Patterson Belknap Webb & Tyler LLP

1133 Avenue of the Americas New York, NY 10036-6710 212.336.2000 fax 212.336.2222 www.pbwt.com

Investigation of Milbank Memorial Fund Historical Activities

I. Executive Summary

The Milbank Memorial Fund ("MMF") engaged Patterson Belknap Webb & Tyler LLP ("PBWT") to undertake a review of MMF activities from its origin to present day to identify potentially unethical medical research activities—measured by current ethical standards—that MMF may have supported or carried out. The investigation involved reviewing MMF's Board of Directors minutes from 1921 to present day, minutes of the Technical Board and other MMF records archived at Yale University and articles published by MMF research staff members, and flagging any studies from that review that contained indicia of possible unethical activities. PBWT engaged medical ethics and history expert Dr. Jason Schwartz to review the flagged materials and conduct follow-up research to determine whether the studies involved unethical activities. We were also instructed that it would not be necessary for us to investigate MMF's involvement with the "Tuskegee Study of Untreated Syphilis in the Negro Male" (the "Tuskegee Study"), which has been separately reviewed by others.

We found several research programs supported by MMF or carried out by its employees or grantees that may have violated current standards of medical ethics, mainly in that we could find no evidence that the requisite informed consent had been obtained or that subjects in the control group were provided with available remedies at the conclusion of the study. Our principal concern is with nutrition studies conducted on the Northern Manitoba indigenous community in the 1940s and 50s (the "Manitoba Studies"), in part because it had already been identified in prior publications as part of an unethical series of experiments. In addition, in two cases the programs selected for study a population that was not logically or uniquely connected

to the subject of the study, suggesting that those populations were selected out of convenience rather than scientific or medical necessity. In all cases, however, including the Manitoba Studies, we found mitigating circumstances, including the facts that (i) several of the studies were not invasive and were of minimal risk to the subjects, including in some cases consisting of nothing more than external examinations, (ii) in some instances remedial treatments were provided or proposed to be provided to the subjects, and (iii) in no case did the research result in a new or improved standard of care that was subsequently withheld from study participants. Moreover, in the majority of the cases we reviewed, the population selected for study was particularly relevant to the matter studied, so that the study population was in a position to benefit from any medical advances prompted by the research. The Manitoba Studies, and several others that presented indications of possible lapses of ethical standards, are discussed below. Key documents discussed in this report are collected under separate cover as Annexes to the report.

II. Assignment

After discovering that the MMF in decades past had financially supported aspects of the ethically indefensible Tuskegee Study, the MMF engaged PBWT to conduct a review of MMF activities throughout its history to seek to identify any other possibly unethical activities that MMF had supported or carried out.

III. Review Team

Attorneys Robert P. LoBue and Scott Kim of PBWT conducted the investigation, assisted by three temp attorneys who were retained to conduct first-level review of some of the original records, due to their large volume, under the direct supervision of PBWT. In addition, PBWT retained the services of Jason L. Schwartz, Ph.D., Associate Professor of Health Policy and the History of Medicine at the Yale School of Public Health, to review historical records as needed, and to advise on all issues and questions concerning ethical standards in medical research. Professor Schwartz subsequently retained the services of Elizabeth O'Neil, a Ph.D. student in Yale's Program in the History of Science and Medicine, to work under Professor Schwartz's supervision in reviewing the archives of the MMF housed at Yale and not publicly accessible at this time due to Covid-19 restrictions. This report is authored by PBWT, but is informed by the vital input and counsel provided by Professor Schwartz, who has reviewed and agrees with its content and conclusions.

IV. Guidelines Adopted

In consultation with MMF leadership and Professor Schwartz, PBWT adopted a number of principles and practices to guide the investigation:

1. The ethical standards of the present day (summarized in section VII below) would be applied to assess the propriety of any questioned activities.

2. Both projects of the research staff employed by the MMF and research conducted by outsiders using grants from the MMF would be considered relevant activities.

3. On the other hand, the fact that MMF employees or others funded by MMF merely joined in academic discussion about and even expressed opinions on subjects that today would be considered morally and ethically questionable, if not indefensible, would not be flagged as problematic, unless it appeared that they had conducted or facilitated unethical research activities in support of their expressed views.[1]

4. We did not consider research by non-MMF personnel that was merely published in the *Milbank Quarterly*, without further involvement of the MMF, to be within scope.

5. The conduct of unethical research would almost inevitably involve direct interaction with human subjects. Thus, our investigation focused on the funding or conducting of experiments on a human population. By contrast, mere retrospective analysis of data previously collected by others without involvement of MMF would be unlikely to raise an ethical question, and was considered outside scope.

6. Throughout its history, the MMF has made grants of funds in the form of fellowships or otherwise to named individuals. In many cases, the grant is simply to fund education and there is no indication what the grantee is specifically studying or researching. Where the MMF records were silent as to the nature of the activities the grantee intended to carry out while benefitting from MMF funding, we did not independently research the grantee to identify all activities he or she may have carried out with the benefit of the grant.

7. We proceeded with awareness of some inherent limitations to the investigation. Because the MMF has been in existence well over a century, and direct research activity by its own staff ended some 50 years ago, persons who likely would have had knowledge of any such activities were not available to be interviewed and we were limited to the documentary record. It is possible that persons associated with the MMF may have engaged in improper activities but left no mention of them in any of the extensive materials we reviewed, either intentionally or by happenstance.[2] On the other hand, exculpatory information—for example, the fact that proper informed consent was obtained from a subject population—might have been omitted from a report or scientific publication because the author's purpose was principally to report

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[1] As an example, from time to time MMF-affiliated persons published articles on eugenics and forced sterilization—pursuits that were once mainstream but are now recognized to be based largely on pseudo-science and morally objectionable (*see* **Annex 23)**. However, we found no evidence that the MMF financially supported these practices or that its employees had carried them out or facilitated them, beyond joining in academic discussion in the journals about these topics.

[2] It is not inevitably the case, however, that ethically questionable activities would go unreported. For example, in "Milbank Memorial Fund—Thirty Five Years in Review" (1940), the report candidly stated that the Fund supported the "study of untreated syphilis in the Negro, undertaken by the United States Public Health Service, the Alabama State Board of Health, the Macon Country Health Department, the Tuskegee Normal and Industrial Institute, and the Milbank Memorial Fund." (p. 53). Even in 1940, this would have been enough to put persons on notice that the methods used in the study were subject to question.

experimental results, and not to describe or justify methodology in an age when awareness of ethical constraints was far less developed than the present day. For these reasons, some conclusions about ethically questionable behavior are, unavoidably, cautiously stated.

