Neutral Citation Number: [2025] EWCA Civ 1032

Case Nos: CA-2024-002295, 002325

IN THE COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE HIGH COURT OF JUSTICE, BUSINESS AND PROPERTY COURTS OF ENGLAND AND WALES, INTELLECTUAL PROPERTY LIST (ChD), PATENTS COURT
Mr Justice Meade
[2024] EWHC 1695 (Pat)

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 1 August 2025

Before :

LORD JUSTICE MOYLAN
LORD JUSTICE ARNOLD
and
LORD JUSTICE SNOWDEN

- -

Between :

MODERNATX, INC.	**Claimant/ Respondent**
- and -	
(1) PFIZER LIMITED **(2) PFIZER MANUFACTURING BELGIUM NV** **(3) PFIZER INC.** **(4) BIONTECH MANUFACTURING GMBH** **(5) BIONTECH SE**	**Defendants/ Appellants**

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- -

Tom Mitcheson KC and Alice Hart (instructed by **Taylor Wessing LLP**) for the **Pfizer Appellants**
Michael Tappin KC (instructed by **Powell Gilbert LLP**) for the **BioNTech Appellants**
Piers Acland KC and Stuart Baran (instructed by **Freshfields LLP**) for the **Respondent**

Hearing dates : 10-11 July 2025

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Approved Judgment

This judgment was handed down remotely at 10.30am on 1 August 2025 by circulation to the parties or their representatives by e-mail and by release to the National Archives.

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Lord Justice Arnold:

Introduction

1. This is an appeal by the Defendants ("Pfizer/BioNTech" or "PBNT" for short) against an order made by Meade J on 25 September 2024 in so far as it relates to European Patent (UK) No. 3 590 949 ("EP949"), which is owned by the Claimant ("Moderna"). The order was made following a 19 day trial in April and May 2024 that in effect amounted to two separate trials, one concerning EP 949 and one concerning European Patent (UK) No. 3 718 565 ("EP565"), which is also owned by Moderna. In a meticulous judgment running to 747 paragraphs dated 2 July 2024 the judge held that EP949 was valid and had been infringed by PBNT, whereas EP565 was invalid.

2. PBNT appeals with permission granted by the judge against his conclusion that EP949 is valid. There is no challenge to the claimed priority date of 1 October 2010. PBNT contends that EP949 lacks novelty over, alternatively is obvious in light of, International Patent Application No. WO 2007/024708 filed by the Trustees of the University of Pennsylvania and published on 1 March 2007 ("UPenn"). Other validity attacks advanced by PBNT before the judge are no longer pursued. Furthermore, Moderna now only relies upon claim 3 of EP949, whereas the judge also had to consider claim 5. Moderna was refused permission to appeal in respect of EP565 both by the judge and by myself.

3. EP949 concerns modified messenger ribonucleic acid (mRNA). The alleged infringements relate to PBNT's mRNA-based SARS-CoV-2 vaccine marketed under the trade mark Comirnaty.

Technical introduction

4. The following brief introduction to the science is based on the helpful explanation given to us by counsel for PBNT.

5. By 2010, there had long been a desire to try to get cells to express proteins of choice. This was commonly attempted by the use of fluorescent reporter proteins, which spanned wide areas of biomedical research, but there were also specific therapeutic targets, such as generating proteins for vaccination, or substituting proteins that were derived from faulty genes in conditions such as cystic fibrosis. One way of making a protein in a cell is by inserting deoxyribonucleic acid (DNA) into the cell, but the drawback of that is that the DNA has to enter the nucleus in the cell to be transcribed into mRNA and then translated into the protein. There is also a risk that, if you use DNA, that might be incorporated into the genome (i.e. the permanent DNA in the cell).

6. Scientists had thought about using mRNA instead. mRNA is the only type of RNA that can be translated into a protein. The advantage of using mRNA instead of DNA is that it does not need to enter the nucleus to be translated, and there is therefore no risk of it entering the genome permanently. It was also easier to synthesize than DNA. Nevertheless, there were problems, in particular with the stability of mRNA, if you inject it into the cell. Foreign RNA is recognised by the immune system and broken down because foreign RNA can be indicative of infection. In addition, mRNA, if it is injected, is not always translated successfully into protein.

7. A breakthrough in this field was made by the team led by Katalin Karikó and Drew Weissman at the University of Pennsylvania in the early 2000s. They first focused on the immune system pathways which attacked the RNA when it was injected into the cell. They noticed that some mRNAs, which contain naturally-occurring modified nucleotides, were not so susceptible to attack by the innate immune system. In these modified nucleotides some of the so-called "canonical" bases, referred to by the letters A, C, G and U, are replaced by modified versions of those bases. U stands for uracil. Uridine is a nucleoside consisting of uracil attached to ribose (a sugar). For present purposes the distinction between uracil and uridine can be ignored. So too can the distinction between a nucleoside and a nucleotide (a nucleoside with a phosphate group attached).

8. In their seminal 2005 paper ("Suppression of RNA Recognition by Toll-like Receptors: The Impact of Nucleoside Modification and the Evolutionary Origin of RNA", *Immunity*, 2005(23), 165-175 ("Karikó 2005")), Karikó and Weissman identified that the substitution of uridine with pseudouridine (Ψ) in mRNA, amongst other substitutions, reduced the innate immune response that was triggered by the introduction of exogenous RNA into cells. They also showed that the level of suppression of the immune response was proportional to the number of modifications. Using these modified nucleotides, the mRNA lasted longer in the cell and that also gave it more chance to be translated into protein.

9. In their 2008 paper ("Incorporation of Pseudouridine Into mRNA Yields Superior Nonimmunogenic Vector With Increased Translational Capacity and Biological Stability", *Molecular Therapy*, 2008, 16(11), 1833-1840 ("Karikó 2008")), Karikó and Weissman went further and showed that, not only was the immune response reduced for mRNA containing pseudouridine instead of uridine, but such mRNAs were also translated more efficiently, so that more protein was produced.

10. UPenn built upon Karikó 2005 and Karikó 2008. Karikó 2005 and Karikó 2008 were subsequently included in the citation of Karikó and Weissman for the Nobel Prize in Physiology or Medicine in 2023, but as the judge rightly noted at [12] that is hindsight knowledge.

The skilled person

11. The judge found at [263] that EP949 was addressed to a person skilled in the art with a knowledge of RNA biology, with a practical interest in improving the use of mRNA in relation to translation and immunogenicity in any of nine sub-fields. PBNT challenge this finding as part of their appeal on obviousness, and I shall consider it in that context. Neither party suggests that it is material to the issues on novelty.

The expert witnesses

12. Moderna called Professor Josef Rosenecker. PBNT called Dr Anton Enright. The judge found at [66] that, while both witnesses were helpful in assisting him to understand the technology involved, Prof Rosenecker was a more useful witness in helping him to understand how the skilled person would think and reason at the priority date of EP949. PBNT again challenge this finding as part of their appeal on obviousness, and I shall consider it in that context. As will appear, the challenge is linked to the challenge as to the attributes of the skilled person.

Common general knowledge

13. The judge set out the common general knowledge of the skilled person, which was almost entirely agreed, at [160]-[251]. Rather than repeat it all again, I shall take that exposition as read.

EP949

14. The judge summarised the disclosure of EP949 at [267]-[287]. For the purposes of the appeal the details do not matter. It is sufficient to note that it is common ground that it does not demonstrate that $m^1\Psi$-mRNA is superior to Ψ-mRNA.

15. As noted above, the only claim now in issue is claim 3, which is in the following terms:

> "An mRNA wherein 100% of nucleotides comprising uracil in the mRNA are replaced with nucleotides comprising N1-methyl-pseudouridine."

16. This claim has three elements: (i) an mRNA (as opposed to, in particular, another type of RNA, of which there are a number); (ii) wherein 100% of nucleotides comprising uracil are replaced with; (iii) N1-methyl-pseudouridine ($m^1\Psi$).

