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9 April 2019

Dr. Michael A. Baker

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Tel. 416 340-5300
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Dear Michael,

**Re: Terms of Reference for Inquiries into Potential Violations of Medical, Ethical, and Legal Standards in the Thalassemia Program at the UHN after 2009**

We understand that plans are underway to undertake inquiries into (i) the adequacy of patient care, and (ii) compliance with legal and ethical standards, within the Thalassemia Program at the UHN related to the switching of UHN patients from licensed, first-line chelation therapy to deferiprone (then-unlicensed in Canada, and licensed in other jurisdictions only as last resort therapy) by UHN physicians beginning in 2009.

We understand that you have undertaken to lead the first inquiry. We write to raise concerns and offer what we hope are constructive suggestions about the composition and the terms of reference for your Inquiry.

First, it is our understanding that member(s) of the Inquiry Panel (apart from yourself) have not been finalized. We have the utmost respect for your long-standing clinical expertise, as well as your demonstrated integrity. However, we agree with you that it is important that there be at least one additional member on the Panel, and particularly, to include an individual entirely independent of UHN and Apotex. Given that we understand that your Inquiry will be confined to the clinical aspects of this situation, as we have discussed this person should also have clinical expertise sufficient to: evaluate the data that was revealed through our recently published study (so that drug regulators can be informed in their decision-making, and clinicians can be informed about prescribing). Fundamentally, it must determine whether patients in the Thalassemia Program were placed at risk or experienced harm beginning in 2009 (so that UHN's ethical and legal obligations to inform them may be met), as well as determine whether any patients in the Program are currently at risk.

In addition, it is our understanding that written terms of reference for your Inquiry have not been established. We do not believe that an Inquiry should be initiated without clear, explicit

and public terms of reference to guide the members of the Inquiry Panel and which can be shared with individuals whose participation in the process is requested. The Inquiry Panel must know its mandate in order to meet it. Participants need to know the terms of reference in order to decide whether and, if so, how to participate. UHN patients and the public need to know to what UHN has committed so that the trust in the institution can begin to be rebuilt.

There are some elements that we believe must be present in the written terms of reference for your Inquiry (and no doubt there will be others):

Guiding Principles for Inquiry

- Expertise
- Independence
- Transparency

Mandate

- To evaluate the data that was uncovered through our recently published study and determine whether any patients in the Thalassemia Program were placed at risk, experienced harm, and/or are currently at risk as a result of the use of deferiprone (unlicensed from 2009 to 2015, and presently licensed as "last resort" therapy).

- To determine whether any other patients (whose EMRs were not reviewed in our study) in the Thalassemia Program were were placed at risk, experienced harm and/or are currently at risk as a result of the use of deferiprone.
- To make recommendations for remedial steps to be taken by UHN in relation to what has taken place from a clinical perspective:
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    - internal
        - patients put at risk or harmed?
        - other patients in the Thalassemia Program
        - staff
        - committees and departments (e.g., Research Ethics Board, legal services)
    - external
        - drug regulators
        - journal editors
        - clinicians
        - the public
        -
- To issue a public report on findings and recommendations (obviously protecting the identity of patients)

To put some flesh on the bones of the mandate set out above, we have attached two

appendices, the first setting out specific questions whose significance should be clear (**Appendix I**), and the second setting out more detailed specific questions accompanied by explanations of their significance (**Appendix II**). Having spent the better part of many years reviewing these EMRs and recognizing the highly complex processes and details involved in the switching of patients to deferiprone, we do not believe that it is possible to reach an assessment of risks and harms without addressing these specific questions. We offer these Appendices pariticularly Appendix II as a minimum set of goals, expecting that the members of the Inquiry Panel will have their own additional questions.

We are also writing to request your assistance with the establishment of another necessary Inquiry: that is, into potential violations of *ethical and legal standards* in the Thalassemia Program at the UHN after 2009. We acknowledge that you do not have any authority over that Inquiry. However, we are well aware of the respect the UHN administration has for you, and believe that it will take seriously any advice you might offer them about another Inquiry.

It is our understanding that a second Inquiry Panel has not been named but,as you noted, a committee consisting of Drs. Kevin Smith (CEO), Brian Hodges (Exec VP), Anil Chopra (Medical Affairs), Ed Cole (Physician-in-Chief), Amit Oza, Brad Wouters, Mansoor Husain, and Mr. Marc Toppings (Head of Legal for UHN). We are not certain of the tasks with which this Committee has been charged but it already presents a number of problems. First, the Committee is entirely internal, which is fatally problematic because the actions of the institution itself are, in part, the subject of the inquiry. Indeed, the actions of some of the people identified as serving on the Committee, and/or their Departments, must be reviewed. This includes, but is not limited to, the involvement of the Research Ethics Board, the Division of Medical Oncology and Hematology, The TGH Research Institute, and The Offices of the CEO (until recently occupied by Dr. Peter Pisters), the Vice-President, Medical Affairs & Quality Care (until recently occupied by Dr. Charles Chan) and UHN's legal team (until recently, headed by Ms Bella Martin). Drs, Pisters, Chan and Wouters were fully informed in writing (over two years ago) while the UHN legal team lead by Ms Martin was informed in writing (over nine years ago) that unlicensed deferiprone was being administered widely at UHN, and many others in authority had considerable previous knowledge of the situation now under formal review. Second, this committee does not have clear, explicit, and public terms of reference. Third, it does not have experts in research ethics and the regulation of drugs – the two key areas for any review of the legal and ethical aspects of what happened in this situation. Finally, it does not have experts in ethical and legal analysis of institutional conflicts of interest, an issue brought into this situation by the long and deep connections between UHN and Apotex.

We plan to write separately to UHN's CEO, Dr. Kevin Smith, as well as the Chairman of the UHN Board of Trustees, Mr. Brian Porter to raise our concerns about the legal and ethical review. We hope that you will speak up in support of the guiding principles of expertise, independence, and transparency for what can be described as a sister inquiry to yours, both because the weight of your views will help to persuade the UHN to do the right thing and because weaknesses in the legal and ethical review will threaten the reception and reputation of your clinical review.

We would be happy to meet with you at any time to discuss the issues we have raised in this letter. We hope that your full Panel will soon be named and terms of reference finalized.

We then hope to be able to fully cooperate with your Inquiry.

Please do not hesitate to contact us if there is anything further we can do to be of assistance.

Sincerely,

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Yours sincerely,

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