V. Materials Reviewed

The primary documentary sources reviewed were:

1. Previously published histories of the MMF, specifically:
    a. "Milbank Memorial Fund—Thirty-Five Years in Review" (1940);
    b. Kiser, "The Milbank Memorial Fund—Its Leaders and Its Work 1905-1974";
    c. "The Milbank Memorial Fund at 90" (1995);
    d. "Centennial Report: Milbank Memorial Fund 1905-2005."
2. The Board of Directors minutes of the MMF from 1921[3] to the present. These minutes are believed to provide the most complete catalogue of approved grants and activities of the MMF, albeit in a very summary form.
3. A bibliography of publications by the MMF staff members during the years in which they were employed by the MMF, compiled by a graduate intern at Columbia University following a request by the MMF. A full list of the publications from the bibliography reviewed in full is provided in **Annex 1**.
4. The minutes of the MMF's Technical Board from 1923 to 1971, available as part of the MMF archives at Yale. The time span was determined based on the years during which MMF maintained a staff of researchers who directly conducted medical research programs under the general oversight of the Technical Board. This review of Technical Board minutes was subsequently expanded to 1985, in an effort to locate additional information about specific programs mentioned in Board of Directors minutes for the more recent time period.
5. During the investigation, specific concerns were raised about research on nutrition conducted by MMF staff member Dr. H.D. Kruse among indigenous Canadians in Manitoba in the 1940s. A number of publications on the subject provided by MMF were reviewed by PBWT and Dr. Schwartz. Using those publications, PBWT made requests for original documents from the Library and Archives of Canada (LAC), and also retained a Canadian researcher to personally obtain documents at LAC that were

[3] With the guidance of MMF, activities pre-1921 were excluded because they were grants to a limited number of charitable organizations.

restricted in access to Canadian citizens.[4] In addition, Dr. Schwartz obtained from the National Institutes of Health's PubMed database a full list of Dr. Kruse's publications, and selected two (not involving the Manitoba work but suggestive of human experimentation) for closer study:

a. Adamson JD, Jolliffe N, Kruse HD, et al. Medical Survey of Nutrition in Newfoundland. *Can Med Assoc J*. 1945; 52(3):227-250.

b. Wiehl, D.G., & Kruse, H.D (1946). Hemoglobin variations for women on iron therapy for thirty-one months. *The Milbank Memorial Fund Quarterly*, 24(4), 373-400.[5]

6. During the investigation, we raised specific concerns about research on rheumatic disease supported by MMF and conducted by Dr. John Paul in the 1930s on indigenous populations and also on schoolchildren in New Haven. Dr. Paul's publication list was also scrutinized and a number of his publications (listed in **Annex 2**) and his personal papers on file at Yale were reviewed by Dr. Schwartz.

7. Miscellaneous news reports collected from internet searches concerning flagged studies from the review of MMF's Board of Director minutes, and other historical mentions of activities of MMF.

VI. Methodology

As instructed by Professor Schwartz, the team first sought to identify, from the documentary sources, those activities that called for deeper scrutiny because they had features indicative of a relatively higher risk of possible unethical conduct ("flags") such as experimentation on vulnerable or captive populations or on diseases where there was a known history of questionable research methods. The list of such flags used to conduct the first-level review follows. It is important to bear in mind that none of these features is, without more, *evidence* of unethical behavior; they are merely the filters used to identify activities worthy of closer study:

- Involved Human Test Subjects
- International – whether the research was conducted outside the United States
- Eugenics/Sterilization
- Population/Pregnancy/Fertility/Reproduction
- Nutrition

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[4] At this writing, we have received all of the "open" files requested from the LAC, but not the "restricted" files. As noted below (see footnote 11), we will update this report if subsequently-obtained records change any of our conclusions.

[5] Upon review, these reports did not disclose any indicia of unethical conduct and are not further discussed in this report.

- Infectious Diseases (sexually transmitted or otherwise)
- Prison – whether the study was conducted at a prison
- Military – whether the study involved the military
- Children – whether the study involved children
- Racial Minorities – whether the study involved or concerned minorities
- Mental Health
- Vaccines
- Cancer
- Migrant Health

Team members first reviewed the published histories listed above (see section V.1) to gain an overall sense of the historical activities and interests of the MMF and to identify the individuals affiliated with the MMF most likely to have been directly involved in experimental activities.

PBWT engaged temp attorneys to review all of the MMF Board of Directors minutes from 1921 through the present. Typically, the Board of Directors met four times per year and the minutes provide a high-level overview of the MMF's activities. PBWT prepared a review protocol directing the temp attorneys to catalog all of the MMF's grants, research projects, travel grants, and fellowships mentioned in the minutes and record the salient details for each activity listed, with the above "flags" in mind. In addition to recording any description provided of the activity, the protocol asked the temp attorneys to catalog (i) whether the activity involved human test subjects and if it did, the population involved, (ii) the subject matter area of research, and (iii) the location of the research. The minutes proved to be too sparse to reveal this information in many cases. Nonetheless, the temp attorneys, with oversight from PBWT, created a catalog of MMF activities from 1921 through the present (the "Catalog").[6]

At intervals during the temp attorneys' cataloguing activity, PBWT and Professor Schwartz reviewed the work in progress and flagged the activities that might plausibly invite further scrutiny. It was believed that the minutes of the MMF Technical Board archived at Yale would be the most likely source of additional information about the flagged activities. Professor Schwartz engaged Elizabeth O'Neil, a Ph.D. student in Yale's Program in the History of Science and Medicine, to search for and review any Technical Board minutes of the flagged activities, along with selected financial records, progress reports submitted by MMF employees, and Milbank Newsletters in an effort to locate additional information.

MMF's Technical Board was set up in 1923 to advise the Board of Directors about funding decisions and the details of the MMF's research projects. While its composition and purpose evolved over time, the Technical Board played a continuing role in MMF's projects

[6] Due to the Catalog's volume, it can be made available separately but is not included as an Annex to this report.

and work, and their discussions were aimed at the general development of public health and medicine in the United States and how MMF could support that development.

As we discovered, the Technical Board minutes themselves rarely discussed specific MMF research activities in any detail and when they did, they did not shed light on the ethical aspects of those activities. When specific research activities were discussed, it was generally with an eye to the broader relevance of the research, rather than the details of grant disbursement or methodologies of a specific MMF project. As such, it was difficult to match the flagged activities from the Catalog with what was recorded in the Technical Board minutes. However, where possible, the Catalog was updated with additional notes on the flagged activities that could be matched up to the Technical Board minutes. Any other activities discussed in the Technical Board minutes that raised ethical concerns but could not be matched to an activity in the Catalog were also flagged.

The team was initially instructed to limit the time scope of its review to the period when the MMF had its own staff of researchers, i.e., approximately the early 1920s to the early 1970s, when the risk of engagement in improper activities was considered to be the highest. We were later instructed to extend the investigation to the present day, and did so.

VII. Key Ethical Principles

According to the Belmont Report,[7] a leading statement of ethical principles applicable to medical research on human subjects, the three fundamental ethical principles for using any human subjects for research are:

1. Respect for persons: protecting the autonomy of all people and treating them with courtesy and respect and allowing for informed consent. Researchers must be truthful and conduct no deception;
2. Beneficence: the philosophy of "do no harm" while maximizing benefits for the research project and minimizing risks to the research subjects; and
3. Justice: ensuring reasonable, non-exploitative, and well-considered procedures are administered fairly—the fair distribution of costs and benefits to potential research participants—and equally.

