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By Claire Duddy,
Nikki Sutherland

Debate on a motion on hormone pregnancy tests

1 Overview

A debate will be held in the Commons Chamber on 7 September 2023 on hormone pregnancy tests. The subject for the debate has been selected by the Backbench Business Committee, and it will be opened by Yasmin Qureshi MP (Labour) and Hannah Bardell MP (SNP).

The motion for the debate is:

> That this House notes that children were born with serious deformities due to the hormone pregnancy test drug Primodos, which was taken by expectant mothers between 1953 and 1975; further notes that official warnings were not issued about Primodos until eight years after the first reports indicated possible dangers; observes that the report by the Commission on Human Medicines' Expert Working Group on Hormone Pregnancy Tests in 2017 was inconsistent with other academic reports; notes that the Independent Medicines and Medical Devices Safety Review, First do no harm, found that Primodos caused avoidable harm; further notes that the Government has refused to acknowledge the recommendations by the Independent Medicines and Medical Devices Safety Review relating to Primodos families; and calls on the Government to fully implement the recommendations in the Independent Medicines and Medical Devices Safety Review and to set up a redress fund for families affected by Primodos.

2 Background

2.1 Use of hormone pregnancy tests

Drugs containing synthetic versions of the hormones progesterone and oestrogen were taken as a form of pregnancy test from the late 1950s until 1970s. Primodos was the most commonly used of these medications in the UK; others included Norlestrin and Amenorone. These medications were used for both the investigation and treatment of menstrual irregularities and for the diagnosis of early pregnancy (usually between five and ten weeks). It is the latter use which has proved controversial.

To diagnose pregnancy, Primodos was usually given as two doses, 12 hours apart. If there was no episode of menstrual bleeding after taking the medication, the test was positive (i.e. pregnancy was indicated).[1]

At the time hormone pregnancy tests were introduced, pregnancy was usually medically diagnosed later than it is today, without chemical tests, once it was obvious that there had been two or more missed periods, and a pregnant uterus could be felt. Hormone pregnancy tests were thought to allow a relatively confident earlier diagnosis of pregnancy.[2]

2.2 Withdrawal of hormone pregnancy tests

Studies in the UK and elsewhere from the late 1960s to early 1970s suggested a link between the use of hormone pregnancy tests and a wide range of serious congenital abnormalities (sometimes called birth defects). These included cleft lip and palate, limb reduction deformities and heart disease.[3]

Although the evidence was not conclusive, in 1975, the Committee on Safety of Medicines (CSM) (an independent advisory committee to the UK medicines licencing authority) recommended that hormone pregnancy tests should no longer be used. Following an editorial highlighting the risks of exposure to sex hormones during pregnancy,[4] the CSM published a letter in the British Medical Journal (BMJ) on 26 April 1975 that stated that there was "little justification"

1 CJ Dewhurst, "Current practice: Obstetrics in general practice", British Medical Journal, 7 March 1964, Vol 1, p 612
2 As above
3 I Gal, "Hormonal pregnancy tests and congenital malformations", British Medical Journal, 23 October 1976, Vol 2, p 1014
4 BMJ, Synthetic sex hormones and infants, 30 November 1974, Vol. 30, No. 4, p485

for the continued use of hormone pregnancy tests, as alternatives were available.[5]

In June 1975, the CSM sent an alert letter (PDF) to all doctors in the UK, advising them of a possible association between hormone pregnancy tests and an increased incidence of congenital abnormalities. The letter recommended that doctors "should not normally prescribe" these products as pregnancy tests.[6]

A yellow warning notice was placed on product containers from 1975 onwards, stating that use in pregnant patients should be avoided. The CSM published a further notification in November 1977. However, it has been reported that Primodos sometimes continued to be used as a pregnancy test within the NHS until it was withdrawn from the market by the manufacturer, Schering Chemicals Limited, in 1978.[7] [8]

The CSM letters from 1975 and 1977 on the safety of a number of hormonal medications, including Primodos, and other relevant documentation is available in the House of Lords Deposited Papers.[9]

2.3 Campaigns and legal cases

The Association for Children Damaged by Hormone Pregnancy Tests was formed in 1978 by Valerie Williams, the mother of a child with congenital abnormalities attributed to Primodos. With support from Jack Ashley MP and others, the Association pursued its aims of obtaining compensation and justice for member families. Mr Ashley secured an Adjournment Debate on hormone pregnancy tests on 26 May 1978, calling for a public inquiry.[10] [11]

In 1977, the Association initiated legal proceedings against Schering Chemicals Limited on behalf of two children with heart defects.[12] [13] The

5 G Greenberg and others, "Hormonal Pregnancy Tests and Congenital Malformations", British Medical Journal, 26 April 1975, Vol 2, p 191

6 Committee on the Safety of Medicines, Hormonal pregnancy tests: A possible association with congenital abnormalities, 5 June 1975 (PDF)

7 C Brewer, "Continued use of hormonal pregnancy test", British Medical Journal, 18 February 1978, Vol 1, p437

8 "Pregnancy test drug 'still prescribed after babies-at-risk warning'", The Times, 17 April 1978 (subscription required)

