IN THE HIGH COURT OF JUSTICE
KING'S BENCH DIVISION
ADMINISTRATIVE COURT

CLAIM NUMBER:

In an application for judicial review
B E T W E E N:

THE KING
on the application of
(1) BAYSWATER SUPPORT GROUP
(2) MS KEIRA BELL
(3) MR JAMES ESSES

Claimants

-and-

(1) HEALTH RESEARCH AUTHORITY
(2) THE SECRETARY OF STATE FOR HEALTH AND SOCIAL CARE

Defendants

-and-

(1) KINGS COLLEGE LONDON
(2) SOUTH LONDON AND MAUDSLEY NHS FOUNDATION TRUST

Interested Parties

STATEMENT OF FACTS AND GROUNDS

A table of abbreviations and acronyms is attached. References in the form [CB] are to pages in the core claim bundle. References in the form [SB] are to pages in the supplementary bundle.

A. INTRODUCTION

1. This is an application for judicial review of the decisions by the Defendants to give ethical and regulatory approval to the clinical trial element of a research programme entitled Puberty Suppression and Transitional Healthcare with Adaptive Youth Services ("PATHWAYS"), a decision which was announced on 22 November 2025.

2. The PATHWAYS trial ("**the Trial**") is intended to evaluate the benefits and risks of using a form of medication called gonadotropin-releasing hormone analogues ("**GnRHa**" or "**puberty blockers**") for puberty suppression in children and young people with gender incongruence.[1] The broader PATHWAYS research programme involves a group of inter-related studies looking at the care needs and treatment of children and young people attending NHS specialist gender services. The Claimants do not seek to challenge the other elements of this programme.

3. The proposal for the Trial, and its approval, arises in the following context:

   3.1 The Trial has been approved against the background of several years of intense debate and controversy about the appropriate way to treat gender incongruence in children and young people. An important element in that background has been an

[1] The definitions of 'gender incongruence' and 'gender dysphoria' are explained at paragraph 13 below.

independent review conducted Dr Hilary Cass (now Baroness Cass), who produced her final report in April 2024.

3.2 Concerns about the risks to patient safety posed by puberty blockers have led to a prohibition on their sale and supply to persons under 18, as of 29 May 2024. This ban was initially temporary and then made permanent on 11 December 2024.[2] There is an exception to the general ban where treatment is part of a National Institute for Health and Care Research ("**NIHR**") clinical trial.

3.3 The approval of the Trial, which is the subject of this challenge, has attracted very considerable public interest and disquiet in the UK[3] and internationally.[4] That wider debate and controversy is part of the factual background but the present challenge focuses on the legality of the approval decisions and the processes that led to them.

3.4 The Trial raises important issues about the legislative framework for the approval of clinical trials and compliance with those requirements in the context of research on children and young people who are vulnerable not only as a result of their age and presentation, but also due a high incidence of a range of neurodivergent conditions present in the potential study group.

3.5 The legal issues raised in this claim have not, to the Claimants' knowledge, been litigated before.

The Parties

4. The First Claimant, Bayswater Support Group ("Bayswater"), is a company limited by guarantee which represents approximately 800 parents and guardians of children and young adults who identify as trans or nonbinary. It was established in 2019 to provide advice and support to families with trans identified children. It has members in all regions of the United Kingdom, as well as in the Republic of Ireland. Its members are overwhelmingly parents whose children are adolescents or young adults but also includes parents of younger children. They are at different stages of gender transition and have different experiences of NHS services.

5. The Second Claimant, Ms Keira Bell, was the lead claimant in previous judicial review proceedings brought against the Tavistock and Portman NHS Trust. She was treated with GnRHa for 'gender identity disorder' (as gender incongruence was then described) as a teenager by the Tavistock's (now closed) Gender Identity Development Service ("**GIDS**"). At age 17 she went on to receive cross-sex hormones in the form of testosterone, and she had a double mastectomy at age 20. She has subsequently regretted her decision to undergo these interventions and sought to 'detransition', but she continues to suffer from the long-term effects of the medication and surgery.

6. The Third Claimant, Mr James Esses, is a practising psychotherapist whose clients include children suffering from gender dysphoria. He is the founder of the therapeutic

[2] Under the NHS (General Medical Services Contracts) (Prescription of Drugs etc.) (Amendment) Regulations 2024, SI 2024/728.
[3] Streeting rejects calls to stop puberty blocker trial - BBC News
[4] NHS Launches Trial of Puberty Blockers for Kids Amid Debate Over Risks and Evidence | IBTimes UK

organisation Thoughtful Therapists and Just Therapy. He is an advocate for ethical, evidence-based treatment for gender dysphoria.

7. The First Defendant is the Health Research Authority ("**HRA**"), a non-departmental public body sponsored by the Department of Health and Social Care ("**DHSC**"). It is responsible for the establishment and regulation of Research Ethics Committees ("**REC**") under ss.109 to 117 of the Care Act 2014. The approval of a REC is required in order for a human clinical trial of investigational medicinal products ("**CTIMPS**") to be given regulatory authorisation pursuant to the relevant legislation, the Medicines for Human Use (Clinical Trials) Regulations 2004 ("**the 2004 Regulations**"). The HRA is required to publish a policy which specifies the requirements with which RECs must comply, and to monitor RECs' compliance with that policy (s. 112(3) Care Act 2014). The current policy in place is the Governance Arrangements for Research Ethics Committees ("**GAfREC**"). The HRA has confirmed in pre-action correspondence that it is the appropriate Defendant, rather than any individual REC for which it is responsible.

8. The Second Defendant is the Secretary of State for Health and Social Care, who is the Minister responsible for the work of the Medicines and Healthcare Products Regulatory Agency ("**MHRA**"), an executive agency of the DHSC. The MHRA has confirmed in pre-action correspondence that the Secretary of State is the appropriate Defendant, on its behalf. The approval of the MHRA is also required in order for a clinical trial to be given regulatory authorisation under the 2004 Regulations.

9. The First and Second Interested Parties (King's College London, "**KCL**", and the South London and Maudsley NHS Foundation Trust, "**SLAM**") are the co-sponsors of the Trial. The lead investigator is Professor Emily Simonoff of KCL. The Interested Parties are responsible under the UK Policy Framework for Health and Social Care for the organisation of appropriate and proportionate arrangements to set up, run and report on a research project. A sponsor is, in relation to a clinical trial, the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial (reg 3 of the 2004 Regulations).

Summary of claim

10. The central elements of the Claimants' case are that:

    (i) The ethical approval ('favourable ethical opinion') granted by the REC, on behalf of the HRA, was substantively and procedurally flawed. The REC was not properly constituted by reference to the requirements of the regulations for lay and expert members; it did not follow the prescribed procedures; it failed to address significant matters that were required by the legislation to be considered; and it failed to take into account relevant matters as to the established evidence of risks of harm and/or take steps to acquaint itself with that evidence.

    (ii) The REC decision was also flawed by reason of the HRA and the REC chair having decided to withhold from the REC members relevant material, thus preventing the REC from even considering for itself the relevance of that material. In particular, there were representations and evidence submitted to the HRA by two separate groups of professionals (as set out in the witness

statements of Professor Curtis and Dr Irvine respectively) that were unjustifiably withheld from the REC members.

(iii) The approval given by the MHRA on behalf of the Secretary of State was also flawed, including on the basis that it could not rationally have been satisfied that the requirement of 'some direct benefit' was met, having pointed out to the applicants (the Interested Parties) that this condition was not met. No documents generated by the MHRA in the course of its decision-making have been disclosed – the subject of a specific disclosure application – and the Claimants necessarily reserve their position as to further public law errors pending such disclosure.

(iv) Both decisions were flawed on the basis of irrationally approving a clinical trial on a group that is vulnerable not only because of their age, as children below the age of 16 who may potentially be as young as 10 (or, even as the trial sponsors suggest as the likely lower age of 12) but also their vulnerability from a high incidence of other conditions such as autism and ADHD, and social difficulties. The trial design is inherently flawed; it lacks a rational scientific purpose; and it is incapable of yielding clinically meaningful data. The Claimants seek permission to rely on the expert opinion of Professor Sallie Baxendale in relation to these fundamental scientific flaws.

11. The Claimants' case is put on the basis of the information which is currently publicly available. The Defendants have repeatedly refused to disclose relevant documents which would allow the Claimants and the Court to understand in more detail the process and reasoning behind the approval decisions, to scrutinise their legality. Even since the pre-action protocol process was started there has been partial and selective disclosure (see below). The Claimants reserve the right to apply to amend this Statement of Facts and Grounds following receipt of the Defendant's Acknowledgments of Service and any further disclosure pursuant to the duty of candour and/or an order for specific disclosure.

Standing

12. In pre-action correspondence the Defendants have questioned whether the Claimants have standing to bring this claim. The Claimants each contend that they clearly have the required "sufficient interest" to give them the legal standing to bring this claim and have set that out in correspondence. In case standing remains in issue the Claimants have set out their case on this in **Appendix A** to the SFG.

B. FACTUAL BACKGROUND

Gender incongruence, its diagnosis and treatment

13. The clinical definitions of **gender incongruence** and **gender dysphoria** may be conveniently found at Appendix 10 of the final Cass report [SB 958]. Gender dysphoria is associated with "*clinically significant distress*" or impairment of function and is the more commonly used term in research publications, as well as clinical settings. However, the PATHWAYS trial protocol uses the term gender incongruence, which as is apparent from the definitions does not involve a necessary element of distress or loss

of function. It is thus based entirely on the subjective reporting of the patient and not on any objective clinical findings.

14. The current state of scientific knowledge in relation to gender incongruence and dysphoria indicates that these presentations are not linked to physical pathology (i.e. they do not constitute disease or illness requiring physical medical intervention). Under DSM-5 gender dysphoria is categorised as a mental disorder. However, the ICD-11 does not define gender incongruence in this way – perhaps unsurprisingly, given that it does not include the need for a clinical finding of patient distress or functional impairment – thus rendering it a subjectively determined condition that is neither a physical nor a mental illness. This raises a question of why it should require any kind of medical intervention or treatment at all, and is relevant to the assessment of any justification advanced for such treatment on an experimental basis (see the explanation of this point at §§94-101 of Prof Baxendale's report [CB 113-114]).

15. Prior to the introduction of puberty blockers, clinical experience of patients who had been gender incongruent (whether or not also fulfilling the criteria for dysphoria) since childhood suggested that in the majority of cases it was resolved during puberty or early adulthood.[5] The introduction of puberty blockers has masked that natural resolution, as set out below.

16. Children and young persons suffering from gender dysphoria are highly vulnerable and demonstrate higher than expected rates of Autism Spectrum Disorder ("**ASD**"), Attention Deficit Hyperactivity Disorder ("**ADHD**"), anxiety, depression, eating disorders, suicidality, self-harm, and Adverse Childhood Experiences (such as physical, sexual, and emotional abuse or neglect).[6]

17. There is no international consensus on the best practice for care and treatment of children and young persons with gender dysphoria or incongruence. Early gender services in this area focused on therapeutic work and psychosocial approaches. However, the approach to treatment changed following the 'Dutch protocol', which emerged from a single case study in 1998 involving a female to male transition via puberty blockers at age 13. There was a subsequent expansion of the Dutch protocol to a larger group of patients, but it is difficult to draw conclusions from the results of this study due to concerns regarding bias and the confounding factor that all patients were also provided with psychological treatment whilst on the puberty blockers.[7]

18. Since then, however, there has been an increasing trend towards a 'gender affirming model' which presumes that a "*child of any age may be cognisant of their authentic identity and will benefit from a social transition at any stage of development*".[8] Gender

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[5] See e.g. Cass Review Final Report at §2.6: "***2.6*** *Several studies from that period (Green et al., 1987; Zucker, 1985) suggested that in a minority (approximately 15%) of pre-pubertal children presenting with gender incongruence, this persisted into adulthood. The majority of these children became same-sex attracted, cisgender adults. These early studies were criticised on the basis that not all the children had a formal diagnosis of gender incongruence or gender dysphoria, but a review of the literature (Ristori & Steensma, 2016) noted that later studies (Drummond et al., 2008; Steensma & Cohen-Kettenis, 2015; Wallien et al., 2008) also found persistence rates of 10-33% in cohorts who had met formal diagnostic criteria at initial assessment, and had longer follow-up periods. It was thought at that time that if gender dysphoria continued or intensified after puberty, it was likely that the young person would go on to have a transgender identity into adulthood (Steensma et al., 2011)*."

