Neutral Citation Number: [2020] EWHC 435 (Admin)

Case No: CO/2966/2019

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

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 28/02/2020

Before :

MR JUSTICE CAVANAGH

- -

Between :

THE QUEEN (on the application of)

CAIT COTTER **Claimant**
(a child, by her mother and litigation friend,
NATASHA COTTER)

- and -

THE NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE ("NICE") **Defendant**

-and-

THE SECRETARY OF STATE FOR HEALTH AND SOCIAL CARE **Interested Party**

- -
- -

Ian Wise QC (instructed by **Hodge, Jones and Allen**) for the **Claimant**
Daniel Stilitz QC and Michael White (instructed by **DAC Beachcroft**) for the **Defendant**
Julia Smyth (instructed by **Government Legal Department**) for the **Interested Party**

Hearing date: 30 January 2020

- -

Approved Judgment

Mr Justice Cavanagh:

INTRODUCTION

1. The Claimant is an 11-year old girl who suffers from a disease called Phenylketonuria ('PKU'). PKU is a rare inherited metabolic condition which inhibits the body's ability to metabolise protein. This prevents the breakdown of an amino acid known as phenylalanine ('Phe') which is extremely toxic to the brain. If PKU is not treated, most children with PKU will develop brain damage leading to profound and irreversible intellectual disability, delayed speech, seizures, and behavioural abnormalities. If this happens, the brain damage will be irreversible. Other adverse outcomes include impaired executive function, reduced processing speed, attention problems and fine impaired motor skills.

2. The standard treatment for PKU is by way of dietary management. The nature of the treatment was explained by Mrs Justice Andrews in another recent case about PKU (though raising completely different legal issues), **R (SB) v NHS England** [2017] EWHC 2000 (Admin); [2018] PTSR 576, as follows:

> "7. The standard treatment for PKU is dietary management. This involves restricting the amount of natural protein consumed, often to only 10–20% of the amount contained in a normal diet, coupled with the taking of a supplement (a protein substitute) to promote normal growth and development. With the exception of fruit and some vegetables, there are few foods that can be eaten without severe limitation. The carefully supervised dietary management of a child with PKU aims to provide enough protein and phenylalanine for adequate growth, but not so much that the levels go too high. Regular blood tests are used to monitor the levels of blood phenylalanine. Dietary adherence is essential, but problematic, and provides a huge burden to families. It can be difficult to achieve, especially as the child gets older. It is recommended that the diet is continued for life."

3. In practice, those with PKU are limited to a very restricted diet which severely limits what and how much can be eaten. For example, those with PKU cannot eat any meat, fish or eggs. Kate Learoyd, Campaign Manager for the National Society for PKU (NSPKU), which supports people with PKU, their families and their carers, who provided a witness statement for these proceedings, described the PKU diet as "one of the most extreme diet regimes ever devised". Understandably, the Claimant finds her dietary restrictions to be limiting and frustrating. She struggles with persistent hunger and is clinically underweight. The special low protein foods that she can eat are unappetising. The protein substitutes that she has to take are also unappetising and cause discomfort. The burden of managing her diet, which is so different from that enjoyed by her friends, and her fear of becoming brain damaged, causes her to suffer from anxiety. It is undoubtedly a huge burden on the Claimant, which she and her parents cope with impressively.

4. There is a drug which can be used to treat PKU. This is sapropterin dihydrochloride (which I will refer to by its brand name, "Kuvan"). This is a synthetic form of the compound (BH4) which is naturally absent in patients with PKU. The Claimant has undertaken a trial of Kuvan and has been found to be responsive to it. Not all persons

with PKU are responsive to Kuvan. Kuvan enables responsive patients such as the Claimant to metabolise Phe and thus to increase their food intake to a considerable extent. The risks of brain damage are reduced. As Andrews J put it in **SB,** at paragraphs 11 and 12:

> "11. ….. In simple terms, for patients who are responsive, Kuvan reduces the level of phenylalanine in the blood, thus making the patient more protein tolerant and enabling them to eat more "normal" foods. In those who respond to Kuvan, the diet is likely to be relaxed and the dietary supplement reduced by 50%. The use of special low protein foods will be decreased or even stopped altogether. Kuvan significantly ameliorates the effects of PKU: however, even in a responsive patient there still has to be some dietary management, and the patient will still have to take supplements (albeit a smaller amount). The European Commission granted a marketing authorisation for Kuvan, valid throughout the European Union, on 2 December 2008.
>
> 12. The group of patients who are responsive to Kuvan are those with "mild to moderate" PKU; around 20% of children with the condition aged four and above…."

5. The benefits of Kuvan have been described in the witness evidence of Professor Anita MacDonald, Consultant Dietician in Inherited Metabolic Disorders at Birmingham Women's and Children's Hospital, who is probably the country's leading expert on PKU. Professor MacDonald said that patients who take Kuvan have little need for specialist low protein foods and may stop or considerably reduce their protein substitute requirements. The overall burden of care is reduced, and overall it has a great impact on their daily life, well being and, in the case of children, their carers' quality of life.

6. There is no dispute between the parties as to the potential highly beneficial effects of Kuvan for patients with PKU who are responsive to it. Kuvan is routinely provided in about 50 countries worldwide. Kuvan was for many years provided in England at a low cost, on a named-patient/compassionate basis, by Schircks Laboratories. In 1999, after it was found that a larger group of PKU patients responded to the drug than was previously thought, the rights to manufacture Kuvan in the UK were bought by a pharmaceutical company, BioMarin.

7. The Defendant ("NICE") is responsible for recommending health technologies, including drugs, for NHS use in England. The NHS is allowed to buy drugs that NICE has not appraised or has not recommended, but NHS bodies are obliged to fund treatments which have been recommended in NICE guidance. If NICE recommended Kuvan for use in the NHS, therefore, responsive patients such as the Claimant could be sure of being prescribed it. Without a NICE recommendation, a patient's prospects of being prescribed Kuvan would depend upon a decision of their local NHS Trust to do so voluntarily. As Kuvan is relatively costly, and would potentially benefit relatively few patients (see paragraph 121, below), and as the demands on NHS Trusts are so great, the chances of this happening may be low.

8. In July 2018, NICE was asked by the Interested Party, the Secretary of State for Health, to assess Kuvan and to make a recommendation as to whether it should be provided by the NHS. Before doing so, NICE had to determine whether it should carry out the assessment under its standard Health Technology Appraisal ("HTA") process, or under the alternative Highly Specialised Technology ("HST") process, which is reserved for highly specialised technologies which meet specified criteria.

9. The choice of assessment process may potentially affect the prospects of a drug being recommended by NICE for use in the NHS. In conducting its assessments, NICE makes use of a criterion known as ICER, the "Incremental Cost Effectiveness Ratio". This focuses upon the "cost per QALY gained". "QALY" is the "Quality Adjusted Life Year", a measure of the state of health in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to one year of life in perfect health. The cost per QALY is a standardised measure of cost-effectiveness that is used across all health technologies. Under the standard HTA process, NICE will recommend a treatment for use in the NHS if the cost per QALY gained is under £20,000, and will generally recommend a treatment at a cost per QALY gained of up to £30,000. Under an HST, however, the upper limit rises to £100,000. It follows that the test for drugs and treatments under HST is, in this key respect, easier to satisfy, and some drugs or treatments may obtain a recommendation from NICE if the HST assessment process were used, but would not obtain such a recommendation if the HTA process is used.

10. This gives rise to the issue that is at the heart of this case. NICE decided to assess Kuvan under HTA. The Claimant contends that NICE erred in law in so doing, and that NICE misunderstood and misapplied its own guidance in failing to make use of an HST process. If HST had been used, the Claimant submits, the prospects of a positive decision being made in relation to Kuvan would have increased significantly. In the event, in September 2019, shortly after these judicial review proceedings commenced, the manufacturer, BioMarin, withdrew the drug from the process altogether. It is not practicable to continue with the assessment process without the manufacturer's participation, and so no final decision has yet been taken as to whether to recommend Kuvan for use in the NHS.