9 DEP2010-1878 (The former Committee on Safety of Medicines (CSM) advise on the safety...)

10 HC Deb 2 March 1978 c390-392W

11 HC Deb 26 May 11978, c2002-9

12 "Group to sue firm over hormone pregnancy tests", The Times, 30 November 1978 (subscription required)

13 "Primodos actions to go ahead: no preliminary hearing on causation", The Times, 10 June 1980 (subscription required)

damage claims were discontinued on 2 July 1982 after the judge found there was insufficient evidence linking Primodos to the conditions.[14]

In early 2014, a new campaign called for an independent public inquiry into hormone pregnancy tests. This was prompted by the discovery of documents from the 1960s that reportedly showed that studies suggested that the drugs caused miscarriages and congenital abnormalities at that time.[15]

In 2019, new legal proceedings were initiated against three pharmaceutical companies who manufactured hormone pregnancy tests (Bayer Pharma AG, who purchased Schering Healthcare in 2006, Aventis Pharma and Amenorone Forte) and the Secretary of State for Health and Social Care, who was responsible for the regulation of the supply and use of medicines.[16]

In response to a PQ on 13 October 2022, the Parliamentary Under-Secretary for the Department of Health and Social Care, Lord Markham, outlined the Government's response to these proceedings:

> The Department is, with others, defending court proceedings which were issued in December 2019 by claimants who contend that hormone pregnancy tests (HPTs), such as Primodos, caused birth defects.
>
> The Department has made an application to strike out the claim by individuals which allege that HPTs caused them harm, which is due to be heard in May 2023. The scientific evidence has been reviewed on a number of occasions and most recently by the Commission on Human Medicines Expert Working Group on Hormone Pregnancy Tests. The Expert Working Group concluded that the available scientific evidence did not support a causal association. It is therefore not considered appropriate to establish an independent mediation process.[17]

In May 2023, these new claims were struck out as an "abuse of process".[18] The defendants had argued that the new claims were an attempt to re-litigate the previous case that failed in 1982, with no new evidence that could help to establish that hormone pregnancy tests caused the injuries affecting the claimants. The defendants also argued that the claim was unviable, as the claimants lacked funding and legal representation at this time.[19] Mrs Justice Yip concluded that no new evidence to establish causation was available, and that there was "no viable plan to progress these claims and no real prospect of success".[20]

14 "Claims dropped", The Times, 3 July 1982 (subscription required)
15 "Is this the forgotten thalidomide?", The Telegraph, 12 May 2014
16 "Wilson vs Bayer Pharma AG. Case Digest", Westlaw, no date (subscription required)
17 PQ HL2291 [on Primodos], 8 September 2022
18 *Wilson & Others v Bayer Pharma AG & Others* [2023] EWHC 1282 (QB)
19 "Wilson vs Bayer Pharma AG. Case Digest", Westlaw, no date (subscription required)
20 *Wilson & Others v Bayer Pharma AG & Others* [2023] EWHC 1282 (QB)

3 Reviews of the evidence on hormone pregnancy tests

3.1 Medicines and Healthcare products Regulatory Agency review 2014

In 2014, the Medicines and Healthcare products Regulatory Agency (MHRA) conducted a review of the historical evidence on hormone pregnancy tests and birth defects (PDF).[21]

The review considered 36 published research studies and additional unpublished data. The findings were published in March 2014. The MHRA reported that the studies "were inconsistent in their findings for an association between use of HPTs and congenital anomalies and are not considered sufficient to conclude that an association exists."[22]

The review authors expressed concerns about the limitations of the studies used, mainly related to their being conducted at a time when research standards were "relatively unsophisticated".[23] The report highlighted that other published reviews expressed similar comments about poor quality data in published studies, and that most other reviews also concluded that the available evidence did not support a causal association between hormone pregnancy tests and congenital abnormalities.[24]

The conclusion from the synopsis of the MHRA report is reproduced below. It states that the evidence on this issue is mixed, but that the MHRA's position was that the data was not sufficient to show a causal link between hormone pregnancy tests and congenital abnormalities:

> The body of evidence for an association between HPTs and congenital anomalies is mixed, with some studies finding a strong association, some finding a weak association and many others finding no association. Although it is understandable to suspect that there may be an association between a medicine and a condition that develops after taking it, particularly when that medicine is taken during pregnancy, this may not necessarily be the case. The timing of exposure is critical and needs to occur during the period of gestation when the fetus is susceptible to the observed outcome. The association also needs to be plausible; in this case the observation of isolated but different anomalies in different studies is particularly difficult to interpret. If HPTs really were teratogenic, all studies should have observed increased numbers of all

21 Medicines and Healthcare products Regulatory Agency, Assessment of historical evidence on Primodos and congenital malformations – a synopsis (PDF), UK Government Web Archive, March 2014, accessed 10 August 2023

22 As above

23 As above

24 As above

> the observed that have been anomalies because women were exposed to HPTs at random times throughout gestation. In addition the scientific methodology needs to be sufficiently robust as to exclude false positive findings ie the possibility that other factors could have been responsible for the observed finding - this is not the case for the vast majority of studies. Having carefully considered the available published evidence, our position therefore remains that the data are not sufficient to conclude that there is a causal association between the use of Primodos (or any HPT) and congenital abnormalities.[25]