[6] Cass Review Final Report §5.68

[7] Cass Review Final Report §§2.7-2.12

[8] Cass Review Final Report §2.14

affirmative care emphasises the use of puberty blockers, cross-sex hormones, and surgery to facilitate gender transition and manage gender dysphoria.

19. In the UK, there was a move towards gender affirmative care at GIDS, which began an early intervention study prescribing puberty blockers between 2011 and 2014. Preliminary findings from that study "*did not demonstrate improvement in psychological wellbeing, and in fact some birth-registered females had a worsening of 'internalising problems (depression, anxiety) based on parental report*". The results showed a significant increase in adolescents scoring the statement "*I deliberately try to hurt or kill myself*" as "sometimes true" following a year of treatment on puberty blockers.[9] However, the results of this study were not published until December 2020.

20. In the interim, from 2014, puberty blockers became available in the UK in routine clinical practice despite the lack of evidence base for this approach. Puberty blockers were made available to those who would not have met the strict inclusion criteria of the Dutch protocol or the UK early intervention study.

The Cass Review

21. Following scrutiny of the risks of hormonal and surgical intervention in vulnerable children, health authorities in an increasing number of countries now recommend **psychosocial** approaches rather than **hormonal** or **surgical** interventions as the primary treatment, and have introduced restrictions on the latter.

22. The increasing national and international concerns over the safety of the administration of puberty blockers on vulnerable children culminated in the UK with Ms Bell's litigation against the Tavistock and Portman NHS Trust in October 2019. Against this background, the Independent Review of Gender Identity Services for Children and Young People chaired by Dr Hilary Cass ("**the Cass Review**") was commissioned by NHS England to make recommendations regarding the provision of treatment for children and young people experiencing gender incongruence and gender dysphoria. The Cass Review published an Interim Report in February 2022 and a Final Report on 10 April 2024.

23. Among the conclusions of the Cass Review were the following, in the 'Summary and recommendations' section of her final report:

    a. The initial movement towards treatment with puberty blockers lacked a sound evidence base. The adoption of such treatment with uncertain benefits without further scrutiny was "*a significant departure from established practice*" and has contributed to "*significant consequences on patient expectations and demand for treatment*" (§§22-23).

    b. The focus on the use of puberty blockers for managing gender-related distress "has overshadowed the possibility that other evidence-based treatments may be more effective" (§69).

    c. The systematic and independent evidence review commissioned by the Cass Review and undertaken by the University of York "*found multiple studies*

[9] Cass Review Final Report, §§2.19-2.20

demonstrating that puberty blockers exert their intended effect in suppressing puberty, and that bone density is compromised during puberty suppression". No changes in gender dysphoria or body satisfaction were demonstrated. There was "*insufficient/inconsistent evidence about the effects of puberty suppression on psychological or psychosocial wellbeing, cognitive development, cardio-metabolic risk or fertility*". Given that "*the vast majority*" of young people started on puberty blockers proceed to cross-sex hormones[10] there was "*no evidence that puberty blockers buy time to think*", which was the original rationale for their use, and "*some concern that they may change the trajectory of psychosexual and gender identity development*" (§§80-83).

d. "*Although a diagnosis of gender dysphoria has been seen as necessary for initiating medical treatment, it is not reliably predictive of whether that young person will have longstanding gender incongruence in the future, or whether medical intervention will be the best option for them*" (§58). Thus, Dr Cass noted that: "[a]*ssessing whether a hormone pathway is indicated is challenging*" and "*the poor evidence base makes it difficult to provide adequate information on which a young person and their family can make an informed choice*" (§§98-99).

24. The final report of the Cass review referred to the proposed clinical trial of puberty blockers, including stating at §16.38:

> *"The Review has already advised that because puberty blockers only have clearly defined benefits in quite narrow circumstances, and because of the potential risks to neurocognitive development, psychosexual development and longer-term bone health, they should only be offered under a research protocol. This has been taken forward by NHS England and the National Institute for Health and Care Research (NIHR)."*

The ban on puberty blockers

25. On 9 May 2024, following the publication of the Cass Review Final Report, the Secretary of State made a temporary emergency order (SI 2024/727) which came into force on 3 June 2024. The Explanatory Memorandum to the emergency order stated that its aim was to "*reduce and remove risks to patient safety*" by (among other measures) prohibiting the sale and supply of puberty blockers to children and young persons under 18, subject to certain exceptions. At the same time, the Secretary of State made regulations (SI 2024/728) restricting NHS Primary Care under 18 prescriptions of puberty blockers to where treatment is part of a NIHR clinical trial, or the person had started a course of treatment on puberty blockers before 26 June 2024.

26. In November 2024 the Secretary of State received advice from the Commission on Human Medicines[11] ("**CHM**") regarding the proposal to introduce a permanent restriction on the administration of puberty blockers. The CHM concluded, among others, that the

[10] Cass Review Final Report at §§14.23-14.25 cites figures of 92-98% (see also Prof Baxendale report at §§44-45 [CB 102]).

[11] The CHM is a non-departmental public body which advises ministers on the safety, efficacy and quality of medicinal products.

prescribing and care pathway for puberty blockers for gender incongruence at the material time constituted an "*unacceptable safety risk*" for children. It noted [SB 1630]:

> *"The reasons for the dramatic increase in the use of GnRH agonists to suppress puberty over the past 10 to 15 years remains unexplained. CHM found no evidence that previous populations in this age range identified as transgender in the volume currently doing so or that similar volumes expressed regret at not receiving GnRH agonists for the suppression of puberty. Of those receiving GnRH agonists for pubertal suppression, the majority do not regret their use when asked 6 to 10 years later. Some suggest this data supports the use in this population. Others consider this a self-fulfilling prophecy. One in 18 do regret the decision and may have lifelong impact from GnRH agonist use. There are valid concerns to be addressed that social constructs are driving behaviours for some transgender youth where children and young people and parents or carers feel compelled to seek pubertal suppression."*

27. The report from the CHM highlighted the following risks:

    a. Cognitive impacts - Under the heading 'Important safety considerations from toxicology studies' (see also Appendix 1 to the CHM advice):

    > *"GnRH agonists provided as medicines can cross from the blood to the brain, and thus long term GnRH agonist treatment may influence brain function and have cognitive and behavioural effects. In animal models studied in a developmental period relevant to puberty, GnRH agonists reduced spatial memory, increased anxiety and depressive behaviours in mice, and had an impact on nerve activity in an area of the brain called the hippocampus which is involved in stress, depression and cognition: GnRH agonists decreased reproductive organ weight with potential effects on reproduction. It is not known whether these animal observations may have corresponding clinical relevance in children and young people" (§23).*
    >
    > and more generally:
    >
    > *"During representation, CHM was provided with valid hypotheses that cognition may be irreversibly impacted by the use of GnRH agonists in the adolescent age range (references 6 and 7). However, further evidence is required to explore this important human development and should be included in the future research agenda" (§29).*

    b. Bone mineralisation:

    > *"It is widely accepted that there are detrimental impacts on bone mineralisation. The degree of impact and ability to recover post puberty suppression has a significant lack of data from large high-quality studies. CHM heard from experts that diet, exercise and vitamin use may be able to support bone health in individuals at risk of loss of bone mineral density. CHM found no data investigating the effect of these measures to offset bone mineralisation impacts when GnRH agonists are used during puberty" (§26).*

c. Fertility - A 'Specific safety consideration with regard to loss of fertility' was discussed at §§30 to 33, concluding:

> *"CHM could not identify any long term safety data on the impact of GnRH agonists on fertility in people with gender dysphoria. Given the complexities, probable finality and experimental nature of these considerations, Gillick competence would be more challenging to achieve than in many other therapeutic areas in paediatric practice. Provision of adequate consent in relation to fertility has been an identified issue raised by GMC with private practitioners providing gender services."*

28. On 11 December 2024, the Secretary of State announced to Parliament his intention to make the temporary ban on puberty blockers permanent, whilst also referring to the establishment of a clinical trial on puberty-suppressing hormones. The announcement confirmed the following:

> *"The Cass Review made it clear that there is not enough evidence about the long-term effects of using puberty blockers to treat gender incongruence to know whether they are safe or beneficial.*
>
> *That evidence should have been established before they were ever prescribed for that purpose. It is a scandal that medicine was given to vulnerable young children, without proof that it was safe or effective, or that it had gone through the rigorous safeguards of a clinical trial."…*
>
> *After thoroughly examining all the available evidence,* [the CHM] *has concluded that prescribing puberty blockers to children for the purposes of treating gender dysphoria, in the current prescribing environment, represents "an unacceptable safety risk".*

Announcement of the PATHWAYS trial and publication of limited information

29. The PATHWAYS Trial was commissioned by NHS England in partnership with the NIHR. It is funded by the National Research Collaboration Programme, an NHS England and NIHR partnership, in the sum of £10,694,902.24. It is sponsored by the Interested Parties.

30. On 21 August 2025, the Defendants received an application for the approval of the Trial. This application was dated 20 August 2025 as a combined application submitted through the Integrated Research Application System ("**IRAS**").

31. On 6 November 2025, the REC gave a "favourable opinion" in respect of the PATHWAYS trial. However, the fact of this opinion being issued was not disclosed to the public until 22 November 2025 when the Defendants announced that the PATHWAYS trial had been approved and the Trial Protocol and some supporting documents were published. At that point the only information as to the REC's decision or its basis was a four-word 'summary' published on the HRA website, which simply stated: '*Further Information Favourable Opinion'* [SB 1418]. The MHRA did not – and

still has not – published or disclosed any information about its decision-making as the licensing authority giving approval.

32. According to the Trial Protocol and supporting documents, the Trial is anticipated to involve 226 children aged up to 15 years and 11 months. Children will be eligible from Tanner Stage 2, the stage of puberty that some children may enter from around age 10: CHM report at §31. The trial sponsors have confirmed that there "*was not a lower age limit*" but have suggested that "*it would be unlikely that children below the age of 12 would be able to display the necessary developments*".[12] Children will be allocated at random to one of two groups: the first group will receive GnRHa immediately; the second group will receive GnRHa after a delay of one year. The Trial's primary objective is stated to be "*to determine the short/medium-term benefits and risks of GnRHa for puberty suppression in CYP with gender incongruence*".[13] The primary outcome measure of the Trial is the 'KIDSCREEN-10' questionnaire, which asks children to rate their responses to simple questions such as "*Have you felt lonely?"* and "*Have you had fun with your friends?*".[14]

33. The participant information sheet states in response to the question 'What might be good about taking part?': "**We do not know whether the treatment may help your child**. By taking part in this study, you and your child **may help us learn more** about what children and young people with gender incongruence find good or not so good about puberty suppressing hormones (GnRHa) treatment,"[15] (emphasis added).

34. The only reference to ethics in the Trial Protocol is at section 12 (page 82, [SB 1125, 1238]) which simply states the Trial "*will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP* [good clinical practice] *and all of the applicable regulatory requirements (specify current legislation).*" There is no further detail or explanation provided. The fact that an obvious placeholder – *"(specify current legislation)"* - is still in the final version and was not picked up on review or updated before publication is an indication of the lack of attention paid to the basic medical ethics of the Trial. The Claimants contend below that this lack of attention to the particular ethical issues to which the Trial gives rise is confirmed on scrutiny of the available documentation in relation to the decision-making process.

35. On 5 December 2025, the Claimants sent a letter before claim to the Defendants challenging the approval of the Trial and seeking disclosure of documents relevant to the decision-making process. The HRA on 19 December 2025 refused to disclose any documents on the basis that the Claimants did not have standing but referred the Claimants to "*publicly available documentation*" on its website [CB 277]. That website was (perhaps not coincidentally) updated on the same date with the publication of several documents in relation to the REC's ethical review of the Trial. The MHRA's response on 22 December 2025 simply stated that its letter of that date sufficed to comply with its duty of candour.

[12] Minutes of REC meeting, 4 September 2025 at p.3 [SB 1347].
[13] PATHWAYS Trial Protocols, p.2 [SB 1045, 1158].
[14] Administered within the KIDSCREEN-52, [SB 1333-1340].
[15] Question 5 of the 'Participant information sheet for parents and legal guardians', p.14 [SB 1295].

