23 October 2019

Dr. Kevin Smith
President & CEO, University Health Network
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Dr. Brian D. Hodges
EVP and Chief Medical Officer
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Dear Dr. Hodges and Smith:

We are writing in respect to the Baker-Odame Review ("Review of chelation therapy practice in the red cell disorders program at UHN") provided to us on 30 September 2019. We have a number of comments and questions.

First, we ask what methods were used to select Dr. Isaac Odame to be the key analyst for the Review. Under the terms of the mandate of this Review as originally stated by Dr. Smith (to provide a non-conflicted, expert, and external individual to assist Dr. Baker) Dr. Odame would clearly have been unacceptable as a reviewer. He is conflicted, although the CV that is provided with the Review makes no mention of his conflicts, which include his ongoing and longstanding mentorship of, and collaboration with, Dr. Ward. In addition, Dr. Odame is not an expert in the field of iron chelation therapy or thalassemia.

Were there other reviewers considered for this review? If so, whose participation was requested? What were the guidelines for selection? How was it judged, and by whom, that Dr. Odame fulfilled guidelines for selection, if these exist?

Our next questions concern the process of the Review itself. What methods were used in undertaking the review? We note that the Review's conclusions contradict directly both the data (all publicly available) and the conclusions of Olivieri et al 2019[1] and, in some cases, those of Binding et al 2019[2]. We ask for the record of analysis of values of the following measurements assessed prior to and following each period of deferiprone exposure for all patients including those receiving (i) deferiprone monotherapy and (ii) varieties of "combination" therapy (deferiprone 'combined' with low-dose and full-dose deferoxamine, and deferiprone 'combined' deferasirox):

- Indications for each patient to have been switched from licensed therapy (that is the documentation that the patients were failing deferoxamine and deferasirox)
- Evidence that severe adverse effects (SAEs) were reported to Health Canada as required by law
- Signed consents by each patient switched to unlicensed deferiprone
- The UHN REB study number which permitted the exposure of these 71 UHN patients to unlicensed deferiprone

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[1] Olivieri NF, Sabouhanian A, Gallie BL. Single-center retrospective study of the effectiveness and toxicity of the oral iron chelating drugs deferiprone and deferasirox. PLoS One. 2019;14(2):e0211942.

[2] Binding A, Ward R, Tomlinson G, Kuo KHM. Deferiprone exerts a dose-dependent reduction of liver iron in adults with iron overload. Eur J Haematol. 2019.

- Liver iron concentration (assessed prior to and following each period of deferiprone exposure)
- Cardiac T2* (assessed prior to and following each period of deferiprone exposure)
- Serum ferritin concentration (assessed prior to and following each period of deferiprone exposure)
- Serum ALT (assessed prior to and following each period of deferiprone exposure)
- Details of complications encountered in each patient
- Documentation of of the deaths of the two patients including copies of reports to Health Canada
- Details of agranulocytosis including copies of reports to Health Canada

Binding et al 2019 indicate that these data are available.

Finally, we ask that you provide all background notes recorded during the process of The Baker-Odame Review, including the names of all patients whose EMRs were examined, as well as the rough and formal notes recorded by Drs. Odame and Baker during the Review. In other words, we are requesting you provide the written individual analysis of each of the 71 patients exposed to unlicensed deferiprone.

We had provided all these details to Dr. Baker on the individual patients in the Olivieri et al. 2019 paper prior to the Baker-Odame Review. It will be critical to compare the data on which the Review was based and the coded individual patient data in Olivieri et al. 2019.

We ask for a reply to this letter at your earliest convenience.

Respectfully submitted,

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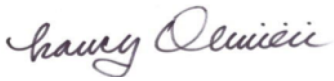

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