These principles are applied in three areas: informed consent, assessment of risk and benefits, and selection of subjects. Informed consent requires that the proposed subjects be given sufficient information concerning such matters as the research procedures, their purposes, risks and anticipated benefits in order to enable a meaningful decision by the subject whether to participate. It also requires that the information is conveyed in a way calculated to ensure comprehension by the subject, and that consent to participate be obtained in an

[7] National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; Department of Health, Education and Welfare (September 30, 1978), *available at https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html*

atmosphere free of coercion or undue influence. The requirement of risk/benefit assessment requires that the researchers systematically balance the risk and potential benefits of the research based on thorough information, and that they minimize risks and consider alternative means of achieving the same ends. The issue of selection of subjects requires that fair procedures be employed, that social, racial, sexual and cultural biases be avoided, and that special care be employed when vulnerable populations are proposed as subjects to protect against their being involved solely for reasons of administrative convenience or because they are ostensibly easy to manipulate as a result of their condition or illness.

The Belmont Report's three fundamental ethical principles served as the foundational background for the U.S. system of protection for human research, which was eventually codified in 45 C.F.R. part 46. This became known as the "Common Rule." This set of regulations governs the conduct of most human experimentation in the United States. Leaning heavily on the Belmont Report, it outlines the basic provisions for the role of institutional review boards, informed consent, and baseline requirements for conducting research involving human subjects.

A vast amount of scholarly literature has built upon the Belmont Report's ethical principles and the subsequent Common Rule, leading to a fuller and richer discussion of the ethics of human subjects research.[8] An influential framework resulting from this discussion relied upon by Dr. Schwartz in this investigation is Drs. Emanuel, Wendler, and Grady's "What Makes Clinical Research Ethical?" (**Annex 3**). Within it are "7 requirements that provide a systematic and coherent framework for determining whether clinical research is ethical." These requirements are presented in the following table:

[8] One such example of this is The Oxford Textbook of Clinical Research Ethics (February 1, 2011), excerpts from which are included in **Annexes 4 and 5**.

Table 2. Seven Requirements for Determining Whether a Research Trial Is Ethical*

Requirement	Explanation	Justifying Ethical Values	Expertise for Evaluation
Social or scientific value	Evaluation of a treatment, intervention, or theory that will improve health and well-being or increase knowledge	Scarce resources and nonexploitation	Scientific knowledge; citizen's understanding of social priorities
Scientific validity	Use of accepted scientific principles and methods, including statistical techniques, to produce reliable and valid data	Scarce resources and nonexploitation	Scientific and statistical knowledge; knowledge of condition and population to assess feasibility
Fair subject selection	Selection of subjects so that stigmatized and vulnerable individuals are not targeted for risky research and the rich and socially powerful not favored for potentially beneficial research	Justice	Scientific knowledge; ethical and legal knowledge
Favorable risk-benefit ratio	Minimization of risks; enhancement of potential benefits; risks to the subject are proportionate to the benefits to the subject and society	Nonmaleficence, beneficence, and nonexploitation	Scientific knowledge; citizen's understanding of social values
Independent review	Review of the design of the research trial, its proposed subject population, and risk-benefit ratio by individuals unaffiliated with the research	Public accountability; minimizing influence of potential conflicts of interest	Intellectual, financial, and otherwise independent researchers; scientific and ethical knowledge
Informed consent	Provision of information to subjects about purpose of the research, its procedures, potential risks, benefits, and alternatives, so that the individual understands this information and can make a voluntary decision whether to enroll and continue to participate	Respect for subject autonomy	Scientific knowledge; ethical and legal knowledge
Respect for potential and enrolled subjects	Respect for subjects by (1) permitting withdrawal from the research; (2) protecting privacy through confidentiality; (3) informing subjects of newly discovered risks or benefits; (4) informing subjects of results of clinical research; (5) maintaining welfare of subjects	Respect for subject autonomy and welfare	Scientific knowledge; ethical and legal knowledge; knowledge of particular subject population

*Ethical requirements are listed in chronological order from conception of research to its formulation and implementation.

(**Annex 3 at p. 2703**).

Applying these current-day principles, the initial question raised by experiments involving humans is whether the issue being tested is a suitable subject for research. For example, in the context of treatment studies, if the current standard of care sufficiently addresses the issue being tested, there would need to be a compelling reason to undertake an experiment at all, such as the possibility of a superior therapeutic approach. If there are questions surrounding the efficacy of the current standard of care, testing a new treatment is ethical, particularly when an intervention being studied is compared to that "standard of care". Using a placebo or control group can also be ethical in the absence of a known, effective treatment; and only if the study concludes that the experimental treatment provided (whether it be a vaccine, education, or something else) changes the current standard of care does the experimental provision need to be offered to the placebo or control group at the conclusion of the

study.[9] To change the current standard of care is a high bar given that results typically need to be replicated and the results of the study confirmed.

VIII. Findings

Review of the Board of Directors and Technical Board minutes uncovered no evidence of MMF activities that triggered ethical concerns other than those discussed below. However, there were 27 entries from the Catalog with "flags" which PBWT, Professor Schwartz, and Ms. O'Neil were unable to clear of potentially unethical conduct, due to the lack of sufficient (or any) description of the activity in the available records. Some of the entries relate to the same study so there were 20 activities total in this category. In addition, Ms. O'Neil flagged five activities discussed in the Technical Board minutes that were not flagged in the Board minutes as possibly raising ethical questions. A brief description of these 25 activities is included in **Annex 6.**

PBWT ran general internet searches on these 25 activities to see if any further information could be uncovered. We located additional documents relating to studies 4, 6, 8, 21, and 25 listed on **Annex 6**. Dr. Schwartz reviewed the results and agreed that only item 6 (Dr. John R. Paul's rheumatic fever studies among indigenous populations and schoolchildren) required additional follow-up. These studies are discussed in further detail below.

Further research could be attempted on the remaining flagged activities listed in **Annex 6** through searches in medical journals, other archival resources, and the like but in consultation with Dr. Schwartz, it was agreed that the investigation had reached a point of diminishing returns. Thus, unless further investigation is requested, we note these activities as having "flags" of potentially unethical activity that have not been cleared.

A. Dr. H.D. Kruse's Nutrition Studies in Northern Manitoba

A major focus of our investigation was on the Manitoba Studies, a series of investigations of malnutrition among the indigenous populations of Northern Manitoba that are of concern as they involved Dr. H.D. Kruse, a staff member of the MMF from 1937 to 1953. A 2013 article published by Dr. Ian Mosby (**Annex 7**) described this work and raised explicit concerns about the apparently unethical methods used. Mosby's cited sources were largely unpublished papers in the Library and Archives of Canada ("LAC"), which we also sought to obtain and review.