36. On 24 December 2025, the Claimants wrote to the Defendants again, explaining their standing and seeking further information arising from the HRA's published documents, including the Trial sponsors' responses to queries raised by the REC. On 15 January 2026, the HRA responded maintaining its position but referring the Claimants to its website, which it had (once again) updated on that same date to publish further documents in relation to the Trial. The MHRA maintained on 19 January 2026 that it had complied with is duty of candour (notwithstanding that no documents generated by the MHRA in the course of its decision-making process in relation to the Trial have been disclosed) but stated that it would provide an update on further disclosure.

37. As at the date of filing the claim for judicial review, there is a continuing lack of documentation relevant to the decision-making, particularly in relation to the approval granted by the MHRA as licensing authority. The correspondence indicates that the Defendants have resisted further disclosure variously on the basis that (a) the Claimants do not have standing; (b) the duty of candour has been complied with by information set out in correspondence; (c) this is an "early stage" of the proceedings which limits any disclosure required; and (d) that the Defendants understand the duty of candour, and take it seriously, but do not propose to disclose further documents. In the absence of further voluntary production of documents in relation to the decision-making the Claimants propose to make an application for specific disclosure. What the currently available documents show as to the decision-making process is set out below in section D.

C. LEGAL FRAMEWORK

Regulatory framework for clinical trials

38. The legal basis of (i) the HRA under the Care Act 2014; and (ii) the MHRA as an executive agency of DHSC has been set out above at paragraphs 7 and 8. In England the HRA is responsible for establishing RECs under the Medicines for Human Use (Clinical Trials) Regulations 2004.

The 2004 Regulations

39. The relevant regulations are the Medicines for Human Use (Clinical Trials) Regulations 2004. The 2004 regulations are due to be extensively amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025/538, but the 2025 Regulations are not yet in force and do not fall to be considered on this claim. The 2004 Regulations implemented EU Directive 2001/20/EC ('the Clinical Trials Directive') and the relevant parts of the structure are as follows:

- Regulations 5 to 10, and Schedule 2, make provision for ethics committees in the United Kingdom, which are to be responsible, amongst other things, for giving opinions on the ethics of clinical trials involving medicinal products.
- Regulation 5 provides for the United Kingdom Ethics Committees Authority, which is to be responsible for establishing, recognising, and monitoring ethics committees; and for the purposes of England the relevant constituent part is the HRA.

- Regulations 11 to 27, and Schedules 3 to 5, make provision for clinical trial authorisations by the licensing authority (i.e. the MHRA) and for ethics committee opinions. In particular: regulation 12 provides that a clinical trial may be conducted only if it has been authorised by the licensing authority and an ethics committee has given a favourable opinion;
- Regulations 14 to 16 and Schedules 3 and 4 make provision for applications for ethics committee opinions;
- Regulations 17 to 21 and Schedule 3 deal with requests to the licensing authority for authorisation.

40. GnRHa is an 'investigational medicinal product' within regulation 2 as it is not authorised for use to suppress puberty in children with gender incongruence. This means that the Trial is a clinical trial of an investigational medicinal product ("CTIMP"), which may only be conducted if both: (i) a favourable opinion from the relevant REC; and (ii) authorisation from the MHRA, are obtained under regulation 12.

41. Regulation 15(5) provides a list of matters that are required to be considered by the REC, including:

> *(5) In preparing its opinion, the committee shall consider, in particular, the following matters–*
>
> *(a) the relevance of the clinical trial and its design;*
>
> *(b) whether the evaluation of the anticipated benefits and risks as required under paragraph 10 of Part 2 of Schedule 1 is satisfactory and whether the conclusions are justified;*
>
> *(c) the protocol…*
>
> *(g) the adequacy and completeness of the written information to be given, and the procedure to be followed, for the purpose of obtaining informed consent to the subjects' participation in the trial;*
>
> *(h) if the subjects are to include minors or persons incapable of giving informed consent, whether the research is justified having regard to the conditions and principles specified in Part 4 or Part 5 respectively of Schedule 1…*
>
> *(m) the arrangements for the recruitment of subjects.*

42. Further, regulation 15(6) provides:

> *(6) If– (a) any subject of the clinical trial is to be a minor; and (b) the committee does not have a member with professional expertise in paediatric care, it shall, before giving its opinion, obtain advice on the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial.*

43. It may be seen that a significant feature of the regime is the additional set of protections that is provided for clinical trials involving minors (defined for the purposes of the 2004 Regulations at reg 2 as "*a person under the age of 16 years*"), from:

a. an additional suite of conditions and principles (in Part 4 of Schedule 1) on top of those applying to all trials (from Part 2 of Schedule 1).

b. the requirement for "paediatric expertise in paediatric care", either from a member of the committee or otherwise from an external adviser, specifically in relation to "*the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial".*

44. **Part 2 of Schedule 1** to the 2004 Regulations sets out the conditions and principles which apply to <u>all</u> clinical trials. In particular these include:

a. <u>Helsinki Declaration principles</u> - Condition 6 of Pt 2 requires clinical trials to be conducted "*in accordance with the principles of the Declaration of Helsinki*."

b. <u>Benefits justifying risks for individual subjects:</u> - Condition 10 of Pt 2 states (emphasis added):

> *"Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients.* ***A trial should be initiated and continued only if the anticipated benefits justify the risks."***

45. **Part 4 of Schedule 1** sets out additional conditions and principles for a REC considering a trial involving minors)), such as this Trial. All required to be considered by the REC pursuant to reg 15(5)(h) and they include:

a. <u>Direct benefit for the group:</u> Condition 10 of Pt 4 in Schedule 1 requires that "*Some direct benefit for the group of patients involved in the clinical trial is to be obtained from that trial*." The requirement for 'direct benefit' goes further than that, and suggests that benefit to public health or to a wider cohort of potential patients is not sufficient.

b. <u>Necessity to validate other data:</u> Condition 11 of Pt 4 requires that "The clinical trial is necessary to validate data obtained – (a) in other clinical trials involving persons able to give informed consent, or (b) by other research methods." In other words, a clinical trial on children is only justified once there is data that has been derived either from those with full capacity to give informed consent (plainly inapplicable) or other research methods not involving experimenting on minors.

c. <u>Following EMA Guidelines:</u> Condition 12 of Pt 4 provides that "*The corresponding scientific guidelines of the European Medicines Agency are followed*." These are considered below.

d. <u>Prevalence of interests of the patient:</u> Principle 16 states "*the interests of the patient always prevail over those of science and society*". This requirement in Pt 4 is more strongly expressed that the equivalent principle for trials involving adult subjects in Principle 1 of Pt 2: "*the rights, safety and well-being of the trial subjects shall prevail over the interests of science and society*", both because (a) 'interests' is a wider category than 'rights, safety and well-being'; and (b) because it specifies that they must *always* prevail. This principle must be read alongside the requirement risk / benefit balancing and direct benefit, above.

EMA Guidelines

46. As noted above, **Condition 12 in Part 4** requires EMA scientific guidelines to be followed in proposed trials involving minors; and that this must be considered by the REC. The EMA has published specific scientific guidelines for the development of medicines for children on its website. Its guideline on clinical investigation of such products reflects the essence of the 'direct benefit' and 'balancing of risk' requirements, stating (emphasis added):

> *"A fundamental principle in pediatric drug development requires that children should not be enrolled in a clinical study unless necessary to achieve an important pediatric public health need…**Experimental interventions or procedures that present greater than low risk to participants must offer a sufficient prospect of clinical benefit to justify or outweigh exposure of a pediatric population to such risk. Likewise, the balance of risk and anticipated clinical benefit must be at least comparable to the available alternative treatments, such that the child is not disadvantaged by enrolment in the research study. There should be a reasonable expectation that knowledge resulting from the clinical study will contribute to the health of the pediatric population."***

47. The EMA scientific guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products'[16] is also applicable, given that this is an "early clinical trial" of the use of GnRHa in this context. In relation to mitigation of risks this emphasises the risk mitigation strategy of using "non-clinical testing", in particular animal testing. For example (with emphasis added):

> *"The development and evaluation of a new IMP* [investigational medicinal product] *is a **stepwise process involving animal and human efficacy and safety information**. The non-clinical data in PD [pharmacodynamic], PK [pharmacokinetic] and toxicology and their translation to human are **important basis for planning and conduct of a FIH [first in humans]/early CT [clinical trial]**." (section 6)*
>
> and
>
> *"High human-specificity of a medicinal product makes the non-clinical evaluation of the risk to humans more difficult in terms of degree of uncertainty. Although this does not imply that there is always an increased risk in a given FIH/early CT, **an in-depth risk assessment is required**. A cautious approach in the conduct and design of a CT with these products is needed."*

The Helsinki Declaration principles

48. As noted above the regulations include a specific requirement that clinical trials be conducted in accordance with the principles of the Declaration of Helsinki. The current version was adopted in October 2024 and sets out a series of principles for medical

[16] [CB 420, 422]; current version was adopted on 1 February 2018.

research involving human participants. Principles 16 to 18 are significant and relate to 'Risks, Burdens, and Benefits'.

49. Other principles on the Helsinki Declaration include:

> *"21. Medical research involving human participants must have a scientifically sound and rigorous design and execution that are likely to produce reliable, valid, and valuable knowledge and avoid research waste. The research must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation."*
>
> *…*
>
> *"28. … Those persons incapable of giving free and informed consent are in situations of particular vulnerability and are entitled to the corresponding safeguards. In addition to receiving the protections for the particularly vulnerable, those incapable of giving consent must only be included if the research is likely to either personally benefit them or if it entails only minimal risk and minimal burden. "*

and the following, in relation to 'Unproven Interventions in Clinical Practice':

> *"37. When an unproven intervention is utilized in an attempt to restore health or alleviate suffering for an individual patient because approved options are inadequate or ineffective and enrollment [sic] in a clinical trial is not possible, it should subsequently be made the object of research designed to evaluate safety and efficacy. Physicians participating in such interventions must first seek expert advice, weigh possible risks, burdens, and benefits, and obtain informed consent. They must also record and share data when appropriate and avoid compromising clinical trials. These interventions must never be undertaken to circumvent the protections for research participants set forth in this Declaration."*

50. There are specific requirements in relation to RECs (principle 23) which include a requirement that a REC "*must be transparent in its functioning*" and a membership with "*adequate education, training, qualifications,, and diversity to effectively evaluate each type of research that it reviews*."

<u>Procedural requirements</u>

51. RECs are required to operate in accordance with various policies produced by the HRA. The most important are the GAfREC and the REC Standard Operating Procedures ("**REC SOP**"), the latest version of which (v.7.7) is dated April 2025. Relevant sections of this are referred to below in the next section.

52. It may be seen from the regulatory framework that RECs provide a key role in the approval of clinical trials, and that there are specific and detailed requirements in relation to their constitution and procedures. Additional considerations and safeguards are mandatorily imposed in trials involving children (and other vulnerable groups).

Relevant public law principles

The basis of review

53. In this claim the Claimants rely upon the principles that all relevant considerations set out in the statutory framework, and all material factual considerations, must be taken into account for a decision to be lawful. They also bring a rationality challenge.

54. A helpful summary of the law on the need for a decision-maker to take into account relevant considerations was set out recently by Lewis LJ in *Keep Chiswell Green v. Secretary of State for Housing, Communities and Local Government* [2025] EWCA Civ 958 at [81]-[82].

55. There can be "no doubt that the Court is entitled to inquire whether there was adequate material to support [the regulator's] conclusion*": IBA Healthcare Ltd v Office of Fair Trading* [2004] EWCA Civ 142, [2004] ICR 1364 at [93] per Carnwath LJ. Ordinary judicial review principles allow a court "*to determine whether* [the regulator's] *conclusions are adequately supported by evidence, that the facts have been properly found, that all material factual considerations have been taken into account, and that material facts have not been omitted*": *Unichem v Office for Fair Trading* [2005] CAT 8, [2005] 2 All ER 400 at [174].

56. In relation to a rationality challenge there are two aspects, as recently set out by Chamberlain J in *R(KP) v Secretary of State for Foreign, Commonwealth and Development Affairs* [2025] EWHC 370 at [55]-[57]. The first is process rationality, which includes the requirement that the decision-maker must have regard to all mandatorily relevant considerations and no irrelevant ones, as set out above.