11. There is a dispute between the parties as regards the prospects of Kuvan being recommended by NICE if the standard HTA process is used. The Claimant submits that the prospects are next to none. NICE, on the other hand, submits that there is a very real prospect of Kuvan being recommended even if it is assessed under HTA. I will return to this issue when I come on to consider the standard of scrutiny that the Court should apply to NICE's decision-making process.

12. It will be apparent from the above that this case is not a challenge to a decision by NICE to decline to recommend Kuvan for use by the NHS. The matter did not get that far, because BioMarin withdrew from the process. Rather, the challenge is to NICE's decision that the assessment process should be the HTA process, rather than the HST process. As for that, NICE has determined upon, and published, the criteria which must be satisfied if a drug or treatment is to be assessed under HST. These are set out in paragraph 28 of a document entitled "Interim Process and Methods of the Highly Specialised Technologies Programme" ("the 2017 Guidance"), which was issued by NICE in April 2017. Paragraph 28 of this document states as follows:

> **"28**. Topics evaluated through the HST programme will be formally referred to NICE by Ministers. HSTs are selected using the following criteria, **all** of which have to apply:"
>
> - The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS;
> - The target patient group is distinct for clinical reasons;
> - The condition is chronic and severely disabling;
> - The technology is expected to be used exclusively in the context of a highly specialised service;
> - The technology is likely to have a very high acquisition cost;
> - The technology has the potential for life long use;
> - The need for national commissioning of the technology is significant."

13. NICE initially decided that Kuvan should be assessed under HTA. After pre-action correspondence from the Claimant, NICE agreed to reconsider its decision and took the decision again. The outcome of the reconsideration was that Kuvan should, indeed, be appraised under HTA. This decision, which is the decision that is under challenge in these proceedings, was recorded in a Topic Selection Outcome Report ("the TSOR"), dated 30 April 2019.

14. As paragraph 28 makes clear, a drug will only be assessed under HST if all seven of the criteria are satisfied. It is common ground that Kuvan satisfies four of the seven criteria set out above. However, NICE decided that Kuvan does not satisfy three of the criteria. The three criteria which NICE decided were not met were the first, second and fourth:

> - The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS;
> - The target patient group is distinct for clinical reasons; and
> - The technology is expected to be used exclusively in the context of a highly specialised service.

15. It was also common ground between the parties that this judicial review challenge can succeed only if the Claimant is right that NICE erred in law in relation to each of the three criteria which NICE decided were not met.

16. The Claimant does not challenge the lawfulness of the criteria itself, and does not contend that NICE was not entitled to apply the criteria set out in paragraph 28 of the

2017 Guidance. Rather, the Claimant's case is that NICE has misunderstood and misapplied the criteria in a way that is unlawful in public law terms.

17. The Claimant was represented by Ian Wise QC, and the Defendant by Daniel Stilitz QC and Michael White. I am grateful to all counsel for their very helpful submissions, both written and oral. The Interested Party did not make representations, but the hearing was attended by Julia Smyth of counsel, on his behalf.

18. In the remainder of this judgment, I will first set out the statutory framework and the relevant parts of the 2017 Guidance, and I will summarise the TSOR decision. I will then identify the grounds upon which a decision such as this can be challenged by way of judicial review, and will consider the intensity of review that the Court should apply in a case such as this. Finally, I will address the grounds of challenge in respect of each of the three criteria.

THE STATUTORY FRAMEWORK

The establishment of NICE and its general duties

19. NICE was established by section 232 of the Health and Social Care Act 2012 ("the 2012 Act").

20. NICE's general duties are set out in section 233 of the 2012 Act, which provides, in relevant part:

> "233. **General duties**
>
> (1) In exercising its functions NICE must have regard to—
>
> (a) the broad balance between the benefits and costs of the provision of health services or of social care in England,
>
> (b) the degree of need of persons for health services or social care in England, and
>
> (c)the desirability of promoting innovation in the provision of health services or of social care in England.
>
> (2) NICE must exercise its functions effectively, efficiently and economically."

21. As Mr Stilitz QC pointed out, this gives NICE a wide discretion in the performance of its functions.

22. The power conferred on NICE to make recommendations for the use of health technologies is set out in section 237 of the 2012 Act, and in regulations made under section 237. Section 237 provides, again in relevant part:

> "237. **Advice, guidance, information and recommendations**
>
> (1) Regulations may confer functions on NICE in relation to the giving of advice or guidance, provision of information or making of

> recommendations about any matter concerning or connected with the provision of—
>
> (a) NHS services,
>
> (b) public health services, or
>
> (c)social care in England.
>
> (2)The regulations may provide that a function conferred under subsection (1)(a)—
>
> (a)is only exercisable on the direction of the Secretary of State or the Board;….."

23. Pursuant, inter alia, to the power under section 237(2), the Secretary of State made the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 (SI 2013/259, "the 2013 Regulations").

2013 Regulations

24. The 2013 Regulations deal separately with "technology appraisal recommendations" which make use of the HTA process, and "highly specialised technology recommendations" which make use of the HST process.

Technology appraisal recommendations

25. "Technology appraisal recommendations" are defined in regulation 2 as follows:

> ""technology appraisal recommendation" means a recommendation made by NICE following an appraisal of the benefits and costs of a health technology conducted by NICE in accordance with NICE's published methods and processes for appraisal of health technologies that results in a positive assessment (but does not include a highly specialised technology recommendation)."

26. As I have said, this involves use of the "standard" HTA process. Regulation 7 provides, in relevant part:

> "7.—(1) NICE may make a technology appraisal recommendation—
>
> (a)in relation to a health technology identified in a direction given by the Secretary of State;
>
> (b)that recommends that relevant health bodies provide funding within a specified period to ensure that the health technology be made available for the purposes of treatment of patients:
>
> ....

> (6) A relevant health body must comply with a technology appraisal recommendation;
>
> …..
>
> (9) NICE must establish a procedure for the appraisal of health technologies, and must consult such persons as it considers appropriate in establishing the procedure."

27. "Relevant health bodies" are defined in regulation 7(7) to include the NHS Board, and Clinical Commissioning Groups" ("CCGs").

28. The NHS Board (formally, the "National Health Service Commissioning Board") was created by section 1H of the National Health Service Act 2006 ("the 2006 Act"). Section 3B(1) of the 2006 Act provides that, "Regulations may require the Board to arrange, to such extent as it considers necessary to meet all reasonable requirements, for the provision of part of the health service of....(d) such other services or facilities [in addition to dental services and services for the armed forces and those in prison] as may be prescribed." The relevant regulations are The National Health Service Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) Regulations 2012 (SI 2012/2996, "the 2012 Regulations"). I will come back to the 2012 Regulations in a moment.

29. CCGs are bodies established under section 14D of the 2006 Act. CCGs are groups of general practices which come together in each area to commission services for their patients and population. They replaced Primary Care Trusts.

30. It follows from the above that the process begins with a direction from the Secretary of State to NICE to appraise a health technology (which may be a drug). NICE then does so and, if it decides to recommend the technology, relevant health bodies must make the technology available for the purposes of treatment of patients. As I have said, the appraisal or assessment process that NICE uses for the purposes of technology appraisal recommendations is the HTA or HST processes.

Highly specialised technology recommendations

31. "Highly specialised technology recommendations" are also defined in regulation 2, as follows:

> "highly specialised technology recommendation" means a recommendation made by NICE following an appraisal of the benefits and costs of a highly specialised health technology conducted by NICE in accordance with NICE's published methods and processes for appraisal of highly specialised health technologies that results in a positive assessment"

32. "Highly specialised health technology is also defined in regulation 2:

> "highly specialised health technology" means a health technology intended for use in the provision of services for rare and very rare

conditions provided for in regulations under section 3B(1)(d) of the 2006 Act"

33. NICE makes use of the HST process to appraise and assess highly specialised technology recommendations. Regulation 8 provides, in relevant part:

> "8.(1) NICE may make a highly specialised technology recommendation—
>
> (a) in relation to a highly specialised health technology identified in a direction given by the Secretary of State;
>
> (b) that recommends that the Board, in the exercise of the Board's function to arrange for the provision as part of the health service of services specified in regulations made under section 3B of the 2006 Act(1), provide funding within a specified period to ensure that the highly specialised health technology can be made available for the purposes of treatment of patients.
>
> ….
>
> (6) The Board must comply with a highly specialised technology recommendation.
>
> (7) The duty of the Board in paragraph (6) must be taken to require that the Board apply such amounts of the sums paid to it under section 223B(1) of the 2006 Act as may be required to enable the Board to comply with the paragraph (1)(b) recommendation.
>
> (8) NICE must establish a procedure for the appraisal of highly specialised health technologies, and must consult such persons as it considers appropriate in establishing the procedure.
>
> (9) The procedure must include arrangements—
>
> (a) for NICE to consult such persons with an interest in the appraisal of a highly specialised health technology that is the subject of a direction referred to in paragraph (1)(a) as it considers appropriate; and
>
> (b) for the Board to be consulted as such a person."

