COMMISSION ON HUMAN MEDICINES
Chairman: Professor Stuart Ralston

Ms Joanna Wood
Review Team
Independent Medicines and Medical
Devices Safety Review
King's College, London
Shepherd's House
Room 3.25b
SE1 1UL

4th June 2019

Dear Ms Wood,

Thank you for your letter of 24 May offering me, as Chair of the Commission on Human Medicines (CHM), the opportunity to respond to comments made by the All-Party Parliamentary Group (APPG) at its oral hearing on 14th May.

Passage 1 includes the statement that, the Committee on Safety of Medicines (CSM), which was replaced on 30th October 2005 by the CHM, failed to inform doctors in the 1970s, when the indication for Primodos as a pregnancy test was removed. I would like to clarify that the change to the indication for Primodos was at the request of the UK Standing Joint Committee on the Classification of Proprietary Preparations (the MacGregor Committee) and driven by the decision that diagnostic tests should no longer be reimbursed by the health service. To the best of my knowledge neither the CSM nor the CHM were consulted on removal of the indication for Primodos, and so neither committee would have had any reason to communicate this information to the medical profession.

Passage 2 attempts to draw parallels between a comment said to have been made by Sir Derrick Dunlop, Chair of the Dunlop Committee, during discussions about the establishment of the Yellow Card Scheme in the early 1960s and the recent reviews conducted by Expert Groups which the Commission established to evaluate the publication by *Brown et al* in zebrafish and the meta-analysis by *Heneghan et al.* According to documents from the National Archives, Sir Derrick's remarks were made in response to concerns expressed by the British Medical Association (BMA) that reporting could be seen as an admission of liability in cases where a patient sues a doctor for prescribing a medicine which

CORRESPONDENCE TO: [redacted]

subsequently causes harm. However, in the landmark letter that Sir Derrick sent to all doctors in the UK in May 1964 to ask them to report any suspicions of adverse drug reactions (ADRs) to medicines to the Yellow Card Registry no reference is made to the destruction of medical records or reports of suspected adverse reactions, and I am not aware of this ever having been accepted practice.

The two recent Expert Group reviews which the Commission established were carried out by highly respected experts who were selected on the basis of the expertise needed to evaluate the questions before the Group and the type of data that would need to be assessed. None of the experts had any involvement in the original review of HPTs and adverse outcomes of pregnancy and none declared any interests that would prohibit their participation. To further ensure impartiality, the terms of reference which the Commission endorsed for each of the Groups and the information provided to them by the MHRA Secretariat did not refer to the original HPT review.

It is the Commission's duty to remain independent at all times, and to trust its Expert Groups to do the work they have been tasked with. For the two most recent Expert Group reviews on the publications by *Brown et al.* and *Heneghan et al.*, the Commission endorsed in full their findings and conclusions, having had opportunity to hear from the respective Chairs and to question them on any aspect of their work.

I am aware that the MHRA also instigated parallel reviews of the publications through specific European regulatory procedures in which the UK had no involvement. On both occasions, the findings of the European reviews were entirely consistent with those of the CHM Expert Groups.

Passage 2 also queries the expertise and motivations of the two main experts selected by the CHM to sit on the Expert Group on the *Heneghan et al.* meta-analysis. The experts in question are world-class leaders in the field of epidemiology and evidence synthesis who were selected to sit on the group precisely because they have been closely involved in developing the methodology (the ROBINS-I tool) that is at the forefront of current thinking in the meta-analysis of observational studies.

I have asked the MHRA to respond on the point about the recording of discussions of the Expert Group which the Commission established to look at the *Heneghan et al* publication.

CORRESPONDENCE TO: [redacted]

I hope that these clarifications are helpful. My thanks again for providing me with a right to reply.

If you have any queries, please do not hesitate to contact the CHM Secretariat.

Yours sincerely,

Professor S Ralston
Chair of Commission on Human Medicines

CORRESPONDENCE TO: [redacted]