UPenn

17. UPenn is entitled "RNA Containing Modified Nucleosides and Methods of Use Thereof". The inventors are Karikó and Weissman. The specification (which, as is conventional, is double-spaced) runs to 291 paragraphs on 74 pages. There are also 78 claims spread over eight pages, and 16 pages of figures. The judge summarised the disclosure of UPenn at [294]-[306]. In the light of the arguments on the appeal, I would summarise it as follows, using the headings and sub-headings in the specification.

Field of the invention

18. The specification states at [001]:

> "This invention provides RNA, oligoribonucleotide, and polyribonucleotide molecules comprising pseudouridine or a modified nucleoside, gene therapy vectors comprising same, methods of synthesizing same, and methods for gene replacement, gene therapy, gene transcription silencing, and the delivery of therapeutic proteins to tissue *in vivo,* comprising the molecules. The present invention also provides methods of reducing the immunogenicity of RNA, oligoribonucleotide, and polyribonucleotide molecules."

Background of the invention

19. The background to the invention is briefly summarised at [002], with reference to the RNA Modification Database ("RNAMD").

Summary of the invention

20. This section of the specification begins:

> "[003] This invention provides RNA, oligoribonucleotide, and polyribonucleotide molecules comprising pseudouridine or a modified nucleoside, gene therapy vectors comprising same, gene therapy methods and gene transcription silencing methods comprising same, methods of reducing an immunogenicity of same, and methods of synthesizing same.
>
> [004] In one embodiment, the present invention provides a messenger RNA comprising a pseudouridine residue."

21. Each of paragraphs [005] to [0022] commences with the words "In another embodiment" and sets out more detailed features of the invention.

Brief description of the figures

22. This section describes the figures from [0023] to [0037]. These contain experimental data from Examples 1-15.

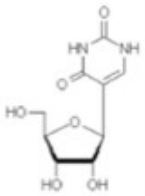
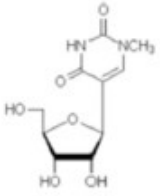
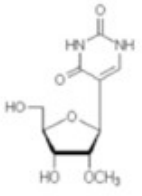
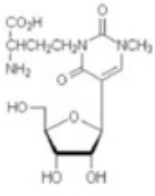
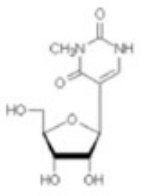
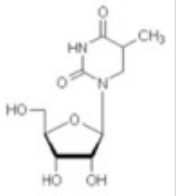
Detailed description of the invention

23. This section of the specification begins with [0038] and [0039], which essentially repeat [003] and [004]. All of the succeeding paragraphs from [0040] to [00175] either begin with, or include, the words "In another embodiment", and set out more detailed features of the invention.

24. At [0056] the specification states:

> "'Pseudouridine' refers, in another embodiment, to $m^1acp^3\Psi$ (1-methyl-3-(3-amino-3-carboxypropyl) pseudouridine. In another embodiment, the term refers to $m^1\Psi$ (1-methylpseudouridine). In another embodiment, the term refers to Ψm (2'-O-methylpseudouridine. In another embodiment, the term refers to m^5D (5-methyldihydrouridine). In another embodiment, the term refers to $m^3\Psi$ (3-methylpseudouridine). In another embodiment, the term refers to a pseudouridine moiety that is not further modified. In another embodiment, the term refers to a monophosphate, diphosphate, or triphosphate of any of the above pseudouridines. In another embodiment, the term refers to any other pseudouridine known in the art. Each possibility represents a separate embodiment of the present invention."

25. The skilled person would be aware that $m^1acp^3\Psi$, $m^1\Psi$, Ψm and $m^3\Psi$ are all naturally-occurring pseudouridine derivatives whereas m^5D is not a pseudouridine derivative (because the six-membered ring has a carbon atom and a nitrogen atom in swapped positions). The judge reproduced the helpful diagram below taken from Dr Enright's first report which sets out the names, abbreviations and structures of these five molecules together with Ψ.

Pseudouridine	1-methyl pseudouridine	2'-O-methyl pseudouridine	1-methyl-3-(3-amino-3-carboxypropyl) pseudouridine	3-methyl pseudouridine	5-methyldihydrouridine
Ψ	$m^1\psi$	ψm	$m^1acp^3\psi$	$m^3\psi$	m^5D
					

26. At [0069] UPenn states:

> "In another embodiment, the modified nucleoside of methods and compositions of the present invention is m^5C (5-methylcytidine). In another embodiment, the modified nucleoside is m^5U (5-methyluridine). In another embodiment, the modified nucleoside is m^6A (N^6-methyladenosine). In another embodiment, the modified nucleoside is s^2U (2-thiouridine). In another embodiment, the modified nucleoside is Ψ (pseudouridine). In another embodiment, the modified nucleoside is Um (2'-O-methyluridine)."

As explained below, these six modifications were tested in the experiments reported in UPenn.

27. In [0070] the specification sets out a further list of 92 modified nucleosides. These were not tested.

28. At [0074] the specification states that in different embodiments the following percentages of the residues of a given nucleotide (U, C, G or A) are modified: 0.1%, 0.2%, 0.3%, 0.4%, 0.5%. 0.6%, 0.8%, 1%, 1.5%, 2%, 2.5%, 3%, 4%, 5%, 6%, 8%, 10%, 12%, 14%, 16%, 18%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 80%, 90% and 100%.

29. In [0076] the specification states, among other things, that RNA may be variously transfer RNA, small nuclear RNA, ribosomal RNA, mRNA, anti-sense RNA, small inhibitory RNA, micro RNA and ribozymes.

30. At [00143] the specification states:

> "In another embodiment, a method of the present invention comprises increasing the number, percentage, or frequency of modified nucleosides in the RNA molecule to decrease immunogenicity or increase efficiency of translation…. "

Experimental details section

31. This section describes 31 examples. Examples 1-16 are experiments which have been carried out, the results of which are reported. Experimental data are reported for the

six modified nucleosides listed in [0069]. They vary in structure quite widely. There are *in vitro* experiments, experiments in cultured cells and *in vivo* experiments. The only modification taken into the *in vivo* experiments is Ψ. Examples 17-31 are "prophetic", meaning that they describe in the present tense experiments which have not yet been performed and predict the results that will be obtained.

32. For present purposes the most important of the actual examples are Example 2 (described at [00187]-[00195]), Example 7 (described at [00209]-[00218]) and Examples 13 and 14 (described at [00234]-[00246]).

33. Example 2 is a general method for the *in vitro* synthesis, or more specifically *in vitro* transcription, of RNA molecules with modified nucleosides. Four of the five RNAs used in this example are mRNAs. Although not spelled out, it would be apparent to the skilled person that the method involves replacement of 100% of the chosen nucleoside (A, G, C or U).

34. Example 7 shows that (to quote the title) "suppression of RNA-mediated immune stimulation is proportional to the number of modified nucleosides present in RNA". In a first experiment RNAs with three modified nucleosides, including Ψ, were tested with percentage replacements ranging from 1% to 100%. In a second experiment three oligoribonucleotides with modified nucleosides were tested. The specification summarises the results of the experiments at [00218] as follows:

> "In summary, each of the modifications tested (m6A, m5C, m5U, s2U, Ψ and 2'-O-methyl) suppressed RNA-mediated immune stimulation, even when present as a small fraction of the residues. Further suppression was observed when the proportion of modified nucleosides was increased."

35. Example 13 demonstrates (to quote the title) "enhanced translation of proteins from pseudouridine-containing RNA *in vivo*", while Example 14 shows that "pseudouridine modification enhances RNA stability *in vivo*". The specification summarises the results of these experiments as follows:

> "[00241] Thus, pseudouridine modification increases RNA translation efficiency *in vitro*, in cultured cells, and *in vivo* in multiple animal models and by multiple routes of administration, showing its widespread application as a means of increasing the efficiency of RNA translation.
>
> …
>
> [00244] These findings confirm the results of Example 12, demonstrating that ψmRNA is more stable than unmodified RNA.
>
> [00245] Further immunogenicity of ψ-mRNA was less than unmodified RNA, as described herein above (Figure 7 and Figure 12C, right panel).

> [00246] To summarize Examples 13-14, the 3 advantages of Ψ-mRNA compared with conventional mRNA (enhanced translation, increased stability and reduced immunogenicity) observed *in vitro* are also observed *in vivo*."

