DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Washington, D.C. 20201

April 6, 1988

Mr. Klaus-Gerhardt Firshow
Publisher
Spectrum der Wissenchaft
Moenchhofstrasse 15
D-6900 Heidelberg
Federal Republic of Germany

Dear Mr. Firshow:

We are writing on behalf of the United States Department of Health and Human Services with respect to a book entitled AIDS: von Molekul zur Pandemie authored by Michael G. Koch and published by your firm. After carefully reviewing certain salient portions of the publication, the Department has serious concerns that the publication in question contains significant scientific, historical and legal errors which may not only undermine its overall utility as a legitimate scientific publication, but also reflect adversely on your firm's reputation. The purpose of this letter is to apprise you of these concerns.

Before addressing the book's substantive shortcomings, we wish to call your attention to the fact that the publication in question, if introduced into commerce, would violate certain provisions of the United States Copyright Act of 1976 and the Lanham Act of 1947. This point is discussed in greater detail later in this letter.

As noted above, the publication in question contains numerous significant scientific, historical and legal errors which deserve careful consideration. These errors in our opinion represent, at the least, a serious misunderstanding both of the dispute between the Institut Pasteur and this Department concerning the patent rights to the AIDS antibody test-kit and its eventual resolution. At most, these errors in our opinion wrongly impugn either directly or through innuendo the integrity of the Department, certain of its scientists and the United States Patent and Trademark Office.

As we understand it, the gist of the author's thesis is that certain scientists at the National Cancer Institute (NCI) downplayed the achievements of the Pasteur scientists, failed to acknowledge in a timely fashion that LAV was the causative agent of AIDS, improperly made use of Pasteur's LAV specimens, and as

a result, obtained a patent on the AIDS antibody test-kit. The author goes on to imply that the Settlement Agreement between the two institutions was artificial and in the author's words "seems somewhat strained." The author's thesis is seriously flawed in all respects. First, it is based on certain factual allegations which are not true. And second, it is based on a total misunderstanding of the United States patent laws and procedures.

At the outset, it must be recognized that the dispute between Pasteur and this Department was a highly technical legal disagreement over patent rights and was not a dispute between scientists over which team first isolated the HIV. This is not surprising given the fact that the author fails to appreciate the difference between a scientific discovery, on the one hand, and a patentable invention, on the other hand. By definition, the discovery of a virus and even proof that the virus causes a specific disease, are not in and of themselves patentable. A patent can only be obtained for an invention, and not an idea or natural phenomenon. The development of the method for detection of antibodies to the AIDS virus and related test-kit, which was at the heart of the legal dispute, was dependent on a series of innovations, some of which, on their own would not have been patentable. Specifically, the AIDS antibody test-kit requires (1) a virus or portion thereof; (2) proof that the isolated virus is the etiologic agent of AIDS; (3) a method for propagating the virus; and (4) a technique for measuring the presence of antibodies to that virus. As such, discovery of the virus represented but one element of the patent application, and by itself, was not patentable.

The actions of the United States Patent and Trademark Office (PTO) in November 1987, clearly indicate that, based on the scientific record as a whole, the development of the test-kit was the joint invention of the Pasteur and NCI teams. This scientific record includes, in addition to the published articles of both teams, pertinent portions of their laboratory notebooks.

The record relied upon by the PTO in making its independent assessment reveals that both teams isolated HIV in 1983 and that beginning in 1982, scientists in Dr. Gallo's laboratory undertook the dual task of isolating a retrovirus in patients with AIDS and then attempting to develop a continuous cell line capable of propogating the virus. This proved to be a difficult undertaking because the retrovirus was cytopathic and appeared to kill any cells which he attempted to use to grow the virus. Ultimately, in November 1983, Dr. Popovic and co-workers in the Gallo laboratory developed a cell line clone (H9) of a human T4 lymphoctye which was relatively resistant to the retrovirus and could be effectively used to produce the virus in relatively large amounts of consistent composition. Without the discovery of such an immortalized cell line, large scale tests would not have

been possible. The Department eventually obtained a patent on that cell line which was licensed on a royalty free basis to Institut Pasteur. The development of the immortalized cell provided the break through necessary to undertake the testing required to establish the cause of AIDS. In fact, it was a series of blind tests of hundreds of sera and multiple virus isolates from patients with AIDS and individuals in risk groups throughout the later part of 1983 and early 1984 that lead Dr. Gallo and his colleagues to conclude that the new retrovirus was indeed the cause of AIDS. Later, in early 1984, under the auspices of the Centers for Disease Control in Atlanta, Georgia, a series of blind tests was undertaken to ascertain whether the sera from patients with AIDS contained antibodies to HIV. Of significance is the fact that both NCI and Pasteur participated in these tests. Each laboratory was provided with sera and asked to judge whether each specimen contained antibodies to the virus. The results of those tests unequivocally established that HTLV-III/LAV was the presumptive causative agent of AIDS.