57. In addition, the process of reasoning "should contain no logical error or critical gap"; in other words, "*does the conclusion follow from the evidence or is there an unexplained evidential gap or leap in reasoning which fails to justify the conclusion*?": *KP*, at [56]. Moreover, the decision-maker cannot have "*failed to grapple with the relevant evidence*" (*R (Kerman) v Charity Commission* [2025] EWHC 1223 (Admin) at [59].

58. The present claim also includes a rationality challenge in its second aspect: outcome - that is, where the challenged decision is outside the "*range of reasonable decisions open to a decision-maker*": *KP*, at [57].

The standard of review

59. The standard of review is context- and fact-sensitive. The degree of intensity of review will depend on considerations such as the gravity of the issue to be determined and the nature of the rights engaged (*PJSC VTB Bank v HM Treasury* [2025] EWHC 3359 (Admin) at [143]).

60. A heightened standard of review is required where fundamental interests are at stake. This has been described as the test of 'anxious scrutiny', as formulated by Lord Bridge in *R v Home Secretary, ex p Bugdaycay* [1987] AC 514 at p531 (approved by the Court of Appeal in *R (Hoareau) v Secretary of State for Foreign and Commonwealth Affairs* [2020] EWCA Civ 1010 at [154]) as follows:

> *"The limitations on the scope of that* [judicial review] *power are well known and need not be restated here. Within those limitations the court must, I think, be entitled to subject an administrative decision to the more rigorous examination, to ensure that it is in no way flawed, according to the gravity of the issue which the decision determines. The most fundamental of all human rights is the individual's right to life and when an administrative decision under challenge is said to be one which may put the applicant's life at risk, the basis of the decision must surely call for the most anxious scrutiny"*

61. 'Anxious scrutiny' therefore requires the Court to adopt a more rigorous scrutiny of the decision-maker's reasoning process; such that the latitude afforded to the decision-maker may be narrowed. It means "*the reviewing court has to do more; and also the reviewing court needs more*". The starting point of such review is that a "*high quality of reasoning*" is required in the decision (*R (Alnoor) v Secretary of State for the Home Department* [2025] EWHC 922 (Admin), per Fordham J at [28]). Further:

> *"This practical consequence of this closer scrutiny is illustrated by the identification of a 'need for decisions to show by their reasoning that every factor which tells in favour of the applicant has been properly taken into account'....The language is 'every factor' not 'every obviously reasonable factor'; and 'properly taken into account' not "taken into account".*

62. This form of 'anxious scrutiny' is required where there is a risk of harm or of damage to the interests of vulnerable children – see *R (Hillingdon London Borough Council) v Lord Chancellor* [2008] EWHC 2683 (Admin) per Dyson LJ at §50 ("*at the heart of this case is the risk posed to vulnerable children*") and §67 ("*I agree that, because the interests of vulnerable children are potentially at stake, the court should consider the issue of irrationality with anxious scru*tiny"). That principle clearly applies to the decision to approve the Trial.

Duty to make reasonable inquiries

63. A decision-maker is also under a duty to make reasonable inquiries to obtain relevant information, also known as the *Tameside* duty. In assessing whether there has been a breach of the *Tameside* duty: "*the question for the court is, did the Secretary of State ask himself the right question and take reasonable steps to acquaint himself with the relevant information to enable him to answer it correctly?"* (*Secretary of State for Education and Science v Tameside Metropolitan Borough Council* [1977] AC 1014, HL, at p1065B per Lord Diplock).

64. The general principles relating to this duty were set out by the Court of Appeal in *Balajigari v Secretary of State for the Home Department* [2019] 1 WLR 4670 at [70], and include that "*the court should establish what material was before the authority*" and should only strike down a decision if on that material, no reasonable authority could suppose their inquiries were sufficient. Thus, where a judgment requires a factual foundation, it is necessary for the Court to examine the soundness of that foundation (*Tameside*, p1047 per Lord Wilberforce):

> *"If a judgment requires, before it can be made, the existence of some facts, then, although the evaluation of those facts is for the Secretary of State alone, the court must inquire whether those facts exist, and have been taken into account, whether the judgment has been made upon a proper self-direction as to those facts, whether the judgment has not been made upon other facts which ought not to have been taken into account. If these requirements are not met, then the exercise of judgment, however bona fide it may be, becomes capable of challenge."*

Procedural irregularity and failure to comply with published policy

65. A public authority must follow procedural requirements set out in statute or a statutory instrument. Procedural irregularities can render a decision or action unlawful depending on the answer to three questions and taking account of the statutory intent of the legislation as a whole: (i) has there been substantial compliance with the statutory requirement; (ii) is the non-compliance capable of being waived and should it be in this particular case; and (iii) if it is not capable of being waived or is not waived what is the consequence of the non-compliance? (see *R (Akin) v. Stratford Magistrate's Court* [2015] 1 WLR 4829, applying *R v Secretary of State for the Home Department, Ex p Jeyeanthan* [2000] 1 WLR 354). In this case, where the decision concerns approval of a clinical trial involving vulnerable children, procedural irregularities are of considerable importance, particularly where they could have led to a different outcome or a relevant consideration not being taken into account.

66. Moreover, a decision-maker must follow his published policy unless there are good reasons for not doing so: *R (Lumba v Secretary of State for the Home Department* [2011] UKSC 12). This is an aspect of the rule of law, which calls for "*a transparent statement by the executive of the circumstances in which the broad statutory criteria will be exercised*", so that an individual may know the criteria to be applied to his case and challenge any adverse decision: *Lumba*, [34]-[35]*; R (Knot Builders) v Construction Industry Training Board* [2025] EWCA Civ 6, [31]. A policy will be given effect particularly if it gives rise to a legitimate expectation, but even in the absence of such expectation, the authority may be required to comply unless departure is justified: *R (A), Secretary of State for the Home Department* [2016] EWCA Civ 597 at [3].

D. THE PROPOSED TRIAL AND THE APPROVAL DECISIONS

The REC decision-making process

67. It appears from the published documents that the decision-making process by the REC was as follows.

68. The only meeting of the REC was on **4 September 2025**. There were nine members in attendance, 2 'expert, 3 'lay' and 4 'lay plus'. The names of the members have been redacted but their occupations have been disclosed.

69. As they appear in a subsequent communication from the REC dated 11 September 2025, the members of the REC were as follows (with those not attending the meeting shaded in the table below), with Ex, Lay and LP designating their expert, lay, or 'lay plus' status according to the disclosed list, and letters added for identification:[17]

A	Health Economist / Psycho-social Researcher	LP
B	Lead Pharmacist in Clinical Trials[18]	Ex
C	Pharmacy Graduate	LP
D	Senior Research Nurse / Coordinator	Ex
E	Private Client and Litigation Paralegal	LP
F	Head of Clinical Operations	LP
G	Retired Nurse	Lay
H	Research Scientist - immunohaematology	Lay
I	Academic Lead for Research, Ethics and Compliance	Ex
J	Chief Regulatory Officer	Ex
K	Senior Research Manager (Clinical Study Management Lead)	Lay
L	Paediatric Intensive Care Consultant – written comments	Ex

70. Neither the Chair of the committee nor the lead reviewer have been identified in the minutes. Written comments were provided for the 4 September 2025 meeting by another 'expert' member, a paediatric intensive care consultant, who did not attend the meeting. Those written comments are a single page of bullet points, none of which appear to be based on paediatric expertise.

71. On **11 September 2025** the REC issued a 'Provisional Opinion' and asked the Trial sponsors to provide 16 items of further information before a final ethical opinion could be issued. This opinion stated (emphasis added) that: "*The REC delegated authority to confirm its final opinion on the application* ***to a meeting of the full Committee,***" [SB 1356]. This note indicates that Member B was the REC Chair. There is no indication of the members of the REC to whom any delegation was intended to be made.

72. On **9 October 2025** the Trial sponsors wrote to both the REC and the MHRA providing their response to the 16 requests for further information from the REC (covered under two headings – 'Part 2: REC Queries' and 'Part 4 – GNA Remarks: REC Queries') as well as the 19 clinical grounds for non-acceptance ("**GNA**") and 3 non-clinical GNA which had apparently been issued by the MHRA on an unknown date, there having being no disclosure in relation to the MHRA's refusal itself despite the Claimants' specific requests.

73. On **28 October 2025** a sub-committee of the REC comprised of five members (again not including the paediatric intensive care consultant) met and identified five further items of information required from the Trial sponsors, or amendments that had to be

[17] As explained below, the Claimants understand that a 'Lay' member is a retired health or social care professional or someone involved in clinical research or a health service body, and that a 'Lay Plus' member is one who has never been a registered health or social care professional or involved in clinical research or a health service body.

[18] According to the later note of 11 September 2025 it appears that member B was the Chair, but that does not appear from the disclosed version the minutes of the 4 September 2025 meeting.

made to the Trial documentation, before a final opinion could be confirmed. The minutes indicate that there was no further consideration of the significant number of issues outstanding from the questions asked previously by the REC. Although the full Committee was not present on this occasion, the minutes state that "*The REC delegated authority to confirm its final opinion on the application to a meeting of the Sub-Committee*" [SB 1392]. There is no explanation of how this delegation could be made or the reasons for it. Those attending are identified as follows (with the same lettering as applied in the table above):

B (Ex) - Chair[19]	Lead Pharmacist in Clinical Trials
E (LP)	Private Client and Litigation Paralegal
F (LP)	Head of Clinical Operations
H (Lay)	Research Scientist - immunohaematology
K (Lay)	Senior Research Manager (Clinical Study Management Lead)

74. On **29 October 2025** a request was issued by the REC Approvals Manager to the Trial sponsors for "*a more complete response*" [SB 1395] to five of the issues raised in the 4 September 2025 Provisional Opinion, reflecting the five items discussed at the 28 October 2025 sub-committee meeting. The note refers to a meeting of the Sub-Committee but makes the request in the name of the Committee.

75. On **31 October 2025** the Trial sponsors provided a further response to these five issues.

76. On **6 November 2025**, a differently constituted 'sub-committee' of the REC met and issued a favourable ethical opinion for the Trial. This sub-committee comprised three members who attended – two 'expert' and one 'lay plus' – of whom only Member B, the Chair, had attended the previous sub-committee meeting. Very brief written comments (four lines in total) were sent in by two other members, one 'lay' and one 'lay plus'. None of the members appears to have had paediatric expertise and two (shaded) did not attend the meeting but sent in (very brief) written comments.

A (LP)	Health Economist/Psycho-social Researcher
B (Ex) - Chair	Lead Pharmacist in Clinical Trials
J (Ex)	Chief Regulatory Officer
F (LP)	Head of Clinical Operations – written comments
H (Lay)	Research Scientist – immunohaematology – written comments

77. The decision-making process by the MHRA remains opaque. From what has been published the Claimants have understood the following:

[19] The reference to the 'Chair' was redacted from the version originally disclosed but appears on the version currently on the website.

a. On **20 August 2025**, the Trial sponsors made a request for authorisation through the IRAS (the consolidated system) which included the request to the MHRA as the licensing authority under reg 17 of the 2004 Regulations.

b. At some point between then and 9 October 2025, the MHRA issued a written notice to the Trial sponsors setting out 19 grounds for not accepting the request, (GNA as 'Grounds for non-acceptance'), pursuant to reg 18 of the 2004 Regulations. That refusal has not been disclosed, nor was it referred to in the pre-action protocol letter on behalf of the MHRA. On 30 January 2026 the MHRA provided the Claimants with the minutes of an extraordinary meeting of the CHM on 18 September 2025 which showed that the CHM had seen and agreed with the GNA, and the Final Advice attached to those minutes concluded that "*on the evidence before them, the CHM had reason to think that on grounds relating to safety they might be unable to advise the grant of a Clinical Trial Authorisation for this trial at present*" [SB 1367].

c. On **9 October 2025**, as noted above, the Trial sponsors wrote to both the REC and the MHRA setting out their response to the GNA.

d. At some point between then and **22 November 2025**, when the approval of the trial was publicly announced, the MHRA must have issued a written notice to the Trial sponsors stating that it accepted the request for authorisation. That has not been disclosed, so there is no indication of the reasoning that led to it, against the grounds on which the application had previously been refused by the MHRA. There has been no explanation of, or disclosure relating to, discussions between the MHRA and CHM, and whether or how the CHM came to change its position from that expressed on 18 September 2025.