It is common ground that the skilled person would regard the results concerning Ψ-mRNA as very promising.

36. The only prophetic example which is relevant is Example 31:

> "**EXAMPLE 31: TESTING THE EFFECT OF ADDITIONAL NUCLEOSIDE MODIFICATIONS ON RNA IMMUNOGENICITY AND EFFICIENCY OF TRANSLATION**
>
> [00290] Additional nucleoside modifications are introduced into in vitro-transcribed RNA, using the methods described above in Examples 2 and 7, and their effects on immunogenicity translation efficiency are tested as described in Examples 1-8 and 9-15, respectively. Certain additional modifications are found to decrease immunogenicity and enhance translation. These modifications are additional embodiments of methods and compositions of the present invention.
>
> [00291] Modifications tested include, e.g.: m^1A; m^2A; Am; ms^2m^6A; i^6A; ms^2i6A; io^6A; ms^2io^6A; g^6A; t^6A; ms^2t^6A; m^6t^6A; hn^6A; ms^2hn^6A; Ar(p); I; m^1I; m^1Im; m^3C; Cm; s^2C; ac^4C; f^5C; m^5Cm; ac^4Cm; k^2C; m^1G; m^2G; m^7G; Gm; $m^2{}_2G$; m^2Gm; $m^2{}_2Gm$; Gr(p); yW; o_2yW; OHyW; OHyW*; imG; mimG; Q; oQ; galQ; manQ; $preQ_0$; $preQ_1$; G^+; D; m^5Um; $m^1\Psi$; Ψ m; s^4U; m^5s^2U; s^2Um; acp^3U; ho^5U; mo^5U; cmo^5U; $mcmo^5U$; chm^5U; $mchm^5U$; mcm^5U; mcm^5Um; mcm^5s^2U; nm^5s^2U; mnm^5U; mnm^5s^2U; mnm^5se^2U; ncm^5U; ncm^5Um; $cmnm^5U$; $cmnm^5Um$; $cmnm^5s^2U$; $m^6{}_2A$; Im; m^4C; m^4Cm; hm^5C; m^3U; $m^1acp^3\Psi$; cm^5U; m^6Am; $m^6{}_2Am$; $m^{2,7}G$; $m^{2,2,7}G$; m^3Um; m^5D; $m^3\Psi$; f^5Cm; m^1Gm**;** m^1Am; τm^5U; τm^5s^2U; imG-14; imG2**;** and ac^6A."

Claims

37. It is only necessary to refer to claim 1, which is as follows:

> "A messenger RNA comprising a pseudouridine residue."

Lack of novelty

The law

38. The judge set out the law in some detail at [118]-[146]. He discussed lack of novelty together with added matter since the tests are very similar, although applied in different contexts. For the purposes of the appeal added matter can be ignored.

39. A patent claim lacks novelty if there is a prior disclosure of something within the claim which is enabled. For present purposes the requirement of enablement can be ignored. The test for prior disclosure was authoritatively stated by Lord Hoffmann in *SmithKline Beecham Plc's (Paroxetine Methanesulfonate) Patent* [2005] UKHL 59, [2006] RPC 10 at [22]:

> "… the matter relied upon as prior art must disclose subject-matter which, if performed, would necessarily result in an infringement of the patent. That may be because the prior art discloses the same invention. In that case there will be no question that performance of the earlier invention would infringe and usually it will be apparent to someone who is aware of both the prior art and the patent that it will do so. But patent infringement does not require that one should be aware that one is infringing …. It follows that, whether or not it would be apparent to anyone at the time, whenever subject-matter described in the prior disclosure is capable of being performed and is such that, if performed, it must result in the patent being infringed, the disclosure condition is satisfied. The flag has been planted, even though the author or maker of the prior art was not aware that he was doing so."

40. Prior disclosure is a strict test. It requires either clear and unambiguous disclosure in the prior document, or clear and unmistakable directions to do something which in fact falls within the claim. It is not sufficient that it would be obvious to carry out or modify the prior art in a manner which falls inside the claim.

41. As the judge rightly observed at [126]:

> "… the whole document has to be considered, but that does not mean that it is a reservoir from any part of which a feature can be taken to combine with a feature from some other part, in the absence of a clear teaching to do so. Similarly, the CGK informs, as ever, what the skilled person understands from the document but it does not make the CGK a reservoir from which features can freely be drawn to be plugged in at will. …"

42. It is often the case that the prior art contains a disclosure in the form either of a list of items or a class of items. I shall have to return to the difference between a list of items and a class of items, and consider the extent to which it is a relevant distinction, below, but for the moment I shall confine myself to explaining what I mean by these expressions. A list of items consists of individual items written out sequentially: A, B, C and so on. A class of items consists of a single description which embraces a number of items. In the field of organic chemistry, a commonly-encountered type of class is a Markush formula. (I explained Markush formulae in *Sandoz Ltd v G.D. Searle LLC* [2017] EHWC 987 (Pat), [2019] ECC 3 at [12]-[18].) As the example of a Markush formula illustrates, it is usually the case that a class could also be expressed as a list, but the class description is used for brevity. Conversely, it is often the case that a list could be expressed as a class (although finding a way to articulate the class accurately might require some thought).

43. There is a considerable body of case law of the Boards of Appeal of the European Patent Office addressing the circumstances in which an item selected from a list or

class of items is novel. As discussed in more detail below, the test applied by the Boards is whether the prior art contains an "individualised description" of the item in question. There is also case law which establishes that an item selected from a combination of two or more lists of some length will generally be regarded as novel.

44. *Individualised description*. The courts in this jurisdiction have adopted the principles established by the consistent case law of the Boards of Appeal. The leading authority is *Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co Ltd* [2009] EWCA Civ 1362, [2010] RPC 9, which concerns selection from a class. The judge cited at [128] a lengthy extract from the judgment of Jacob LJ in that case. I reproduce the major part of this below:

> "23. Olanzapine is one of the 10^{19} compounds of formula (I) and one of the 86,000 compounds of the 'preferred' class. It is not mentioned specifically.
>
> 24. DRL contends that nonetheless this specific compound lacks novelty - that in the language of EPC Art.54 it formed 'part of the state of the art' having been 'made available to the public by means of a written ... description.' The contention amounts to this: that every chemical class disclosure discloses each and every member of the class. …
>
> 25. I reject the contention for two reasons: firstly as a matter of a priori reasoning and secondly because it is inconsistent with settled EPO Board of Appeal case law.
>
> 26. First then, the a priori considerations apart from case-law. An old question and answer runs as follows: 'Where does a wise man hide a leaf? In a forest.' It is, at least faintly, ridiculous to say that a particular leaf has been made available to you by telling you that it is in Sherwood Forest. Once identified, you can of course see it. But if not identified you know only the generality: that Sherwood Forest has millions of leaves.
>
> 27. The contention has no logical stopping place. If there is disclosure of olanzapine here, why would one not regard an even more general disclosure as a disclosure of it. Suppose the prior art had merely been of '3-ringed organic compounds?' Such a description would encompass much much bigger numbers than the 10^{19} of formula I. Yet the logic of the argument would be the same - that there is a disclosure of each and every member of the class.
>
> 28. I would add that I would regard the listing out of a great number of compounds as opposed to the use of a Markush formula in the same way. To say a particular book is identified by saying 'the books in the Bodleian' is no different from saying it is identified by providing access to the catalogue of the Bodleian.

29. Similarly it makes no sense to say that a generalised prior description discloses a specific matter falling within in. The judge's example illustrates the point. A prior disclosure of 'fixing means' is not a disclosure of a particular fixing means e.g. welding or riveting even though you could list out a whole number of ways of fixing things together which would include these means.

