

RESPONSE TO THE CHARGE TO THE CONSULTANTS TO
THE DIRECTOR OF THE NATIONAL INSTITUTES OF HEALTH
CONCERNING THE INVESTIGATION OF DRS. GALLO AND POPOVIC

January 29 and 30, 1992

General Comments:

Every aspect of this case of alleged misconduct is unique including the existence of this group of advisors.

In early 1990 the National Academy of Sciences and the Institute of Medicine were asked to provide a list of individuals, representing a broad range of backgrounds and interests, who would be willing to serve as consultants to the NIH as it carried out inquiries into the laboratory of Dr. Robert Gallo and his associates. This group was not taken through the process of formal appointment as an advisory committee, but rather brought in as individual consultants to the Director. The charge was to advise on the process involved in the various steps of the inquiry and later to comment on the final written report. At no time was this group actively involved in the actual investigations or the interviews that were carried out.

The first meeting of the advisors with the Acting Director and the members of OSI was in April of 1990 at which time the Inquiry phase had already been underway for about 2 months. During the ensuing 2 years there have been major changes in personnel in both the Director's Office and in the OSI. This has undoubtedly contributed to the length of this investigation.

The nature of the AIDS epidemic and the prominence of Dr. Gallo's laboratory as the focus of the NIH attack on this problem ensured press attention from the very early '80s. Many of the general problems discussed in the present report were brought out in the press at that time. Most interested citizens considered that whatever the actual facts might be, the issues were decided in a practical sense by the agreement between the French and American governments concerning the patents on the blood test.

The real origin of the current claims of misconduct remains obscure, but the most visible whistle blower is an investigative reporter, Mr. John Crewdson of the Chicago Tribune. This is not the usual case of an individual who is personally knowledgeable of, and engaged in the events leading to the accusation. The case was built by reading documents and interviewing those who were directly involved. The results of this effort appeared in the

late fall of 1989 in an extensive article in the Chicago Tribune. The principal focus of the article was on events that had occurred 5 to 6 years earlier.

THE SPECIFIC CHARGES AND RESPONSES;

1. Does the report show that the investigative process was thorough and pursued the issues appropriately?

We believe that the collection of physical evidence, the investigation of the facts, and the interviews of the witnesses were thorough and appropriate. However, we believe that certain of the analyses and conclusions of these investigations are flawed. The problems are discussed below.

2. Are the issues/allegations stated properly in the proposed final report?

Yes. This aspect of the Report represents a very good job.

3. Does the Proposed Final Report address all the issues that should be addressed?

Yes.

4. Are all of the issues appropriately covered?

No.

Each of the allegations raised against the Popovic et al. paper is considered independently in the Report and in no obvious or stated order of priority. This tends to trivialize the significance of the findings. The Conclusion section castigates the overall level of accuracy of the paper, but fails to integrate the findings into a larger context, namely a pattern of behavior on Dr. Gallo's part that repeatedly misrepresents, suppresses and distorts data and their interpretation in such a way as to enhance Dr. Gallo's claim to priority and primacy.

Consider the following sequence of events; it appears to be well established by the report and is largely or entirely undisputed.

A. LAV (LAI) was grown successfully in the Gallo laboratory during the fall of 1983. In particular, LAV was successfully propagated using HUT78 cells. Thus, a crucial fact was established -- HUT78 cells were permissive for the growth of LAV (i.e. the causative agent of AIDS). The Gallo lab "went to school" with the French virus, yet they later failed to mention the fact that they had propagated the French virus. In fact, they denied propagation of the French virus and stated (in the Popovic et al. manuscript) that the French virus had never been transmitted to a permanent cell line. Given the quality of the information derived from propagation of the French virus, we believe that this constitutes intellectual recklessness of a high degree -- in essence, intellectual appropriation of the French viral isolate.

B. With knowledge of the fact that HUT78 was permissive for the growth of LAV, members of the Gallo laboratory attempted to propagate their own isolate in November of 1983 using HUT78 (the pool experiment). Subcloning of HUT78 was initiated at the same time. Freshly subcloned, HUT78-derived, H9 cells ultimately were added to the pool culture. The name of HUT78 was changed to HT, and subclones were ultimately designated (H4, H9, etc) without reference to HUT78.

C. the so-called HTLV-III virus was thus established and introduced to the world with no reference to or discussion of two crucial facts. (1) Culture conditions were established using the French virus, and (2) the cell line utilized (HUT78) was one that had been obtained from the Minna laboratory. Against the backdrop of comments from Gallo about the need for speed to counteract the growing AIDS epidemic, we note that the Report states that Gallo refused to distribute uninfected H9 cells unless collaborative agreements had been secured from the other investigators. Although others could have obtained HUT78 cells from the ATCC (American Type Culture Collection), the essential identity of HUT78 with H9 had been effectively obscured. We consider failure to distribute uninfected H9 cells freely after publication of the article by Popovic et al. to be essentially immoral in view of the growing seriousness of the AIDS epidemic. Finally, the description of the pool culture experiment and the convenient definition of "continuous culture" obscure the true methodology and chronology and lend an entirely unwarranted impression of rigorous science to a haphazard set of circumstances. Their haphazard nature is established by the fact that the "HTLV-III culture" was, indeed, ultimately shown to represent another example of the continuous culture of LAV (LAI) in the Gallo laboratory.