Appeals

34. Regulation 9 of the 2013 Regulations provides that a person aggrieved by a recommendation made under regulations 7 and 8 may appeal to an appeal panel on the basis, inter alia, that NICE acted unreasonably in the light of the evidence submitted to NICE. The Claimant could not have brought an appeal in the present matter, because Kuvan's manufacturer, BioMarin, withdrew from the process. The appraisal process cannot proceed without the participation of a drug's manufacturer.

The 2012 Regulations

35. The 2012 Regulations make specific provision for the Board to arrange for specified services for rare and very rare conditions. Regulation 11 provides:

> "11. The Board must arrange, to such extent as it considers necessary to meet all reasonable requirements, for the provision as part of the health service of the services specified in Schedule 4."

36. Schedule 4 sets out a list of over 150 services for rare and very rare conditions. Paragraph 63 of Schedule 4 specifies "Highly specialist metabolic disorder services". It is common ground that this covers treatment for those with PKU. It is also common ground that it is not the case that any treatment or service for a rare or very rare condition falling within Schedule 4 has to be provided by the NHS. It is only services that are recommended by NICE under regulations 7 and 8 of the 2013 Regulations which must be provided by the NHS. The fact that a service is listed in Schedule 4 does not mean that any treatments for the conditions covered by the service will be appraised under HST.

THE 2017 GUIDANCE

37. The 2017 Guidance is non-statutory guidance which has been issued by NICE to explain how, and in what circumstances, NICE will approach conducting assessments of highly specialised technologies under regulation 8, under the HST process. There is an equivalent non-statutory guidance document for standard technology appraisals, dated April 2018, entitled "Guide to the processes of technology appraisal", which it is not necessary to refer to. Although the guidance is non-statutory, the definitions of "technology appraisal recommendations" and "highly specialised technology recommendations" in regulation 2 of the 2013 Regulations (above) each state that the appraisals will be conducted by NICE in accordance with its published methods and processes for appraisal of the relevant technologies. In my judgment, this must cover the decision as to which process to use, and it follows that NICE is bound to act in accordance with its published method for deciding whether a particular technology should be assessed under HTA or HST.

38. For highly specialised technologies, under HST, NICE makes use of an Evaluation Committee, which is an independent advisory body, made up of people who work in the NHS, patient and carer organisations, relevant academic disciplines, and people from pharmaceutical and medical device companies. The Evaluation Committee makes recommendations to NICE regarding the benefits and costs of highly specialised technologies for national commissioning by NHS England. There is a detailed, many-stage, process before a recommendation is made as to whether NICE should recommend a highly specialised technology for NHS use, including consultation and evidence-gathering stages.

39. The first stage is the selection of highly specialised technologies which will be appraised under the HST process, rather than under the HTA process. As I have said, there are seven criteria which must be satisfied, as set out in paragraph 28 of the 2017 Guidance (see paragraph 12, above). Paragraphs 35 and 36 of the 2017 Guidance state as follows:

> "35. The methodological approach to the evaluation of highly specialised technologies (HST) is based on the NICE Guide to the

> Methods of Technology Appraisal with variations required to evaluate technologies for very rare conditions, as described in this document. The following sections should be read in conjunction with that Guide.
>
> "36. As described in the Guide to the Methods of Technology Appraisal, when formulating its recommendations to the Institute, the Evaluation Committee has discretion to consider those factors it believes are most appropriate to each evaluation. In doing so, the Evaluation Committee has regard to the provisions and regulations of the Health and Social Care Act 2012 relating to NICE, and NICE's legal obligations on equality and human rights. The Act expects NICE, in undertaking its general duties, to have regard to:
>
> - The broad balance between the benefits and costs of providing health services or social care in England.
>
> - The degree of need of people in England for health services or social care.
>
> - The desirability of promoting innovation in providing health services or social care in England."

40. The rationale for having different, and more generous, criteria for recommending highly specialised technologies, as compared with other technologies, is set out in paragraph 39 of the 2017 Guidance:

> "39. Given the very small numbers of patients living with these very rare conditions a simple utilitarian approach, in which the greatest gain for the greatest number is valued highly, is unlikely to produce guidance which would recognise the particular circumstances of these very rare conditions. These circumstances include the vulnerability of very small patient groups with limited treatment options, the nature and extent of the evidence, and the challenge for companies in making a reasonable return on their research and development investment because of the very small populations treated. Nevertheless, as part of its consideration of the value 8 for money of the technology, the committee must give consideration to the balance between the costs and the benefits."

41. Paragraphs 50-52 of the 2017 Guidance say, in effect, that when the ICER for the technology is less than £100,000 per QALY gained, the technology is likely to be recommended (though this is an oversimplification of the summary of the "value for money" assessment that is set out in the 2017 Guidance). Paragraph 53 makes clear that there would need to be compelling evidence to justify a recommendation where the ICER is more than £100,000 per QALY gained. As I have said, under the standard HTA process, it is unlikely that a technology will be recommended if its ICER is more than £30,000 per QALY gained.

THE TSOR DECISION

42. The TSOR decision was issued on 30 April 2019. It followed on from a meeting of the joint topic selection decision-making group ("the decision-making group"), which was made up of NICE, the Department of Health and Social Care and NHS England, on 15 February 2019. The decision-making group took the decision on behalf of NICE, and there is no challenge to this delegation. The TSOR decision states that the decision-making group understood that for Kuvan to be eligible for the HST programme all criteria must be met. The group accepted that, despite the availability of a very strict diet, PKU is chronic and severely disabling. The group further accepted that the technology has the potential for life-long use, that the technology is likely to have a very high acquisition cost, and that the need for some form of national commissioning of the technology is significant. The TSOR decision then addressed the three criteria which the decision-making group decided were not met. I will set out what was said about these criteria later in this judgment when I deal with the grounds of challenge. The conclusion was as follows:

> "The decision-making group concluded that although sapropterin for treating PKU meets some of the criteria for routing to the highly specialised technologies programme, it does not meet all the criteria.
>
> The assessment of the topic through the technology assessment programme should be resumed, therefore, and the Secretary of State will be advised accordingly."

THE NATURE OF THE CLAIMANT'S CHALLENGES AND THE INTENSITY OF REVIEW

43. Needless to say, it is not open to me simply to substitute my view for the view of NICE as regards whether the HST process should have been used to appraise Kuvan. The Court can only intervene to quash NICE's decision if the decision was unlawful on public law grounds. Mr Wise QC, on behalf of the Claimant, relies on two interlocking grounds. First, he submits that NICE applied the wrong test, because NICE misread and misunderstood the three criteria in the 2017 Guidance which led to NICE's decision not to assess Kuvan under the HST process. In other words, NICE did not ask itself the right questions. Second, he submits that the conclusion reached by NICE was irrational.

The correct approach to the interpretation of a passage in non-statutory Guidance

44. So far as the first issue is concerned, this depends upon the correct interpretation of the relevant parts of paragraph 28 of the 2017 Guidance. As Andrews J said in the **SB** case, at paragraph 29,

> "The correct interpretation of a policy is a matter for the Court. Its application is a matter of judgment for the decision maker. However, that judgment must be formed on the basis of a proper understanding of the evidence available to him, taking into account all relevant factors: a material mistake of fact or law, or a material misunderstanding can lead to an invalid conclusion."

45. It is clear that a misreading or a misunderstanding of the criteria, as set out in paragraph 28 of the 2017 Guidance might lead NICE to ask itself the wrong question and so to come to an invalid conclusion.