3.2 Commission on Human Medicines Expert Working Group review 2017

In response to a Backbench Business Committee debate on oral hormone pregnancy tests in October 2014, the then Minister for Life Sciences, George Freeman, confirmed that there would be an independent review of evidence on this issue.[26]

The MHRA issued a call for evidence (PDF) in March 2015.[27] This stated that the Commission on Human Medicines (the body that advises ministers on the safety, efficacy and quality of medicines) had endorsed the need for a review of the evidence relating to hormone pregnancy tests. The document also stated that the review would not be a political inquiry but would examine the evidence to see if there were grounds for accepting a link between the use of hormone pregnancy tests and adverse outcomes.[28]

An Expert Working Group (EWG) was established, and its terms of reference agreed in December 2015. These are set out in its 2017 report:

- To consider all available evidence on the possible association between exposure in pregnancy to hormone pregnancy tests (HPTs) and adverse outcomes in pregnancy (in particular congenital anomalies, miscarriage and stillbirth) including consideration of any potential mechanism of action
- To consider whether the EWG's findings have any implications for currently licensed medicines in the UK or elsewhere
- To draw any lessons for how drug safety issues in pregnancy are identified, assessed and communicated in the present regulatory system and how the effectiveness of risk management is monitored

25 As above

26 HC Deb 23 October 2014, c1138

27 Medicines and Healthcare products Regulatory Agency, Hormonal pregnancy tests (including Primodos) and possible association with birth defects: Call for evidence (PDF), UK Government Web Archive, 25 March 2015

28 As above

- To make recommendations.[29]

In an October 2016 Backbench Business Committee debate, concerns were raised that the agreed terms of reference did not permit the EWG to investigate reports of regulatory failure by Government bodies in the 1960s and 1970s.

In response, the then Under-Secretary of State for Health, David Mowat, said that "nobody on the Government side of the House has any interest in anything other than getting to the truth, and the process that was put in

[29] Commission on Human Medicines, Report of the Commission on Human Medicines Expert Working Group on Hormone Pregnancy Tests, October 2017

place two years ago had that at its heart".[30] He noted that the Association for Children Damaged by Hormone Pregnancy Tests did not have confidence in the inquiry, describing this as "unsatisfactory". He said that if the EWG found a clear causal link between hormone pregnancy tests and adverse outcomes, further action would be taken on regulation and liability.

He went on to address concerns that the EWG were not impartial:

> The second concern is that the expert working group is not impartial. The MHRA has taken a vigorous approach to evaluating and handling potential conflicts of interest. No member of the expert working group can have any interest in any of the companies that were involved or their predecessors. Members should not have publicly expressed a strong opinion, favourable or unfavourable, about the possibility of birth defects arising from these drugs. We heard that one of the members had tweeted. If there is evidence of that, we will follow it up. It is true that one member not of the expert group, but of the advisory group was removed because it was felt that he had a conflict of interest that was not properly declared. Action was taken very quickly in respect of that. The inquiry is chaired by a consultant gynaecologist from the Chalmers centre in Edinburgh. The group has 14 scientists drawn from some of the best universities in the UK. We have no reason to believe that any of them have any more reason not to want to get to the truth than Members on both sides of this House.[31]

1 Sky news documentary March 2017

In March 2017, a Sky News documentary, Primodos: The Secret Drug Scandal, provided an account of its six year investigation into the history of hormone pregnancy tests. This included reviewing archived documents from a number of organisations.

The programme expressed concerns about the actions of the then regulator, the Committee on Safety of Medicines, at the time when hormone pregnancy tests were in use. It reported that the findings of studies of adverse effects associated with the drugs were not made public.[32]

The documents reviewed by the documentary team were submitted to the Expert Working Group.

A March 2017 Lord's Parliamentary Question asked about the Government's response to the documentary. The then Under-Secretary of State for Health, Lord O'Shaughnessy, stated that any new evidence identified would be provided to the Expert Working Group for consideration:

30 HC Deb 13 October 2016, c544

31 HC Deb 13 October 2016, c546

32 Sky News, Primodos: Sky News exposes pregnancy drug cover-up, 19 March 2017

> An Expert Working Group of the Commission on Human Medicines is conducting a comprehensive scientific review on the evidence for a possible causal association between Hormone Pregnancy Tests (HPTs), including Primodos, and birth defects. Any important new evidence identified in the Sky News documentary will be reviewed by the Medicines and Healthcare products Regulatory Agency and provided to the Expert Working Group for their consideration and advice.
>
> While the evidence for any association between HPTs and congenital defects is still under consideration it would be premature to comment on the need for a public inquiry [...][33]

More information about the investigation can be found on the Sky News website.[34] The documentary can be viewed on the Sky News YouTube channel.[35]

Publication of the Expert Working Group Report

In November 2017, the Commission on Human Medicines' Expert Working Group published its report. The group's overall conclusion was that "the scientific evidence does not support a causal association between the use of HPTs such as Primodos and birth defects or miscarriage".[36]

The report summary sets out three key issues addressed by the group in relation to hormone pregnancy tests and the conclusions that they reached in relation to each of these (bold text from the original document):