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[9] The Oxford Textbook of Clinical Research Ethics' Chapter 25 contains a discussion on the ethics of research involving placebos that supports the principles discussed herein (*see* **Annex 4**). More specifically concerning whether an experimental provision needs to be provided to a placebo or control group, Chapter 31 states that "researchers have an obligation to provide whatever benefit can be derived from the study to those who participate in the research." (**Annex 5 at p. 328**).

According to Mosby, the studies began with a physical examination commencing in March 1942 of malnourished subjects at Norway House,[10] a settlement of indigenous populations in Manitoba. The findings from those examinations were published in 1946 by the research team, consisting of Drs. P.E. Moore (of the Canadian Indian Affairs Branch), F.F. Tisdall (of the Royal Canadian Air Force), R.S.C. Corrigan (Medical superintendent of the Norway House Agency), and Dr. Kruse, identified in the publication as affiliated with MMF **(Annex 8)**. The published report makes clear that malnutrition and resulting ailments were pervasive among the population studied. According to Mosby, following or at some point during this initial survey, the research team conducted controlled experiments on the effectiveness of vitamin supplements by separating the subjects into a study group and a control group. The results of that experiment were described as inconclusive and were not published (**Annex 7 at p. 166 note 66)**. Mosby concludes that the Canadian nutritional research concerning the indigenous peoples on which he reports ultimately did little to improve the health of the malnourished subjects (**Annex 7 at p. 148).**

A second study described by Mosby is the "1947-1948 James Bay Survey" which appears to have been similar in design to the experimental phase of the Norway House work. Mosby states that Drs. Moore and Tisdall were involved in this portion of the work. He does not affirmatively state Dr. Kruse was not involved, but provides a listing of funders and affiliations of the researchers involved in the study—and that list does not include MMF or Dr. Kruse (**Annex 7 at pp. 153-154**).

The third study in this series of events consisted of nutrition experiments conducted in residential schools from 1948 to 1952 that involved altering the diets of indigenous schoolchildren to observe the effects on their nutrition in comparison with a control group selected within the schools. These studies also involved medical and dental examinations, blood tests, and intelligence and aptitude tests.[11]

All of the research detailed by Mosby—at Norway House, James Bay, and the residential schools—raises ethical concerns because of the vulnerable populations and lack of evidence of informed consent. The nutrition research at the residential schools was, however, of greatest ethical concern. In particular, investigation of the residential schools before the experiments began showed, according to Mosby, "overwhelmingly poor conditions . . . the food provided typically failed to meet the government's own stated nutritional requirements." (**Annex 7 at p. 159**). The controlled experiments at the schools consisted of a series of lengthy five-year

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[10] The same studies carried out at Norway House were also carried out on indigenous populations at Cross Lake, God's Lake Mine, Rossville, and The Pas but our investigation led us to focus on Norway House where "the survey was concentrated" (**Annex 8 at p. 228**).

[11] The residential schools system in Canada involved nonconsensual relocation of indigenous children from their homes and boarding them at the schools in an effort to deprive them of both their family ties and native culture. This system has been the subject of significant disapprobation in recent years.

experiments, in which the control groups, and to some extent the experimental population, were denied adequate nutrition and even "treatment that other students would have had access to…." (***id*. at p. 163**). We therefore examined closely the extent of Dr. Kruse's personal involvement in all of these studies, and the degree of awareness and support provided by MMF leadership.

The minutes of the MMF Board of Directors reflect some knowledge of the experimental program and related activities. The March 1938 minutes include a report that Dr. Boudreau (the Executive Director of the MMF starting April 1937) "had been in touch with Canadian government agencies for some time with respect to a nutrition program which is being developed there" (**Annex 9 at p. 575**). The October 1942 minutes reference Dr. Kruse "working on the early diagnosis of mild nutritional deficiencies" in "connection with the Fund's nutrition program" and spending time on nutrition problems of the Canadian Air Force (**Annex 10 at p. 684**). The October 1943 minutes describe the two Canadian activities on which Dr. Kruse was active, including the first direct reference to the studies of indigenous populations:

> Dr. Kruse has made a nutritional survey of several hundred Cree Indians in Northern Manitoba and he is now a Consultant of the Canadian Department of Indian Affairs.
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> During the last two years, the Medical Branch of the Royal Canadian Air Force has been consulting Dr. Kruse regarding nutritional problems among the personnel, and he is a Consultant of the Secretary for War on studies of K rations at Camp Lee.

(**Annex 11 at pp. 710-711**).

There are no further details provided and no other references to these activities in Board minutes. The minutes of the Technical Board contain a reference to Dr. Kruse's Manitoba studies, but without providing much further information. It states:

> Dr. Tisdall visited Dr. Moore and discussed possibilities of a nutritional survey among Indians of the North. The final outcome was a study of some 400 natives in northern Manitoba. The Milbank Memorial Fund contributed the services of Dr. Kruse and cooperation was secured from the Hudson's Bay Company, the [Royal Canadian Air Force], and the Province of Manitoba." (**Annex 12 at p. 1481**).

None of the published histories of the MMF (see "Materials Reviewed," V.1) discusses Dr. Kruse's work in Manitoba, but Kiser's 1973 book notes that Dr. Boudreau (an American born and educated in Canada) made nutrition a major research focus of MMF and hired Dr. Kruse for that purpose (p. 72-73). Kiser writes:

> With his Canadian background, Boudreau naturally became interested in that country's work in nutrition. Dr. Frederick W. Tisdall, Wing Commander of the Canadian Royal Air Force, became a frequent visitor at the Fund and a virtual co-worker with Dr. Kruse. He and several Canadian colleagues, all in uniform, were

> frequently at Technical Board meetings during the early forties, reporting on progress made in fortifying foods with the essential vitamins.

(**Kiser at p. 75**). Dr. Tisdall, as seen earlier, was part of the research team that conducted the Norway House and James Bay studies.

We also obtained Dr. Kruse's 1940 to 1945 Report on Activities, in which he wrote of his involvement in the Manitoba Studies:

> In March, 1942, under the auspices of the Medical Division of the Indian Affairs Branch of the Dominion of Canada, the Royal Canadian Air Force, the Hudson's Bay Company, and the Milbank Memorial Fund, I participated in a nutritional survey of 400 Indians in Northern Manitoba, Canada. In this survey the methods of tissue examination were applied. The results were incorporated in a report submitted to the appropriate Dominion authorities which stated that the nutritional condition of the Indians generally, was exceedingly poor. Severe acute riboflavin and vitamin C deficiencies were extremely common; pronounced advanced, chronic lesions of all deficiency states were seen in almost every Indian. Upon obtaining these facts, the Indian Affairs Office instituted an active and vigorous campaign towards improvement of the Indians' nutritional condition. The Indians with their high tuberculosis rate and poor physical stamina have for many years presented seemingly insoluble problems to the Dominion. For the first time the Department envisions a positive, constructive program for improvement of the Indians' health.

(**Annex 13 at p. 12**).