46. Helpful guidance as to the approach that the Court should take to the interpretation issue can be found in the well-known passage from the judgment of Lord Reid (with which all of the other members of the Supreme Court agreed) at paragraphs 18 and 19 of **Tesco Stores Ltd v Dundee CC** [2012] UKSC 13; [2012] PTSR 983. The **Tesco Stores** case was concerned with the interpretation of a development plan. Lord Reed said:

> "18. In the present case, the planning authority was required by section 25 to consider whether the proposed development was in accordance with the development plan and, if not, whether material considerations justified departing from the plan. In order to carry out that exercise, the planning authority required to proceed on the basis of what Lord Clyde described as "a proper interpretation" of the relevant provisions of the plan. We were however referred by counsel to a number of judicial dicta which were said to support the proposition that the meaning of the development plan was a matter to be determined by the planning authority: the court, it was submitted, had no role in determining the meaning of the plan unless the view taken by the planning authority could be characterised as perverse or irrational. That submission, if correct, would deprive sections 25 and 37(2) of the 1997 Act of much of their effect, and would drain the need for a "proper interpretation" of the plan of much of its meaning and purpose. It would also make little practical sense. The development plan is a carefully drafted and considered statement of policy, published in order to inform the public of the approach which will be followed by planning authorities in decision-making unless there is good reason to depart from it. It is intended to guide the behaviour of developers and planning authorities. As in other areas of administrative law, the policies which it sets out are designed to secure consistency and direction in the exercise of discretionary powers, while allowing a measure of flexibility to be retained. Those considerations point away from the view that the meaning of the plan is in principle a matter which each planning authority is entitled to determine from time to time as it pleases, within the limits of rationality. On the contrary, these considerations suggest that in principle, in this area of public administration as in others (as discussed, for example, in **R (Raissi) v Secretary of State for the Home Department** [2008] QB 836), policy statements should be interpreted objectively in accordance with the language used, read as always in its proper context.
>
> 19. That is not to say that such statements should be construed as if they were statutory or contractual provisions. Although a development plan has a legal status and legal effects, it is not analogous in its nature or purpose to a statute or a contract. As has often been observed, development plans are full of broad statements of policy, many of which may be mutually irreconcilable, so that in a particular case one

> must give way to another. In addition, many of the provisions of development plans are framed in language whose application to a given set of facts requires the exercise of judgment. Such matters fall within the jurisdiction of planning authorities, and their exercise of their judgment can only be challenged on the ground that it is irrational or perverse: **Tesco Stores Ltd v Secretary of State for the Environment** [1995] 1 WLR 759, 780, per Lord Hoffmann. Nevertheless, planning authorities do not live in the world of Humpty Dumpty: they cannot make the development plan mean whatever they would like it to mean."

47. The position is, therefore, as Andrews J said in **SB,** that the meaning of a passage in a policy document should be interpreted objectively in accordance with the language used, subject to the important caveat that the passage must be read in its proper context. A passage in a policy document cannot be read by the decision-maker to mean whatever the decision-maker would like it to mean, if that meaning is not consistent with the words used. The passage should not, however, be read as if it were a statute or a contract.

48. I think that it is also important to bear in mind the primary readership for which the policy document was designed. In the present case, paragraph 28 of the 2017 Guidance was designed to give direction to the expert decision-making group, and to provide information to the wider readership of interested parties who will, in the main (though not exclusively) be medical professionals and persons engaged in the pharmaceutical industry.

The intensity of the irrationality review

49. Mr Wise QC, for the Claimant, submitted that, for three main reasons, this is not a case in which a substantial degree of deference, or margin of discretion, should be granted to the decision-maker, when examining the way that the criteria were applied to the particular facts.

50. First, Mr Wise QC said that the intensity of the review will depend on the impact of the determination under challenge. He referred to **R(KM) v Cambridgeshire CC** [2012] UKSC 23; [2012] PTSR 1189, in which Lord Wilson said, at paragraph 36, "I agree with Langstaff J in **R(L) v Leeds City Council** [2010] EWHC 3324 (Admin) at [59] that in community care cases the intensity of review will depend on the profundity of the impact of the determination." The same holds true for all types of cases, not just community care cases: see **R (Rogers) v Swindon NHS Primary Care Trust** [2006] EWCA Civ 392; [2006] 1 WLR 2649, at paragraphs 55-56.

51. Second, Mr Wise QC submits that this is not a case in which the decision is specialist in the sense that the decision-makers have particular expertise which makes them better placed than the Court to decide the issue before them.

52. Third and, in any event, he submitted that the Court should not shy away from a thorough review of a decision even if it was taken by experts on a matter requiring specialist expertise. In **R (British Academy of Songwriters, Composers and Authors) v Secretary of State for Business, Innovation and Skills** [2015] EWHC 1723 (Admin), Green J said, at paragraph 144:

> "144 … It is an error to suggest that simply because the subject matter of a decision, or the evidence used to justify it, is "economic" or "technical" that courts should recoil in terror and move gratefully into judicial reticence mode by reference to "margin of appreciation". If this were the judicial default position courts would find it hard indeed to hold in favour of claimants in clinical negligence cases where, almost invariably, the case turns on complex scientific evidence. In **R (Rotherham MBC)** [2015] PTSR 322 the Supreme Court recognised the dangers of "judicial timidity": para 65, per Lord Neuberger of Abbotsbury PSC. Decisions of the utmost importance to individuals, to companies and to society are routinely "economic" and "technical" and errors in those decisions should be as much susceptible to judicial review as other equivalent but less technical decisions. There should be no lacuna in judicial review simply because the nature of the decision under challenge is a difficult one."

53. Mr Stilitz QC, for the Defendant, takes issue with the points made by Mr Wise QC.

54. As for the first one, Mr Stilitz QC submits that, without wishing to downplay the impact of PKU on a sufferer, there is already a treatment available, in the form of dietary management, and this case is not concerned with a life and death matter.

55. In addition, Mr Stilitz submits that it would be wrong to assume that the use of the standard HTA assessment process means that there is no hope of any recommendation by NICE in favour of Kuvan. Put bluntly, the issue is cost-effectiveness. Whilst the manufacturer's list price of Kuvan might suggest that there is no real prospect of it passing the "cost per QALY gained of up to £30,000" test, in reality, he submits, the position is much more nuanced. The cost saving from the reduction in, or elimination of, protein substitutes resulting from the use of Kuvan would be set off against the cost of Kuvan in the cost-effectiveness evaluation. These can cost £14-18,000 per year for a single patient. Moreover, the evidence of behalf of NICE states that in practice manufacturers are often willing to offer very substantial discounts to the NHS, sometimes as much as 80% off list price, because the NHS is such a big customer and because if a drug is recommended for use in the NHS this may well open it up for markets in other countries. Though NICE was not in a position to say anything about the negotiations that had taken place with BioMarin in relation to Kuvan, Mr Stilitz QC submitted that it would be wrong to assume that there was little or no chance of Kuvan being recommended by NICE if the HTA route was used. If BioMarin were prepared to offer a large discount, it may well be possible that Kuvan would be recommended under HTA. He suggested that the fact that BioMarin withdrew from the process once the judicial review proceedings were underway might be explained by the fact that BioMarin may feel that they would expect to be able to negotiate a higher price for Kuvan from the NHS if the HST route was used, not that BioMarin felt that the HTA route was hopeless. I should add that there was no evidence whatsoever before me that the Claimant or those who supported her were in league with BioMarin in any way, and there was no evidence from BioMarin, or from anyone else, to support Mr Stilitz's suggestion about its possible motivation.

56. The thrust of Mr Stilitz QC's submissions on this issue was that it would be wrong for the Court to decide on the intensity of review issue on the basis that the choice of

assessment process would make all the difference between success and failure for Kuvan obtaining a recommendation.

57. As for the second and third considerations, Mr Stilitz submitted that it is well-established that a decision of a specialist body exercising expert judgment should be subject only to a light touch review: see **R (Campaign to End All Animal Experiments) v Secretary of State for the Home Department** [2008] EWCA Civ 417, per May LJ at paragraph 1; **R (Centro) v Secretary of State for Transport** [2007] EWHC 2729 (Admin) per Beatson J at paragraph 36, and **R (London and Continental Stations and Property) v The Rail Regulator** [2003] EWHC 2607 (Admin), per Moses J, at paragraphs 27-34.

