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McMaster Research Ethics Board [MREB]
McMaster University
1280 Main Street West
Hamilton, Ontario
L8S 4L8

RE:McMaster Research Ethics Board PET Trials declared unethical by Canadian Association of Nuclear Medicine [CANM].

Dear Board Members

PREAMBLE:

The Ontario government made the decision in the late 1990's that it was not going to pay for Positron Emission Tomography [PET] scanning because of cost concerns. Cancer Care Ontario was told to discredit, delay and block PET. They would partner with the McMaster School of Evidence Based Medicine to accomplish this task. McMaster University controlled most of the funding for PET, up until at least some scans were covered by OHIP. The McMaster group continues its arrangement with CCO to assess PET which ultimately leads to government policy. These efforts to block PET have lead to unprecedented accusations, condemnation and official motions declaring the PET Trials on cancer patients to be "unethical and bordering on immoral."

- *These experiments continue to this day, and the MREB will presumably be involved in approving and following these PET Trials in their various forms.*

The Ontario government medical experts evaluating the existing medical literature on PET, as well as designing and interpreting the data from their experimental design, have publicly claimed that this process would be open and transparent and that experts were invited to participate. Cancer Care Ontario [CCO] committees partnered with McMaster University School of Evidence Based Medicine in the assessment of PET in Ontario on behalf of the Ontario Ministry of Health.

In reality, the trials were written in secret and repeated attempts by the Ontario Association of Nuclear Medicine [OANM] and others who were PET experts to be part of the trial designs were rejected by the PET STEERING Committee [PSC]. In a 2009 JCO paper by Evans et al, and in

statements made in the press this process is presented as one of the best examples of cooperation amongst physicians in Ontario to introduce PET.

> *"First, oncologists and nuclear medicine physicians, who, in Canada, have rarely collaborated on research have worked together to design and execute clinical trials."*
>
> *'..standardizing how PET scans were performed and reported**, and gaining acceptance by health professionals for the evaluative program.'***

The only way that the OANM physicians were able to see what was happening in the trial design was that someone from the PSC leaked copies to the executive.

The PET TRIALS assessed by MREB lead to unprecedented outrage and disturbing accusations and official motions condemning the Ontario PET Trials by Canadian and International PET experts starting in at least 2005. This included but was not limited to:

1. The PET Trials were declared "unethical", with demands to be halted and that a panel of Canadian experts in ethics and health policy assess the "ethical" nature of these trials.
    a. These motions were dismissed by the Minister of Health, Mr. George Smitherman, and the CCO committees.
2. In 2009, Dr. Al Driedger, the most senior member of the CCO PET Steering Committee resigned at a national meeting on PET in Toronto and stated among other things that *"what those who were evaluating PET in Ontario were doing, bordered on immoral."*
3. Professor Rodney Hicks, a recognized world expert in PET from Australia stated to me in a 2016 email:
    a. *"Ontario has the most egregious and politically motivated agenda against PET in the world."*
4. That none of the government 'medical experts' assessing PET, when challenged, is claiming that there is any scientific validity or justification to assess diagnostic imaging equipment such as PET with 'health technology assessment", a tool being developed at the McMaster School of Evidence Based Medicine.
5. That repeated attempts since at least 2004 by the Ontario Association of Nuclear Medicine [OANM], the Canadian Association of Nuclear Medicine [CANM] as well as from medical professionals and other individuals to get answers from the various experts and their committees as to how PET was being evaluated have gone either unacknowledged, or when acknowledged, not a single question of relevance was addressed.
6. In 2011 an extensive publication with respect to the status of PET in Canada was published by TRIUMF from the University of British Columbia. The sections detailing Ontario's unique approach to PET are detailed and will accompany this document.

7. In the 2017 Ontario Auditor General's Report it is noted that Ontario has the least number of PET scans/1,000 population in medical jurisdictions offering PET. *This is a direct result of the assessment of PET by CCO and the McMaster group.*
8. That the Senior Executive of Cancer Care Ontario with the knowledge of the Chairman of the Board, and the Chairman of the PET Steering Committee have threatened to block my hospital privileges. As it currently stands:
    a. If I continue to speak to physicians and/or patients about how PET is being assessed in Ontario, or supply them with the supporting documentation, or use PET case examples publicly to demonstrate my points, and even without patient identifiers, they will block my hospital privileges.