30. Thus logic dictates rejection of the argument that a disclosure of a large class is a disclosure of each and every member of it. So also does EPO case-law. Mr Carr accepted that was so, so I can take the matter quite shortly, going to just one case, *Hoechst/Enantiomers* T 0296/87, 30 August 1988, which effectively sums up earlier cases. It said:

> '6.1 Here the Board is guided by the conclusions it reached in its *Spiro compounds* decision T 181/82 (OJ EPO 1984, 401) concerning the novelty of chemical entities within a group of substances of known formula. With regard to products of the reaction of specific spiro compounds with a (C1-C4)-alkyl bromide defined as a group, the Board drew a sharp distinction between the purely intellectual content of an item of information and the material disclosed in the sense of a specific teaching with regard to technical action. Only a technical teaching of this kind can be prejudicial to novelty. If any such teaching is to apply in the case of a chemical substance, an individualised description is needed.'
>
> So what one must look for by way of an anticipation is an 'individualised description' of the later claimed compound or class of compounds. This case is miles from that. …

31. It is not necessary here to go into what is sufficient to amount to an 'individualised description.' Obviously the question may partly be one of degree, but other considerations may come in too, for instance the specificity of any indicated purpose for making the compounds. A mere woolly indication of the possible use of the prior class may require less specificity than a precise one.

32. This view of the law accords with … *SmithKline Beecham plc's (Paroxetine Methanesulfonate) Patent* … Where you have a patent for a particular chemical compound and a prior art general disclosure, performance of the general disclosure … does not necessarily result in infringement of the patent. …"

45. Counsel for PBNT submitted that Jacob LJ's obiter statement at [28] that there was no difference between a class and a list was incorrect, and contradicted by the case he

cited at [30], T 296/87 *Hoechst/Enantiomers* [1990] OJ EPO 195. In that case the Board went on in [6.1] to say:

> "Thus, as the Board decided in that case, the purely intellectual content of the term (C1-C4)-alkyl comprises the eight groups methyl (C1), ethyl (C2), n- and isopropyl (each C3), and n-, sec.-, iso- and tert.-butyl (each C4). Only the methyl group is disclosed in individualised form, however, since this is synonymous with the lower basic value C1-alkyl. In contrast, the special alkyl groups with two or three carbon atoms—included but not enumerated are not disclosed in this way; nor are the four individual groups comprised in the upper basic value (C4), which discloses butyl groups only as a generic term."

46. Furthermore, in *Hoechst/Enantiomers* itself, the Board held at [6.2] that a disclosure in the prior art of a structural formula which constituted a racemate (in other words, the formula did not show the chirality of the relevant carbon atom and thus did not distinguish between enantiomers) did not disclose the enantiomers in individualised form. It went on at [6.3]:

> "The situation is different if the state of the art includes enantiomers – howsoever designated (D, d, L, l or + or -) – which are specifically named and can be produced."

47. I do not accept this submission for two reasons. First, as a matter of principle, I cannot see any distinction between a list and a class in this context. A list may be very long, while a class may contain a small number of members. Either way, the question is whether there is an individualised description of the item in question. This is a question of fact and degree depending on the precise content of the prior art, as Jacob LJ explained at [31].

48. Secondly, I do not consider that, upon analysis, the submission is supported by *Hoechst/Enantiomers*. The key point that the Board made was that it was necessary to distinguish between "the purely intellectual content of an item of information" on the one hand and "a specific teaching with regard to technical action" on the other hand. This distinction does not correlate with the difference between a class and a list. In some circumstances a disclosure of a class (particularly a small class) might constitute a specific teaching with regard to technical action, while in some circumstances disclosure of a list (particularly a large list) might not constitute a specific teaching with regard to technical action.

49. The earlier case T181/82 *Ciba-Geigy/Spiro Compounds* [1984] OJ EPO 401 which the Board cited was concerned with a class, "C1-C4 alkyl". It is important to note that the issue in that case was one of inventive step, and specifically the application of the problem and solution approach used for the assessment of inventive step by the EPO. In that context there was a question as to whether a reference to "C1-C4 alkyl" (more specifically, "C1-C4 alkyl bromide") in claim 9 of the prior art document disclosed methyl (i.e. C1-alkyl), with the consequence that methyl was the closest prior art with which the claimed invention fell to be compared to see if it provided superior properties. On the facts, it was held that this was an individualised disclosure of C1-alkyl. Although the Board stated at [9] that "Claim 9 cannot be regarded as a list of all

the eight alkyl bromides which it covers", that statement was drawing the familiar distinction between what a claim covers and what it discloses. Furthermore, this statement was made in the context I have described.

50. As for *Hoechst/Enantiomers* itself, this was concerned with a very particular problem in organic chemistry. Structural formulae are often drawn in a manner which ignores the chirality of one or more carbon atoms. There is a difference between such a formula and a disclosure of one or more specific enantiomers. The difference is significant because enantiomers can have quite different properties to each other.

51. I do not consider that the Board can have been intending in either case to draw a rigid distinction between a class and a list when considering novelty.

52. The judge concluded at [131]:

> "Each side before me accepted that there is no fixed numerical cut-off for individualisation (although this did not stop them bandying about small, large and middling numbers from cases). I will proceed on the basis that the overall test is whether there is an individualised disclosure and that the size of the list/class is one relevant factor. Often, no doubt, it will be a major factor and in the right case it might be decisive."

I agree with this.

53. *Selection from multiple lists*. In the frequently-cited decision T 12/81 *Bayer/Diastereomers* [1982] OJ EPO 296 the Board of Appeal held at [13]:

> "… If … two classes of starting substances are required to prepare the end products and examples of individual entities in each class are given in two lists of some length, then a substance resulting from the reaction of a specific pair from the two lists can nevertheless be regarded for patent purposes as a selection and hence as new."

Although expressed by reference to two classes of starting materials, this principle has been applied generally to selections from multiple lists.

54. As the judge noted at [136], the approach is not mechanistic. As the Board of Appeal held in T 783/09 *Novartis/Antidiabetic compositions* (unreported, 25 January 2011) at [5.6]:

> "… given the term 'can' in the citation from decision T 12/81, the absence of a direct and unambiguous disclosure for individualised subject-matter is not a mandatory consequence of its presentation as elements of lists. Thus, the 'disclosure status' of subject-matter individualised from lists has to be determined according to the circumstances of each specific case by ultimately answering the question whether or not the skilled person would clearly and unambiguously derive the subject-matter at issue from the document as a whole."

55. This statement was made in the context of added matter, but it is equally applicable to novelty. The same is true of what the Board of Appeal said in T 1878/19 *KCI/Re-Epithelialization Wound Dressings* (unreported, 3 August 2023) (cited in *Case Law of the Boards of Appeal* (11th edition) at II.E.1.6):

> "1.1 … According to well-established case law of the boards of appeal, a single feature may normally be taken from a single list and incorporated into a filed claim without contravening Article 123(2) EPC. If features from more than a single list are combined, there generally needs to be a pointer for each of the selections made such that the combination of selected features can be considered disclosed in the application as filed. …
>
> 1.2 … An individual list may be short and even only comprise two alternatives. Yet, it further adds to the number of choices a skilled person already has to make to arrive at the claimed subject-matter. The decisive question is thus not how long an individual list is, to be classified as a 'list', but merely from the fact that alternatives are present among which the particular combination of features is to be selected. Further it has to be questioned whether there is a pointer not only to each individual selected feature, but also to the specific combination of the selected features. As regards the proprietor's argument of a 'concretisation', the Board does not find this convincing if, as in the present case, the general feature of the claim in the application as filed can be concretised in several ways which are presented as mere alternatives without any specific preference to one or the other being given …"

56. As the judge noted at [145], it is important to consider whether the lists are independent of one another. It may be that the choice from one list affects the choice from another so that there is in fact no need to select from both lists, as opposed to one. The judge discussed T 1581/12 *GlaxoSmithKline/Neisseria antigens* (unreported, 15 September 2016) as an example of this.

57. The judge concluded at [146]:

> "Finally, and at the risk of repetition, the test of clear and unambiguous disclosure is emphatically not an obviousness test. Pointers, in particular, are a facet of deciding the question of clear and unambiguous disclosure and not a licence for holding something to be disclosed merely because it was an obvious choice. This may be easier to say than to apply, but on novelty of EP949 I think it is of some importance."

Again, I agree with this.

