 10-20,000 cpm. Accordingly, pooling of inocula resulted in that the uninfected H9 cell line was exposed to multiple viruses. The subsequent virus-releasing cell subline, designated HTLV III_B, has multiple DNA proviruses in it, based on hybridization and DNA sequence data. Two of these have been cloned and they are related but not identical. Neither of these proviruses is identical to LAV, and although they are close, they differ significantly by about 1-2% from LAV.

It was implied that this could occur as a DNA sequencing error. Four independent laboratories sequenced the DNA clones from the III_B cell line. Essentially no differences were seen. In the rare cases where a discrepancy was observed, it could be readily accounted for and corrected.

Second, one could suppose that with time, mutational drift could occur in the cell line. Data from Gallo's laboratory can document that provirus remains stable. Furthermore, based on available data, simple laboratory transmission of HTLV III_B to a cell line also did not lead to significant sequence variation.

Third, the allegation was made that it is uncanny that since HTLV III/LAV isolates differ from each other, the HTLV III_B and the LAV were so close to each other. This can also be discounted, because recent DNA sequence data show that exceedingly closely matched pairs of viruses have been isolated from different individuals. These pairs are as close as, or closer in relationship than LAV is to HTLV III_B. Gallo's group first discovered and published on variation. On detailed analysis of their more than 130 isolates, the conclusion is that there are not a few strains of HTLV III/LAV but a continuum.

Any one isolate has closely related "relatives" (1 to 2% difference) and distantly related "relatives" (more than 5% genomic diversity.

D. Gallo possessed privileged information from the Institut Pasteur prior to the general public and about one year prior to applying for his own patents.

When the Barre-Sinoussi manuscript, describing the detection of a retrovirus in a single patient with lymphadenopathy (not AIDS) was submitted to Science, in April 1983, it was sent out for review. The policy of Science is to send the manuscript out to several reviewers at different institutions. Dr. Gallo and his colleagues reviewed the manuscript and sent back a highly laudatory response (Attachment). Although the evidence was limited, Dr. Gallo suggested rapid publication. He discussed the manuscript with other colleagues who were quite critical in their comments, and recommended outright rejection. The comments of the other official reviewer(s) are not known. Upon our oral request, Science did not wish to release any information, even without reviewers' identification. At that time, in April of 1983, it was unclear that lymphadenopathy (which can be due to many causes) and AIDS were directly caused by a single etiological agent.

The paper was published rapidly and became public knowledge in May 1983. Thus Dr. Gallo had the above information one month prior to its egress into the public domain. Several emminent scientists had significant reservations about the validity of the French work. A Dr. Siegel sent a letter to Science disagreeing that a retrovirus was identified by the Institut Pasteur group. That letter was not published, and it was Dr. Gallo who asked Science not to publish the critical comments in order to give the Pasteur group a chance.

If, for whatever reason, a competing scientist would feel threatened by information in a manuscript, it is tacit knowledge that a negative or lukewarm response from a reviewer will make it difficult for a paper to be published in a journal such as Science. Even more simply put, a reviewer can request difficult and/or lengthy experiments which must be carried out prior to the acceptability of the manuscript. Thus publication can be significantly delayed. This was clearly not the motivation of Dr. Gallo. His very positive response was instrumental in having the paper published ultra rapidly.

Has Dr. Gallo obtained any key evidence in that manuscript which helped him unduly toward the application of his patents? The answer is no, in that the base of general knowledge was not increased, and that no specific key element was used later in his U.S. patent application. Dr. Gallo used virus from AIDS patients, not primarily lymphadenopahy patients; used a continuous cell line rather than short-term lymphoid cells to obtain adequate amounts of virus; and described and used a specific reactivity with a viral antigen, which was disavowed by the French patent.

Another important aspect which deals with motivation is the documentable fact that the Gallo laboratory already had very analogous data from AIDS patients as early as December 1982. They had a virus expressing positive reverse transcriptase activity, a negative HTLV p19 antigen, and the cells which failed to persist in culture. Thus the Institut Pasteur observations corroborated analogous pre-existing data in the NCI laboratory. It appears to us that in contrast to getting some proprietary information form the manuscript review process, Dr. Gallo displayed a commendable sense of generosity and scientific goodwill by ensuring a rapid publication of possibly competing

data, and by providing the Institut Pasteur reagents to HTLV I and HTLV II. These latter reagents enabled the Institut Pasteur scientists to show that they had something new which then enabled them to publish.