With this background, we summarize our conclusions as to both the nature and extent of Dr. Kruse's involvement in the Manitoba work, and the ethics of that work.

a. *Nature and Extent of Dr. Kruse's involvement*

At the time of the Manitoba research. Dr. Kruse was a renowned expert in nutrition, and likely would have been influential in guiding research activities with which he was associated.[12]

It is indisputable that Dr. Kruse was personally present for at least the first phase of survey work at Norway House, and personally examined some of the subjects. This is confirmed by the 1946 publication by the researchers reporting on the survey results, which Dr. Kruse co-authored (**Annex 8**), and Dr. Kruse's 1940 to 1945 Report on Activities in which he wrote "I participated in a nutritional survey of 400 Indians in Northern Manitoba" (**Annex 13 at**

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[12] *See* New York Times, July 14, 1977, Page 19 (obituary)("Dr. Kruse, whose fields were biochemistry and nutrition, held three doctorate degrees, a medical doctor of science degree from Johns Hopkins University and a doctorate in chemistry from Dickinson College.")

p. 12). Controlled experiments were also conducted at Norway House following the "survey" in which Dr. Kruse participated. We have seen no evidence that Dr. Kruse personally conducted this portion of the studies. However, they are closely associated in time, place and objectives with the initial examinations of the subjects, and there is contemporaneous evidence that Dr. Kruse had detailed awareness of the controlled experiment. For these reasons, it is fair to attribute responsibility to Dr. Kruse for this activity as well.

Dr. Kruse's awareness of the controlled experiment is documented in a 1944 report by Dr. Moore (one of the Manitoba Studies' lead doctors) to the Special Committee of the Canadian Parliament on Postwar Reconstruction and Re-Establishment of Indian Population, and associated testimony given by Dr. Moore when presenting the report to Parliament (**Annex 14**). It confirmed that Dr. Kruse was present for the first phase of the study beginning in 1942, but Dr. Moore also told the Committee that the Norway House study was proposed to be continued for another year or more. Dr. Moore stated that Dr. Kruse would be returning to that location to analyze the results. Moreover, Dr. Moore referred to the Norway House controlled experiment as a "study" being conducted by Dr. Corrigan and Ms. Wilson, and testified that "[i]n the opinion of Dr. Moore, Dr. Kruse and Dr. Tisdall, this study is being coordinated by Dr. Corrigan and Miss Wilson in an exemplary and commendable manner." (**Annex 14 at 316**). This statement strongly supports the conclusion that Dr. Kruse had detailed knowledge of not merely the objectives of the controlled study, but its methodology.

We could not ascertain whether Dr. Kruse was involved in, or how much he knew about, later phases of the Canadian nutrition studies discussed by Mosby—the experimentation at James Bay in 1947-48 or at the residential schools in 1948-52.[13] Given that the James Bay Survey was performed by some of the same researchers (Tisdall and Moore) who had partnered with Kruse to perform the initial survey at Norway House, and the reportedly close working relationship of Drs. Tisdall and Kruse, it seems highly likely that Kruse at least was informed of the James Bay nutrition research among the Canadian indigenous populations. The residential schools work, however, was conducted by Dr. L. B. Pett, Chief of the Nutrition division of the Canadian Department of National Health and Welfare. Dr. Pett was not involved in the earlier work. Although Mosby discusses the Norway House, James Bay, and residential schools research together in one article, it would not be fair to consider them all as one research program, as they were separated in time and geographical location. We have seen no evidence that Dr. Kruse worked with Dr. Pett or had any input into the design of the residential school studies.

[13] We received and reviewed all open files requested from the LAC cited by Mosby pertaining to these studies and found no evidence of Dr. Kruse's involvement. There remain restricted files that have not been released to us. In consultation with MMF, it was decided that the remaining files were unlikely to provide materially new information about Dr. Kruse's involvement in the studies in question and those files are not being pursued.

b. *Ethical Lapses in the Manitoba Studies*

i. The Norway House research

Mosby found no evidence that the initial controlled experiment at Norway House was conducted with the informed consent of the subjects or, if minors, their parents. We concur that the available documentation does not evidence such consent. In addition, when Dr. Pett, the researcher who carried out the residential schools experiments, was challenged years later about the ethics of the work, he did not contend that informed consent was obtained (**Annex 15**).[14]

Dr. Moore made recommendations in 1944 to the parliamentary committee to address some of the issues his research uncovered, including measures seeking "immediate results" such as providing "multi-vitamin therapy" and that the food eaten by the Native populations be used "as a vehicle to carry these food substances which have been found to be lacking in their diet." Dr. Moore's report also provides some helpful context and even provides some reassurance regarding ethical concerns in that the researchers appeared to be conducting the studies to identify issues relevant to the test subjects' own health and there was at least some effort by the researchers to provide remedies for the medical issues they identified in conducting their research. Likewise, Dr. Kruse's 5-year report quoted earlier maintains that, as a result of his research, "Indian Affairs Office instituted an active and vigorous campaign towards improvement of the Indians' nutritional condition." (**Annex 13 at p. 12**).

Our conclusion, and that of Dr. Schwartz, is that the initial "survey" phase of the nutrition studies at Norway House, in which Dr. Kruse was clearly physically present, was of minimal ethical concern in that it consisted solely of non-invasive examination, but the issue remains whether the subjects consented to being involved in the study. The next phase, in which controlled vitamin supplement experiments were carried out at Norway House, would not comport with modern requirements of ethical research in that, while the research was relevant to the medical problems of the subject community, we found no evidence that informed consent was obtained. The degree of ethical lapse is mitigated (even assuming that informed consent was not obtained), in that the researchers intended to ameliorate the condition of the subjects at the end of the study and apparently took steps to do so. We believe Dr. Kruse's close connection with the Norway House research program as a whole renders him (and, derivatively, MMF) accountable for whatever ethical lapses occurred there.

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[14] With regard to the Norway House activity, Dr. Moore told the parliamentary committee that the subjects "cooperated in a wholehearted spirit" but this is undercut by references to participants in the study being as young as six years old. Regarding the later work at the schools, Mosby quotes an "Outline of Talk to Children in Indian Schools Prior to Taking Dietary Records in Autumn," 1948 (**Annex 7 at p. 165, fn, 64**), which indicates that the subjects were only given a vague statement to the effect that a study was being done to improve their health.

We have also considered the ethical implications of the observation of Mosby concerning the Norway House experiment that:

> Clearly the research team was well aware that these vitamin supplements only addressed a small part of the problem and that, if they really wanted to deal with the immediate problem of malnutrition and hunger, emergency food relief that met all of the nutritional needs of the community was badly needed.

(**Annex 7 at 152**). This suggests a possibility that the researchers were intent on testing and, at best providing, a partial and less costly solution (vitamin supplements) to a much larger problem of general malnutrition, which would include such problems as insufficient caloric and protein intake. Those deficiencies, which the researchers documented at the outset of their work, could not be alleviated by vitamin supplements alone but would require far more comprehensive, costly, and systemic interventions such as massive food relief to the indigenous population. As advised by Dr. Schwartz, we believe this is a serious issue but one which ultimately does not cause us to consider the Norway House study unethical beyond the concern expressed above about the lack of informed consent.