> **1. To consider all available evidence on the possible association between exposure in pregnancy to HPTs and adverse outcomes in pregnancy (in particular congenital anomalies, miscarriage and stillbirth) including consideration of any potential mechanism of action**
>
> The EWG's overall finding is that the available scientific evidence, taking all aspects into consideration, does not support a causal association between the use of HPTs, such as Primodos, during early pregnancy and adverse outcomes, either with regard to miscarriage, stillbirth or congenital anomalies. All the available relevant evidence on a possible association has been extensively and thoroughly reviewed with the benefit of up-to-date knowledge by experts from the relevant specialisms.
>
> **2. On whether the Expert Working Group's findings have any implications for currently licensed medicines**
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> The findings of the review for HPTs, including Primodos, on a possible association between exposure in pregnancy to HPTs and adverse outcomes in

33 PQ HL6207 [on Primodos], 21 March 2017
34 Sky News, Primodos: Sky News exposes pregnancy drug cover-up, 19 March 2017
35 Sky News, Primodos: The Secret Drug Scandal, YouTube, 22 March 2017
36 Commission on Human Medicines press release, Independent Expert Working Group finds totality of scientific evidence does not support a causal association between the use of hormone pregnancy tests and birth defects, 15 November 2017

> pregnancy do not have implications for any currently licensed medicines. They are in fact considered to be reassuring for women who may inadvertently become pregnant whilst taking these hormones for contraception or gynaecological indications.
>
> **3. To draw any lessons for how drug safety issues in pregnancy are identified, assessed, and communicated in the present regulatory system and how the effectiveness of risk management is monitored**
>
> There have been substantial and far-reaching advances in all areas of the development, regulation, study and use of medicines in pregnancy since HPTs were available in the UK, whereas there was a lack of transparency in the past. Nevertheless, ways to strengthen further how safety concerns in pregnancy are detected, managed, evaluated and communicated should be taken forward.[37]

The Expert Working Group also made a number of recommendations. These included undertaking an annual review of congenital anomalies. They also recommended that genetic testing is offered to families wherever there has been an adverse pregnancy outcome following the use of hormone pregnancy tests, to determine if there is an underlying genetic cause.

> The EWG considered that a number of steps could be taken to safeguard future generations through strengthening the systems in place for detecting, evaluating, managing and communicating risk with exposure to medicines in early pregnancy. These include:
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> - undertaking an annual review of all reported congenital anomalies with independent scientific advice of CHM, published in its annual report
> - facilitating research by optimising the collection of, access to and use of data on medicines in pregnancy
> - safeguarding future generations through improved training and guidance of healthcare professionals
> - working to improve the impact of safety messages on the risks of medicines in pregnancy.
>
> In addition, families of the Association for Children Damaged by HPTs, whose lives have been impacted by adverse pregnancy outcomes and who were given HPTs to diagnose pregnancy should be offered a full up-to-date genetic clinical evaluation.[38]

The Chair of the Commission on Human Medicines, Professor Stuart Ralston, reported that the review was comprehensive and that it was reviewed and endorsed by the Commission:

> This was a comprehensive and wide ranging scientific review of all the available evidence on the possible association between HPTs and birth defects by internationally leading experts across a broad range of specialisms. The

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37 Commission on Human Medicines, Report of the Commission on Human Medicines' Expert Working Group on Hormone Pregnancy Tests, 15 November 2017

38 As above

> report of the EWG was carefully reviewed and discussed by the Commission on Human Medicines CHM who fully endorsed the EWGs conclusions and recommendations.[39]

Alongside the report, the Expert Working Group published a range of material that they considered in the course of their review, including documents from the UK National Archives and documents produced by the pharmaceutical company Schering AG.[40]

Response to the Expert Working Group report

There were widely reported criticisms of the Expert Working Group report. These included that the report did not examine regulatory issues and that a number of documents had not been included in the review.

Families who believe they have been affected by hormone pregnancy tests called the review a "whitewash" and "a cover-up".[41]

The Guardian reported:

> Marie Lyon, chair of the Association for Children Damaged by Hormone Pregnancy Tests, said: "It's truly shocking and I am appalled by the report. We all feel betrayed, and I feel like I have no faith in government health agencies now. I am distraught for our members, who still haven't had the answers they need."[42]

Parliamentary debate on the Expert Working Group report

In an Urgent Question debate shortly after the publication of the report, and a Backbench Business Committee debate in December 2017, members from across the House expressed criticisms of the report. Content from both of these debates is included below.

Concerns raised in the debates included that the review was asked to look at a "possible association" but reported on a "causal association" and that evidence relating to the actions of the Committee on the Safety of Medicines in the 1960s and 1970s had not been looked at by the expert working group. In response to these criticisms in the Backbench Business Committee debate, the then Under-Secretary of State for Health, Steve Brine, said that he did not think that the terms of reference of the review had changed:

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39 Commission on Human Medicines press release, Independent Expert Working Group finds totality of scientific evidence does not support a causal association between the use of hormone pregnancy tests and birth defects, 15 November 2017

40 Commission on Human Medicines, Report of the Commission on Human Medicines' Expert Working Group on Hormone Pregnancy Tests - Documents, 15 November 2017

41 "Primodos pregnancy test report criticised as 'whitewash' by MPs", The Guardian, 16 November 2017