It should also be emphasized that Dr. Gallo and his co-workers described 48 independent isolates of the AIDS virus, not just one, and mass produced in permanent culture six of these, not just one.

We wish to emphasize that the PTO would not have issued the two patents unless the record demonstrated that the inventions at issue were in fact jointly developed by both teams. Indeed, the provisions of Settlement Agreement of March 30, 1987, between Pasteur and the Department were contingent on certain PTO actions. Those actions were not controlled by either Pasteur or the Department. In short, notwithstanding the Settlement Agreement, if the PTO had found that the record was not sufficient to justify the claim of joint inventorship, then PTO would not have issued the patents that it did in fact issue.

Given the brief factual and legal account of what in fact occurred, it may be worthwhile to compare that account with the author's unfortunate rendition. The following few examples, we believe, aptly illustrate the author's basic misunderstanding of the events surrounding the development of the test-kit, the dispute between Pasteur and the Department and the eventual resolution of that dispute.

1. On page 94, the author in German states:

> Then in May, 1984 the first successful isolation from Gallo's laboratory was published (Popovic et al., 1984). The American scientists named their virus HTLV-III (human T-cell leukemia/lymphoma virus type III), although morphologically it could not be differentiated from LAV.

The above paragraph is scientifically and historically incorrect. The author implies that the HTLV-III, isolated by Gallo et al. and the LAV, isolated by Montagnier et al., must have been identical, since they could not be morphologically differentiated. However, as all virologists know, it is impossible to say that any two viruses are even reasonably closely related, let alone that they are the same, from morphological studies alone. In fact, here, an appropriate generic name was not even possible until the development by the Gallo group of the first specific reagents to these types of viruses.

The above paragraph explicitly states that Gallo's first successful isolation was the subject of the 1984 publication. In addition, the above quoted paragraph implies that the Gallo team decided, sua sponte, in 1984 to name the virus. Neither assertion is correct. First, the 1984 Science publication did not report on the "first successful isolation from Gallo's laboratory" of HTLV-III. The Popovic et al. article reported not on the first isolates of the virus, but rather on isolates of the virus that had been grown in a perpetual cell line. The PTO recognized this critical distinction, when in 1987 it issued a patent on the H9 and CEM cell lines.

Second, Dr. Gallo did not, as the author implies, name the virus on his own initiative. Instead, Dr. Gallo and his colleagues named it HTLV-III in their May 1984 publications according to a recommendation made in September 1983 by a group of ten European, Japanese and American retrovirologists. The group suggested that names of human retroviruses discovered in the future related to but distinct from Human T Lymphotropic Virus be named sequentially, HTLV-III, HTLV-IV, etc., if the retrovirus infected T-cells.

2. On page 94, the author in German states:

> In the face of all this, Gallo persisted unswervingly for an entire year (1983/1984) to propagate the HTLV-I as the cause of AIDS.

The above statement is patently false. First, Gallo never suggested, let alone advocated, that HTLV-I was the cause of AIDS. Rather, he suggested in 1982 and early 1983 that a retrovirus, probably a variant of HTLV-I, would be the most likely candidate. Second, as noted above, beginning in early 1983, the Gallo group devoted considerable effort to developing a permanent cell line which would enable them to mass produce HTLV-III [now HIV]. Mass production of the virus was essential in order to ascertain whether it was in fact the causative agent of AIDS. Thus, it would make little sense to devote 9 months of effort in an attempt to mass produce an irrevelant virus, when

the goal of the research was to obtain adequate amounts of the virus so that extensive tests could be carried out to ascertain HIV as the cause of AIDS. In January 1984, NCI and CDC scientists demonstrated that HTLV-III/LAV was the causative agent. Publication of these results did not occur by the Gallo group until May 1984. The patent application filed by Gallo et al. in April 1984 stated that HTLV-III was the cause of AIDS. In July 1984, the French group copublished with the CDC scientists proof that HTLV-III/LAV was the causative agent of AIDS. In short, Koch's statement that Gallo advocated unswervingly for an entire year (1983/84) that HTLV-I was the cause of AIDS is flatly contradicted by the record.

3. On page 95, the author in German states:

> By this time [May 1984, when Gallo first published the micrographs of HTLV-III] it had already been completely confirmed that the LAV of the Paris group was the causative agent of AIDS and that it looked like a typical lentivirus.