Balancing benefit/risk and identifying 'direct benefit'

78. As set out above (paragraphs 44 to 45) the REC was required to consider distinct questions of (a) whether the anticipated benefits of the Trial justified its risks; and (b) whether "*some direct benefit*" for the group of patients involved in the Trial is to be obtained from the Trial. The extent to which these were identified and addressed by the REC and MHRA is addressed below.

79. At the 4 September meeting the REC recorded that [SB 1348]:

> *"The Committee asked for assurance that the researchers* ***were confident that the risk/benefit balance was appropriate*** *for the study. The applicants stated that there was genuine equipoise at the minute and that* ***there was no data at present on the cognitive impacts of puberty blockers.*** *They also stated that there would have been a series of clinical assessments made by* ***the gender service and national MDT which will consider the overall risk/benefit of the treatment*** *and that participants would be monitored closely throughout the study. The Committee accepted the response"* (emphasis added).

80. The Claimants make the following points in relation to this answer:

a. It was inaccurate and significantly misleading because there is data on the cognitive impact of puberty blockers from animal studies (see the CHM report [SB

1621-1664] and Professor Evans' statement [CB 209-219]) which confirm that there may be significant harmful effects, as well as Professor Baxendale's report at §§15-18 [CB 94-95]).

b. There were also other established risks of harm that the applicants' answer did not identify and the REC did not purse in the context of its query as to risk / benefit balance. The applicants' assertion of "*genuine equipoise*" could not be justified: again, see the CHM report and the basis on which the statutory ban was imposed, as well as Professor Baxendale's explanation of the need to consider Number Needed to Treat against Number Needed to Harm at §§172-187 [CB 129-133].

c. It failed to alert the REC to the fact that up to 98% of those who took puberty blockers would go on to cross-sex hormones,[20] entailing very significant further risks over and above those incurred by puberty blockers themselves. On any view this was a factor that had to be weighed in the risk/benefit balance, especially given the "*concern that* [puberty blockers themselves] *may change the trajectory of psychosexual and gender identity development*" as outlined by the CASS review above at paragraph 23c. The REC did not consider this.

d. The answer did not provide any basis on which the REC could have been satisfied that the 'direct benefit' requirement for clinical trials involving children (Condition 10 of Pt 4, Sch 1, 2004 Regulations) was met, and which was not separately addressed. Indeed that is not a question that the REC (or its purported sub-committees) ever appears to have recognised as needing to be answered. See Professor Baxendale's analysis at §§106-116 [CB 115-117] and §§143-147 [CB 122-124].

e. It was not sufficient for the Trial sponsors to say that the gender service and national multi-disciplinary team will consider the overall risk/benefit of puberty blockers for participants in the study. In order to give approval, the REC had to be able to reach a reasonable conclusion that there would be "[s]*ome direct benefit for the group of patients involved in the clinical trial*". The sponsors were unable to give them that assurance; they instead simply said that the gender service/MDT would make that assessment. That cannot be adequate in the context of the consistent evidence, as noted in the Cass Review (and accepted by the trial sponsors, e.g. in the FAQs referred to above), is that it is not possible to identify consistently or accurately which children with gender incongruence may or may not benefit from puberty blockers (see Professor Baxendale's analysis at §§148-171 [CB 124-129]).

81. The REC followed this up with a request for further information in its 11 September letter [SB 1353]:

> *"Please provide additional information around the current and previous standard of care treatments for this group of patients as well as what potential future standard of care may look like if the results of this application reveal that puberty blockers are not beneficial."*

[20] The Cass Review Final Report, 14.23 – 14.25.

82. The answer received on 9 October from the Trial sponsors was [SB 1381]:

> *"Previous UK practice: psychosocial care as first line; puberty suppression with GnRHa available initially under research study (until 2014, non-randomised), then adopted in routine care at the Tavistock GIDS for selected cases. Current UK practice (from 2024): NHS England does not routinely commission GnRHa for gender incongruence/dysphoria in under-18s. Cross-sex hormones can be considered for those older than age 16. Private supply and dispensing routes have been restricted by government, with an indefinite ban on sale/supply for this indication to under-18s outside NHS-led pathways; ongoing NHS reforms are implementing the Cass Review. If PATHWAYS shows no benefit / net harm of GnRHa: likely future standard would continue to exclude routine NHS use, with focus on holistic, multidisciplinary psychosocial care within the CYPGS service model being rolled out; puberty blockers would remain restricted to research or be decommissioned for this indication pending new evidence. Conversely, if benefit/risk is favourable, NHS England has signalled access would be through an ongoing research programme leading to possible commissioning decisions."*

83. On 28 October 2025, the REC sub-committee agreed that the 9 October 2025 answer was insufficient and on 29 October the REC asked the Trial sponsors for more information (emphasis added) [SB 1391]:

> *"In order to provide assurance to the Committee that **the potential benefits of this application outweigh the risks**, please provide a justification for implementing a trial involving GnRHa at this point in time as opposed to investigating other areas related to transitional healthcare such as psychosocial care."*

84. The answer given by the Trial sponsors was as follows (emphasis added) [SB 1399]:

> *"The PATHWAYS trial responds directly to the urgent evidence gap highlighted by NHS England, the Cass Review, and the Commission on Human Medicines (CHM). CHM's November report concluded that "the current prescribing and care pathway for GnRH agonists for gender incongruence and/or gender dysphoria presents an unacceptable safety risk for children and young people under 18 years without significant additional safeguards" and recommended that restrictions remain until robust evidence and governance frameworks are in place. NHS England has ceased routine prescribing of GnRHa due to insufficient evidence of safety and effectiveness. This was further confirmed by UK Parliamentary law, which banned prescription of GnRHa for this indication and called for a clinical trial. CHM reinforced this by advising a permanent restriction on private prescribing until evidence from controlled trials becomes available. **The absence of evidence is itself a risk.** Families and clinicians face decisions without clear data on benefits, risks, or long-term outcomes. This trial provides a structured, monitored environment to generate high-quality evidence. Psychosocial care is essential and remains part of standard care. For some adolescents, this distress is severe and linked to mental health risks,*

including self-harm. The Cass Review strongly supports a biopsychosocial model as the foundation of care for young people with gender incongruence. It highlights that many referred adolescents present with co-occurring conditions such as: anxiety and depression; eating disorders; self-harm and suicidality; neurodevelopmental conditions (Autism, ADHD) and recommends that these should be assessed and managed through currently available evidence-based psychosocial interventions before or alongside any medical treatment. Psychosocial care has a well-established evidence base for improving mental health outcomes and reducing risk behaviours in these populations. However, psychosocial interventions alone cannot halt pubertal progression, which is often requested by adolescents. The trial therefore integrates psychosocial support provided by new clinical services as part of standard care ***while evaluating whether GnRHa adds additional benefit beyond this. It is thought that temporary suppression of puberty may reduce gender-related distress, improve engagement with psychosocial support, and improve quality of life. However, the current evidence to support or refute this is uncertain and hence the need for the trial. Many of the possible risks with GnRHa are poorly evidenced and uncertain including reduced bone mineral density, metabolic changes, and uncertainty about long-term cognitive and psychosexual outcomes.*** *These will be mitigated through strict eligibility criteria, comprehensive monitoring (DEXA, ECG, blood tests), and fertility counselling. The trial operates under NIHR and GCP standards, with multidisciplinary oversight, aligning with CHM's recommendations. Psychosocial interventions are embedded in the trial and remain core to care.* ***Investigating GnRHa under controlled conditions is essential to determine whether its benefits outweigh risks****."*

85. The MHRA's grounds for non-acceptance (as they appear in the applicants' response, in the absence of the grounds themselves) also included the following (emphasis added) [SB 1368]:

> *"The inclusion criterion #5 is vague and open to subjective interpretation. Terms such as "possibility", "may benefit" and "might be achieved" do not provide sufficient clarity to ensure consistent eligibility determination. In accordance with ICH E11(R1), eligibility criteria must be specific enough to define the study population****. The inclusion criterion must therefore be revised as follows****: a. The clinician in the CYPGS [children and young persons gender services] leading on care for that CYP believes "the CYP, with persistent gender incongruence despite other appropriate care,* ***is likely to" benefit*** *from GnRHa for puberty suppression.* ***This benefit "is expected to" be achieved*** *in relation to quality-of-life parameters (e.g., confidence in peer and family relations, participation in school and/or leisure activities, improved sense of well-being), mental or physical health."*

86. The answer to the MHRA's GNA received on 9 October from the Trial sponsors included the following in response to the MHRA's request quoted above (emphasis added) [SB 1375]:

*"Answer: the protocol inclusion criterion has been modified to: 'The clinician in the CYPGS leading on care for that CYP considers that GnRHa for puberty suppression offers **a reasonable prospect of benefit**. This benefit **might be** achieved in relation to quality-of-life parameters (e.g., confidence in peer and family relations, participation in school and/or leisure activities, improved sense of well-being), mental or physical health.'"*

87. This exchange illustrates that (i) the MHRA (unlike the REC) sought to establish the 'direct benefit' criterion and recognised that the application did not fulfil it, highlighting why the proposal did not meet the test and proposing wording that would do so; and (ii) the Trial sponsors' answer confirmed that the criterion could not be established; they did not (because they could not) adopt the wording that was required by the MHRA by way of revision. This position is also reflected the 'Participant Information Sheets' produced by the trial applicants, for both parents and children. The sheet for children and young people includes the following question and answer (emphasis added):

"What might be good about taking part?

*"**We do not know** whether the treatment may help you. … "* [SB 1320].

88. As Professor Baxendale concludes (see §90) "*puberty blockers are better understood as part of a research experiment rather than as treatment offered for the direct benefit of the child. Research of that kind, where there is no clear expectation of benefit to the individual child, is classed as non-therapeutic research*". The Trial falls well short of the ethical threshold required for such non-therapeutic research and could not be approved under the 2004 Regulations on that basis.

89. Similarly, in relation to the balancing of risks and harms condition, it was apparent from the sponsors' own answer that the balance criterion could not be met: "*Investigating GnRHa under controlled conditions is essential to determine whether its benefits outweigh risks,"* [SB 1399]. In these circumstances a clinical trial involving administering drugs to children could not lawfully be justified as the precondition that *"the anticipated benefits justify the risks"* could not be satisfied.

<u>Necessity to validate data</u>

90. No consideration appears to have been give by either the REC or the MHRA to the mandatory consideration of the condition identified at paragraph 45b above, namely data obtained by those with capacity to consent or "*other research methods*". Had the required factor been considered it is hard to see how it could have been rationally found to have been present.

91. In particular if considered, it would or should have been concluded that the data-linkage study drawing on the experience of NHS patients previously treated with GnRHa for gender incongruence, and further studies on the effects of GnRHa on animals, should have been carried out before approval was considered for a clinical trial on children.

92. *Animal studies:* Various concerns raised about GnRHa side-effects from animal studies were highlighted in the CHM advice, particularly in relation to effects on bone density, cognition and fertility. Yet there is nothing in the publicly available information about the

Trial approval process to suggest that this was taken into account or further research using animals considered by the REC.

a. The Helsinki Declaration (principle 21), to which both the REC and the MHRA have to have regard under the 2004 Regulations, expressly requires that research should be informed by animal experimentation where appropriate.

b. The EMA guidance on risk mitigation (see paragraph 46 above), which was required to be followed by the REC, highlights the importance of evaluating data from animal studies in early clinical trials.

93. As Professor Evans sets out in his witness statement (see §12-22) he has conducted extensive animal research on GnRHa already and has recently been commissioned to undertake further studies. There was obviously relevant information he could have provided to the MHRA or REC had he been asked, which would have been highly relevant to their decision-making. Yet no questions appear to have been asked about this issue, whether of Professor Evans or otherwise. Indeed, as set out above (paragraph 80) the REC appear to have been actively misled by the applicants' response in relation to the REC's request for assurance in relation to the risk/benefit balance, when the applicants stated that "*there was no data at present on the cognitive impacts of puberty blockers*" [SB 1348].