Test on appeal

58. Novelty is a binary question which depends on the application of the correct legal standard to the prior art. The interpretation of the prior art is a question of law once

the court has been properly instructed by the expert evidence as to the common general knowledge with which the skilled person reads the document, and hence the technical considerations which bear upon its interpretation. It follows that there is a right answer to any question of novelty. It is not a matter of evaluation taking into account multiple factors and applying an imprecise standard like obviousness.

PBNT's case in outline

59. As the judge explained at [307]-[312], [318] and [334], at trial PBNT advanced three different routes to anticipation by UPenn. Route 1 was PBNT's primary case. Route 2 was a relatively minor variant on route 1. Route 3 was PBNT's secondary case, although the judge found it simpler and more persuasive.

60. On the appeal PBNT did not rely on route 2 given that Moderna no longer relied on claim 5. More importantly, PBNT advanced route 3 as its primary case. This is despite the fact that route 3 was not mentioned in PBNT's skeleton argument for trial. The first iteration of it was mentioned in oral opening submissions and maintained in PBNT's written closing submissions. Route 3 only reached its final form after the judge asked for further written submissions on novelty in chart form. As Moderna submitted, the late emergence of route 3 and its evolution during the course of trial are powerful indications that it is a hindsight-driven construct. This is further emphasised by PBNT's deployment of additional arguments in support of route 3 on appeal. Although PBNT still rely upon route 1, it is difficult to see how this can succeed if PBNT fail on route 3.

Route 3

61. Route 3 starts from [004], corresponding to claim 1, of UPenn. This discloses mRNA comprising a pseudouridine (Ψ) residue. [0056] defines what is meant by "pseudouridine", namely Ψ itself, $m^1\Psi$, three other named possibilities and "any other pseudouridine known in the art". [0074] discloses a list of percentage replacements, including 100%. Example 2 discloses a general method for making RNAs with modified nucleosides which can be used to achieve 100% replacement and which is used in a number of subsequent Examples. PBNT argue that, because UPenn discloses each of $m^1\Psi$ and 100% replacement as part of a list, each is individually disclosed. Furthermore, PBNT argue that there is a strong pointer to combining 100% replacement with each "pseudouridine" disclosed in [0056] because the clear teaching of UPenn as a whole is that 100% replacement is preferred because it confers improvements in both efficiency of translation and reduction in immunogenicity. (I did not understand counsel for PBNT to pursue in oral argument a suggestion made in PBNT's skeleton argument that [004] and claim 1 should be interpreted as referring to 100% replacement because 100% replacement is the default in an *in vitro* transcription reaction, but in any event I do not accept that argument. As Moderna pointed out, there is no teaching in UPenn that the mRNA of claim 1 or [004] must be made by *in vitro* transcription, and the skilled person would understand that it could be made by chemical synthesis.)

62. I agree with the judge that route 3 does not destroy the novelty of claim 3 of EP949. My reasons, which are essentially the same as the judge's, are as follows.

63. First, [0056] is a definition. It provides for "pseudouridine" to be given an extended meaning for the purposes of (*inter alia*) [004] and claim 1. It does not contain any technical teaching with regard to the items in the list. There is no indication as to why the five specified modifications have been listed. By contrast, [0069] lists modified nucleosides which have been tested. $m^1acp^3\Psi$, $m^1\Psi$, Ψm and $m^3\Psi$ are all naturally-occurring Ψ derivatives whereas m^5D is not. As discussed in more detail in connection with obviousness, the only apparent explanation for the inclusion of m^5D is that it shares structural similarities with the others. Furthermore, the list is an open-ended one. Although the skilled person who considered the matter could readily ascertain (by searching the RNAMD) that there were no other known naturally-occurring pseudouridines, that was not common general knowledge. In any event, the words "any other pseudouridine known in the art" are apt to capture any other modified pseudouridine that (unbeknownst to the skilled person) had already been made or which might be made in the future. Accordingly, the skilled person would understand that UPenn was trying to ensure that the claims covered future developments. $m^1\Psi$ is not said to be preferred. It is debatable whether, when read together with [004]/claim 1, this is an individualised disclosure of $m^1\Psi$-mRNA, but it is not necessary to decide this question.

64. Secondly, [0074] is a list of 33 percentage replacements for a given nucleotide base (U, C, G or A). In substance, it covers everything from 0.1% to 100%. It is not said that 100% is preferred. Nor is there any clear statement anywhere else in UPenn that 100% is preferred. Indeed, there is no reference to 100% replacement either in the summary of the invention or in the claims. The most one can say is that (i) Example 2 teaches the reader how to make RNAs with 100% replacement of a chosen base by *in vitro* transcription, (ii) there is a general teaching in [00218] that reduction in immunogenicity is proportional to the extent of the replacement for each of six modified nucleosides tested and (iii) there is a general teaching at [00241]-[00246] that Ψ-mRNA (implicitly with 100% replacement) also increases translation efficiency. Again, it may be debatable whether this is an individualised disclosure of 100% replacement, although PBNT has a stronger case on this than on $m^1\Psi$, but it is not necessary to decide this question. Nor is it necessary to consider an enervating dispute between the parties as to whether, as Moderna contended, Examples 10 and 11 show that it is not inevitable that 100% replacement achieves both enhanced translation and reduced immunogenicity (a contention that Moderna accepted was partly new, but said was being advanced in response to a new argument of PBNT concerning Example 7.)

65. Thirdly, and crucially, PBNT's case is in substance one of selection from two lists. There is no pointer whatsoever to the combination of $m^1\Psi$ and 100% replacement. PBNT argue that the lists are not independent, because someone who decides to synthesise an mRNA with $m^1\Psi$ in place of U necessarily has to choose a percentage of modified nucleotide to use. I agree with the judge that this argument is fallacious because the facts that a choice is necessary and that 100% replacement would be an obvious choice in the light of UPenn does not mean that there is a clear and unambiguous disclosure of 100% replacement of U with $m^1\Psi$ in mRNA.

66. On the other hand, I should explain for completeness that I do not accept Moderna's argument that route 3 involves selection from three lists, the third being the list of

RNAs in [0076]. The reason for this is that [004] and claim 1 of UPenn are confined to mRNA.

Route 1

67. Route 1 involves starting with Example 31. This refers back at [00290] to use of the methods described in (*inter alia*) Examples 2 and 7. The list of 96 nucleosides in [00291] includes $m^1\Psi$. PBNT argues that $m^1\Psi$ is individually disclosed in [00291] and that [00290] individually discloses the use of the methods of Examples 2 and 7 with each of the modified nucleosides, either of which would result in 100% replacement.

68. Again, I agree with the judge that route 1 does not destroy the novelty of claim 3 of EP949. My reasons, which are essentially the same as the judge's, are as follows.

69. First, Example 31 is not merely prophetic, but also a bare proposal to test many further modified nucleosides in a range of different experiments. Unlike some of the other prophetic examples, it does not predict the results that will be obtained. Carrying out all of these tests would take a very long time. It is, to use Jacob LJ's word, a woolly proposal.

70. Secondly, the list of modified nucleosides is not merely long, but also open-ended because the list starts with the words "include e.g.". It seems to be a laundry list of modified nucleosides to test, selected without rhyme or reason. In my judgment there is no individualised disclosure of $m^1\Psi$, because there is no specific teaching with regard to technical action concerning $m^1\Psi$.

71. Thirdly, in my judgment there is no individualised disclosure in Example 31 of 100% replacement of U in mRNA. It refers back to the use of Examples 2 and 7, but only also as being amongst the experiments that can be carried out. Example 2 is not confined to mRNA. Example 7 uses a range of percentage replacements including 100%. Again, there is no specific teaching with regard to technical action concerning 100% replacement of U in mRNA.

72. Fourthly, there is in any event no pointer whatsoever to combining the selection of $m^1\Psi$ with the selection of 100% replacement of U in mRNA.

Conclusion

73. For the reasons given above I conclude that claim 3 of EP949 is novel over UPenn.

Obviousness

Basic principles

74. The judge discussed the law at [147]-[159]. There is no dispute as to the accuracy of that account. For the purposes of the appeal it is sufficient to note the following points, most of which are drawn from the judgment of Lord Hodge in *Actavis Group PTC EHF v ICOS Corp* [2019] UKSC 15, [2019] Bus LR 1318.