As noted earlier, the desire to test a "superior therapeutic approach" is commonly recognized as one justification for medical experimentation on humans. However, that does not necessarily mean that only the optimal therapy (or intervention) can ethically be researched. The issue whether it is ethical to test a less expensive yet less effective intervention in the context of public or population health has been hotly debated in recent years, as discussed in Buchanan and Miller, A Public Health Perspective on Research Ethics, 2006 J. Med. Ethics 729 (**Annex 24**). The Buchanan article takes note of studies in two areas—antiretrovirals and lead paint abatement—in which researchers came under criticism for studying such less expensive remedies that would be less efficacious than the optimal remedy, but due to their lower cost might make it possible to afford some relief to a larger population given the constraints of limited resources and public will to spend on such remedies. While Buchanan and Miller acknowledge that conventional ethical doctrine would find fault with this approach, they argue that the public health perspective should allow greater freedom to pursue such studies, where, for example, "economic or political constraints . . . do not allow universal provision of the higher standard." Thus, the authors conclude:

> Research on less expensive, less effective interventions is justified by giving due moral consideration to the feasibility of providing population-wide protections, provided the risks to participants are reasonable and proportionately balanced in relation to the prospective health benefits to them and the value of the knowledge to be gained. Concerns about reducing pressure to provide the most effective intervention need to be assessed in the specific historical context of the health problem under consideration and to be balanced against the likelihood that the status quo of neglect will be maintained if a less expensive alternative is not developed**.**

This approach suggests that the totality of circumstances must be considered before condemning a research approach that studies a less than optimal or 'total' remedy as unethical. In this case, while the nutritional needs of the population went far beyond vitamin deficiencies, that was one recognized problem needing to be addressed. Moreover, it was not known at the time whether vitamin supplements could be just as effective as more robust food relief to solve that *particular* aspect of the overall nutritional problem, an important difference from the paradigmatic studies in this ethical conversation—antiretrovirals and lead paint abatement—for which the inferiority of the interventions being studied (relative to the respective 'gold standard' approaches) was beyond dispute.

Equally important, our review of Dr. Moore's testimony and report to the Parliamentary committee overseeing this work leads us to believe that the researchers were cognizant of the larger nutritional needs of the population in question and sought to address those needs. For example, Dr. Moore's report called for "investigations as to the best foods to which Vitamin A and Vitamin C might be added," viewing this as a "widespread Therapeutic program for the correction of chronic deficiency states universally present amongst the Northern Indians." (**Annex 14 at 317**). The report further proposed, as one of several longer-range solutions, "that children in every Indian day school be given a noonday meal based on the best available food that would provide a large share of their daily nutritional requirements." (Id.). These recommendations suggest that the researchers were not seeking to cut corners by finding a low-cost and partial remedy to the exclusion of larger measures, but were focused on remediating vitamin deficiencies as the most urgent measure to implement among a wider array of nutritional needs of the population. For these reasons, we and Dr. Schwartz do not conclude that the decision to focus research at Norway House on vitamin supplements, as opposed to more general improvements in the food supply, was unethical.

ii. The Later Studies

With regard to the phase of nutritional studies carried out at James Bay in 1947-48: there is no indication that informed consent was obtained, and while the researchers were seeking solutions to the nutritional problems of the indigenous population, it is not clear whether the study results identified specific means of improving the condition of the subjects and whether any of the subjects was provided with any such remedies. As Mosby laments, too often the only upshot of these studies was a call for "more such studies." (**Annex 7 at pp. 151 and 164**). As to James Bay, however, unlike Norway House, it is fairly clear that Dr. Kruse and MMF were not involved in the design or implementation of the research even if Dr. Kruse knew it was occurring.

The research conducted at the residential schools raises deeper concerns about ethical propriety. The subjects were not merely vulnerable but a captive population and clearly had no ability to opt out of the studies; the experiments continued for lengthy time periods during which proper diets were withheld from obviously malnourished children; even the experimental subjects were denied needed care (such as dental care) when doing so was thought to interfere

with the experimental needs of the study; and there is no indication that at the end of the study remedial measures were afforded to improve the condition of the subjects. Again, however, there is no evidence that Dr. Kruse or MMF participated in these studies in any capacity. Moreover, unlike the James Bay work there is no overlap in research personnel with the original Norway House studies, which appear to have ended at least four years before the residential schools work began. For this reason, while the residential schools nutrition research was clearly unethical judged by modern standards, it is fair to say it was a separate project from the Norway House activities and we cannot attribute responsibility to Dr. Kruse or MMF for this research.

The chart that follows summarizes the research among the indigenous populations in Canada described by Mosby:

Summary of Canadian Studies					
Experiment		**Years**	**Description**	**Known Researchers**	**Known Sponsors and/or Contributors**
Norway House Survey	Survey	1942-44	Survey of the dietary habits and nutritional status of 400 indigenous persons.	-Dr. Percy Moore -Dr. Frederick Tisdall -Dr. Harry D. Kruse -Dr. Cameron Corrigan	-Department of Indian Affairs -MMF -Royal Canadian Air Force -Hudson's Bay Company
	Experiment	1942-44	Vitamin controlled experiments involving 125 indigenous persons provided with a variety of supplements while 175 acted as a control.	-Dr. Percy Moore -Dr. Frederick Tisdall -Dr. Cameron Corrigan[15]	
James Bay Survey		1947-48	Nutrition study on indigenous populations' diet, including controlled studies involving changes to diet.	-Dr. Percy Moore -Dr. Frederick Tisdall -G. Gordon Brown	-Department of National Health and Welfare -Department of Mines and Resources -Canadian Life Insurance Officers Association -United States Public Health Service

[15] As discussed above, Dr. Kruse was not present but was familiar with and reportedly approved this phase of the research.

Residential School Experiments	1948-52	Nutrition study on indigenous schools to examine the students' known malnutrition and conduct control experiments involving changes to the students' diet.	-Dr. Lionel Pett	

B. Dr. John Paul's Rheumatic Fever Studies

The investigation flagged two articles by Dr. John R. Paul, a prominent virologist, concerning rheumatic fever studies on schoolchildren: (1) Paul, J., & Dixon, G. (1937). Climate and Rheumatic Heart Disease: A Survey Among American Indian School Children in Northern and Southern Localities. *The Journal of the American Medical Association*, 108(25), 2096-2100 (**Annex 16**), and (2) Paul, J., Harrison, E., Salinger, R., & DeForest, G. (1934). The Social Incidence of Rheumatic Heart Disease: A Statistical Study in New Haven School Children. *The American Journal of the Medical Sciences*, 301-309 (**Annex 17**). Both studies are from the 1930s and were supported by MMF, as stated in the initial footnote in each article. The ethical concerns raised by the articles led Dr. Schwartz to conduct follow-up research. Dr. Paul was a faculty member at Yale, associated with what is now the Yale School of Public Health. His personal papers are housed at Yale and were available to Dr. Schwartz.[16] Dr. Schwartz accessed and reviewed those records to see if there was additional information about the questioned studies, and also performed a general search of the medical literature to see if there were any other reports authored by Dr. Paul indicating a tie to MMF.