BODY OF DOCUMENT:

Although the Ontario Government PET Trials with Cancer Care Ontario [CCO] and McMaster referred to above occurred a number of years ago, there are two issues that need to be finally dealt with.

1. How did the MREB approve to five PET Trials between 2004 and 2006. In particular I will be focusing on the PET PREDICT TRIAL on women with early stage breast cancer that precipitated the 2005 CANM motions declaring the PET Trials "unethical".
2. I am concerned that "unethical trials", approved by the MREB, are still being performed on patients at the McMaster School of Evidence Based Medicine.

ISSUE 1:

MREB APPROVAL FOR PET TRIALS DECLARED UNETHICAL AND BORDERING ON IMMORAL:

I will include all the relevant documents with background information on the PET PREDICT TRIAL. Once they have been reviewed I would like to address these questions to MREB.

CANM MOTIONS:

Thursday, May 12, 2005
17:00 – 18:00
Pacific Ballroom, The Fairmont Hotel Vancouver
Vancouver, B.C.

MINUTES OF THE ANNUAL GENERAL MEETING
CANADIAN ASSOCIATION OF NUCLEAR MEDICINE

Present:
Steven Burrell
Tom Carr
Frank Cheeseman
Sandor Demeter
Albert Driedger
Rick Dubeau
Karen Gulenchyn
Peter Hollett
Gilbert Hurwitz
Ingrid Kaslowsky
Guy Lamoureux
Rosie Lawrence
Bill Leslie
Daniel Levin
Sandy McEwan
Christopher O'Brien
Daniel Picard
Curtis Mohamed
Jean-Paul Soucy
Thomas Ruth
Mandy Van Vliet
Kathy Yip
Pam Zabel
Hélène Samson

MOTION:
Be it resolved that:

The CSNM strongly recommends that the PET Trial sites in Ontario immediately suspend their participation in the four Ontario clinical PET trials and not participate in the upcoming registry trials until the ethical, operational and financial concerns raised by these trials are satisfactorily addressed by the provincial PET steering committee and the Ontario Ministry of Health.

Moved by Kevin Tracey, seconded by Jean-Luc Urbain.

CARRIED

MOTION:
Be it resolved that:

The CSNM strongly urges the Ontario Ministry of Health to immediately and adequately fund clinical PET in the province using the CMS guidelines as an interim template until such time that provincial guidelines for its use can be put in place.

Moved by Kevin Tracey, seconded by Jean-Luc Urbain.

CARRIED with two abstentions (one being Karen Gulenchyn)

MOTION:
Be it resolved that:

The CSNM recognizes that the scientific evidence available to the medical community is such that these trials cannot be regarded as ethical because they impede medical access to patients for whom the technology has been proven to be of value. The CSNM recommends an external review by a nationally recognized institute in health care and medical ethics be conducted to resolve this issue.

Moved by Al Driedger, seconded by Christopher O'Brien.
CARRIED with one abstention (not Karen Gulenchyn)

<u>THE MCMASTER RESEARCH ETHICS BOARD:</u>

No one from CCO has ever disputed that the PET PREDICT TRIAL were "unethical" from several perspectives. Yet this trial would have had to have been reviewed by the McMaster Research Ethics Board [MREB]. This raises several very disturbing issues that have yet to be addressed.

<u>PET TRIAL DESIGN:</u>

The Declaration of Helsinki is clear that researchers cannot deliberately design a trial to fail. As detailed in the accompanying documents, there were two versions of the PET PREDICT TRIAL. Both were deliberately designed to fail given that:

- *The subjects specifically chosen for the PET PREDICT Trial were women with early stage breast cancer assumed to be Stage I or Stage II. This would imply that the primary tumour in the breast could not be greater than 50 mm AND that axillary metastasis had to all less than 2mm in dimension with only one axillary metastasis greater than 2mm.*
- ***There was not then or now a macroscopic diagnostic imaging device that can detect disease of the size these patients were carefully chosen and assumed to have, and then entered into the trial.***

The stated purpose of the PET PREDICT TRIAL was to see if a PET scanner would be appropriate to detect axillary metastasis *<u>which by deliberate selection could not be detected with the PET scanners</u>*.