42 As above

> The terms of reference set out the scope of the review, and I do not believe that they changed. They were endorsed by the CHM in December 2014 a few weeks after the previous debate, and confirmed by the then Minister, my hon. Friend the Member for Mid Norfolk, in a letter to the all-party group in September 2015. In the same letter, the all-party group was informed: "it is important to review the scientific evidence to establish whether there is any causal association between use of HPTs and subsequent birth defects in the child." It is implicit and integral to any scientific assessment of evidence on medicines and associated harms to see whether the medicine is actually responsible for causing the harm rather than simply being associated with it.[43]

He also reiterated that historic regulatory issues were outside of the scope of the Expert Working Group's review.[44]

Members also stated that patients and campaigners had described the review as a whitewash.[45] [46] They expressed concerns about a sentence that had been removed from the draft report before the final report had been published.[47] The Minister acknowledged these concerns and said that the report had been revised to better reflect the scientific conclusions:

> [..] I know that many Members are concerned about differences in the draft and final reports, and especially over the removal of the sentence that said: "limitations of the methodology of the time and the relative scarcity of the evidence means it is not possible to reach a definitive conclusion."
>
> That sentence in the draft report was followed immediately by the group's overall finding "that the available scientific evidence does not support a causal association between the use of HPTs such as Primodos, during early pregnancy and adverse outcomes."
>
> The CHM quite rightly considered the two sentences together to be misleading, and advised that the report should be revised to better reflect the scientific—I stress, scientific—conclusion of the group, and that is set out on page 100 of the final report.[48]

Concerns were also expressed about the treatment of the families who were invited to give evidence to the review.[49] Mr Brine acknowledged that this could have been improved.[50] In response to the Backbench Business Committee debate he said that he had discussed this with the Expert Working Group and asked them to "report back to me as to how they will do things better next time."[51]

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43 HC Deb 14 December 2017 c714
44 As above
45 HC Deb 16 November 2017 c581
46 HC Deb 14 December 2017 c693
47 HC Deb 16 November 2017 c581
48 HC Deb 14 December 2017 c714
49 HC Deb 16 November 2017 c581
50 As above
51 HC Deb 14 December 2017 c715

3.3 University of Oxford systematic review

In October 2018, a group of researchers published a systematic review and meta-analysis of research on hormone pregnancy tests. This review included 26 research studies. The researchers concluded that:

> The evidence of an association has previously been deemed weak, and previous litigation and reviews have been inconclusive. However, we believe that this systematic review shows an association of oral HPTs with congenital malformations.[52]

The lead author of this study, Professor Carl Heneghan, raised concerns about the 2017 Expert Working Group review in an interview with Sky News. His criticism focused on the approach taken by the Expert Working Group in their earlier review of the evidence.[53]

A spokesperson from the MHRA responded, describing the new research as a re-analysis of existing data, and defending the review produced by the Expert Working Group:

> This publication, which is currently awaiting peer review, does not contain new data. It is a different approach to the analysis of existing historic observational data which was reviewed by the Commission on Human Medicines' Expert Working Group on Hormone Pregnancy Tests.
>
> The review by the Expert Working Group was comprehensive, scientifically robust and independent. Based on the totality of the data, the review concluded the available scientific evidence did not support a causal association between the use of HPTs such as Primodos during early pregnancy and birth defects or miscarriage.
>
> In line with our commitment to review any new evidence, we will be consulting independent scientific experts for their views.[54]

The Commission on Human Medicines convened an ad hoc Expert Group to consider the findings of this new research. In March 2019, this group met to consider the study and an evaluation of its approach and findings produced by the MHRA.[55]

Members of the Expert Group raised concerns about the methods employed by the researchers in relation to how data were selected and assessed for

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52 Carl J Heneghan and others, Oral hormone pregnancy tests and the risks of congenital malformations: a systematic review and meta-analysis, F1000 Research Vol 7, No 1725, 29 January 2019

53 Jason Farrell, Oxford University study links pregnancy drug Primodos to birth defects, Sky News, 28 November 2018

54 As above

55 Commission on Human Medicines, MHRA report: CHM Ad Hoc Expert Group on Systematic Review and Meta-Analysis of Studies on Oral Hormone Pregnancy Tests by Heneghan et al, March 2019

quality, and the approach to statistical analysis. The Expert Group concluded that "the study could not be considered robust".[56]

An additional assessment of this study was undertaken by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP). Their report was published in April 2019 (opens pdf) and identified limitations in the study itself and in the quality of the studies included in the review.[57] The report concluded:

> [...] the quality of most studies used is questioned and, as a result, the conclusions of the meta-analysis cannot be considered reliable."[58]

2 Research on zebrafish embryos

In October 2018, an ad hoc Expert Group of the Commission on Human Medicines met to consider the findings of a study examining the effect of two component ingredients of Primodos on zebrafish embryos.[59] This study found that norethisterone acetate (NETA) and ethinylestradiol (EE) could cause developmental abnormalities in zebrafish embryos.[60]

The Expert Group recognised that zebrafish could provide a useful model to help understand the effects of chemicals on development, and that this study was well conducted. However, they noted that the findings of this study could not be directly translated to human pregnancy outcomes. The Expert Group concluded that the study should be considered alongside existing evidence, but that it did not raise new safety concerns about drugs that contain NETA and EE.[61]