As noted above, the fact of the matter is that the causal link between AIDS and both LAV and HTLV-III was established as part of experimental work conducted between December 1983 and January 1984. Prior to that date, there were insufficient quantities of the virus available and hence, insufficient data to establish the casual link. Prior to the 1984 May and July publications, noted above, there was no scientific publication which confirmed the causal link between LAV or any other retrovirus and AIDS, and indeed, the author cites no authority for his incorrect statement, as none exists.

4. On pages 95-96, the author implies that Gallo was less than fully candid when he stated that the LAV specimen sent to him by Montagnier did not survive. The author goes on to note that the records were redacted in order to conceal the contamination of certain HTLV-III specimens with LAV.

The author's rendition is grossly inaccurate. As the author notes, Gallo received two shipments of LAV, one in July and the other in September. The July shipment failed to survive; the September shipment was studied by the scientists at NCI and others at the Frederick Cancer Research Facility. Indeed, there would have been no need to request a second shipment had the first shipment survived. At first, it was thought that that second shipment of virus could not be grown in a cell line. However, further analysis using electron microscopy revealed that it did grow in a cell line, but only transiently

The author goes on to imply that Gallo attempted to hide the fact that portions of the second shipment survived by redacting laboratory records to conceal the existence of LAV. In fact, the

unredacted letter was obtained from Gallo's laboratory. The Department has no idea where the redacted copy came from, but it appears that it came from a non-government source and further that the redaction was done by someone outside Gallo's laboratory. Moreover, it is obvious that if Gallo or any of his co-workers wanted to do what Koch has accused them of doing, they would not have labeled the samples as "LAV." Further, an analysis of the original six isolates that were produced in permanent culture, as described in the original Gallo publications, revealed that five were very different from LAV; the sixth isolate, although more closely related to LAV than the other five, was nevertheless distinct.

5. On page 98, the author in German states:

> Gallo's patent application was granted in January, 1985 . . .

This statement is incorrect and belies a basic failure on the part of author to appreciate detail, a failure which as noted above affects many aspects of his publication. The Gallo patent issued on May 28, 1985 (No. 4,520,113) and not, as the author states, in January 1985.

The above delineation of the various errors in the book is not intended to be exhaustive, but merely illustrative of the author's repeated failure to accurately report on the scientific history of AIDS. Part of this may be due to the fact that the author, as we understand it, is neither a scientist nor historian. Whatever the reason, the Department urges that you correct the record in future editions and seriously consider deleting any polemic statements that impugn the integrity of the United States, its agencies and by implication its employees.

In addition to the wealth of substantive errors contained in the subject publication, certain portions of the book violate provisions of the various United States laws relating to intellectual property. Specifically, the book contains a number of micrographs which are the property of the United States. Many of these micrographs are reprinted in the book with copyright notices indicating ownership by a private entity. For example, Figure 10.50 which is a micrograph of HTLV-I bears the notation "(Gallo et al., Science 1983;220:865. Copyright, 1985, AAAS)." This copyright designation, as well as others throughout the book, is incorrect as matter of both fact and law. First, although the micrograph did appear in Science it is the property of the United States government and hence, not subject to copyright. Moreover, if the copyright designation was intended to refer to the issue of Science from which article containing the micrograph was drawn, then the publisher must indicate which

portion of republished matter is not subject to copyright. Specifically, 17 U.S.C. § 403 (Copyright Act of 1976) provides as follows:

> Whenever a work is published in copies or phonorecords consisting preponderantly of one or more works of the United States Government, the notice of copyright provided by section 401 and 402 shall also include a statement identifying, either affirmatively or negatively, those portions of the copies or phonorecords embodying any work or works protected under this title.

Thus, if a copyright designation is included it must also contain a proviso indicating that the item republished (e.g., the micrograph) is in fact not subject to copyright (See, 17 U.S.C. § 105) and is the property of the United States Government. Inasmuch as the copyright designations used throughout the book improperly cognate ownership or origin of the micrographs, those designations, and hence, the book as a whole, violate Section 43(a) of the Lanham Act. Consequently, the Department of Health and Human Services formally requests that before you introduce the subject publication into commerce you correct the copyright designations so that they conform to the provisions of the Copyright Act of 1976.

In conclusion, it should be noted that the errors in question may be viewed by some as defamatory, thereby possibly subjecting the author, your firm and its distributors to such civil actions as the aggrieved private individuals may deem appropriate. This letter, however, is written neither to advance the private interests of any federal employee or other person nor to advocate their legal positions. Instead, this letter is being written to make certain that your firm appreciates the concerns of this Department in ensuring that scientific publications dealing with AIDS accurately reflect what has occurred.

Sincerely,

Robert Windom, M.D.
Assistant Secretary for Health

Ronald E. Robertson
General Counsel