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

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Mark Wilkinson
Head of Legal & Compliance

Bayer plc
400 South Oak Way
Green Park
Reading
Berkshire RG2 6AD
United Kingdom

[redacted]
www.bayer.com

Bayer plc is registered
in England No. 935048
Registered office:
Bayer plc
400 South Oak Way
Reading
Berkshire RG2 6AD

Dear Ms Wood

Thank you for your letter of 12 July enclosing an extract of the transcript of evidence given at an oral hearing attended by the All-Party Parliamentary Group (APPG) on Hormone Pregnancy Tests. Our comments are as follows:

1. The analogy with thalidomide, made by Jacob Rees-Mogg (passage 3) in relation to the issue of proof of causation is misconceived. While it is true that the mechanistic pathway whereby thalidomide ingestion caused malformations was never firmly established, that is not the same issue as determining whether general causation has been established between exposure to thalidomide and an increased incidence of malformations. Various issues are typically examined in considering whether causation is established, including whether the epidemiological evidence reveals an increase in the incidence of malformations following exposure to the product in early pregnancy, whether there is any correlation between the time of exposure in early pregnancy and the type of malformation that follows, whether the relevant malformations can be produced in animal experiments (i.e. there is an animal model for teratogenicity), whether there is any indication of a correlation between supply of the relevant product and the incidence of malformations and whether there is an increase in the incidence of a unique syndrome or "finger-print" for the product in question.

   In the case of thalidomide the scientific evidence was positive for all these elements. In the case of Primodos it is negative for all these elements. If a plausible mechanism exists for the causation of malformations this reinforces the available evidence of teratogenicity, but it is not necessary to establish causation. It was such an analysis that caused one of the scientists who first alerted the world to the teratogenicity of thalidomide (Professor W Lenz) and who had a special interest in the causes of congenital malformations to conclude in an expert report to the court in the UK litigation that was discontinued by the claimants in 1982 that Primodos could not be considered as teratogenic.

2. In passages 2, 3 and 4, Jacob Rees-Mogg seems to concede that it may be difficult to prove causation of congenital abnormalities by Primodos, but argues that it was known to be an abortifacient and patients should have been informed of this. Such a conclusion of abortifacient effect is unjustified, as it is not supported by the scientific evidence. We respectfully cross-refer to the points made in our last letter to you of 18 July 2019. We also do not recognise the basis for the statement in Passage 3 to there being only two safety tests before marketing in 1958 and these never being "updated". It is unclear whether the reference is to animal tests or to clinical trials, but in either case the statement is erroneous. In relation to clinical trials, we respectfully refer to our answer to question 3 of your May 2019 list of questions and in relation to animal testing we would refer to the EWG's detailed analysis of Schering and third party animal data and the implications of them at Section 5 of their Report of 2017.

3. In passage 3, Jacob Rees-Mogg criticises the fact that regulators allowed Primodos to be marketed despite, as he viewed the position, the absence of any therapeutic effect and its propensity to cause abortions. The unqualified reference to an absence of therapeutic effect is unjustified. Prior to 1970, the product was recommended for use as a pregnancy test or for the treatment of secondary amenorrhoea not due to pregnancy. From 1970, the product was marketed in the UK only for the treatment of secondary amenorrhoea not due to pregnancy where it and products like it were viewed by the UK authorities and by other regulators across Europe as having a therapeutic effect. For this reason products continued to be available for that therapeutic use long after the indication of pregnancy testing was deleted either as a response to regulatory direction or through voluntary removal of the indication by the companies concerned.

Thank you for giving us the opportunity to respond to the arguments advanced by the APPG.

Yours sincerely

Mark Wilkinson

Mark Wilkinson
Head of Legal and Compliance, Bayer plc