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May 4, 2000

Dr. Jane E. Henney
Commissioner, Food & Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

Enclosed are copies of two pages sent to the Great Lakes College of Clinical Medicine (GLCCM) from Steven Masiello, Director of the Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, at the Food & Drug Administration (FDA), who challenges our IRB approval. We have an earlier letter from the FDA indicating that the FDA has no authority over our research, since we are "not interested in developing a 'product' or filing an investigational application ('IND') . . ." On what authority, therefore, is Mr. Masiello challenging our IRB approval? If the FDA has no such authority, kindly rescind Mr. Masiello's demands immediately.

Furthermore, statements in Mr. Masiello's letter are inaccurate, defamatory and ethnically biased. I ask that you investigate this matter and take appropriate action regarding the responsible FDA employee.

Quotes from the FDA letter are in (bold), followed by responses and clarifications in standard print.

FDA 7A: **The protocol is inadequate in that it does not describe what testing is done to screen the malarial parasite donors.**

Our protocol states that: 1) the blood should only contain *Plasmodium vivax*, 2) that repeated thick and thin blood smear examination for parasites other than desired *Plasmodium* should be carried out, 3) negative antibody screens for syphilis, hepatitis, HIV, CMV, and any other infections suggested by history and physical examination are required. This is in accordance with standard blood screening procedures used for transfusion blood.

FDA 7A: **The direct injection of blood from a malaria parasite donor into a study subject would not be permitted in the U.S. because cultured malaria parasites are available.**

In the United States, from 1931 to 1965, U.S. Public Health Service laboratories provided malaria blood for the direct injection of blood from malaria parasite donors into tens of thousands of neurosyphilis patients. The safety and effectiveness of the procedure was reported from the Harvard School of Public Health in a peer-reviewed medical journal.

Vienna's Wagner von Jauregg won the 1927 Nobel Prize in medicine for discovering malariotherapy. The procedure was discontinued only after malariotherapy eradicated neurosyphilis, and penicillin cured early syphilis.

The Heimlich Institute met with the head of malariology at Walter Reed Army Hospital. He informed us that *P. falciparum* can be cultured, but *P. vivax* cannot. The reasons why we chose to use *P. vivax* should be obvious to the FDA. Furthermore, we have correspondence from the Centers for Disease Control (CDC) offering to provide us with malarial blood for injecting into patients receiving malariotherapy in the United States.

In light of the above, the FDA investigator's lack of knowledge and his apparent ethnic bias in assuming that the Chinese government or Chinese physicians would undertake a procedure "that would not be permitted in the U.S." certainly deserve rebuke.

FDA 7B: **The statement in the response letter that "the IRB's approach (to this study) was no different than if the research was conducted in the U.S." demonstrates that the IRB appears to lack the expertise or experience to ascertain the acceptability of proposed research in terms of Institutional commitments and regulations, applicable law, and standards of professional conduct and practice.**

That is a false and prejudicial statement (see below). The IRB statement is correct. The FDA investigator's biased statement is without basis in fact.

FDA 7C: **We reject your position that the IRB was able to consider the community attitudes of the Chinese population in which the research was to be conducted.**

The IRB approval was given with the knowledge that Dr. Heimlich has had an ongoing fifty-five-year relationship with the people of China and is known by the U.S. government to be an authority on Chinese culture. He was officially named a "Friend of the Chinese People," when honored with a banquet in the Great Hall of the People two days after President Reagan received a similar banquet. The FDA investigator's false accusation against GLCCM, without knowing the facts, is, again, evidence of bias against GLCCM and the Chinese.

FDA 7C: **Given the great differences between Chinese and American cultures, we do not accept that the GLCCM was capable of understanding Chinese attitudes about the research. This is one reason, among many, that the academic institution in China that was associated with the research, as referenced in your response letter, should have obtained governmental and approval from a local IRB (or equivalent body).**

The FDA investigator makes the ridiculous and biased assumption that IRB approval

from GLCCM was all that was necessary for this project to proceed in China. Our Chinese-American consultant resents this ethnic harassment against the attitudes of the Chinese people. The research is being carried out by the Chinese government's equivalent of the U.S. Public Health Service, which is under their Ministry of Health. The senior Chinese scientific investigator is the Director of the Center for AIDS Control and Research of the Centers for Public Health and Disease Control (i.e., the Chinese Public Health system). He speaks English fluently and has been to the U.S. and other countries many times to attend conferences and to present data on AIDS treatment. In addition, he underwent additional specialized immunological training at a leading university in the U.S. as part of this project. His work is carried out in the Chinese Public Health System. What prejudice leads the FDA investigator to assume otherwise?