56 Commission on Human Medicines, Minutes of meeting held on 18 March 2019 of CHM Expert Group on Systematic Review and Meta-analysis of Oral Hormone Pregnancy Tests, 6 May 2019

57 Committee for Medicinal Products for Human Use, Assessment Report Procedure under Article 5(3) of Regulation (EC) No 726/2004. INN/active substance: norethisterone and ethinylestradiol, EMA/745160/2018 18 October 2018 (opens PDF)

58 As above

59 Commission on Human Medicines, CHM ad hoc Expert Group: evaluation of new research on the developmental effects of norethisterone acetate and ethinylestradiol in zebrafish embryos, 19 October 2018

60 Samantha Brown and others, The Primodos components Norethisterone acetate and Ethinyl estradiol induce developmental abnormalities in zebrafish embryos, Scientific Reports, Vol 8 No 2917, 13 February 2018

61 Commission on Human Medicines, Minutes of meeting held on 5th October 2018 of zebrafish ad hoc Expert Group, 19 October 2018

3.4 The Independent Medicines and Medical Devices Safety Review

In February 2018, the then Secretary of State for Health and Social Care, Jeremy Hunt, announced a Government review on medicines and medical device safety. The Independent Medicines and Medical Devices Safety Review was chaired by Baroness Cumberlege. The aims of the review were to "make recommendations for improving the healthcare system's ability to respond where concerns have been raised about the safety of particular clinical interventions, be they medicines or medical devices".[62]

The Library briefing on The Independent Medicines and Medical Devices Safety Review provides an overview of the review, its findings and Government action in response to its recommendations.[63]

The review examined three issues of concern: the use of Primodos; the use of the anti-epileptic drug sodium valproate in pregnancy and the use of pelvic mesh. For each of these, the review investigated:

- the robustness, speed and appropriateness of those processes and actions followed by the relevant pharmaceutical/ medical device manufacturers and applicants for and holders of licenses to manufacture and sell pharmaceutical products and medical devices, the regulatory authorities, healthcare providers, public and clinical bodies and policy makers;
- whether problems could have been recognised by the relevant bodies, authorities, manufacturers and license holders and others sooner and more effectively;
- whether the same bodies could, and should, have acted upon concerns sooner and if they did not, the reasons why.[64]

In addition, in relation to Primodos, the review focused on two specific questions of interest:

1. where the science is not broadly acknowledged or accepted, whether the available historic and scientific evidence (and its assessment to date) can reasonably preclude 'a possible association' between Hormone Pregnancy Tests and their teratogenic effects, and/or needs to be revisited, in the opinion of the Review;

62 The Independent Medicines and Medical Devices Safety Review: Terms of Reference, accessed 25 August 2023

63 Commons Library research briefing CBP-9274, The Independent Medicines and Medical Devices Safety Review

64 The Independent Medicines and Medical Devices Safety Review: Terms of Reference, accessed 25 August 2023

2. given the knowledge on Hormone Pregnancy Tests available to the manufacturers, regulators and clinicians at the time, the consideration, advice and practice with regard to the use of alternative, non-invasive pregnancy tests.[65]

Publication of the First Do No Harm report

The report of the review, First Do No Harm, was published in July 2020.[66] In her press conference speech accompanying the publication of the report, Baroness Cumberlege stated (bold text from the original document):

> In our view Primodos continued to be given as a pregnancy test for years longer than it should. In the face of growing concerns it should have ceased to be available from 1967. A non-invasive alternative was available by then, and the concerns that were being expressed should have led to action by the regulator. It continued to be given to women for years longer. While there is disagreement between experts about whether Primodos caused birth defects, the fact remains that thousands of women and unborn children were exposed to a risk that was acknowledged at the time. That should not have happened. This is not a case of us judging the actions of the past by the standards of today. This was discussed at the time, but not acted upon. **The system failed.**[67]

A detailed timeline of key research studies, manufacturer, regulatory and patient actions, media coverage, media coverage and parliamentary activity relating to hormone pregnancy tests was produced as part of the review.[68]

The review concluded that hormone pregnancy tests should not have been available from 1967 onwards, given that an alternative pregnancy test was available and that there were concerns about risks. Although determining causation was outside the review's scope, the report also noted that "a possible association between HPTs and malformations exists and cannot be precluded" and found that those affected were entitled to support.[69]

The review made nine overarching recommendations, as follows:

- Recommendation 1: the government should immediately issue a fulsome apology on behalf of the healthcare system to the families affected by Primodos, sodium valproate and pelvic mesh.

- Recommendation 2: the appointment of a Patient Safety Commissioner who would be an independent public leader with a statutory responsibility. The commissioner would champion the value of listening to

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65 The Independent Medicines and Medical Devices Safety Review: Terms of Reference, accessed 25 August 2023

66 The Independent Medicines and Medical Devices Safety Review, First Do No Harm, 8 July 2020

67 The Independent Medicines and Medical Devices Safety Review, Press Conference Speech, 8 July 2020

68 The Independent Medicines & Medical Devices Safety Review, Annex B Hormone Pregnancy Tests Timeline, July 2020

69 The Independent Medicines and Medical Devices Safety Review, First Do No Harm, 8 July 2020

patients and promoting users' perspectives in seeking improvements to patient safety around the use of medicines and medical devices.