94. *'Linkage' studies:* Recommendation 5 in the Cass Review was to look at longitudinal health data from patients treated by GIDS between 2009 and 2020. It is clear that this would shed significant light on long-term harms relevant to the justification for the Trial. As stated by NHS England in August 2024 in relation to 'Implementing the Recommendations of the Cass Review'[21]:

- *NHS England has assumed responsibility from the Cass Review team to complete a study that links the data from the services provided by the former Tavistock GIDS to an adult data set.* ***Recommendation 5****.*
- *This required legislation from the Secretary of State for Health and Social Care (statutory instrument) to be laid that allowed the linkage of the NHS number given at birth and the new NHS number after a change of gender recognition.*
- *Such studies can provide a wealth of knowledge that may lead to greater understanding of long-term health benefits and harms.*

95. The reason for the delay in undertaking the data-linkage study appears (see §92 of the final Cass Report) to have been lack of cooperation from the NHS adult gender clinics. This remains the position to date. A study of 9000 patients, now adults, has full HRA approval and NHS England has encouraged gender clinicians to cooperate, describing it as an opportunity to gather "*high quality evidence*." Despite this, those clinicians have refused to share their data. Dr Cass has recently made a public statement that this is "*extraordinary*".[22] It is certainly not an adequate reason to proceed with the PATHWAYS Trial before ascertaining the longer term effects on those who have previously received

[21] https://www.england.nhs.uk/long-read/children-and-young-peoples-gender-services-implementing-the-cass-review-recommendations/ [SB 986].
[22] https://www.bmj.com/content/391/bmj.r2660

puberty blocking drugs for gender dysphoria or incongruence, given the known risks (including as highlighted by the CHM itself and in the Secretary of State's announcement to Parliament on 11 December 2024 – see paragraphs 27 and 28 above).

96. The Claimants' case is that approval of the trial without securing the potentially available data from other sources (i.e. animal studies and linkage studies) that would provide significant information as to the potential risks and harms, and any benefits, of GnRHa hormones was (a) in breach of the mandatory requirement imposed by condition 11 of Pt 4; but also (b) a failure of the *Tameside* duty; and in any event (c) irrational.

Lack of scientific rationale and fundamentally flawed trial design

97. It has been seen that reg 15(5) requires the REC to consider *"(a) the relevance of the clinical trial and its design*"; and "*(c) the protocol*".

98. The Trial does not have a clear or consistent scientific rationale, nor a clear hypothesis linking the proposed mechanism of action to the specific symptoms of a defined condition. This fundamental flaw does not appear to have been specifically considered by the REC (or the MHRA). The minutes of the REC meeting indicate that a range of specific matters were considered in relation to the trial, but not its underlying rationale. As Professor Baxendale puts it at §74 of her report, "*Since their introduction into gender clinics, no one has gone back to first principles to examine whether these medications should be used. In my opinion this was a critical failing in the trial proposal that any assessment of it for approval was required to address*".

99. The Claimants rely upon the expert evidence of Professor Baxendale, who explains in detail the lack of a clearly articulated scientific rationale and inability of the Trial to produce clinically useful answers. Professor Baxendale explains that the Trial involves exposing children to an intervention that deliberately interferes with normal development, in the absence of a clear scientific rationale, a testable hypothesis, reliable outcome measures, or any evidence-based method of identifying who is likely to benefit and who is likely to be harmed. Decisions about enrolment are therefore necessarily based on belief rather than evidence. Given these concerns, it was irrational for the Defendants to approve the Trial.

100. As Professor Baxendale explains in her report (§§86-105), at different times and in different places at least three different rationales for GnRHa in gender incongruence have been put forward: 'time to think', a mental health intervention to improve mental wellbeing, and future ability to pass as the opposite sex if a person in due course decides to undergo further medical and surgical gender transition. The Protocol states that the objective of the Trial is "*to determine the short/medium-term benefits and risks of GnRHa for puberty suppression in children and young people with gender incongruence*" [SB 1045, 1158]. This is, as Professor Baxendale explains at §§106-116, insufficiently clear and not consistent with the Declaration of Helsinki requirements. There is no falsifiable hypothesis with testable outcomes. Rather, the Trial is "*an exploratory experiment designed to catalogue possible effects of a treatment across multiple domains, rather than to test a specific claim of benefit with an evidential foundation*" (§116).

101. Moreover, the purported primary objective of the Trial as set out in the Protocol does not appear to be in reality the underlying (or at least the only) rationale. As examined by Professor Baxendale at §§68-72, the Trial sponsors have expanded their rationale to include wider public health or socio-political reasons for conducting the Trial, which are impermissible under Principle 16 of Pt 4 to the 2004 Regulations and the Declaration of Helsinki. In an interview with the BMJ published in December 2025 Dr Cass said that the main justification is a concern that young people with gender incongruence are taking puberty blockers from illegal websites or dealers and the Trial "*would allow researchers to gather evidence safely within a structured study, rather than leaving young people to experiment on themselves."*[23] Prof Simonoff did not demur from this suggestion. Indeed, it is a similar point to that made by the Trial sponsors in their response to the REC's 29 October 2025 questions, where they said "*The absence of evidence is itself a risk. Families and clinicians face decisions without clear data on benefits, risks, or long-term outcomes. This trial provides a structured, monitored environment to generate high-quality evidence*" [SB 1399].

102. As Professor Baxendale set out in her report, there are at least three fundamental errors in the trial design that mean it cannot produce meaningful results. **First**, a single year's delay for one of the two cohorts of participants before receiving GnRHa cannot provide statistically sufficient data on changes in cognitive abilities or bone density (see §§117-126). **Second**, the trial design does not properly compare 'puberty being halted' with 'puberty continuing' as all the participants will receive GnRHa (see §§127-130). **Third**, the KIDSCREEN-10 questionnaire is not a sufficiently accurate measurement nor sufficiently clearly linked to the rationale for the medical intervention (see §§131-142).

103. Finally, the fact that the vast majority (92-98%) of children given GnRHa go on to take cross-sex hormones creates serious difficulties in obtaining any meaningful data in long-term follow-up. This was recognised by the Trial sponsors in their 9 October 2025 answer to the MHRA's GNA[24] but the only solution offered was a request to participants to opt-in to adult follow-up through the NHS Register after the Trial finishes, which does not address the problem.

Relevant evidence excluded from the REC

104. Evidence filed on the claim establishes that the following expert groups wrote to the HRA setting out various highly relevant concerns and questions, none of which were passed to the REC.

105. The Clinical Advisory Network on Sex and Gender ("**CAN-SG**") engaged in extensive correspondence with both the HRA and MHRA, and also wrote directly to the Chair of the London – City and East REC, as explained in the witness statement of Dr Louise Irvine. In particular, CAN-SG raised concerns about whether there was clinical equipoise, the that anticipated benefits of the trial did not justify the risks, and the availability of alternative sources of data or potential interventions which could be

[23] "This is why the trial is necessary": experts behind the puberty blockers study respond to mounting opposition | The BMJ
[24] "*We agree that long-term follow-up is important in establishing the safety of the IMPs* [investigational medical products] *into adult life and physical maturity. We note the scientific challenges that are associated with disentangling long-term effects of GnRHa and cross-sex hormones as most of those remaining on a trans-gender hormonal pathway will commence the latter post-16 years of age while young people desisting will stop puberty suppressing hormones*" [SB 1376].

carried out first. CAN-SG includes experts in child and adolescent psychiatry, clinical pharmacology and the design of clinical trials. However, the HRA did not provide the REC with CAN-SG's correspondence on the basis that all these concerns would be covered in the application for ethical approval, and instead treated it as a 'complaint'. As Dr Irvine notes, this "*comprised a fundamental failure to ensure that the REC was properly briefed on the issues relevant to its decision*" (§24). As she also notes, having now seen the redacted minutes of the REC committee and sub-committee meetings which the HRA has published, there was no consideration of the concerns raised by CAN-SG.

106. Professor David Curtis, together with nine other clinicians and researchers with expertise in neuroendocrinology, psychiatry, psychology and medical ethics, wrote to the First Interested Party and the HRA. As he explains in his statement (see §9) this correspondence raised concerns in particular about the effectiveness of a two-year follow-up period for the proposed trial and the risk of serious and irreversible harm. The HRA informed him that it had shared the letter with the Chair of the REC who had decided there was no basis to share it with the rest of the REC.

Procedural flaws in the REC process

107. There is an obvious importance in compliance with the procedural safeguards embedded in the processes and procedures devised by the HRA in its statutory role under the 2004 Regulations. These safeguards include specific provisions to ensure appropriate lay and expert representation. The provisions reflect the inherent sensitivity and risks that may arise from clinical trials generally, which is particularly acute in the present context of a controversial proposal using children as the subjects of research, with public concerns as to the safety of what is proposed.

108. Under paragraph 3.2.4 of the GAfREC, REC review is to be proportionate to the scale and complexity of the research proposed. In light of the highly charged background to this trial and the significant respects in which it is unusual and unprecedented, it was particularly incumbent upon the HRA to ensure that the REC review was rigorous and that care was taken to give effect to the procedural safeguards in place. As set out below there have been a series of procedural failings in the process leading to REC approval.

Constitution of the REC

109. Schedule 2 to the 2004 Regulations sets out "Additional provisions relating to Ethics Committees". Paragraph 3 of Schedule 2 relates to "Membership" (which is reflected in §4.2.6 of the GAfREC) and provides as follows:

> *3.—(1) An ethics committee shall consist of—*
> *(a) expert members; and*
> *(b) lay members.*
> *(2) An ethics committee shall have no more than 18 members.*
> *(3) The members of an ethics committee shall be appointed by the appointing authority.*
> *(4) A person shall not be eligible for appointment as a lay member of an ethics committee if, in the course of his employment or business, he—*
> *(a) provides medical, dental or nursing care, or*

(b) conducts clinical research.
(5) An appointing authority shall, in relation to an ethics committee, exercise their power under sub-paragraph (3) so as to ensure that—
(a) at least one third of the total membership shall be lay members; and
(b) at least half of the lay members must be persons who are not, or who never have been—
(i) health care professionals,
(ii) persons involved in the conduct of clinical research, other than as a subject of such research, or
(iii) a chairman, member or director of—
(aa) a health service body, or
(bb) a body, other than a health service body, which provides health care; or
(cc) an integrated care board.
(6) References in sub-paragraph (5) to a health service body include—
(a) a Strategic Health Authority,
(b) a Primary Care Trust,
(c) the National Institute for Health and Care Excellence,
(d) the Health and Social Care Information Centre.
(e) Health Education England, and
(f) the Health Research Authority.

110. Under paragraph 2 to Schedule 2 "'lay member" means a member of an ethics committee, other than an expert member."

111. The following is apparent in relation to the requirements for lay members on the REC:

(i) A REC must be comprised of at least one-third lay members;

(ii) At least half of the lay members must be persons who are not, and who have never been, health care professionals, persons involved in the conduct of clinical research or a chairman, member or director of any health service body or healthcare provider.

(iii) There is no provision in the regulations or procedures made under them for 'Lay Plus' members, but it appears that 'lay plus' is intended to be used as a label used to describe the subset of lay members who meet the additional requirement in paragraph 3(5)(b) of Schedule 2.

112. As far as can be established from the minutes of the only meeting of the REC constituted to consider this Trial only one, or maybe two, of 'Lay' or 'Lay Plus' members of the 12 members of the REC (of whom 9 attended) met the requirement at paragraph 3(5)(b). By reference to the table at paragraph 67 above:

- Of the three designated 'Lay' members, G is a retired nurse; H is a research scientist in immunohaematology; and K is a "Senior Research Manager (Clinical Study Management Lead)". Of these only G could properly constitute a lay member of the REC.

- Of the four designated as 'Lay Plus', A was a Psycho-social Researcher; C was a Pharmacy Graduate; E a "Private Client and Litigation Paralegal"; and F "Head of Clinical Operations". Of these only E, and possibly C (subject to further

information), would appear to be capable of meeting the requirements of a lay member, let alone a 'lay plus' member meeting the requirement of paragraph 3(5)(b).