75. As Lord Hodge noted at [58]-[59], section 3 of the Patents Act 1977 provides that:

> "An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art …"

The notional skilled person has no inventive capacity.

76. As Lord Hodge noted at [60], it is common for English courts to adopt the structured approach to the assessment of obviousness described by Jacob LJ in *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588, [2007] FSR 37 at [23]:

> "(1) (a) Identify the notional 'person skilled in the art'; (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the 'state of the art' and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?"

This approach is not mandatory, however. In this case the parties did not adopt it in their arguments at trial, nor did the judge in his judgment.

77. At [63] Lord Hodge said:

> "In *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc* [2008] 4 All ER 621, para 42, Lord Hoffmann endorsed the fact-specific approach which Kitchin J set out in *Generics (UK) Ltd v H Lundbeck* [2007] RPC 32, para 72 where he stated:
>
> > 'The question of obviousness must be considered on the facts of each case. The court must consider the weight to be attached to any particular factor in the light of all the relevant circumstances. These may include such matters as the motive to find a solution to the problem the patent addresses, the number and extent of the possible avenues of research, the effort involved in pursuing them and the expectation of success.'
>
> Kitchin J's list of factors is illustrative and not exhaustive. Another factor which needs to be considered in the present case is the routineness of the research. …"

78. Lord Hodge went on to consider nine factors which are often relevant considerations. Four of these are particularly pertinent for present purposes:

"65. First, it is relevant to consider whether at the priority date something was 'obvious to try', in other words whether it was obvious to undertake a specific piece of research which had a reasonable or fair prospect of success: *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc* , para 42, per Lord Hoffmann; *MedImmune Ltd v Novartis Pharmaceuticals UK Ltd [*2013] RPC 27, paras 90–91, per Kitchin LJ. In many cases the consideration that there is a likelihood of success which is sufficient to warrant an actual trial is an important pointer to obviousness. But as Kitchin LJ said in *Novartis AG v Generics (UK) Ltd* [2012] EWCA Civ 1623 at [55], there is no requirement that it is manifest that a test ought to work; that would impose a straitjacket which would preclude a finding of obviousness in a case where the results of an entirely routine test are unpredictable. As Birss J observed in this case (para 276), some experiments which are undertaken without any particular expectation as to result are obvious. The relevance of the 'obvious to try' consideration and its weight when balanced against other relevant considerations depend on the particular facts of the case.

…

69. Fifthly, the existence of alternative or multiple paths of research will often be an indicator that the invention contained in the claim or claims was not obvious. If the notional skilled person is faced with only one avenue of research, a "one-way street", it is more likely that the result of his or her research is obvious than if he or she were faced with a multiplicity of different avenues. But it is necessary to bear in mind the possibility that more than one avenue of research may be obvious. In *Brugger v Medic-Aid Ltd (No 2) [1996] RPC 635* , 661, Laddie J stated:

> 'if a particular route is an obvious one to take or try, it is not rendered any less obvious from a technical point of view merely because there are a number, and perhaps a large number, of other obvious routes as well.'

I agree. As a result, the need to make value judgements on how to proceed in the course of a research programme is not necessarily a pointer against obviousness.

70. Sixthly, the motive of the skilled person is a relevant consideration. The notional skilled person is not assumed to undertake technical trials for the sake of doing so but rather because he or she has some end in mind. It is not sufficient that a skilled person could undertake a particular trial; one may wish to ask whether in the circumstances he or she would be motivated to do so. The absence of a motive to take the

> allegedly inventive step makes an argument of obviousness more difficult. …
>
> …
>
> 72. Eighthly, the courts have repeatedly emphasised that one must not use hindsight, which includes knowledge of the invention, in addressing the statutory question of obviousness. That is expressly stated in the fourth of the *Windsurfing* / *Pozzoli* questions. Where the pattern of the research programme which the notional skilled person would undertake can clearly be foreseen, it may be legitimate to take a step-by-step analysis. In *Gedeon Richter plc v Bayer Schering Pharma AG* [2011] EWHC 583 (Pat); [2011] Bus LR D153, Floyd J stated, at para 114:
>
> > 'I think that the guiding principle must be that one has to look at each putative step which the skilled person is required to take and decide whether it was obvious. Even then one has to step back and ask an overall question as to whether the step-by-step analysis, performed after the event, may not in fact prove to be unrealistic or driven by hindsight.'
>
> The obvious danger of a step-by-step analysis is that the combination of steps by which the inventor arrived at his invention is ascertained by hindsight knowledge of a successful invention. … "

The judge's assessment

79. As the judge explained at [33], he found it convenient to address all the issues concerning the expert witnesses together at the beginning of his judgment before turning to other issues. For the purposes of the appeal it is more convenient to set out the relevant parts of the judgment in a different sequence.

80. *The skilled person*. As the judge explained at [256], there was a dispute between the parties as to the identity of the skilled person:

> "i) Moderna and Prof Rosenecker said that EP949 is directed to a scientist with a good understanding of the biology of RNA who is working on, or has an interest in, developing mRNA for the purposes of transcript therapy;
>
> ii) Pfizer/BioNTech and Dr Enright said that EP949 is directed to an RNA biologist who is interested in using RNA for research, whether fundamental or applied to therapeutic purposes."

81. At [257]-[258] the judge noted that it was common ground that, subject to a nuance which did not matter, the problem which EP949 aimed to solve was to increase

translation and reduce immunogenicity of mRNA. The judge went on in a passage which is necessary to set out almost in full:

> "259. This agreement identifies the problem at a scientific and somewhat conceptual level but leaves open the question of why it mattered, and to what practical end a solution to it could be put. So the issue still remains of whether the skilled person would be someone working on using mRNA for transcript therapy (Moderna) or someone who also would have an interest in fundamental research (Pfizer/BioNTech). I am not bound to choose between the parties' two formulations and indeed I go on below to reject both, although the upshot is more in favour of Moderna.
>
> 260. As I identify in addressing the specification of EP949, the practical application of what it teaches is not limited to transcript therapy. It also covers immunotherapy and direct vaccination, as well as non-therapeutic uses. I need not go into the details, but Counsel for Pfizer/BioNTech established in cross-examination that there were real teams in the following relevant areas where a solution to the problem could be useful (but it was not suggested and would be unreal for any of those teams to be working in *all* of them, and indeed I think most if not all were only active in one):
>
> i) Cellular reprogramming studies;
>
> ii) Immunotherapy;
>
> iii) Direct vaccination;
>
> iv) Studying gene expression and the efficacy of RNA platforms;
>
> v) Studying mechanisms of translation and immune response;
>
> vi) Studies on zinc finger nuclease technology;
>
> vii) Neuroscience research;
>
> viii) Developmental research; and
>
> ix) Gene (or protein) replacement therapy.
>
> 261. So Moderna is wrong in seeking to define the skilled person as being someone working on, specifically, transcript therapy. They could be working in any of those fields. Pfizer/BioNTech described some of the above fields as 'study' or 'research'. That tended to favour its argument that Dr Enright was close(r) to those teams, but I think it is not a fair way of looking at things. The above teams were looking for

practical results and I do not think an overview of them supports the position that the correct field was one of pure research, whatever its scope.

262. A further reason to reject Moderna's narrow definition of the skilled person, as Pfizer/BioNTech submitted and as I accept, is that the claims of EP949 are not limited to therapy.

263. I therefore identify the skilled person as being someone with a knowledge of RNA biology, with a practical interest in improving the use of mRNA in relation to translation and immunogenicity in any of the fields above.

264. That means that there was not *any* real team corresponding to the notional skilled person in the breadth of their interest, in the sense that no team covered so much ground. It also means that it would have been impossible for Moderna, or indeed either side, to call a single witness who in fact matched that breadth of interest. ….

