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May 15, 1990

Dr. Claude Lenfant
Director, NHLBI
Building 31, Room 5A52
National Institutes of Health
Bethesda, MD 20892

RE: 1RO1 HL 41166-01A2

Dear Dr. Lenfant:

I am writing to express my concern regarding the grant application submitted by Dr. Darwin R. LaBarthe, "Pediatric Epidemiology of Cardiovascular Risk Factors: US/Japan." As I indicated at the Working Group On Program meeting, April 30, 1990, the failure to include minorities in the U.S. study population raises some serious questions.

High blood pressure, high blood cholesterol levels, and cigarette smoking have been identified as the three major modifiable risk factors for cardiovascular disease. While these risk factors affect the entire U.S. population, Blacks and Hispanics are particularly vulnerable. This increase vulnerability is often the result of socioeconomic factors, cultural and lifestyle differences.

Cardiovascular diseases are the number one cause of death in Blacks. Of the six causes of excess deaths listed in the 1986, Report of the Secretary's Task Force on Black and Minority Health, cardiovascular diseases were listed as number one.

Consideration of a study of this magnitude that does not include a population representative of the prevalence of the disease is difficult to understand. In addition, it appears that the National Institutes of Health guidelines, as well as those of NHLBI, regarding the inclusion of minorities are not adhered to in this study.

This study could possibly provide new and important data about the development of cardiovascular risk factor and the early manifestations of this disease. However, the validity of this study would be seriously questioned without a population representative of those primarily affected by the disease. I am not convinced that the findings of this study, as currently designed, would be cross-cultural. The differences in diet, life-style, smoking rates and socioeconomic factors are significant enough to impact study findings.

I request that my concerns be shared with other members of the NHLBI Advisory Council.

Thank you.

Sincerely,

Jacqueline C. Flowers, MPH, M.ED
Director, Office of Minority Affairs

JCF/fh

CONFIDENTIAL

June 6, 1990

Dear Colleague:

I write this letter seeking your counsel in regard to NHLBI policy requiring inclusion of minority populations in all epidemiological studies and clinical trials, a recent interpretation of 1987 NIH policy, attached to this letter. Everyone supports wholeheartedly the increasing diversity of NHLBI programs and initiatives. There are few institutions in our society that have more directly and effectively addressed problems of health and risk in minority populations than the NHLBI program. This is a highly necessary, priority strategy.

But a policy that requires inclusion of a statistically adequate and representative population of minorities, in each and every investigator-initiated grant application for a population study or clinical trial, raises major issues of science, ethics and funding. Such a policy is de facto now in place as a result of Council actions on May 25, 1990. This letter is to apprise you of that fact and something about how it came about, and to seek your counsel about the wisdom and feasibility of the policy and your opinion on its impact on the design, peer review and funding of proposals in our field.

I was confronted with this policy issue unexpectedly, serving as the primary Council reviewer of the Labarthe grant, a few of the pink sheets of which are enclosed. It had been reviewed three times, with progressive adjustments and attention by the review group to this policy issue. It received approval with the highest enthusiasm, at a 3.7 percentile funding level.

At the meeting of the Committee on Program a month prior to the Advisory Council meeting in May, 1990, Ms. Flowers, a member of the Advisory Council, raised a question about the program appropriateness of the application. She wrote a letter, attached, which was received by Council members a few hours before we were to make a policy and program review of the approved grant. After my primary review for the Council, the grant was immediately challenged by Ms. Flowers who made an extensive, detailed claim that it was clearly in violation of existing NHLBI policy, along with a number of other scientific and policy issues, more and less relevant, with a conclusion that the population proposed to be studied is an inappropriate one.

During the meeting, staff response to the points I felt obliged to make as a Council member (summarized in the enclosed) was that a clear, unambiguous NHLBI policy had been in place since 1987, that the policy had repeatedly been made known to the scientific community, in general, and to Dr. Labarthe in particular. When the policy was read aloud, including the several exceptions, based on feasibility and appropriateness, that the policy clearly allows, the "parenthetical remarks" were judged irrelevant to the core content and intent of the policy, and thus, were inoperative.

Council then judged that NIH policy had been abrogated and the proposal should be rejected. It was maintained that it was important to reject this application or other epidemiological investigators would go on doing this. It should be nipped in the bud.

Action was deferred and staff will interpret the deferral to the investigator.

I am enclosing the entirety, I believe, of written NHLBI policy from 1987, along with a March 1990 update made by staff to clarify existing policy. Its question and answer format does indeed provide some clarification, but this, to my knowledge, has not been circulated widely to the scientific community.

The issue is that the NHLBI now has in effect a policy which requires not just the inclusion of a representative population, or of any minorities encountered in a population, but an hypothesis about, and an adequate sample of minorities in which to study definitively any disease or risk

issue that pertains particularly to minority health. This means, of course, all cardiovascular diseases and their risk characteristics. This seems to me a remarkable and unique requirement to be imposed on all population studies, and only on them (and trials). Their design, feasibility, and cost, as well as academic judgment and freedom are major issues here. All this is within the context of an overall NHLBI program that is already highly responsive to, and focused on minority health issues. Staff was unresponsive when I requested, in my responsibility as a Council member, a formal process be initiated to provide careful estimates of the immediate, in fact, retrospective application of this policy, as well as its forward-going impact.

I was, of course, extremely uncomfortable to be so surprised by this issue, and to be the sole representative of our discipline on the Council, and having to respond to what I perceived were unjust charges against the investigator as well as a highly discriminatory impact on the design and funding of all studies in the field. I believe that scientific and policy issues were seriously misrepresented, both in the challenge to this grant and in Councils' and staffs' acceptance of this policy, without careful examination of the procedure used to single out this grant, larger issues of scientific import, or of the feasibility and cost impact of disseminating this policy. Again, all this is to be enforced selectively on population studies and trials, within the context of a wholly ethical and appropriate general program priority of the Institute, centrally concerned as it is with health issues among minorities.