58. The Defendant's Summary Grounds for Resisting the Claim also pointed out that, immediately after the passage at paragraph 144 of the **Songwriters** case relied upon by the Claimant, Green J went on to say:

> "145. But this does not imply that the Courts will substitute their own view of the correct decision for that of the decision maker. There is a wealth of difference between the court exercising proper supervisory jurisdiction over an "economic" decision and a court acting as the decision maker itself."

59. In my judgment, the appropriate level of intensity of review for the irrationality challenge in the present case falls between the submissions made by the parties.

60. On the one hand, I think that Mr Wise QC is right to emphasise the importance of this issue for the Claimant and others in a similar position to her. Even though the availability of Kuvan may not be literally a matter of life of death for responsive sufferers of PKU, I think that it is clear, on the evidence, that the benefits, in terms of quality of life improvements, of the availability of Kuvan on prescription are very significant indeed.

61. Also, whilst I accept that it is not a "given" that Kuvan would not be recommended by NICE, if the HTA route were used, in my judgment the fact remains that the prospects would have been substantially improved if the HST route had been available.

62. Accordingly, I think that Mr Wise QC is right that the impact of the decision under challenge was very significant for the Claimant and for others in the same position, and the intensity of review should reflect this.

63. On the other hand, I think that Mr Stilitz QC is right that the criteria in question are matters that, to some extent at least, require the exercise of expert judgment, and the use of expert knowledge.

64. In **International Transport Roth GmbH v The Home Secretary** [2003] QB 728 (CA), at paragraph 87, Laws LJ said:

> "Greater or lesser deference will be due according to whether the subject matter lies more readily with actual or potential expertise of the democratic powers or the courts."

65. Though NICE is not a "democratic power", it is a body which has been vested by Parliament with responsibility for this matter. Those charged by NICE with taking this decision will

generally be in a better position than a judge to make the evaluations that are inherent in the criteria.

66. Further assistance on the right approach to be taken by a Court can be obtained from **R (Campaign to End All Animal Experiments) v Secretary of State for the Home Department** [2008] EWCA Civ 417. In that case, the Court of Appeal was concerned with a "substantial severity" limit in Guidance about the treatment of animals. The guidance described the substantial severity limit as being reached by "Protocols that may result in a major departure from the animal's usual state of health or well-being." "Major" was contrasted with "mild" and "moderate". At paragraph 57 of the judgment, May LJ said:

> "The scientific expert must form a judgment as to which of these categories should apply. Much of the language is not technical, but the scientist will not derive much real help from the lawyer in making the necessary judgment. This is not, after all, a tax statute. Pages of cerebration about the meaning of ordinary words, "mild", "moderate", "major" and "substantial" are not likely to help."

67. At paragraph 60, May LJ said;

> "The judge correctly stated that in practice there had to be an exercise of judgment; and that the views of scientists and veterinary surgeons who make the judgments must be given proper respect up to the point at which their judgment can be shown to be vitiated by legal error or clearly wrong."

68. It is true that the questions to which the three relevant criteria give rise do not involve highly technical scientific questions. However, they raise questions of degree which someone who is familiar with the approach to, and treatment of, rare and very rare conditions in the NHS will be better placed than a judge to answer. So, for example, the question whether the target patient group is distinct for clinical reasons is a question for which expertise and experience will help to provide the answer.

69. As Green J made clear in the **Songwriters** case, this does not mean the Court should simply defer to the decision-makers, but I think that it is appropriate to bear in mind that this decision involved issues of judgment and was vested in a group of people with particular experience and expertise to take it. The views of the decision-makers should be given proper respect, whilst also bearing in mind, as I have said, that the impact of the decision was very significant on those whose chances of obtaining Kuvan on the NHS were thereby reduced.

70. I also bear in mind that, wherever one ends up with the issue of intensity of review, the central question, to which intensity of review is relevant, is whether the decision was irrational or perverse. There is always a high threshold for irrationality cases.

THE CHALLENGE IN RELATION TO CRITERION 2

71. It is convenient to begin, as the parties did in their submissions, with Criterion 2, the second of the three criteria that were "failed" by Kuvan. This was that "The target patient group is distinct for clinical reasons".

72. The decision-making group, on behalf of NICE, decided that this criterion was not met because, "To be clinically distinct the total population should be an entire

population in its own right and not a subset of a larger group of patients. In the case of this population patients eligible for sapropterin are a subset of patients with PKU and only distinct from the wider PKU population because they can be identified [as responsive] either by a short trial using sapropterin, or through gene mutation analysis."

73. Mr Wise QC, for the Claimant, had three points as to why this conclusion was an error of law.

74. First, he submitted that the way that the decision-making group took its decision was inconsistent with the criterion, ie they misinterpreted the criterion. He submitted that the criterion does not say that, in order to be distinct, the target group has to be an entire population in its own right, or that it cannot be a subset of patients with a particular condition, such as PKU. Even if the target group of patients is a sub-set of patients with PKU, it is still clinically distinct.

75. Second, Mr Wise QC submitted that NICE's conclusion is irrational, because it simply does not make sense to interpret "distinct" as meaning "entire population". There is no logical reason why a "distinct" patient group cannot be a subset of patients with a particular condition.

76. Third, Mr Wise QC submitted that the approach taken by NICE was inconsistent with the purpose of this criterion, because its purpose was to ensure that highly specialised technologies, which are likely to be expensive, are given to those who need them, and are not given to patients with no clinical need for them.

77. Mr Wise QC also relies upon the witness evidence of Professor MacDonald. Professor MacDonald said that patients with PKU who may benefit from Kuvan can be identified before a treatment with Kuvan is commenced. At paragraph 20 of her second statement, Professor MacDonald said:

> '… in summary, in order to identify BH4 [ie Kuvan] responsive patients effectively and efficiently, it requires a 2 stage process: 1) mutation analysis – this will exclude patients with two null mutations who are unlikely to respond to BH4; followed by 2) a BH4 loading test. This means that BH4 responsiveness will be confirmed before treatment with BH4 commences.'

78. For NICE, Mr Stilitz QC submitted that a target group was clinically distinct, for the purposes of this criterion, if its members could be identified as such beforehand. This is because it is important, before the HST process is used, that it is clear how many people will benefit of the treatment, so that the cost of recommending the treatment can be assessed.

79. Mr Stilitz QC drew my attention to the European Medicines Authority's ("EMA's") Summary Of Product Characteristics for Kuvan. This formed the basis for its market authorisation. Paragraph 4.1 of this document says that Kuvan is indicated for the treatment of hyperpheynlalaninaemia (HPA) in adults and paediatric patients of all ages with PKU who have been shown to be responsive to such treatment. Responsiveness is defined in paragraph 2 which says, in relevant part:

> "Response to this medicinal product is determined by a decrease in blood phenylalanine. Blood phenylalanine levels should be checked before administering Kuvan and after 1 week of use at the recommended starting dose. If an unsatisfactory reduction in blood phenylalanine levels is observed, then the dose can be increased weekly to a maximum of 20 mg/kg/day, with continued weekly monitoring of blood phenylalanine levels over a one month period. The dietary phenylalanine intake should be maintained at a constant level during this period.
>
> A satisfactory response is defined as a greater than or equal to 30% reduction in blood phenylalanine levels, or the attainment of the therapeutic blood phenylalanine goals defined for an individual patient by the treating physician. Patients who fail to achieve this level of response within the described one month test period should be considered non-responsive, these patients should not be treated with Kuvan and administration of Kuvan should be discontinued."

80. Mr Stilitz QC submitted that this shows that the target patient group cannot be defined in advance, and consists simply of those who achieve a 30% reduction in blood Phe levels on test, or who meet bespoke goals set by the treating doctor.