- Recommendation 3: a new independent Redress Agency for those harmed by medicines and medical devices should be created based on models operating effectively in other countries. The Redress Agency will administer decisions using a non-adversarial process with determinations based on avoidable harm looking at systemic failings, rather than blaming individuals.

- Recommendation 4: separate schemes should be set up for each intervention – hormone pregnancy tests (HPTs), valproate and pelvic mesh – to meet the cost of providing additional care and support to those who have experienced avoidable harm and are eligible to claim.

- Recommendation 5: networks of specialist centres should be set up to provide comprehensive treatment, care and advice for those affected by implanted mesh; and separately for those adversely affected by medications taken during pregnancy.

- Recommendation 6: the Medicines and Healthcare products Regulatory Agency (MHRA) needs substantial revision particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.

- Recommendation 7: a central patient-identifiable database should be created by collecting key details of the implantation of all devices at the time of the operation. This can then be linked to specifically created registers to research and audit the outcomes both in terms of the device safety and patient reported outcomes measures.

- Recommendation 8: transparency of payments made to clinicians needs to improve. The register of the General Medical Council (GMC) should be expanded to include a list of financial and non-pecuniary interests for all doctors, as well as doctors' particular clinical interests and their recognised and accredited specialisms. In addition, there should be mandatory reporting for the pharmaceutical and medical device industries of payments made to teaching hospitals, research institutions and individual clinicians.

- Recommendation 9: the government should immediately set up a task force to implement this review's recommendations. Its first task should be to set out a timeline for their implementation.[70]

The report made specific recommendations in relation to those affected by hormone pregnancy tests:

[70] As above

- Establishing specialist centres for families affected by medicines taken in pregnancy, to provide diagnostic services (including genetic testing) and referrals to other services in a single setting, and to conduct research

- Establishing an *ex gratia* scheme to provide discretionary payments to provide redress for the stress, anxiety, psychological harm and toll of fighting for recognition experienced by those affected by hormone pregnancy tests.[71]

In addition, the review found that regulatory action on hormone pregnancy tests was inadequate and failed to prevent the continued use of these tests after concerns were raised.[72]

Government response and reaction

In January 2021, the then Minister of State for Patient Safety, Suicide Prevention and Mental Health, Nadine Dorries, gave a Written Statement to Parliament which provided an interim response to the review.[73] The full Government response to the review was published on 21 July 2021.[74]

The Government accepted the overarching conclusion of the review that the system had failed to listen to patients. It issued an unreserved apology to those affected by Primodos, sodium valproate and pelvic mesh, and announced the creation of the new role of the Patient Safety Commissioner and a national registration system for medical devices.[75]

The Government did not accept the report's recommendation that a new independent Redress Agency should be created. Their response highlighted existing legal routes for redress. In addition, the Government did not accept the recommendation that specialist services should be established for those adversely affected by medicines in pregnancy. Instead, they stated that they would undertake work to improve care pathways for those affected, and to improve the safety of medicines used in pregnancy more widely.[76]

In July 2021, the then co-chairs of the All-Party Parliamentary Group on First Do No Harm, Jeremy Hunt and Baroness Cumberlege, responded to the Government's response:

> We welcome the government's acceptance of four of the Review's nine recommendations and a further one in principle. We are particularly pleased there will now be a Patient Safety Commissioner, and we urge the government

71 As above
72 As above
73 Department of Health and Social Care and The Rt Hon Nadine Dorries MP, Update on the government's response to the Independent Medicines and Medical Devices Safety Review, 11 January 2021
74 Department of Health and Social Care, Independent Medicines and Medical Devices Safety Review: government response, 21 July 2021
75 As above
76 As above

> to move swiftly to appoint the person and establish the post. We are confident that the Commissioner will be able to reduce the risk of avoidable harm in future, and spare individuals and families from the appalling consequences witnessed by the IMMDS Review.
>
> But we are deeply disappointed the government has rejected calls for an independent redress agency or any redress for families whose lives have been devastated by medicines or medical devices. For those families justice has not been done today.[77]

The Patient Safety Commissioner is currently undertaking work to explore options in relation to redress. However, the scope of this project is limited to options for redress for those affected by pelvic mesh and sodium valproate.[78] It should also be noted that the Patient Safety Commissioner's remit extends only to England.

Health and Social Care Committee follow-up

In December 2022, the Health and Social Care Committee held a one-off evidence session to examine the progress made on the report's recommendations.[79] The committee noted that they had been unable to receive evidence from Marie Lyon on behalf of the Association of Children Harmed by Hormone Pregnancy Tests due to ongoing litigation (see section 2.3 above) but stated an intention to return to examine this issue later.[80]

77 First Do No Harm APPG, Statement from Baroness Julia Cumberlege CBE and the Rt Hon Jeremy Hunt MP, 21 July 2021

78 Patient Safety Commissioner, PSC Redress project, no date, accessed 30 August 2023

79 Health and Social Care Committee, Follow-up on the IMMDS report and the Government's response, Sixth Report of Session 2022-23, HC 689, 20 January 2023

80 As above

4 Parliamentary material

4.1 House of Commons Health and Social Care Committee publications

2022/23 follow-up on the IMMDS report and government response

HC 689 2022/23 and HC 1286 2022/23

4.2 Debate

Cumberlege Report

HC Deb 3 February 2022 | Vol 708 c213WH -

4.3 PQs

Pregnancy Tests

Asked by: Lloyd, Tony

To ask the Secretary of State for Health and Social Care, what recent assessment he has made of the potential merits of providing redress for victims of Hormone Pregnancy Tests.