E. Dr. M. Popovic received LAV from the Institut Pasteur and signed a noncommercialization agreement:

The implicit impact of receipt of LAV has a bearing only if LAV had been used to develop the HTLV III_B stock in H9 cells which eventually became the basis for the blood antibody detection test.

The Gallo laboratory does not contest the existence of such a document signed by Dr. Popovic upon receipt of LAV. The document was evidently returned to the Institut Pasteur, and Dr. Popovic did not retain a copy. It is proper and normal procedure that NCI reciprocally requests a "Confidentiality Agreement Form" from the hundreds of recipients of HTLV III_B or H9 cells.

It is clear from other sections of this document that LAV was not used in generating the HTLV III_B virus strain advertently or inadvertently. As a matter of fact, Dr. Popovic later attempted to infect the parental uninfected H9 cells with the LAV isolate from the Institut Pasteur. The total amount of reverse transcriptase activity obtained ($\sim$20,000 cpm) was inadequate to initiate an infection of continuous cells.

F. Comments on Some Scientific Aspects of Respective French and US Patent Applications

Several components of the various patent applications which relate to the diagnosis of past infection with the AIDS causative virus, termed HTLV III/LAV, deserve special mention on the scientific level:

1. The existing blood test for past viral infection is now a highly accurate and sensitive reality. It was made possible only because the first U.S. patent applied for was based on the solution of the critical process of availability of sufficient virus mass to conduct the test beyond the laboratory scale. This meant the achievement of symbiosios for a usually lethal virus for normal T_4 cells to grow in a continuous T_4-containing human leukemia cell line. However interesting the small scale technology may be, the specific survival-adaptation process which comprised the first patent application was a sine qua non. However, that patent did not issue conjointly with the Serological Detection Patent which is already out (#4,520,113).

2. It may be the above factor, and that of point 3, which wholly or in part contributed to a low percentage of diagnosis in virus-exposed people using the LAV Institut Pasteur technology. In their patent application, only 20% of AIDS patients scored positive, while 63% of LAS patients were positive for LAV antiviral antibody. These technical aspects were so onerous that no significant conclusion could be safely drawn. Even in July 1984, the LAV-containing test systems picked up only 41% of AIDS patients. The U.S. patent-derived test procedures at the time of application identified 88% of AIDS patients and 79% of LAS patients, and shortly thereafter, essentially all the patients.

3. The U.S. patent application itself relies on the fact that the pathognomonic (i.e., the diagnostically critical) antibody is directed against the envelope component of HTLV III. This was true for the ELISA, and especially for the Western Blot test. The French application specifically disclaimed that fact, i.e., it contended that human antibodies do not exist which detect

immunological determinants on the envelope proteins of the virus. Their major thrust of reactivity has been geared toward the major internal core protein of the virus, the p25. We now know that many AIDS patients do not have detectable anti p25 antibodies, while all have antibodies to the envelope gp41 component.

4. To get the LAV ELISA operational, the Institut Pasteur and their U.S. licensees also had to adapt LAV to a continuous human leukemic T cell line. It is of interest that they eventually used the HUT 78 cell line which is a relative of the HT cell line developed by Dr. Gallo. The HUT 78 cell line was first described by NCI scientists and was characterized years ago by them in collaboration with Dr. Gallo.