We are all aware of the sensitive and important political issues involved here. In later discussions with a "highly placed official in HHS," when outlining this NHLBI problem, the response was: "You just have to live with it." I think, however, that it would be irresponsible of the scientific community and its leaders not to address these issues in a more open, rational and orderly way, rather than in a purely political and bureaucratic way. At the very least, I believe the community of investigators should insist on the policy being more carefully specified and more detailed than is provided in the enclosed, and that this detailed policy and its rationale be resubmitted as a proposal and discussed at highest levels in NIH and HHS. This discussion should take place in the context of a thoroughgoing examination of the need for a specific regulation, in the presence of the current broad and diverse programmatic strategy of the Institute, and be accompanied by a careful report on the feasibility and cost of

implementation of this policy with every population study proposal. Finally, should consideration be made of how these policies might apply to clinical and bench researches, if this policy controlling the scientific directions of population researches and clinical trials is judged a valid and appropriate one? I hope you will advise me on how to proceed, and then address this matter at every level, personal and institutional, making your thoughts known to Claude Lenfant and members of the Advisory Council whose names and addresses are appended. To keep me informed, I would be very grateful if you would copy me on any communications.

Cordially,

Henry Blackburn, MD
Professor and Director

This is the gist of H. Blackburn's comments on the absence of minority populations, after Council and staff claimed the Labarthe proposal violated NIH policy.

I agree that it would clearly be desirable to have similar information in minority groups in this country. There are important scientific questions for Hispanics and Blacks, for example, in regard to obesity, insulin activity, glucose tolerance, body composition, diet and blood pressure. However, the review of any major NIH proposal requires a sensitivity to, and scrutiny of, the environmental setting. Reviewer judgments have to be made about feasibility and cost. Both of these population studies, U.S. and Japanese, are already in place. Their communities are organized, preliminary data are collected and other related studies are in progress. All of this demonstrates the great likelihood of success. If this study should prove infeasible in the Woodlands or in the Japanese at Shimane, it would be unlikely that it could be done anywhere with any less community experience or support.

The investigators intend to explore these questions in minorities, which they are now doing in a pilot study in Corpus Christi, Texas, comparing

Hispanic and Anglo populations. But, according to the chairperson of the review group, with whom I consulted, there is apparently no comparable community setting for blacks or hispanics available to them where the investigators could, at this time, propose, with confidence that such an undertaking is feasible. For example, feasibility requires a defined community, prior work experience, an established institutional identity, an adequate sample size, and reasonable homogeneity within populations, to give adequate power of analysis with stratification on major variables.

Inclusion of a minority population now would increase the cost of this proposal. Neither the investigators nor reviewers considered that the added cost could be justified or proposed at this time. Successful mounting of this project would, however, put them in a position to propose such a study.

It is, of course, essential that NIH, both in policy and in practice, stimulate, organize, support and give priority to studies where cultural differences or exposures of minorities are suspected to play a role in disease susceptibility and risk. It may not be appropriate, however, that NIH fail to support well-designed studies that seek answers to

fundamental and universal health questions, simply because they do not include minority populations due to feasibility, absence of experience or accessibility of populations. An analogy might be the NIH or the VA failing in the 1970s to support the initial trials of antihypertensive therapy because they were not specifically designed to include and address minority susceptibility, but from which minorities have gained much in health applications. Another would be failure to support studies on the risk and prevention of coronary artery disease in the absence of women in the sample, due to obvious feasibility-cost issues in the critical first-generation studies. A many times greater sample size and resources, and much feasibility testing, would have been required to study these issues in women.

It is, of course, highly appropriate that such studies include minority populations when available and feasible, as it states in NIH policy. The Cincinnati, Minneapolis and Bogalusa school projects have, indeed, involved such subgroups. There would surely be cultural differences in the impact of culture on physiological risk of minority and white populations of youths in Texas, or for that matter, in Japan, (they have two minorities, Koreans and Aino). But it is difficult to conceive of science and the public

health moving forward if approved investigator-initiated projects were rescinded by programmatic review for not always pinpointing those particular questions in minorities. Inclusion of such populations in proposals should clearly be a programmatic priority for NIH. But programmatic rejection of excellent projects because of failure to include those questions in a project, due to current information on feasibility, it seems to me, would defeat the progress of science and impede the health of all.

Let us then push forward with the superb initiatives of NHLBI to address the special cardiovascular health and risk problems in minority populations and continue to provide them priority. Let us not, however, for arbitrary or unscientific reasons, impose a discriminatory requirement on all proposals for epidemiological studies and clinical trials by the mandatory inclusion of "adequate samples" of minority populations in each and every project, irrespective of experience, feasibility, cost or the scientific questions addressed. Particularly, let us not proceed with policy without full examination of the discriminatory nature of such a policy applied, in fact, in retrospect, or applied without a thoroughgoing working group evaluation of the implications of such a

policy.

Program diversity and priority is now in place in NHLBI, which has been as responsive as any other institution in our society to this need. The Council must carefully consider, further than it has done at this meeting, whether it can always be expected of, or imposed on, every study, that these issues be addressed with adequate design, samples, and pilot experience, irrespective of scientific questions, feasibility and cost.

Finally, more than any other discipline, epidemiology is basically concerned with and sensitive to ethnic and racial and population differences in disease and risk. This is the meat of its existence; more than any other scientific discipline. However, feasibility and careful evaluation of the likelihood of getting results at a given cost are essential parts of the review process for such epidemiological applications. Where these issues are ignored, then the policy may be discriminatory, and generally unwise.