- The REC did not therefore have at least one third of lay members, at least half of whom were 'lay plus' as properly designated by reference to the requirements of the regulations.
- The Claimants solicitors have requested to be provided with the identities of the members of the REC so that their status and eligibility may be properly assessed. The position as it currently appears is set out in the table below with the member, designation, and comment in each case where the member was designated as lay or lay plus (with those not attending, all designated as experts, shaded):

A	Health Economist / Psycho-social Researcher	LP	Not eligible as lay, as apparently conducts clinical research; nor lay plus subject to confirmation of employment history
B	Lead Pharmacist in Clinical Trials	Ex	
C	Pharmacy Graduate	LP	Possibly eligible as lay (and lay plus) subject to further information as to past and current employment and business.
D	Senior Research Nurse / Coordinator	Ex	
E	Private Client and Litigation Paralegal	LP	Apparently eligible as lay (and lay plus), subject to further information to confirm as to employment history
F	Head of Clinical Operations	LP	Not apparently eligible as lay, as provides medical, dental or nursing care; nor lay plus subject to confirmation of employment history
G	Retired Nurse	Lay	Eligible as lay, but not lay plus
H	Research Scientist - immunohaematology	Lay	Not eligible as lay, as conducts clinical research
I	Academic Lead for Research, Ethics and Compliance	Ex	
J	Chief Regulatory Officer	Ex	
K	Senior Research Manager (Clinical Study Management Lead)	Lay	Not eligible as lay, as apparently conducts clinical research.
L	Paediatric Intensive Care Consultant – written comments	Ex	

113. There is an additional requirement under GAfREC that does not appear to have been met, which is to ensure that the REC was representative of public opinion on the subject of puberty blockers. The GAfREC makes clear the importance of a REC being independent and impartial and free from conflicts of interest (§2.3.6), and having members who reflect the diversity of society and not representing vested interests, but rather current ethical norms in society, the currency of public opinion and the diversity of the adult population (§§4.1.1, 4.2.2-4.2.5). On the basis of the information published or disclosed to the Claimants it does not appear that these requirements have been fulfilled, noting that approximately two-thirds of the British public believe puberty blockers should never been given to under-18s to treat gender incongruence, even as part of a clinical trial,[25] yet this majority opinion does not appear to have been reflected in any way in the questions raised by the REC or the decision made to approve the trial.

Lack of requisite expertise

114. As set out in paragraph 42 above, reg 15(6) of the 2004 Regulations imposes a requirement for access to expert advice, either within the REC membership or otherwise externally. This applies where a clinical trial involves minors. Specifically, that advice is "*on the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial*": see reg 15(6) and §2.49 of the REC SOP.

115. The REC SOP provides at §2.53 that: "If the relevant member cannot attend the meeting, they should be invited to submit written advice prior to the meeting. A copy of the advice received should be made available to members prior to the meeting or tabled at the meeting. The substance of the advice should be recorded in the minutes."

116. In circumstances where the REC does not have a member with the relevant expertise the SOP at §2.54 sets out various steps that may be taken to secure such expert input.

117. An individual (Member L) who is described as Paediatric Intensive Care Consultant was a member of the REC. It is not apparent that this individual was regarded as the relevant expert in paediatric care to provide advice "*on the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial".*

118. Noting the requirement under the regulations for the advice on paediatric care to address "*clinical, ethical and psychosocial problems*" in that field:

    (a) A paediatric intensivist would not be in a position to provide the input necessary expertise in the present context;

    (b) In any event they did not even purport to do so, having neither attended the only REC meeting (submitting brief written comments which did not provide specific consideration of the "*clinical, ethical and psychosocial problems*"), and not being a member of either purported sub-committee; nor having referred to them the applicants' responses in response to either the REC's points or the first sub-committees' points; and

    (c) There is no indication from the minutes that the written comments were considered or discussed by those who were present at the meeting.

[25] See e.g. https://www.whitestoneinsight.com/puberty-blockers

(d) The requirements of §2.53 of the REC SOP do not appear to have been met in relation to the availability of the written advice to members in advance of the meeting; nor was it recorded in the minutes, which contain no reference to that advice.

Invalid delegation to a sub-committee

119. Paragraph 6(1) of Sch 2 to the 2004 Regulations permits the appointment of sub-committees by a REC, as follows:

> ***6.***—*(1) An ethics committee may—*
>
> *(a) appoint sub-committees consisting of members of the committee; and*
>
> *(b) make arrangements for the exercise, on behalf of the committee, of any of its functions by such a sub-committee, in accordance with the standing orders and operating procedures adopted under sub-paragraph (3).*

120. Specifically, in relation to "the final determination" paragraph 6(4A) provides:

> *(4A) Where a full meeting of an ethics committee has considered a valid application and reached a provisional opinion, it may delegate the final determination of its opinion in accordance with regulation 15 to the Chairman of the ethics committee or a sub-committee of specified members.*

121. These discretionary powers are mirrored by paragraphs 4.2.24 to 4.2.26 (there being no 4.2.25) of GAfREC which also make clear that the general power of delegation must be in accordance with standard operating procedures.

122. Only the REC has the power to appoint a sub-committee. There is no indication that the power was validly exercised in the present case. The minutes of the REC meeting on 4 September 2025 say nothing about appointing a sub-committee, let alone "*of specified members*".

123. An email dated 11 September 2025 from the REC Approvals Manager to the sponsors adds a note at the end of 16 points raised by the REC: "*The Committee delegated authority to confirm its final opinion on the application to a meeting of the full Committee* [sic]*"* [SB 1356]. That note is, on its face, meaningless. In the context of purported delegation it presumably was intended to refer to "*a sub-committee*" rather than "*the full Committee*" but (a) as set out above, there is nothing on the face of the minutes of the 4 September meeting in relation to delegation by the REC; and therefore (b) there was there no record of the specified members of the proposed sub-committee. Accordingly, the Claimants submit that there has been no valid delegation to a sub-committee by the REC.

124. If there was to be a delegation the decision to do so should not only have been recorded with reasons and specified members. The specification of members is not a technicality as the REC in exercising a power of delegation would need to ensure that the sub-committee had relevant expertise within its composition. Paragraph 7.11 of the REC SOP requires that the REC Manager is responsible for ensuring the appropriate expertise is available to any sub-committee (presumably by external advice if such expertise is not available within the sub-committee). There is no evidence this was done

in the present case. The paediatric intensive care consultant was not present at any of the sub-committee meetings.

125. A sub-committee met on 28 October 2025 which consisted of five members. None of them had paediatric expertise. They did not issue a final opinion, but instead posed five more requests for further information or changes to the trial sponsors. The first and fourth of these were absolutely fundamental – the first was a request for justification that the potential benefits outweigh the risks (a core mandatory consideration for approval, as explored above) in order to provide assurance to the Committee (as a whole, not just the Sub-Committee), and the fourth was a concern that the proposed follow-up to the trial would not be sufficient to provide meaningful evidence of long-term impact of GnRHa. Despite this, the final opinion was again delegated to a sub-committee, but no reasoning was given for this, even though the first request was made explicitly in order to assure the whole Committee.

126. It is apparent that the membership of the sub-committees which met on 28 October 2025 and 6 November 2025 was different: see paragraph 76 above. Even assuming it to have been validly appointed (contrary to the position set out above) there sub-committee had no power to appoint a further sub-committee. Apart from the Chair (Member B) the only other two individuals attending the final meeting on 6 November 2025 (Member A and Member J) had not been members of the previous sub-committee that met on 28 October 2025.

127. There is no evidence that the whole Committee was informed of the responses from the trial sponsors to the further requests made by the Sub-Committee, let alone given any opportunity to express their views. Rather, the final decision to approve the Trial was made by a sub-committee attended by three members (two of which had not been members of the previous sub-committee) who gave their final opinion on 6 November 2025 (with very minimal written comments – two lines each – from two other members who did not attend). None of the members in attendance had any relevant medical expertise. The final favourable opinion was issued despite it being recorded previously that the situation was "*Further Information: Response Not Complete*" [SB 1391].

128. The Claimants contend that the delegation, and sub-delegation, were both invalid. The process adopted was procedurally flawed in the respects set out above, and contrary to the provisions of Schedule 2 of the 2004 Regs and the applicable REC SOP.

Failure to appoint (and consider appointing) a lead reviewer

129. Whilst appointing a lead reviewer is not mandatory under the applicable procedures, paragraph 2.19 of the REC SOP provides:

> *2.19 It is strongly recommended that RECs appoint one or more members as lead reviewers for each application for full applications in consultation with the Chair as necessary. A lead reviewer must also be appointed for each application to be reviewed by a proportionate review sub-committee. Use of the lead reviewer form is mandatory.*

In the circumstances of the ethical issues arising from the Trial, the REC should at least have considered appointing a lead reviewer, as "strongly recommended". No lead

reviewer is identified in the publicly available REC documents, nor is there any indication that this was considered. This failure to follow published policy is a public law error.

No summary or opinion published

130. Paragraph 5.6.1 of GAfREC provides:

> *5.6 Transparency*
>
> *5.6.1 RECs should publish a summary of the research they have reviewed, together with their opinion, whether favourable or otherwise*

131. The need for transparency is particularly acute in the context of the ethical assessment of a proposed trial that is so contentious, involving administering drugs to children with potentially lifelong implications, well-established risks of harm, and highly contested benefits. The REC in the present case has not (even by way of disclosure) provided (a) the summary of the research that they have reviewed; or (b) their opinion.

(a) The decision of 6 November 2025 lists documents relating to the conduct of the trial (such as questionnaires and information leaflets), but not any "*research that they have reviewed*". Either the REC did not review any research or they have not listed the research that they have reviewed. In either event that constitutes a significant failure.

(b) It cannot sensibly be suggested that the publication of the words '*Further Information Favourable Opinion*' constitutes the required opinion. No other summary has been published, nor any disclosed in the course of the pre-action protocol process. The public is therefore entirely in the dark as to the conclusions drawn by (or on behalf of) the REC as to the matters that required to be considered under reg 15(5) or its consideration of what it viewed to be the expert advice required by reg 15(6). This constitutes an unlawful breach of the requirement for transparency imposed by the HRA's own policy.

<u>The MHRA's role and decision-making</u>

132. In accepting the request for authorisation the MHRA had to be satisfied that the Trial would be in accordance with the conditions and principles set out in Sch 1 to the 2004 Regulations (see reg. 28 which provides that no person shall conduct a clinical trial or perform the functions of a sponsor otherwise than in accordance with those conditions and principles). In particular, as set out above, under paragraph 12 of Part 2 of Schedule 1 to the 2004 Regulations a trial shall be initiated only if the MHRA comes to the conclusion that "*the anticipated therapeutic and public health benefits justify the risks*".

133. The MHRA has neither published nor provided to the Claimants any information about the basis upon which it decided to accept the request for authorisation following receipt of the trial sponsors' answers to its 19 grounds for non-acceptance, or came to this conclusion about the benefits justifying the risks specifically. On its face, its decision was irrational, including given the inability of the applicants to provide the confirmation that had been (correctly) sought by the MHRA and agreed with by the CHM as to the 'direct benefit' to individuals in the trial: see paragraphs 85 to 87 above.

134. The Claimants reserve the right to amend their case upon disclosure of information pursuant to the duty of candour, but at present submit that there is insufficient evidence that the MHRA adequately considered relevant considerations and therefore fell into material public law error.

E. GROUNDS OF CHALLENGE

135. The Defendants' decisions to approve the PATHWAYS clinical trial were unlawful in the following respects, as subdivided into the grounds which follow:

1) Failure by the REC failed to take account of mandatory considerations set out in the 2004 Regulations, particularly Condition 10 ("direct benefit"), Condition 11 ("necessity to validate data obtained elsewhere") and Condition 12 ("compliance with the EMA").

2) Failure by both the REC and the MHRA to take into account relevant considerations and/or to take reasonable steps to acquaint themselves with the relevant information before making a decision, contrary to the *Tameside* public law duty.

3) Procedural illegality in failing to constitute the REC in accordance with the statutory requirements as to both (a) lay representation; and (b) relevant scientific expertise).

4) Procedural illegality in failing to follow the procedures and processes set out in the 2004 Regulations, GAfREC and the REC SOP, including by flawed delegation of the substantive approval to subcommittees.

5) Irrationality in failing to identify a clear scientific rationale for the trial and failing to identify how the trial will produce meaningful data that will answer the questions it is intended to answer, which mean that the decisions by both the REC and the MHRA to approve the trial were decisions which no reasonable public authority could have reached.

GROUND 1: illegality due to failure by the REC to consider and/or evaluate mandatory considerations set out in relevant legislation

136. The REC failed to consider the following matters which were statutorily required, properly or at all:

(a) The requirement under reg 15(5)(h) and Sch 1, Part 4 condition 10 for 'some direct benefit for the group of patients involved in the trial', as set out at §§78 to 89 above.