FURTHER CONSIDERATIONS BASED ON THE DOCUMENTS

SENT TO HHS BY THE INSTITUT PASTEUR DIRECTOR, DR. DEDONDER

Several topics addressed by the French as evidence for priority of discovery have not been discussed in the original response, and four of these need further elaboration:

I. Enclosure H.

The letter from Dr. A. Karpas exhorted the Institut Pasteur to send out a package of information to scientists all over the world. Many scientists have subsequently received several such items, one of which is a part of Dr. Gallo's letter, Exhibit 42, 42bis. A key point in Dr. Gallo's letter to an eminent European scientist which was somehow obtained by Dr. Karpas, is that Dr. Gallo has never seen "the virus Luc Montagnier has described, and I suspect he might have a mixture of the two". At that time, Dr. Gallo had just received the LAV sample which was active, whereas the previous LAV sample sent was non-viable. The reference to a possible mixture deals with a scientific fine-point which is elaborated upon in the enclosed statement from Dr. Gallo. Dr. Gallo does consider that he already had evidence at that time of an agent which could have been the cause of AIDS. However, up to the May 4, 1984 Gallo publication, there was no clear relationship of any viral isolate as being the cause of this disease.

2. Enclosure E.

The Cold Spring Harbor Symposium of September 15, 1983, presented a summary of French data up to that time. Dr. Gallo also had a presentation at the same meeting. In a meeting report compiled on October 7, 1983, it is

stated that Dr. Gallo discussed that HTLV was isolated from 25-30% of AIDS cases, and that it did kill T cells. Dr. Gallo also published, as a part of his talk, a picture of HTLV III, and cited early serological evidence connecting AIDS and HTLV III. However, Dr. Gallo admits that he updated his presentation between the meeting and the publication. The French statement that Dr. L. Montagnier has presented his results in September 1983, "in the same terms" as they have been published in 1984 is not clear in that Dr. Montagnier might also have used the same prerogative, and that the actual data presented might not have been the ones appearing in the final version.

A component of priority is that Dr. Montagnier allegedly developed an ELISA test using LAV, and assessed antibody response in virus-exposed individuals prior to Dr. Gallo. However, an aspect of both quality and quantity has to be considered, and that the approaches chosen by the two scientific groups represent a philosophical bifurcation. Dr. Montagnier ran his test - an accepted ELISA technology - with minimal available virus quantity. However in that format, the test could never be used extensively, and clearly, the French never did manage large-scale testing until over a year-and-a-half later, when they adopted the continuous cell-line technology pioneered by Dr. Gallo. Second, the French ELISA test was intrinsically unreliable as a diagnostic tool, because they focused on the wrong antigen - the internal core p25. At that time, they found that only 20% of AIDS patients had positive antibody, and even in July 1984, only 41% of AIDS patients scored positive for LAV-antibody as performed by the French. Thus, although the French tried to state that they

had a functional ELISA test, their data could not be considered acceptable for diagnostic purposes. In fact, this represents a res ipsa loquitur because if the French had a real test, they would have developed a generally applicable test.

The Gallo approach focused on developing a mass test with close to a hundred percent reliability, which is what would be needed in the real world. This took longer and culminated in the development of the continuous HTLV III-producing cell line, which led to the first U.S. patent application, and the first unambiguous linkage of this virus to the disease in May 1984.

3. Enclosure J.

A major corroboration for the French primacy of invention was the statement in the New York Times on April 22, 1984, by Jr. J. Mason, then head of the CDC. Dr. Mason was quoted as saying he believed that a virus discovered earlier in France (LAV) was the cause of AIDS. Dr. Mason was very prudent in that he also stated that LAV had yet to be confirmed and validated as the cause of the disease. Dr. Mason stated that the researchers at CDC had not yet received a copy of the manuscripts that Dr. Gallo's team was about to publish. It was on the next day, April 23, 1984, that HHS Secretary M. Heckler and Dr. Gallo announced that HTLV III was the probable cause of AIDS, based on solid immunological data presented in one of the manuscripts. Reprints of these were handed out to all reporters. At that time, the French-CDC team had not yet submitted for publication their data linking LAV to AIDS. Their manuscript

was first received by Science on May 5, 1984, and was published on July 20, 1984. The stress on the LAV was a natural consequence of the French-CDC collaboration. Had CDC known of the imminent presentation of the unambiguous Gallo data, it is suspected that a different and a more balanced attribution would have been probable.

The content and the impact of the other enclosures/documents has either been discussed, or is already in the public domain, or has limited significance in the determination of events which led to the discovery.