QUESTION 1:

Why did the MREB approve the PET PREDICT TRIAL given that PET camera's were NOT physically capable of identifying the axillary metastasis the patients were told the researchers were trying to detect?

INFORMED CONSENT TO ENTER PET TRIALS:

The principles of ethical human experimentation demands that subjects being asked to enter an experiment are expected to be given a far more detailed discussion of not just all the aspects and intentions of the trial, but *controversies* related to the experiment, and detailed discussion of risks. The following is from a course on ethical human research that I completed at the National Institute of Health in Bethesda Maryland under the section on INFORMED CONSENT it was stated: (emphasis added)

> "Informed consent in research means more than simply obtaining the signature of the potential research participant. It is a process that involves *conveying accurate and relevant information about the study and its purpose*; disclosing known risks, *benefits, alternatives*, and procedures; answering questions; and *enabling the potential participant to make an informed decision about whether to participate."*

Under ELEMENTS OF CONSENT: (again emphasis added)

> "***The research team must DISCLOSE all relevant information to the potential participant***. The information must be sufficient to allow the potential participant to decide whether to participate. It is generally accepted that the potential participant must be given the following information: the purpose of the study; nature of the procedure; reasonable alternatives to the proposed intervention; and risks, benefits, and uncertainties of each possible intervention."

QUESTION 2:

In light of the CANM motions, and fundamental and critical job of Ethics Review Boards to make sure that subjects considering or entering into the PET PREDICT Trial were appropriately informed, how is that the McMaster Research Ethics Board was unaware of the following facts and thus approved the PET PREDICT TRIAL?

In particular those subjects considering entering the PET PREDICT TRIAL were NOT informed of the following critical information in order for them to make a fully informed decision to take part in the trial or not.

- *1a. That there was NO validation to support the use of HTA in the design and/or evaluation of this trial?*
- *1b. That the PET cameras were not physically capable of detecting the cancers the women were suspected to have that entered the trial?*
- *1c.That at the time of the trial the science based medical literature had already confidently shown that PET was not of any use in Stage I or II breast cancer because of the small size of the metastasis of which the PET cameras were not capable of detecting?*
- *1d. Given that patients are supposed to be informed of any issues of potential contentiousness relevant to the proposed experiment, why were these women not told of the unprecedented and serious concerns raised by Canadian and International PET experts with respect to the trial design including the fact that the PET PREDICT TRIAL in both versions had been declared "unethical"?*
- *2e.Were the trial subjects told that the significant radiation dose they would receive from the PET experiment was not medically indicated, and the subsequent lifetime risks from this radiation exposure in light of the fact that risks from radiation are cumulative?*

In a 2009 discussion with Dr. Julian Dobranowski, Provincial Head of Cancer Imaging, Cancer Care Ontario agreed that there was no scientific basis or validation to use HTA to assess any piece of diagnostic imaging equipment, PET, CT or otherwise. I asked him the following question to which he shrugged his shoulders which I took to indicate agreement, and did not challenge this statement in a subsequent letter I sent to him in 2010.

- *That the purpose of the "PET TRIALS" was not about evaluating PET, but using PET to try and validate health technology assessment."*
- *Those considering entering the trial were not told this critical information. This also becomes very relevant to ongoing experiments on patients through the McMaster School of Evidence Based Medicine.*

QUESTION 3:

Why were the women being asked to participate in the PET Trials not told the true purpose/aim of the PET Trials use PET to try and validate the health technology assessment tool, and not to determine appropriate roles for PET?

THE PRINCIPLE OF EQUIPOISE:

Besides approving trials and experiments on humans, research ethics committees must follow the progress of the trial to ensure that it remains compliant to all the principles of ethics.

Principles of Ethical Experimental design are clear:

A: If it becomes clear during the trial that the principle in question being asked is the correct answer then the trial must be stopped and everyone gets the drug.

B: Equally true *is that if it clear the experiment will fail THEN IT MUST BE STOPPED IMMEDIATELY.*

Given the trial was by its very design meant to fail, the PET PREDICT TRIAL should have been stopped almost immediately after it began and certainly after less than 20 patients had completed the trial.

- *Instead more than 300 women were knowingly and deliberately exposed to non-medically indicated and therefore harmful radiation from the PET scans as a result of taking part in the PET PREDICT TRIAL*.