Dr. Schwartz concluded that Dr. Paul's connection to MMF was limited to the two epidemiological studies regarding rheumatic fever and rheumatic heart disease in the 1930s discussed here.

The first study involved a survey of 1,000 indigenous schoolchildren to determine the prevalence of rheumatic fever at various latitudes in the American west in an effort to determine the role of climate in causing the disease. This population was chosen, according to Dr. Paul's writings, because of factors such as racial homogeneity and similarity of living conditions at the various study locations. The article notes that "[p]ermission for the privilege of proceeding with this work was first obtained from the Office of Indian Affairs, U.S. Department of the Interior," but does not indicate that permission was obtained from the children's

[16] This raised a potential conflict of interest concern for Dr. Schwartz as a Yale faculty member, but both PBWT and MMF agreed that under the circumstances (Dr. Paul passed away in 1971), this should not be considered a disqualifying conflict and instructed Dr. Schwartz to undertake the review of Dr. Paul's records.

parents. There is also no indication that treatment was provided to children enrolled in the study who showed signs of rheumatic fever or other medical conditions. As is usually the case with vulnerable populations such as indigenous persons, the question must be asked why this population was chosen as the study subjects.

The materials at Yale provided greater context to Dr. Paul's research and what was known about rheumatic fever at the time.[17] During the time of Dr. Paul's research, the treatment for rheumatic fever was quite limited as was the treatment for any cardiac damage that resulted from it. Thus there was a pressing need for basic research on the disease, which was prevalent among the population studied.

The materials also explained that Dr. Paul's studies on indigenous children were aimed at investigating the effects of climate on its occurrence. Indigenous children living in reservations from the edge of Mexico to the Canadian border were chosen as the studies' subjects because the social and environmental aspects of life on the various reservations were similar, such that any differences in rates of rheumatic fever could likely be attributed to climate. Dr. Paul examined 1,000 indigenous schoolchildren in Montana, Wyoming, New Mexico, and Arizona, representing latitudes of 45", 43", 37", and 33". The results indicated that rheumatic heart disease was ten times more prevalent in those living close to Canada than in children living on the Mexican border.[18]

Based on this description of Dr. Paul's work, Dr. Schwartz concluded that the study of indigenous children could not be ethically criticized for arbitrarily selecting a vulnerable population, or for failing to offer treatment to those found in the study to be suffering rheumatic disease (because there was no effective treatment available). There is, however, a remaining concern whether the indigenous subjects consented to the study. As noted earlier, the absence of evidence of consent is ambiguous. The fact that Dr. Paul paused to acknowledge the grant of permission from the Bureau of Indian Affairs while not mentioning permission granted by the subjects might suggest that the latter did not occur. There is, however, a significant mitigating factor, in that the examinations appear to have consisted of nothing more than visual examination and listening to the heart by stethoscope for signs of rheumatic disease. This is not an invasive procedure and carries minimal risk of harm to the subject.

Dr. Paul's study of schoolchildren in New Haven was in many respects similar. The studies, carried out in the early 1930s, consisted of medical examination of 758 students in both public and private schools at various locations in New Haven seeking to ascertain whether certain environmental conditions were associated with variant rates of rheumatic disease. A small group of students in the adjacent town of Hamden were also examined. As in the case of the indigenous population investigation, Dr. Paul acknowledges receiving institutional consent, but not individual consent of the patients or their parents or

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[17] *See* **Annexes 18 and 19**.

[18] **Annex 15 at p. 335**.

guardians.[19] Similarly, the methodology appears to have involved nothing more than visual examination and listening to the heart with a stethoscope, so that the risk to participants was minimal.[20]

There is one notable difference in Dr. Paul's report of his New Haven research versus his research among indigenous populations. Dr. Paul reported that when examinations of subjects identified incidental, treatable medical conditions, those individuals would be referred for care elsewhere. No similar statement is made in the reports of the studies of indigenous subjects. This divergence indicates, on the one hand, that Dr. Paul followed a salutary practice of acting in the interest of his subjects at least in the New Haven case. On the other hand, it leaves open the possibility that he acted less favorably toward the indigenous subjects by not arranging for them to be treated for observed medical conditions other than the subject of study (for which, again, there was no effective cure at the time). We caution that the evidence for such bias is relatively weak, since it is possible that Dr. Paul did in fact seek care for the indigenous subjects but simply did not note that fact in reporting the methods and results of his work.

We conclude that Dr. Paul's two studies supported by MMF likely breached modern ethical standards, but in a minor way. While such studies today would likely be characterized as "minimal risk research" for which waivers or alterations of the usual informed consent process may be granted, such waivers typically require researchers to show that the research could not practically be carried out if individual informed consent were required. As that is not the case here, the concern regarding individual consent remains. Individuals involved in research are entitled to know that they are taking part in research and to be able to opt out, even if the risks of their participation are very low. And in this case, as in others we are reporting on here, we do not have affirmative evidence to confirm that knowledge and agreement.[21]

C. MMF Publications

As noted earlier,[22] PBWT was provided with a bibliography of 370 published works authored by MMF personnel during the time those individuals were employed as researchers by the MMF. PBWT narrowed this list down to 29 publications based upon the publications' titles. We then reviewed the 29 publications in full and cleared all of them aside from item 12 (Nutritional Status of Aircraft Workers in Southern California: IV. Effects of

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[19] *See* **Annex 19 at p. 57**: "Sample public and private schools were selected and permission for examination of the pupils was obtained from the Board of Education (or the headmaster in the case of private schools) as well as from the physicians in charge of the health of the school population".

[20] *Id.* at p. 58.

[21] Our conclusion regarding Dr. Paul's studies is therefore similar to our conclusion regarding Dr. Kruse's survey work at Norway House, which was non-invasive and lacked a control group but where the subjects were nonetheless entitled to decide whether to participate. Unlike the later phases of the Manitoba Studies, Dr. Paul's studies did not involve controlled experiments in which a control group was not given potentially beneficial treatment.

[22] See "Materials Reviewed," ¶ 3, and **Annex 1**.

Vitamin Supplementation on Clinical, Instrumental, and Laboratory Findings, and Symptoms), item 18 (Tuberculosis Case-Finding in the Red Hook Area of New York City), and item 22 (The Influence of Nutrition Education in Families of the Mulberry Area of New York City). These three articles were provided to Professor Schwartz for his review (***see*** **Annexes 20, 21, and 22**).

As with the other studies discussed in this report, it is difficult to confirm particular details on how the research was conducted, particularly whether consent was obtained (especially by today's standards) and whether the "placebo" or "control" group was provided post-trial treatment. In many cases, we are unable to determine definitively whether these steps were taken.