(b) The inability, on the trial sponsors' own evidence, for the statutory risk / benefit balance requirement for individual trial subjects under reg 15(5)(b) and Sch 1, Part 2 condition 10 (also as read with condition 16) to be satisfied: see §§78 to 89 above.

(c) The requirement to validate data that had been obtained by other means, under Sch 1, Part 4 condition 11; including consideration of (i) animal studies and (ii) follow-up of individuals who had previous been prescribed puberty blockers for gender incongruence or dysphoria: see §§90 to 96 above.

(d) Compliance with EMA scientific guidelines; in particular as to risk mitigation and trials involving children: see §§46 to 47 above

(e) Failure to consider the trial protocol design, as required by reg 15(5)(a), and in particular failure to ask any or any adequate questions about its underlying scientific rationale and ability to yield clinically meaningful data: see §§97 to 103 above

GROUND 2: illegality due to failure to take into account relevant considerations/*Tameside* failure to enquire

137. As set out above at §§104-106, the HRA withheld relevant material from the REC, in particular the evidence and representations from two separate groups of professionals. This material was unreasonably and unjustifiably withheld from the REC (other than the Chair) by the HRA, so that the others members of the REC were not even able to evaluate its significance (or otherwise) for themselves.

GROUND 3: by the HRA and REC adopting a procedurally flawed procedure in failing to follow the designated processes set out for the REC

138. The REC's procedures were materially flawed in that:

(a) The REC was not properly constituted, with individual members being wrongly designated as lay and/or 'lay plus': see §§109-112 above

(b) There was a failure to meet the statutory requirements for lay membership as to proportions and the requirements of GAfREC that the REC should be representative of public opinion. Its membership has not been shown to be independent, impartial and free from conflicts of interest: see §113- above.

(c) The REC lacked the statutorily required expertise pursuant to reg 15(6): see §§114-118 above.

(d) There was no valid delegation to the first sub-committee, with an absence of the necessary decision by the REC to form a sub-committee of specified members, as required by paragraph 6(1) of Sch 2: see §§119-124 above.

(e) Similarly there was no valid delegation to the second sub-committee nor any lawful basis for it to issue a 'favourable opinion' on behalf of the REC: see §§125-128 above.

(f) There was a failure to consider appointing a lead reviewer, despite this being "strongly recommended" in the REC Standard Operating Procedures: see §129 above.

(g) There is a continuing failure to meet the policy requirements of transparency provided in GAfREC para 5.6, in particular in failing to publish either a summary of the reviewed research or their opinion (beyond merely indicating that it was favourable) - see §§130-131 above.

GROUND 4: Irrationality

139. Both the HRA / REC and the MRHA irrationally approved a trial protocol that lacked the essential components for a clinical trial; in particular (a) a clearly articulated scientific rationale; and (b) the ability to yield clinically meaningful data;: see §§97-103 and §135 above.

F. CONCLUSION AND REMEDY

140. For the reasons set out above, the Defendant's decisions to approve the Trial were unlawful. Accordingly, the Claimant seeks:

    a. A declaration that the Defendants have acted unlawfully in approving the PATHWAYS clinical trial.

    b. A mandatory order quashing the Defendants' approval of the PATHWAYS clinical trial;

    c. An order prohibiting the PATHWAYS clinical trial from enrolling any children or young people.

    d. Such further relief as the Court deems just and appropriate.

141. To the extent necessary the Claimants will seek interim relief to prohibit any steps to recruit children and young people to the trial pending final determination of this claim.

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Instructed by Conrathe Gardner LLP

TABLE OF ABBREVIATIONS

As used in both this Statement of Facts and Grounds and in documents in the claim bundle.

ADHD	Attention Deficit Hyperactivity Disorder
ARSAC	Administration of Radioactive Substances Advisory Committee
ASD	Autism Spectrum Disorder
CHM	Commission on Human Medicines
CAMHS	Child and Adolescent Mental Health Services
CTA	Clinical Trial Application
CTIMP	Clinical Trial of an Investigational Medicinal Product
CYP	Children and Young People
CYPGS	Children and Young People's Gender Service
DHSC	Department of Health and Social Care
ECG	Echocardiogram
EMA	European Medicines Agency
FIH	First In Human
GAfREC	Governance Arrangements for Research Ethics Committees
GCP	Good Clinical Practice
GIDS	Gender Identity Development Service
GNA	Grounds for non-acceptance
GnRHa	Gonadotropin-releasing hormone analogues
HCRW	Health and Care Research Wales
HRA	Health Research Authority
IMP	Investigational Medical Product
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomised Controlled Trial Number

	- despite its name, now is a registry for non-randomised clinical trials as well as randomised ones.
KCL	King's College London
MDT	Multi-Disciplinary Team
MHRA	Medicines and Healthcare Products Regulatory Agency
NIHR	National Institute for Health and Care Research
NMDT	National Multi-Disciplinary Team
PATHWAYS	Puberty Suppression and Transitional Healthcare with Adaptive Youth Services
PD	Pharmacodynamic
PIS	Participant Information Sheet
PK	Pharmocokinetic
POCBP	Patients of Child-Bearing Potential
PPI	Patient and Public Involvement
QoL	Quality of Life
REC	Research Ethics Committee
REC SOP	Research Ethics Committee Standard Operating Procedures
SAE	Serious Adverse Event
SLAM	South London and Maudsley NHS Foundation Trust
SUSAR	Suspected Unexpected Serious Adverse Reaction

APPENDIX A – Standing

1. The statutory requirement of "*sufficient interest*" set out in s. 31(3) of the Senior Courts Act 1981 is interpreted by the courts in a flexible and pragmatic manner, focusing on whether the claimant's interest is sufficient to justify their bringing the application before the court, rather than being unduly restrictive or requiring a direct personal right to be affected. The test excludes "mere busybodies," but allows challenges from those with a genuine interest, which may be personal, public, or representative in nature. Standing is context-specific and assessed in light of the legal and factual circumstances of each case, including the public importance of the issue, whether there are better-placed challengers, and the role of the claimant (individual or organisation) in the relevant area (see R *(Redrow Plc) v Secretary of State for Levelling Up, Housing and Communities* [2024] EWCA Civ 651, the Court of Appeal (quoting Sedley LJ from *R (Bancoult) v Secretary of State for Foreign and Commonwealth Affairs* [2007] EWCA Civ 498) at [27]:

   > *"What modern public law focuses upon are wrongs – that is to say, unlawful acts of public administration. These often, of course, infringe correlative rights, but they do not necessarily do so: hence the test of standing for public law claimants, which is interest-based rather than rights-based."*

2. *R (Kukhtyak) v Hounslow LBC* [2023] EWHC 2914 (Admin) confirmed that the test is generally interpreted liberally, allowing persons with a genuine interest and excluding busybodies.

3. The **Bayswater Support Group** has standing on both a directly affected and a representative basis. Bayswater's membership primarily consists of around 850 parents of trans-identifying children and young adults. The children of these parents may well be giving serious consideration to participation in the PATHWAYS trial. This establishes a direct and practical connection to the decision under challenge, not a remote or hypothetical concern. Bayswater's membership includes parents who disagree with the other parent about their child's participation in the Trial, including in circumstances of separation or divided parental responsibility, or where the other parent has previously facilitated their child's access to hormone treatment without the knowledge or consent of our member.[26] In such cases, one parent's consent may expose a child to recruitment to the Trial notwithstanding the objections of the other. This is not a matter of speculation but a structural feature of the trial design and entirely possible given past judgments by the family courts,[27] and it gives rise to a real and imminent interest in the lawfulness of the approval decision.

4. Bayswater also satisfies the criteria for representative standing. The courts have recognised standing for organisations representing identifiable affected groups, particularly where those most directly affected cannot readily bring proceedings themselves. In *R (McCourt) v Parole Board for England and Wales* [2020] EWHC 2320 (Admin), standing was recognised for individuals raising serious issues of public importance, notwithstanding the absence of direct personal detriment. The key

[26] First Claimant's second statement at [§21, CB 163].
[27] See e.g. *O v. P* [2025] 4 WLR 9

distinction, as drawn in *R (Good Law Project Ltd) v Prime Minister* [2022] EWHC 298 (Admin), is between those with a genuine interest and mere busybodies. The court noted that NGOs and individuals have been granted standing where they act "*in their fields of interest*" (para 28) and are representative of, or closely connected to, those affected by the decision. That reasoning applies here: and it would be fanciful to suggest that children eligible for the PATHWAYS trial would themselves seek to challenge the legality of the trial. Indeed, if the present proposed claimants were not recognised as having standing to bring this challenge it is hard to envisage any individual or group that would be, which would leave any public law errors in the approval decision unsupervisable by the court.

5. Such children who will be subject to this trial do not yet realise that they may be victims (eligible for standing in a human rights claim). Individual parents may be divided, under pressure, or unable to act in time. In those circumstances, the powerful question arises: if not Bayswater, then who? Denying standing where there is unlikely to be a more appropriate challenger risks leaving decisions of major public importance effectively immune from judicial scrutiny, contrary to the well-established principle that there must not be a lacuna in the rule of law.

6. Further, the Trial documentation itself expressly recognises the relevance of those with lived experience. The PATHWAYS FAQs state that young people with lived experience and parents/caregivers have been consulted "*from early in the study's development*" and will continue to be involved through Advisory Groups convened by the National Children's Bureau, contributing to the "*design, implementation, and interpretation of study findings*". It would be incoherent for the Defendants to contend that lived experience is sufficiently relevant to shape the design and oversight of the trial, yet insufficient to ground standing to challenge the lawfulness of the approval decision through the courts. It is only right, and consistent with public law principle, that parents with lived experience — including Bayswater members — are permitted to express their concerns through the court process when they allege unlawfulness in the approval decision.

7. This is also relevant to the Second Claimant, **Keira Bell**, who has standing by reason of her direct personal experience of the treatment pathway to which the PATHWAYS trial relates. In *Bell v Tavistock and Portman NHS Foundation Trust* [2021] EWCA Civ 1363, Ms Bell was a Claimant in the capacity of a former patient who had been treated with puberty blockers, progressed to cross-sex hormones, and later regretted the treatment pathway. That challenge focused on the question of whether children under the age of 16 could give informed consent to the prescription of puberty-blocking medications as part of treatment for gender dysphoria. Her standing to bring a claim was not contested, as her direct experience was sufficient; she had been directly affected by the policy and its implementation. That analysis applies similarly here. The PATHWAYS trial authorises and formalises a treatment pathway materially indistinguishable from that which Ms Bell experienced. Her interest is therefore not abstract or ideological but grounded in personal experience of the very category of intervention now being approved under a research protocol.

8. Finally, the Third Claimant **James Esses** has standing as a professional with direct experience as a psychotherapist with children with gender incongruence. This gives him a genuine and informed interest in the lawfulness of the approval of a clinical trial involving children. The issues raised by the Trial are the same clinical, ethical and safeguarding concerns that Mr Esses has previously raised and successfully litigated upon. Those proceedings directly informed the UK Council for Psychotherapy's decision to issue a formal statement clarifying the legal protection afforded to gender-critical beliefs and affirming the legitimacy of exploratory therapeutic approaches with children. In that statement, the UKCP Chair, Dr Christian Buckland, expressly recognised that "*medical interventions can potentially be irreversible*" and that it is therefore "*imperative that all underlying aspects to someone's dysphoria are given the attention and exploration they deserve through professional psychotherapies … prior to considering medical intervention*." Mr Esses' involvement in the events leading to that clarification demonstrates that his concerns were substantive, credible and sufficiently serious to require formal recognition at national professional level.

9. The Trial will concern a cohort of children who are known to be particularly vulnerable, including children with autism and other neurodevelopmental or mental health difficulties. Mr Esses has personal clinical experience of working with such children experiencing gender dysphoria and professional awareness of the issues arising from the use of puberty blockers in children experiencing gender dysphoria. He has first-hand experience of exploratory therapy with such children, he has a direct and legitimate interest in ensuring that the trial is lawful, ethically defensible, and adequately safeguards the children involved.

10. In summary, Mr Esses' interest arises from sustained engagement with issues concerning the welfare of children subject to gender-related medical interventions and from his professional practice in the alterative area of exploratory therapeutic practice with vulnerable children experiencing gender distress. In circumstances where children cannot litigate and parental interests may be fragmented, recognising standing for a responsible and informed individual challenger accords with the liberal and pragmatic approach endorsed by the authorities.