81. In my judgment, Mr Stilitz QC's submission is correct. The evidence put before me, both by Professor MacDonald and by Mr Meindert Boysen, Director of the Centre for Health Technology Evaluation at NICE, demonstrates that it is possible to use gene mutation analysis to exclude some PKU patients altogether. It is clear from the gene mutation analysis alone that this subset of PKU patients will not be responsive to Kuvan. However, for those PKU patients who are not ruled out by gene mutation analysis, it is necessary to carry out the test described in the EMA document to decide if they will be sufficiently responsive to benefit from Kuvan. The key point, in my view, is that there is no clear bright-line cut off between those who will benefit from Kuvan and those who will not. The definition of a satisfactory (or sufficient) response is that it applies to patients who display a greater than or equal to 30% reduction in blood Phe levels, or who achieve the goals set for them by their treating physician. This is a matter of degree. The upshot is that, as Mr Stilitz QC submitted, the target group is defined solely by Kuvan response, not by anything else, and, even then, there is an element of subjectivity in it, both because the 30% line was drawn at the place where it was felt right to draw it and because responsiveness is, in the final analysis, a matter for the subjective decision of the treating physician.

82. Against that evidential background, I come to the three grounds of challenge relied upon by Mr Wise QC.

83. First, he submits that in treating a clinically distinct group as being one that comprises an entire patient population that can clearly be identified before being eligible for an appropriate treatment prior to the start of that treatment, NICE has misinterpreted and therefore misapplied the criterion. In my judgment, this is not the case. If you do not know which members of a group of patients with a particular disease will benefit from a treatment until you test the treatment on them, they are not "clinically distinct". If the criterion was intended to require that there is a test which shows whether patients in a wider group are sufficiently responsive to the treatment, then the wording used

would have been completely different. The "clinically distinct" criterion is intended to ensure that NICE can work out, in advance, which groups of patients will benefit from the treatment. This enables NICE to carry out the cost/benefit analysis. If this is not clear, NICE cannot do so.

84. In my judgment, this interpretation of "clinically distinct" is consistent with the objective and normal meaning, in accordance with the language used, read in its proper context.

85. Once it is accepted that NICE interpreted and understood the criterion correctly, in my judgment, the irrationality challenge falls away. The pool of patients consists simply of those who are responsive to the treatment. There is no clear dividing line between those who are to be regarded as responsive: ultimately it depends on whether the treating physician thinks that they are. There is nothing that is "clinically distinct" in this pool of patients, as the phrase would normally be understood. Moreover, I agree with Mr Stilitz QC that a group is not "clinically distinct" if, as here, it cannot be identified until its members are subjected to a trial. It is true that some potential candidates can be excluded even before a trial by gene mutation analysis, but the fact remains that the dividing line between those who are in the target group and those who are not is whether or not the test treatment shows that they are responsive, to the necessary degree.

86. Put shortly, if the target group simply consists of those who benefit from a treatment beyond a certain threshold, this is not a group that is "clinically distinct".

87. As for the third point taken by Mr Wise QC, in my judgment the approach taken by NICE was consistent with the purpose of the criterion. It means that the HST process is used only in circumstances where the target patient group for the treatment is identifiable in advance because it is distinct for clinical reasons. This means that NICE can carry out the cost/benefit analysis at the appraisal stage. As Mr Boysen said in his evidence, the HST process is exceptional and departs from the level playing field that is otherwise applied by NICE to health technologies through the HTA process.

88. As Mr Stilitz QC and Mr White put it in their skeleton argument, if a drug is to be routed through the HST, and therefore may cost the NHS a very large amount per patient, it is crucial for cost control that it has a clearly defined patient population. An ill-defined target group, at the appraisal stage, would undermine this objective.

89. A second rationale for this criterion was put forward by NICE. This was that the clinical distinctiveness criterion prevents the system being "gamed" by pharmaceutical companies by the manipulation of marketing authorisations. Since a company has control over what authorisations it applies for, a company could, in theory, seek to bring a drug within the HST process by subdividing a drug into versions for different patient groups. This risk is avoided by requiring drugs that are routed through HST to have a target population that is clinically distinct.

90. There is no suggestion that there has been any "gaming" in relation to Kuvan. Nonetheless, in my judgment this second rationale provides some supporting justification for this criterion.

91. It is important to bear in mind also that the fact that a treatment is not assessed under HST does not mean that it will not be considered for recommendation by NICE at all: rather, it means that the assessment process will be the same that applies to the vast majority of drugs and treatments.

92. As it is accepted by the Claimant that she has to be successful in her challenge to all three "failed" criteria, my conclusion in relation to Criterion 2 means that the judicial review challenge must fail. Nevertheless, I will go on to consider the arguments in relation to the decisions on the other two "failed" criteria.

THE CHALLENGE IN RELATION TO CRITERION 4

93. This criterion is that the technology is expected to be used exclusively in the context of a highly specialised service.

94. The TSOR decision recognised that the reference to a "highly specialised service" was capable of having different meanings attributed to it. The phrase has been given various different meanings by NHS England in public facing documents. The TSOR drew a distinction between the words "specialist" and "specialised". The word "specialist" refers to the level of expertise delivered within a service, with "highly specialist" meaning a very high level of expertise. In contrast, "specialised" and "highly specialised" refer to the commissioning models used by NHS England to commission specialised and highly specialised services, respectively. The TSOR noted that highly specialised commissioned services require national co-ordination for a distinct group of patients where it was agreed when the service was commissioned that national coordination would result in significantly improved outcomes that would be delivered in a more efficient set up.

95. The decision-making group for the TSOR decided that it was this second definition which was to be used for the purposes of the criterion: the treatment must be used in a service that is commissioned as a highly specialised service model.

96. On that basis, Kuvan did not satisfy the criterion. The TSOR said that NHS England provides treatment and services to patients with inherited metabolic disorders in more than 10 specialist metabolic centres across England. PKU is one of the services covered by this service, and the TSOR noted that this service is "highly specialist", in the sense that it is delivered with a very high level of expertise. However, it is not commissioned or organised as a highly specialised service. The specialist metabolic centres are not part of a highly specialised service, and so Kuvan does not satisfy this criterion.

97. Mr Wise QC put forward four grounds of challenge to the approach adopted by the decision-making group to this criterion.

98. First, he submitted that the service for PKU patients that is currently commissioned by NHS England is one in which highly specialist practitioners are providing a Metabolic Disorder Service. He submits that, on any sensible and common-sense understanding, a service provided by highly specialist practitioners must be a highly specialised service.

99. Second, Mr Wise QC points out that services for PKU patients are delivered as part of the "highly specialist metabolic disorder services (adults and children)" which are listed in Manual For Prescribed Specialised Services 2018/19 ("the Manual"), published by NHS England. He submits that this means highly specialist metabolic disorder services, which includes treatment of PKU, are therefore included within the highly specialised services commissioned by NHS England. It does not matter that PKU services are provided as part of a larger group of highly specialist services.

100. Third, Mr Wise submits that if treatment with Kuvan were to be approved, it would inevitably be provided in a specialist service organised or arranged for the purpose.

101. Fourth, Mr Wise QC submits that, in any event, the criterion is not absolute. It says "expected" to be used exclusively in the context of a highly specialised service, not "will" or "would" be used in such a service.

102. I do not accept these submissions.

103. As for the first ground, the starting point is that there is a key difference between a highly ***specialist*** service, on the one hand, and a highly ***specialised*** service, on the other. A highly specialist service is one that involves a very high level of expertise. There is no doubt that treatment for PKU is provided by a highly specialist service. This is made clear by paragraph 64 of Schedule 4 to the 2012 Regulations, which refers to the obligation by the Board to arrange for the provision as part of the health service of "Highly specialist metabolic disorder services" (see paragraph 36, above). This covers the provision of treatment for PKU.

104. However, in my judgment, Mr Stilitz QC is right to submit that, in this context, "highly specialised services" means something else. It is a reference to the commissioning model. Somewhat unhelpfully, the 2017 Guidance does not itself define "highly specialised services". However, in my judgment the Defendant is right that this is a term of art and is used within the NHS to refer to services that are commissioned as highly specialised services. In other words, it is the way that the services are commissioned that make them highly specialised, rather than the degree of expertise of those who provide the services. Just because something is recognised in Schedule 4 to the 2012 Regulations as being highly specialist, or because it is, in the common usage of the phrase, a highly specialist service, does not mean that it is a "highly specialised service" for the purposes of this criterion.