265. I think it is unusual but not unprincipled to identify the skilled person as being someone with a practical interest in the use of mRNA where translation and immunogenicity were relevant, even though in the real world the work of any given individual would inevitably be on only a subset of that broader field. This means that it would be open to anyone challenging the validity of EP949 to show that it was obvious to a skilled person working on mRNA vaccines, or on mRNA immunotherapy, or on mRNA for stem cell development. Had Pfizer/BioNTech called an expert from any of these subfields, had the difference between the subfields mattered, and had Prof Rosenecker not been able to put himself in the position of someone in such other subfield, then Moderna's position might have been quite difficult. But that is not what has happened: Pfizer/BioNTech have called an expert who is not from any of the subfields but rather a pure, basic scientist.

266. I also think that in the present case there is an important interface between the argument over the skilled addressee of EP949 and the argument over the right approach to obviousness. Pfizer/BioNTech's argument is that the skilled addressee is a basic scientist interested in fundamental research. The downstream effect of the contention is problematic: it founds Pfizer/BioNTech's submission that it would be obvious to try a variety of Ψ modifications, including $m^1\Psi$, without any particular practical goal in mind, without any concrete expectation of success (indeed with a willingness to accept null results as a success in the sense of providing information), and without understanding why Ψ itself achieved what it did in the prior art. This is not a proper approach to obviousness. I also think it is not the proper approach to the

> skilled person. The skilled person has a practical interest in the application of an invention, and even if that is not an absolute rule, it is a conclusion that is justified in the present case where EP949 identifies a range of practical applications. The fact that they might be deployed in research in a practical way does not detract from this. I bear in mind that the relevant field may be a research field or a field of manufacture (*Illumina* at [66]) but patents are nonetheless addressed to readers with a *practical* interest (e.g. *MedImmune* at [77]).”

82. *Dr Enright*. As the judge explained at [50], Moderna advanced four criticisms of Dr Enright’s experience and evidence. The judge rejected the third criticism, and no more needs to be said about it. The other three criticisms were as follows:

> “i) First, in relation to his experience:
>
> a) that he had no direct experience of using mRNA for therapeutic purposes or experience with attempting to increase expression of exogenous mRNA;
>
> b) that his interests related to types of RNA which are not translated ..; and
>
> c) that his interests lay in matters of fundamental research and fundamental biology.
>
> ii) Second, that Dr Enright knew that the case related to $m^1\Psi$ at the time of his first report and that parts of his evidence were contaminated by hindsight.
>
> …
>
> iv) Fourth, that Dr Enright’s approach to obviousness was erroneous due to his willingness to entertain modifications which could produce negative (‘catastrophic’) results.”

83. The judge’s assessment of the first and fourth criticisms at [51] was:

> “As to the first point, it would be unfair and inaccurate to say that Dr Enright’s work was purely abstract or computational (although computational analysis was a very strong feature of his work over some periods) and he plainly had considerable experience of ‘wet’ laboratory work. But I do accept that his interests were to do with fundamental research, and well removed from the practical application of mRNA expression, whether for therapeutic or any other applied goals. He pointed out that all work in his field was done with the general goal, ultimately, of improving human health, but that does not change the fact that his work was much more at the theoretical end of the spectrum. As a result, he was given to thinking that things were obvious to do if they would yield information of

> any kind, positive or negative, and whether or not they would give a practical advantage. The fourth point above is a facet of this, and I accept it."

84. The judge considered the second criticism at [52]-[64]. The judge accepted that, in general, Dr Enright had been instructed using the "sequential unmasking" approach to try to avoid hindsight (see *Akebia Therapeutics Inc v Fibrogen, Inc* [2020] EWHC 866 (Pat), [2020] RPC 15 at [36]): he was asked for his views on the common general knowledge and the prior art before he was shown EP949, and to begin with he did not know the modified nucleotides used in Covid-19 vaccines. By the time he finalised his report, of course, he knew that the invention of EP949 was about $m^1\Psi$.

85. The judge went on to consider two examples of hindsight relied on by Moderna in a passage which is necessary to quote in full:

> "56. The first relates to his treatment of [0056] of UPenn. As is discussed below, in that paragraph, the authors refer to the four naturally occurring Ψ derivatives known at the time, plus m^5D. These are defined as being pseudouridines.
>
> 57. An oddity, however, is that m^5D is not a pseudouridine derivative like the others mentioned. It is common ground that the skilled person would think about this and wonder why it was listed. In paragraph 7.16 of his first report, Dr Enright said 'The Skilled Person would note that while m^5D is not literally a Ψ derivative like the others in the group, it does share structural similarities with the others, in particular $m^1\Psi$, which would explain its inclusion.'
>
> 58. It is not in dispute that m^5D is in fact particularly similar to $m^1\Psi$, but Counsel for Moderna put to Dr Enright in cross-examination that he would not have offered the explanation that he did, in the way he did, unless he had an awareness of the importance of $m^1\Psi$ to this case. This was fortified by the fact that Prof Rosenecker, in his second report, pointed out that there are other nucleosides in the RNAMD not mentioned in [0056] which are more closely related to the other modifications in that paragraph than m^5D is to $m^1\Psi$. In particular, he pointed to there being just one difference between Ψm and Um.
>
> 59. Dr Enright agreed that the skilled person would do an analysis similar to Prof Rosenecker's but would not chase 'down the rabbit hole' of every detail.
>
> 60. Counsel for Pfizer/BioNTech said that Dr Enright was doing no more in his paragraph 7.16 than stating a fact about similarity. I do not agree. If unaware of any particular importance of $m^1\Psi$, Dr Enright could have made much the same point without using the words 'in particular $m^1\Psi$'. He also plainly went further than just stating a fact because he was seeking to

explain what the skilled person would think the patentee's logic was that underlay the inclusion of m^5D. I think that without knowledge of the importance of $m^1\Psi$, Dr Enright would have more likely gone on to say something along the lines of there being a potential reason why m^5D was included, but that it was obscure why it was the *only* nucleoside mentioned that was not literally a Ψ derivative, given that there were other derivatives even closer to those mentioned in [0056]. In other words, Dr Enright's express mention of $m^1\Psi$ when it was not entirely necessary to making his general point, and stopping the explanation on the basis of the comparison to $m^1\Psi$ when there was more to be said, are both indicative of a particular focus on $m^1\Psi$ not to be found in [0056] or UPenn generally, feeding into his obviousness analysis.

61. The second example related to a paper by Brand and others from 1978 *Biochem J* referenced in the RNAMD in the entry for $m^1\Psi$, which Dr Enright relied on during his oral evidence as showing that $m^1\Psi$ was present in 18S RNA of certain HeLa cells. I agree with Moderna that Dr Enright's reliance on Brand in this way was inconsistent with his position as to the skilled person's attitude to Charette & Gray (which I deal with in more detail below and which is referenced much more prominently in relation to Ψ in the RNAMD), and also that the inconsistency is hard to explain without reference to hindsight. However, this point does not bear on the preparation of his written reports, only his oral evidence.

62. I also thought that Dr Enright's very heavy focus on [0056] in UPenn relative to [0291] is something that would have been unlikely to the reader of the document without hindsight.

63. For these reasons I conclude:

    i) Based on the [0056]/paragraph 7.16 point, that while Dr Enright generally tried to prepare his written evidence analysing obviousness without knowledge of the importance of $m^1\Psi$, that knowledge came in to at least some degree. It is not possible to be sure to what extent, but I think it was appreciable.

    ii) Based on the Brand point, the emphasis on [0056] and his evidence generally, there was some material hindsight in Dr Enright's approach overall.

64. Neither of these is a personal criticism of Dr Enright. I accept his general evidence about the sequence of his instructions, but it is a reality of the system that his long and detailed report will have continued to be worked on after he did know about the importance of $m^1\Psi$, and it is an understandable thing that it affected the analysis. As to there being some general

> hindsight, this is a factor to take into account and not a reason for rejecting his evidence wholesale."

86. Finally, the judge stated at [66]:

> "Based primarily on the second and fourth points concerning Dr Enright, above, I consider that Prof Rosenecker was a more useful witness in helping me to understand how the skilled person would think and reason at the EP949 Priority Date. But both witnesses were helpful in assisting me to understand the technology involved."