5. Is the Final Report well-written and organized and does it convey thoroughness and objectivity?

The present version of the Report is a great improvement over the earlier draft. However, the discussion of the Inquiry is still somewhat diffuse. This Section is fundamentally a chronological narrative with much useful detail.

We recommend that the current Section I, essentially as is, be made an appendix to the Report, and that a very brief overview of the overall report be written, including the conclusions of the Inquiry phase. This would provide the background and context for the Investigation.

The Inquiry led to the following major findings:

1) The Inquiry concluded that certain of the allegations, notably that the Laboratory had grown no isolates of HIV other than LAV, were incorrect.

(Note: A variety of samples were obtained and sequestered during the Inquiry phase. The subsequent PCR analysis of certain of these samples has shown that the major, and finally sole, viral components in HTLV-IIIb and LAV were identical. It is not possible, from these results, to establish whether the appearance of LAV was accidental or intentional misappropriation.)

2) The Inquiry identified serious questions concerning the validity of the contents of the key paper (Popovic et al. 1984) establishing the culture and identity of HIV.

The Investigation has examined issues related to that paper:

- 1) misrepresentation of data
- 2) distortion of procedures and findings
- 3) misleading statements
- 4) persistent patterns of behavior contrary to standards of intellectual integrity

The thoroughness of the Investigation appears to be excellent. Two sides to each allegation are clearly and well presented. However, we do question the validity of the analysis and conclusions in certain instances. There appears to be a discrepancy in the treatment of Drs. Gallo and Popovic. Different standards appear to have been applied. For example:

Allegation (7) - The sentence on the RT analyses of the samples is found to be a misrepresentation. None of the authors will acknowledge composing the sentence. With no way to identify the actual source, the blame could be

distributed among all the authors. Yet the blame has been specifically placed on Dr. Popovic. This appears to be arbitrary especially in light of other statements that misconduct cannot be charged where data are lacking.

Allegation (11) - In the description of the immunofluorescence assay results, the blame for the discrepancy is placed on Dr. Popovic, again with no obvious basis for a choice between the two individuals involved, and in the absence of specific supporting data.

Allegation (13) - In contrast to the above allegation, where two interpretations of the EM photographs were given, the opinion of Dr. Gallo was accepted over that of Dr. Gonda in spite of the fact that the latter was an acknowledged expert in this technique and was engaged in the evaluation of such photographs on a regular daily basis.

Allegation (8) - The statement that LAV had not been transmitted in a permanent cell line is simply false, and was known to be false at the time the paper was written. This is one of the most glaring faults in the paper and is part of the pattern of misrepresentation in the discussion of the problem of continuous culture. There is no way in which Dr. Gallo can be excused from sharing the blame for this misstatement.

6. Does the report reflect an appropriate and credible investigation to determine whether there has been scientific misconduct?

In one critical area, discussed above, the answer has to be NO.

The public and/or the Congress will perceive a bias in the treatment of the two principals in the Investigation.

Further the Report does not address the overriding issue of the responsibility of the Chief of a Laboratory to monitor the performance of all personnel in the Laboratory and to pay particular attention to the accuracy of major publications which bear his name as an author. The paper at issue was central to the claim of priority in growing the virus. The senior author had an imperfect command of English and a known inadequacy in record keeping. The combination of these facts should have resulted in the most meticulous scrutiny by the Chief of the Laboratory for the benefit of all members of the Laboratory in addition to his own personal responsibility as an author.

ADDITIONAL COMMENTS:

1) In spite of the many faults in the 1984 paper, OSI made no recommendations with regard to the paper itself. Retraction seems inappropriate since some of the conclusions are in fact correct. However, the authors could be asked if, for the record, they would publish a corrected version. In addition to the authors this would require the agreement and advice of "Science" as to how this might best be accomplished. The absence of records at the journal office may or may not complicate such a process. With or without such an agreement, OSI should inform Science of the errors that they have uncovered.

2) It should be made clear, although it is not now, that the responses of Drs. Gallo and Popovic to the Report, which are included as appendices, are, in fact, responses to the first draft prepared in the spring of 1991 and not to the present form of the Report.

3) One might note at some appropriate spot that the frequent reference in the Gallo response to the "pressure to publish" the 1984 papers as a necessary prelude to development of the blood test is pure hyperbole. In science the "pressure to publish" is invariably related to problems of establishing priority and is invariably located solely in the mind of the author(s). The development of the blood test would have been more adequately served by the thoughtful and careful preparation of the papers describing the research. Their timing was irrelevant.

Frederic M. Richards
Consultant.