105. The technical meaning of "highly specialised services" within the context of the health service is most clearly explained in the Manual For Prescribed Specialised Services 2018/19 ("the Manual"), published by NHS England. This is the detailed technical document that describes which elements of specialised services are commissioned by NHS England and which by CCGs. At page 12, the Manual states as follows:

> "Definitions of "specialist" and "specialised"
>
> In this document, the term "specialist" refers to a level of expertise delivered within a service (with "highly" specialist meaning a very high level of expertise). The terms "specialised" and "highly specialised" refer to the commissioning models used by NHS England

> to commission highly specialised and specialised services respectively."

106. One of the services listed in the Manual is "Highly specialist metabolic disorder services (adults and children)". PKU is one such disorder. The Manual says that these services include services provided by Highly Specialist Disorder Centres, and that NHS England (rather than CCGs) commission highly specialist metabolic disorder services for patients with specialist inherited metabolic disorders from Highly Specialist Metabolic Disorder Centres, including services delivered on an outreach basis as part of a provider network.

107. In his witness statement on behalf of the Interested Party, Mr James Palmer, Medical Director for Specialised Services at NHS England, said:

> "The distinction between "highly specialist services" and "highly specialised services" is an important one. "Highly specialist services" are those services identified to be delivered through a national commissioning function rather than by specialist service commissioning enacted through the NHS England regions. [Highly] specialised services are provided to a smaller number of patients compared to specialised services, usually no more than 500 patients per year. For this reason they are best delivered nationally through a very small number of centres of excellence. Examples of highly specialised services include liver transplant services, and proton beam therapy for specific cancer treatments."

108. In other words, the specialised services, listed in the Manual, are so specialised that they are commissioned by NHS England rather than by CCGs. However, most of them are specialised services that are commissioned through NHS England regions. A small sub-group of services are so highly specialised that a different commissioning model is used: these are the "highly specialised services" that are commissioned through a national commissioning function, rather than through the regions, and that are delivered at a very small number of centres of excellence. Dr Palmer said that there are a total of 60 services that are commissioned nationally as "highly specialised services".

109. Dr Palmer said that it does not follow that every service that might benefit from national co-ordination is or should be commissioned as a highly specialised service. NHS England publishes, more or less annually, a list of highly specialised services (the "Highly Specialised Services List"). The most recent list is dated December 2018. This document explains why there is a highly specialised commissioning model, as follows:

> "Each highly specialised service is provided to a smaller number of patients compared to specialised services; usually no more than 500 patients per year.
>
> Due to the small number of patients accessing such services, they are most appropriately delivered and co-ordinated nationally through a very small number of expert centres. This model of delivery makes it easier to recruit appropriately qualified professionals and to ensure that

> they receive the level of training needed to maintain their expertise. It also permits the most effective use of resources by efficient management of patient care and ensuring access to the technology necessary to allow delivery of the services."

110. Against this background, and in this context, it is clear, in my judgment, that the reference in the criterion to "highly specialised services" is a reference to services that are commissioned nationally by NHS England as a highly specialised service, and which are listed in the Highly Specialised Services List. A service is not a "highly specialised service" simply because it is, in colloquial terms, highly specialist or specialised, nor because it is defined in the 2012 Regulations as a highly specialist service. In this context, "highly specialised" and "highly specialist" mean something different. Once again, a service is not "highly specialised" just because it is listed in the Manual. This is how the wording would be understood by the primary target readership for the 2017 Guidance.

111. Neither treatment for PKU, in particular, nor treatment for highly specialist metabolic disorders, in general, is on the Highly Specialised Services List. Services in relation to PKU are not commissioned nationally as "highly specialised services" by NHS England. This means, in my judgment, that the decision-making group was entitled to take the view that Kuvan did not satisfy this criterion. I should add that the great majority of the services that are listed in the Manual are not commissioned as highly specialised services. Such services are the exception.

112. There is a logic and rationale behind making use of this criterion for the purposes of allocating a treatment to the HST process. The restriction to "highly specialised services" means that the treatment will be commissioned through an appropriate model. The fact that the treatment, if recommended, will be commissioned under the highly specialised services treatment model means that there will be close, and central, supervision of the prescription of the drugs or other treatment. One can readily see that NICE might not have made use of this criterion, but it is for NICE, not the courts, to set the criteria (within lawful limits) and is not suggested by the Claimant that NICE was not entitled to adopt this criterion. In my judgment, NICE was entitled to adopt it.

113. The view that this criterion is focused upon whether the treatment, if recommended, would be commissioned as a highly specialised service, is supported by paragraph 30 of the 2017 Guidance, which states that where NICE recommends a treatment under HST, the relevant guidance will be phrased as follows:

> "[Technology x] is recommended as an option for the treatment of [disease y] in the context of national highly specialised commissioning by NHS England."

114. I should add that Mr Wise QC submits that his proposed interpretation of "highly specialised services" is supported by the definition of "highly specialised health technology" in regulation 2 of the 2013 Regulations (see paragraph 33, above). He submits that Kuvan satisfies the definition of a "highly specialised health technology" and so a service providing it must necessarily come within the definition of a "highly specialised service". I do not agree. The relevant question for the purposes of the criterion is whether the service, not the technology, is highly specialised. As I have

said, this depends upon whether it is commissioned by NHS England as a highly specialised service.

115. The second ground relied upon by Mr Wise QC in relation to this criterion is that services for PKU patients are delivered as part of the "highly specialist metabolic disorder services (adults and children)" which are listed in the Manual. I have already dealt with this point. In my judgment is clear that the mere fact that a service is listed in the Manual does not mean that it is a "highly specialised service" for the purpose of the third criterion in paragraph 28 of the 2017 Guidance.

116. The third ground relied upon by Mr Wise QC looks to the future. He submits that if treatment with Kuvan were to be approved, it would inevitably be provided in a specialist service organised or arranged for the purpose. This is not borne out by the evidence. In his witness statement, Mr Palmer said that he would not expect treatment with Kuvan to be placed on the Highly Specialised Services List, if it were to be commissioned. He said that neither the diagnosis for PKU, nor the administration of the drug (oral administration at home) provides a degree of complexity that would require national co-ordination. Mr Palmer said that the mainstay of care in the UK remains the expert dietary advice and support for patients that is provided by the 19 current providers of the specialist metabolic disorder service. If Kuvan were commissioned by NHS England, the existing specialist metabolic disorder service would not need the support of a highly specialised service.

117. Finally, Mr Wise QC submitted that, in any event, the criterion is not absolute. It says "expected" to be used exclusively in the context of a highly specialised service, not "will" or "would" be used in such a service. The fact remains, however, that, on the evidence, Kuvan is not expected to be used in the context of a highly specialised service.

118. For these reasons, I conclude that NICE acted lawfully in concluding that the fourth criterion was not met.

THE CHALLENGE IN RELATION TO CRITERION 1

119. This criterion is that the target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS.

120. This criterion does not make use of absolute criteria. Rather, it requires the decision-maker to make a value judgment, namely whether the treatment will usually be concentrated in "very few" treatment centres in the NHS. There is no definition of "very few" and this is necessarily a matter of judgment, and is dependent on context.

121. In the TSOR, the decision-making group noted that NHS England's clinical commissioning policy of December 2018 identified the potentially eligible population for Kuvan as approximately 500 individuals, with 300-350 patients to access treatment over time, and an estimated additional 28 patients to require treatment per year. The TSOR noted that patients with PKU eligible for Kuvan would be able to receive this treatment in the "more than 10" specialist metabolic centres across England where NHS England currently provides treatment and services to patients with inherited metabolic disorders.

122. The Defendant submitted that the "very few centres" test must be assessed by reference to the relevant context, and that this includes that the vast majority of highly specialised services on the Highly Specialised Services List, 47 out of 60, are provided at four or fewer centres. A small number, 11, are offered at five or six centres, of which nine are for complex organ transplantation services and the complex intensive care treatment of ECMO (extracorporeal membrane oxygenation, a complicated form of life-support). The other two highly specialised services provided at more than four centres are the primary malignant bone tumours service and the lysosomal storage disorders service. Neither of these is provided at more than eight centres. (The lysosomal storage disorders service was designated for national commissioning in 2005, before the 2012 NHS reforms and the establishment of NHS England.) Of the 11 highly specialised services that are provided in more than four centres, none, apart from the lysosomal storage disorders service, concerns more than 500 patients.