QUESTION 4:

> *Why did the MREC not immediately stop the PET PREDICT TRIAL when the early data confirmed that the trial would fail?*

ISSUE 2:
ONGOING PET TRIALS RUN THROUGH MCMASTER UNIVERSITY:

> I am concerned that “unethical trials” are still being performed on patients at the McMaster School of Evidence Based Medicine.

To the best of my knowledge, the McMaster School of Evidence Based medicine is still conducting PET Trials on human subjects to assess further possible indications for the Ontario government to consider funding by OHIP; through a program called PET ACCESS; and through PET Registry Trials and using *health technology assessment.*

As a personal example and what lead directly to the threats against me by CCO and others, in a case of a tragic irony, a patient of mine with cervical cancer ended up having a contraindicated and mutilating radical radiation therapy to her pelvis. This was a direct result of her physicians being forced to investigate this patient not on the current science based and peer reviewed literature but based on the CCO ‘compulsory standards’ not based on science, but based on “an egregious and politically motivated agenda” to quote Professor Rodney Hicks. Had this patient of been allowed to have a PET/CT before her radiation therapy, as was the long accepted ‘standard’ in the science based medical literature, she would not have had the contraindicated therapy. The result for this patient is not long after her contraindicated therapy she was admitted to

hospital with intractable pain and complications, in part because of the damage from the radical radiation therapy to her pelvis. She never left hospital and died some seven months later.

The PET/CT allowed only after her therapy correctly demonstrated that she had untreatable Stage IV cervical cancer from the beginning. In the middle of this case, one of the patients oncologists was asked to review a paper about to be published by the McMaster group as to whether there was any role for PET/CT in cervical cancer patients.

- *The paper concluded there was no role for PET/CT in cervical cancer.*
- *In discussion with a classmate of mine who has practiced gynecology in the US for almost 40 years, he could not comprehend what he was hearing. He said to me:*
    - *"David, where I practise, and for almost 20 years, most oncologists won't even book most patients with cervical cancer until they have had a staging PET scan!"*

It is well understood by the 'science based medicine community' that one of the most attractive features of using HTA, is that the 'outcome' can be 'shaped' to fit with what those sponsoring the experiment, in this case, the Ontario Government and the Institute for Clinical Evaluative Studies [ICES], *need to justify the position the government has already determined it will take with respect to funded uses for PET/CT in Ontario.*

This may sound like a 'conspiracy theory', but consider the following example of what is currently funded by OHIP for routine PET/CT scans.

- *The majority of PET/CT scans covered by OHIP are related to lung nodules and lung cancer.*
- *The OHIP funded indications are the exact opposite of the entire world expert body of opinion regarding appropriate roles for PET/CT in these circumstances.*
- *The consequences for Ontario patients is devastating and may in some cases be fatal.*

If this is in fact true, that HTA is still being used by the McMaster group:

QUESTION 5:

5a. In the current McMaster School of Evidence Based Medicine assessment of PET, is HTA being used in any aspect of the trial design and/or interpretation of the results?

5b. If this is the case, are those considering entering the trials told that there is no scientific validity or basis to use HTA to assess PET/CT for the purpose of the experiment?

5c. Are potential participants told that the true purpose of the experiments is not to assess PET/CT but to try and validate HTA as stated by Dr. Julian Dobranowski?

5d. Are prospective subjects fully informed about the discrepancy between the 'science based and peer reviewed' standards of medical practice regarding the use of PET, versus the position that the McMaster group is taking, including the fact that in most cases, that it has already been established that PET is accepted as the most appropriate diagnostic imaging device to investigate their cancers?

SUMMARY:

As I am sure you can appreciate, these are profoundly serious accusations against the credibility of the McMaster Research Ethics Board. Therefore I would ask that you review the documents I will include and address the questions I have submitted to the MREB. Normally such matters are discussed amongst the various parties in private. However the result of trials approved by the MREB has had unprecedented and profound impact on Ontario's patients. Therefore this discussion will take place in the public sphere. In addition, I have a legal opinion from my CMPA lawyer that those who have been acting as the government's 'medical and scientific advisors' are acting in the capacity of "public servants", and thus are expected to be open, transparent and publicly accountable for their actions to the public.

If you would like further information or documentation please contact me through my email or hospital address.

Respectfully Submitted

Dr. Dave Webster