Answering member: Maria Caulfield | Department: Department of Health and Social Care

The Government's response to the Independent Medicines and Medical Devices Safety Review did not accept the recommendation relating to redress, including for hormone pregnancy tests. We are prioritising improving the future safety of medicines and medical devices through high standards for industry to market and manufacture products.

HC Deb 30 November 2022 | PQ 94687

Hormone Pregnancy Tests Expert Working Group

Asked by: Lloyd, Tony

To ask the Secretary of State for Health and Social Care, whether he plans to publish the findings of the Expert Working Group review on Hormone Pregnancy Tests.

Answering member: Maria Caulfield | Department: Department of Health and Social Care

The 'Report of the Commission on Human Medicines' Expert Working Group on Hormone Pregnancy Tests' was published on 15 November 2017 and is available at the following link:

https://www.gov.uk/government/publications/report-of-the-commission-on-human-medicines-expert-working-group-on-hormone-pregnancy-tests

HC Deb 30 November 2022 | PQ 94686

Pregnancy Tests

Asked by: Davey, Ed

To ask the Secretary of State for Health and Social Care, whether she will reassess the findings of the Expert Working Group review on Hormone Pregnancy Tests.

Answering member: Maria Caulfield | Party: Conservative Party | Department: Department of Health and Social Care

We have no plans to do so.

HC Deb 01 November 2022 | PQ 70951

Primodos

Asked by: Lord Alton of Liverpool

To ask His Majesty's Government, further to their issuing of an apology to Primodos victims in 2017, what plans they have to support those victims to seek justice through the courts.

Answering member: Lord Markham | Department: Department of Health and Social Care

The Government has no plans to do so.

HL Deb 13 October 2022 | PQ HL2293

Primodos

Asked by: Lord Alton of Liverpool

To ask His Majesty's Government whether they will publish all the documents they hold relating to victims of Primodos.

Answering member: Lord Markham | Department: Department of Health and Social Care

All documents relating to hormone pregnancy tests, such as Primodos, other than those subject to legal privilege, have been published in an online only format at GOV.UK.

HL Deb 13 October 2022 | PQ HL2292

Primodos

Asked by: Lord Alton of Liverpool

To ask His Majesty's Government whether they are supporting the pharmaceutical company Bayer in seeking to strike down an attempt by victims of Primodos to have their case heard; if so, why; and whether they will seek to establish an independent mediation process to ascertain whether there is a causal link between Primodos and birth defects.

Answering member: Lord Markham | Department: Department of Health and Social Care

The Department is, with others, defending court proceedings which were issued in December 2019 by claimants who contend that hormone pregnancy tests (HPTs), such as Primodos, caused birth defects.

The Department has made an application to strike out the claim by individuals which allege that HPTs caused them harm, which is due to be heard in May 2023. The scientific evidence has been reviewed on a number of occasions and most recently by the Commission on Human Medicines Expert Working Group on Hormone Pregnancy Tests. The Expert Working Group concluded that the available scientific evidence did not support a causal association. It is therefore not considered appropriate to establish an independent mediation process.

HL Deb 13 October 2022 | PQ HL2291

Primodos: Compensation

Asked by: Moore, Damien

To ask the Secretary of State for Health and Social Care, what steps his Department is taking to support people who have experienced harm as a result of hormone pregnancy drug Primodos.

Answering member: Maria Caulfield | Department: Department of Health and Social Care

The Medicines and Healthcare products Regulatory Agency has established The Safer Medicines in Pregnancy and Breastfeeding Consortium of 16 organisations to meet the information needs of women and healthcare professionals, through accessible and consistent advice.

We have established the role of Patient Safety Commissioner to work with regulatory bodies to improve the safety of medicines and medical devices. The forthcoming Women's Health Strategy will also address the health and wellbeing of women in England. A Women's Health Ambassador will lead the programme to deliver outcomes of the Women's Health Strategy, which will be published later this year.

HC Deb 06 June 2022 | PQ 10005

5 News items

The following is a selection of news and media articles relevant to this debate.

Please note: the Library is not responsible for either the views or the accuracy of external content.

Primodos: Pregnancy test damages claims thrown out by judge

BBC News Online

Philippa Roxby

26 May 2023

Primodos: Mother vows to keep fighting for justice after campaigners lose High Court bid for damages over pregnancy test pill

i News

Serina Sandhu

26 May 2023

UK families lose bid for compensation over Primodos pregnancy test drug

The Guardian

Hannah Devlin

26 May 2023

Baby Nicola died just days after her first birthday – one young 'victim' of a medical scandal that drug chiefs still deny happened... Will there ever be justice for the Primodos children?

The Daily Mail

Ethan Ennals

10 June 2023

6 Useful links

Guardian

26 May 2023

Explainer: What is Primodos and why were 100 UK families seeking compensation?

Association for Children Damaged by Hormone Pregnancy Tests

primodos.org

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