The project received independent approval from review boards from municipal, provincial and Ministry of Health authorities, as well as the provincial scientific committee. GLCCM most certainly understood this situation — apparently much better than the FDA investigator. Perhaps the FDA investigator can explain what he means by the "Chinese attitudes about the research" and why this does not reflect any type of ethnic bias.

FDA 7D: **Although Dr. Heimlich's Foundation is apparently underwriting this research study, he has no responsibilities for subject screening, study procedures, or evaluation of subjects, and appears to have no direct supervisory role over the study.**

Dr. Heimlich is the principal investigator for this research and was personally involved in all procedures mentioned. He made repeated trips to China to oversee patients' treatments. In addition, in 1996, following presentations at the NIH (Bethesda, MD) and the 12th World AIDS Conference (Vancouver), a leading AIDS authority, a professor from a major U.S. university's immunology department, asked to join in this effort. Their doctors also made regular trips to the research site in China to provide independent evaluation of the quality of research being done by our colleagues in China. They also provided independent corroboration of the results from China.

FDA 7D: **Dr. Heimlich is not obligated to obtain IRB approval for his limited involvement in this study, and indeed, in this case, it was inappropriate for him to do so.**

As stated above, Dr. Heimlich was not required to have FDA approval; therefore this statement is wholly false and defamatory. The matter of Dr. Heimlich's involvement has also been addressed. Because of his great respect for the several hundred physician members of GLCCM and their IRB, and to have the benefit of their advice, he sought IRB approval even though it was not required.

More importantly, the FDA investigator's statement indicates his failure to understand the fundamental purpose of the IRB. The IRB's purpose is to review proposed medical

research to determine its risk-benefit ratio and to supervise the progress of the research, particularly with regards to patient safety. How can it be "inappropriate" to seek additional IRB supervision (above that required)?

FDA 7E: **The IRB file for this study did not contain the Chinese translation of the protocol or consent form. In general, when study subjects are non-English speakers, the IRB must assure that the consent form translation is accurate.**

If the Chinese English-speaking Director cannot accurately translate the protocol and consent forms into Chinese, who can? The FDA investigator speaks of non-English speakers in the U.S. Is he not aware that in China, Chinese is not a foreign language?

FDA 7F: **Please describe the IRB's efforts to determine that this study had been approved by the appropriate office in the Ministry of Health and by the local institution(s) where the research was conducted.**

As previously indicated, the position of the FDA investigator is ludicrous, and his statement is false and ethnically prejudicial. He fails to understand that the government of The Peoples Republic of China would not kowtow to US IRB approval. The Chinese authorities conducted their own rigorous, scientific evaluation and confirmed GLCCM's decision by providing their own approval. Again, can the FDA investigator provide a rationale explanation of how having additional IRB oversight not be of benefit to patients enrolled in this study?

FDA: **The IRB should rescind approval of this study and defer the human subject protection responsibilities to the responsible Chinese authorities. Please provide documentation that the IRB has informed the Chinese clinical investigator of his responsibility to obtain appropriate Chinese government and local institutional approval for the research.**

In view of the above, such a statement to the Chinese clinical investigator is highly inappropriate and insulting. It would act against American interests in China and interfere the important research being carried out.

The IRB approval was granted to the Heimlich Institute, not to the Chinese government. To inform the Chinese government that a U.S. IRB approval is withdrawn is insulting. What would the FDA investigator think if the Chinese informed him a Chinese IRB approval of work done in the U.S. had been rescinded?

In conclusion, an FDA investigator has taken action to remove an IRB from a study outside FDA authority. The study does not require FDA approval because it is not a drug, nor a device and it is not being developed as a commercial product. Furthermore, the FDA approval is not required because the study is being conducted by scientists outside of the United States. The FDA investigator's demands delay an important

scientific study, interfere with sound, thorough IRB review of this same study, and defame the principal investigator, coworkers and the IRB which is overseeing this study.

The FDA investigator's actions raise the question of bias against GLCCM regarding his investigation of their other IRB approvals. We ask you, Dr. Henney, to take immediate action vis-a-vis your employee and the unwarranted harm to our research that his bias and false accusations are causing.

Sincerely,

Henry J. Heimlich, M.D., Sc.D.
President

cc: Great Lakes College of Clinical Medicine
Institutional Review Board