123. The Defendant also pointed out that the Rare Diseases Advisory Group ("RDAG"), a non-executive committee of NHS England which is responsible for making recommendations on which highly specialised services or technologies should be prioritised for investment, defines "highly specialised services" as being those prescribed services concerning usually no more than 500 patients and/or provided in four or fewer specialist centres in the UK. The terms of reference for the RDAG also provide that it is the responsibility of the RDAG to provide advice to NHS England and the devolved administrations on the most appropriate service to deliver those highly specialised technologies that receive a positive technology appraisal determination from NICE.

124. Mr Palmer's evidence was to the effect that NHS England commissions highly specialist metabolic disorder services (adults and children) as a specialised service contracting with 19 providers for the full range of services within that definition. There is no specialised or highly specialised service for PKU. Provision is made as part of the wider specialist metabolic disorder services. The best estimate of those with PKU in England is between 4,000 and 5,600, of whom the number of individuals under regular follow-up is about 2,000. Mr Palmer said that NHS England would not consider it appropriate to provide highly specialist metabolic disorder services for these patients from as few as four centres, and that NHS England will continue to maintain access to these services across all 19 current providers. Whilst it is true that it is anticipated that only around 500 PKU patients would benefit from Kuvan, NHS England would not commission a highly specialised service exclusively for the purpose of providing Kuvan to these patients, because they would also require the broader services and expertise available from the existing highly specialist metabolic disorder providers. As I have said, Mr Palmer said that the mainstay of care in the UK remains the expert dietary advice and support for patients that is provided by the 19 providers of the specialist metabolic disorder service.

125. The Claimant's witness, Professor MacDonald says that it is an exaggeration to say that there are 19 centres for highly specialist metabolic disorders. There is a "hub" and "spoke" system. There are 9 full-service, "hub" centres, and a further 10 satellite "spokes", in local hospitals, which do not provide a full service and which rely very heavily on the support and direction provided by the "hub" centres. I accept this evidence and therefore, I address the Claimant's argument in relation to this criterion

on the basis that treatment for highly specialist metabolic disorders is concentrated in 9 full-service centres, with a further 10 "spoke" centres.

126. Mr Wise QC submits that the TSOR does not explore what is meant by "usually concentrated in very few centres" and by failing to understand what is meant by this in the context of highly specialised services, the TSOR is bound to have made an arbitrary and so irrational decision. The number of hospitals providing the service is likely to be "very few" when considered in the context of the well over 1,000 NHS hospitals in the country. Mr Wise QC also submits that NICE erred in law in that it did not consider how many centres it expected that treatment with Kuvan would actually be concentrated in. He said that NICE had made up a definition to suit itself, and so fell into the Humpty Dumpty trap identified by Lord Reed in **Tesco v Dundee.** He also said that NICE failed to give this criterion a meaning that was consistent with the statutory purpose of the HST process, which is that there is a presumption that any technology/treatment for a rare or very rare condition found in Schedule 4 to the 2012 Regulations should be considered through the regulation 8 HST process unless there are good reasons not to do so.

127. In considering the challenge to the decision in relation to this criterion, it must be recalled that the Claimant does not challenge the right of NICE to determine criteria to use when selecting the appraisal process for a treatment, and the Claimant does not challenge the criteria themselves. Rather, the challenge is to NICE's interpretation of its own criteria, and to the alleged irrationality of its decision.

128. The main thrust of the Claimant's submission in relation to this criterion is that NICE has placed an impermissible gloss on the criterion, by drawing on the definition of "highly specialised services" used by the RDAG, and on the figures for the number of centres at which centrally-commissioned highly specialised services are currently provided by NHS England, to determine what the phrase "treatment will usually be concentrated in very few centres" means for the purpose of this criterion. The Claimant submits that the question of "very few centres" should be evaluated by reference to the number of NHS hospitals in England.

129. In my judgment, NICE was entitled to interpret this criterion in the way that it did. As I said earlier in this judgment, when reviewing the authorities on the correct approach to the interpretation of non-statutory guidance, the meaning of a passage in a policy document should be interpreted objectively in accordance with the language used, subject to the important caveat that the passage must be read in its proper context. In my view, the relevant context, for present purposes, is that the treatment must usually be concentrated in broadly the same number of centres as highly specialised services are normally provided in. This gives some content to the words "very few", which are otherwise almost entirely a matter of opinion. Applying this approach, "very few" means, normally, four or fewer, though there are some highly specialist services that are provided in a slightly higher number of centres.

130. In my judgment, this is a good example of a type of case in which the specialist decision-makers are better placed than anyone else to form a view about what general words (such as "very few") mean in the particular context. This is not a case of the decision-maker making up a decision to suit itself, which bears no relation to the language used. Rather, it is a case of a decision-maker taking into account context to give meaning to a general form of words. To use a phrase that is used in other areas

of the law, the meaning ascribed by the decision-making group to this phrase "goes with the grain" of the words used.

131. Furthermore, the interpretation applied by NICE to this criterion did not run counter to the spirit and purpose of the twin-track HTA and HST appraisal processes. There is no basis for the proposition that the statutory scheme presumes that any technology/treatment for a rare or very rare condition found in Schedule 4 to the 2012 Regulations should be dealt with under HST, unless there are good reasons not to do so. Mr Wise QC readily accepted in his submissions that just because a treatment is for a rare or very rare condition found in Schedule 4, it does not automatically follow that it must be appraised under HST, though he submitted that it should be appraised under HST unless there is a cogent reason not to do so. He also accepted that NICE was entitled to set its own criteria for deciding whether to proceed under HTA or HST. This criterion was designed to keep a tight rein on the availability of the HST process, and to ensure that any treatments that were assessed under HST would be tightly controlled if they were recommended. In my judgment, these were legitimate objectives, and this criterion is consistent with those objectives. The objectives are consistent with the reasons why the "highly specialised services" commissioning model is used (see paragraph 109, above). In an ideal world, there would be no restrictions on the availability on the NHS of very useful drugs such as Kuvan, but we do not live in an ideal world, and it is NICE's responsibility to decide which drugs to recommend for use in NHS England, against the background of a finite budget. In exercising that responsibility, NICE must have regard, inter alia, to the broad balance between the benefits and costs of the provision of health services in England, and must exercise its functions effectively, efficiently and economically (section 233 of the 2012 Act, set out at paragraph 20, above). This means, unavoidably, that NICE must make difficult decisions which will disappoint people who have every good reason to hope that a drug or treatment will be recommended for use in the NHS in England.

132. Applying this interpretation to the issue before the decision-making group, I do not think that it can be said to be irrational for the group to decide that a treatment that was provided at 9 hub centres and, at least partially, at a further 10 spoke centres, would not be a treatment that will usually be concentrated in very few centres in the NHS. Even if one ignores the 10 spokes for present purposes, it was not irrational for the decision-making group to conclude that a treatment that would be provided at 9 centres would not be one that would be concentrated in very few centres in the NHS.

133. As for the point that NICE did not apply its mind to the question whether Kuvan would be provided at all of the current centres for highly specialist metabolic disorders, in my judgment it is clear that, if Kuvan were commissioned, it would be prescribed to patients, at least, at all of the current 9 hubs. Kuvan is a tablet which is taken orally by the patient at home. It does not need specialist equipment or expert application, although, as Professor MacDonald explained, patients and their carers need to be counselled, detailed assessments and meticulous blood Phe monitoring must be undertaken, and expert dietetic care provided with corresponding adjustments made to the amount and type of protein permitted in the diet. I do not see why this could not be done, at least, in the 9 hubs which currently deal with highly specialist metabolic disorders. The question whether Kuvan would be limited to only some of the current centres, self-evidently, did not arise. It follows that NICE did not fail to

ask itself the right question in relation to this criterion, in the sense referred to by Lord Diplock in **Secretary of State for Education and Science v Tameside MBC** [1977] AC 1014, at 1065.

CONCLUSION

134. For the above reasons, this application for judicial review is dismissed.