Professor Schwartz's opinions on each study are set forth below. In general, he concluded all three raised only very low levels of ethical concern.

a. *Nutritional Status of Aircraft Workers in Southern California: IV. Effects of Vitamin Supplementation on Clinical, Instrumental, and Laboratory Findings*

This was a nutrition study supported by five separate funders, including the MMF, and one of the article's authors, Jacob W. Dubnoff, was from the MMF (**Annex 20**). It involved an analysis of Southern California aircraft workers' diets for four months followed by a year-long study on the effects certain vitamins had on those workers' diets through the use of one control group of 259 men who received a placebo, a second control group of 185 men who received nothing, and a third group of 262 men who received the vitamins. The study spanned from 1941 to 1943.

While the research subjects were described as "volunteers," the primary ethical concern is that persons in the "placebo" group were described as having vitamin deficiencies that sometimes resulted in health defects and it is unclear whether the placebo group received treatment for those conditions at the conclusion of the study. The second "control" group, who received nothing, did not know they were being included in the study until their medical histories were taken, raising consent issues and also whether they should have been offered treatment for any relevant diagnoses.

Professor Schwartz concluded that it is ambiguous whether the participants provided informed consent by today's standards (the reference to the participants as "volunteers" is relevant but not dispositive on this issue, as the word was sometimes employed in this era to identify subjects without meaning to convey the extent of consent given). There is also a potential issue with withheld treatment as it is unclear whether the researchers followed up with the placebo or control groups. Given that the study concluded further research was necessary to determine whether the vitamins provided "positive therapeutic effects" on the two conditions it showed signs of potentially treating (**see Annex 20 at p. 177**), Dr. Schwartz concluded that the study did not change the standard of care at the time. Thus, there was no obligation on the part of the researchers to offer any follow-up treatment to the placebo or control groups.

b. *The Influence of Nutrition Education in Families of the Mulberry Area of New York City*

As part of a community program for the control of tuberculosis in the Mulberry area of New York City; the Mulberry Health Center, the Bureau of Tuberculosis of the New York City Department of Health, and the MMF also studied the effectiveness of nutrition education on the same families involved in the tuberculosis program (**Annex 21**). The study was carried out from July 1937 through December 1939 and was designed to test whether teaching in the home would improve families' eating habits and living. The study divided 135 families into three equally sized groups: (1) a group that received nutrition teaching from a nutritionist, (2) a group that received nutrition teaching from nurses, and (3) a control group to whom no nutrition teaching was provided. It is unclear from the publication whether the control group ever received the benefit of the nutritional education provided to the study groups (which the study noted as having a positive effect), and it is also unclear whether either the control group or study groups provided consent.

Professor Schwartz concluded that the subject of the study—the diets of families—was relatively benign and that the results did not change the standard of care at that time in nutrition. Nonetheless, if this study were conducted today, the researchers may have needed to provide the control group with nutritional education at the conclusion of the study to meet current ethical standards. It is unclear from the article whether the researchers followed up with the control group at the end of the study but if they did not, it is not overly problematic—especially because the study failed to change the standard of care at that time. The authors noted that "[p]roblems [observed in the study group receiving care from a nutritionist] which were outside the scope of nutrition were referred to the nurse or to the supervisor for attention." It would be an issue if the authors noticed some chronic issue in a control group participant and failed to follow up on it. But again, there is insufficient information here to know whether that was the case, and we are reluctant to draw negative inferences from the omission of information in these reports.

c. *Tuberculosis Case-Finding in the Red Hook Area of New York City*

The death rate from tuberculosis in Central Harlem and Red Hook in the early 1930s was significantly higher than in nearby areas. This study, with funds and personnel provided by the MMF, was initiated to study the effectiveness of using X-ray examinations to detect tuberculosis in these two areas with follow-up of all diagnosed cases (**Annex 22**). This particular article reported on the survey of 9,900 persons aged 15 years and older within homes receiving government assistance from April to May 1933 in Red Hook. The families were described as "fairly typical of wage-earning families in the lower income classes to be found in normal times in the congested areas of New York City." In essence, it was a report of a tuberculosis screening and diagnosis program. It lacked comparison groups, controls, and other features one would typically associate with an "experiment."

Professor Schwartz's primary concern related to the selection of the subjects of the research. The fact that the study population included "members of all families on home

relief in the two areas" during the Depression raises concern about how voluntary the participation of the individuals truly was. We know nothing about how much information was provided to the research population about the purposes of this program, the risks associated with the x-ray screening, and any consequences (express or implied) for not participating in the x-ray screening and follow-up examinations. But even if there was meaningful consent, defining a research population as only those individuals receiving government aid (which is unrelated to the topic being studied) in specific communities would not pass ethical muster today, even if tuberculosis was a significant concern in those groups and their communities.

On the other hand, it is a positive fact that everyone in the research received the screening and any follow-up examinations warranted; nothing was withheld from control groups, for example, since there were not any controls. And research subjects did receive the benefit of diagnosis and follow-up of cases that might not have otherwise been identified through alternative methods in use at the time. (Compared to, say, a hypothetical study that only collected x-ray images en masse, used those images to determine the prevalence of tuberculosis in a community, but did not provide the individual follow-up and family contact examinations that this program did.)

IX. Conclusion

Our investigation identified several research projects involving human subjects in which there was clear MMF involvement and for which there is no evidence that the essential ethical feature of informed consent was obtained. Those projects are: (1) the Norway House nutrition studies in Manitoba in 1942-44, (2) Dr. Paul's rheumatic disease studies in the American west and in New Haven in the 1930s, (3) nutrition studies in Southern California and the neighborhood of Mulberry Street in New York City, and (4) tuberculosis screening in the Red Hook neighborhood in New York.[23]

While these studies should be condemned as unethical due to the apparent lack of informed consent, we also observed mitigating factors in several of them. Although several of the populations studied can fairly be described as vulnerable, in most cases the populations were not arbitrarily selected but rather were particularly relevant to the condition or disease under study and therefore in a position to benefit from any salutary results obtained from the research.[24] In addition, available evidence suggests that the researchers responsible for the Manitoba studies were seeking broad-based improvements to the nutritional situation of the

[23] We also examined one research program—the nutritional experiments at the Canadian residential schools, which addressed some of the same issues among the same population as the Manitoba studies. The research at the residential schools rises to a higher level of ethical concern, but we found no evidence of involvement by MMF or persons affiliated with it.

[24] The exceptions are the x-ray screening for tuberculosis provided to persons "on home relief" in Red Hook, and the vitamin supplement experiments on aircraft workers in Los Angeles. In neither case is there a unique connection between the subject of study and the group selected.

studied population and were not merely attempting to use vitamin supplements as a low-cost substitute for the larger nutritional and other reforms that were clearly indicated by the poor condition of the study population. Finally, while it is unclear whether the programs discussed in this report in which a control group was used provided benefits to control group members at the conclusion of the studies, in none of the cases did the research result in a new standard of care, so there would not have been an ethical obligation to provide access to those study interventions.

These mitigating factors help to contextualize the enumerated programs and should be considered in assessing the overall degree of ethical violation.

P.B.W.T.