87. *Obviousness*. The judge summarised PBNT's case at [360] as follows:

> "i) The data on Ψ in UPenn were very promising and of real interest.
>
> ii) The skilled person would decide to explore other nucleoside modifications.
>
> iii) The ones of interest would be the 'Ψ-like' ones.
>
> iv) It would be possible to make $m^1\Psi$ if that were selected.
>
> v) If the skilled person made $m^1\Psi$ the most obvious thing to do would be to modify 100% of the uracils …..
>
> vi) Carrying out the necessary translation and transfection experiments as in UPenn *in vitro* would take a couple of months."

88. At [361]-[362] the judge noted that there was no material dispute as to points (i), (iv) and (v). As for point (vi), there was a dispute, but not one that independently affected his decision either way.

89. At [365]-[370] the judge considered point (i) in more detail. In this context, the judge found at [366] that the fact that "the skilled person would not understand the reason for Ψ's good results" would "naturally lead them to think that they should first see if Ψ was of practical utility in their own field before branching out". At [367] he cautioned himself that "the presence of a particularly attractive way forward does not necessarily make other obvious things non-obvious".

90. At [371] the judge noted that points (ii) and (iii) were closely interrelated. As he discussed at [372]-[378], the necessary starting point was the disclosure of UPenn concerning modified nucleosides, and in particular [0056]. The judge noted at [374] that he had considered [0056] in the context of lack of novelty and when considering Moderna's submission about Dr Enright's hindsight.

91. The judge's principal reasoning is contained in two passages which it is necessary to quote almost in full. The first reads:

"379. I do not think that [0056] will bear the weight that Pfizer/BioNTech sought to put on it:

i) It does not naturally read as a technical teaching that the listed nucleotides are preferred or particularly beneficial. It is a definition not a scientific statement.

ii) The presence of m^5D makes it unclear what thinking had gone into the list. I cover this above in relation to Dr Enright's hindsight.

iii) It is not a concrete list of 5 possibilities because it also extends to any other pseudouridine known in the art. I agree that if the skilled person went to the RNAMD they would find there were no other natural pseudouridines, but they would not know the position about artificial ones.

iv) There are multiple other lists in the document.

v) The list in relation to which there is a positive teaching to look for other, better, nucleosides is [00291] which is a technical teaching, albeit a broad and prophetic one, accompanied with methods and so on.

380. UPenn has to be read as a whole in this regard, and it is certainly not legitimate, as Pfizer/BioNTech sought to do at one point, to give primacy to [0056] just because it comes first.

381. An additional tension in Pfizer/BioNTech's case on this point is that it seemed to involve the unspoken assumption that there would in fact be modifications better than, or as good as, Ψ among any that the skilled person decided to test. But Dr Enright accepted that he or she would not know even that.

382. A further and closely related point which I think is important and powerfully in Moderna's favour is that UPenn does not say why Ψ had worked so well. Nor did Pfizer/BioNTech have any real case that it was possible to work out why …. The skilled person's reading of [0056] and e.g. [00291] would be informed by this. So to this extent the choice of other modified nucleosides to try would be made 'blind' and there could not be any inference that the choice in [0056] was made on a concrete basis of understanding the mechanisms at work. Indeed, Pfizer/BioNTech's case was in large part, in reality, that the skilled person would set about making modifications in order to understand why Ψ had produced such good results. In another passage of his evidence heavily relied on by Pfizer/BioNTech, Prof Rosenecker agreed that that *could* be done, but it is important that it went no further than *could.*

> 383. The next aspect of Pfizer/BioNTech's case to consider in connection with points ii) and iii) is the RNAMD. Pfizer/BioNTech's case, supported by Dr Enright's evidence, is that the skilled person would cross check the [0056] list against the RNAMD. Assuming that in Pfizer/BioNTech's favour, as I think is reasonable on the evidence, doing so would confirm that there were no other naturally occurring pseudouridines (as I have mentioned above). But I think it would also lead the skilled person to consider what other information was available about the 5 modified nucleosides from [0056]. In relation to $m^1\Psi$ there is a sub-issue, which I regard as an important one, about a review article called Charette & Gray, to which I will digress in a moment.
>
> 384. I also note that Dr Enright was not consistent in his approach to the list in [0056]: he both suggested that the skilled person would prioritise them, and that the skilled person would make and test them all. This inconsistency arose, I think, from the weakness of the skilled person's ability to prioritise in a way in which he or she could have confidence, and it undermines the case for obviousness all the more."

92. After this passage, the judge considered Charette & Gray, which is referred to in the RNAMD, at [385]-[402]. It is sufficient for present purposes to note the judge's conclusion at [400]:

> "… in my view the skilled person would, on balance, be more likely to go to Charette & Gray on the basis that it is the review article commended by the RNAMD, read its summary, and stop there, taking on board that it endorsed the hydrogen bonding theory which, if applied to $m^1\Psi$, would tend to suggest reduced stability. I do accept on the basis of the oral evidence that the skilled person would not think this was a theory that was supported by strong evidence, or the only theory, and they would take on board that its application to mRNA was a matter of uncertainty. Nonetheless, in a situation where the skilled person would otherwise have no basis for working out why pseudouridine achieved what it did, it would be the best information and analysis available. …"

93. The second passage is:

> "403. Returning to Pfizer/BioNTech's reliance on [0056], Dr Enright gave evidence about how the skilled person would think through and rank the list of 5 modifications in [0056] were they to get that far (although as I have mentioned above he was not wholly consistent about this and also said that the skilled person would test all five). He considered structural similarity to Ψ, giving preference to those which were small incremental changes, biological origin, and the existence of methods of synthesis. Without going into all the details, this led him to

reduce the list to Ψm and $m^1Ψ$ as preferred, $m^1acp^3Ψ$ and $m^3Ψ$ further down because they had modifications in the Watson-Crick interface and m^5D also further down by virtue of not being a pseudouridine. ….

404. I note in passing that this rejection, or at least downgrade, of m^5D is hard to justify without hindsight given that the authors of UPenn had consciously included it in [0056], albeit without giving reasons.

405. Little was said by Moderna about biological origin or availability of synthetic methods but there was a good deal of evidence about the effect of, and the skilled person's thinking about, changes in the Watson-Crick interface.

406. On this topic, I think a very important point was the fact that (as both experts said in evidence and as Counsel for Pfizer/BioNTech accepted in closing) small structural changes could make a big difference in effect …. It may be, taking Pfizer/BioNTech's case at something close to its highest, that the skilled person would see changes outside the interface as *relatively* less likely to cause problems, but they would still think that even a small change there could have a major or even, as Dr Enright said, 'catastrophic' effect. I take on board that Prof Rosenecker was himself willing to assess the likelihood of larger or smaller changes having an effect or not, but in the main he was comparing bigger changes with smaller ones and saying that the former were more likely to have an impact. That is not inconsistent with the possibility of small changes having a big effect. He also accepted that a skilled person 'could' do the experiment to see the effect of small changes outside the interface, but as with many of his answers he was just accepting the possibility, not that it was obvious.

407. I also have in mind that Dr Enright did not say that the skilled person would not make changes in the Watson-Crick interface. He said that despite the modifications potentially being catastrophic, the skilled person would still like to test them as part of the 'scientific process', albeit with reduced confidence. I think this was symptomatic of his approach that negative information would be useful in gradually moving to an understanding of what was going on.

408. Pfizer/BioNTech placed some stress on methylation as a specific change. It said that methylation was known to play a role in reducing immunogenicity, from the CGK, and that if Prof Rosenecker was willing to contemplate that some small changes were unlikely to have an effect, he ought to have been willing to consider methylation at the N1 position of Ψ as a possibility. However, Prof Rosenecker was only making comparative statements based on the size of changes, and in the

relevant part of his cross-examination he said that methylation was a bigger change compared to others under discussion. Further, although Pfizer/BioNTech's point about methylation might often be true, there were cases where it was not, as in m6A as tested in Karikó 2005, which was highly immunogenic.

409. Essentially absent from all of Pfizer/BioNTech's evidence, argument and analysis on these points was a consideration of expectation of success. I do not think there would be any positive expectation of success, either in general or in relation to any specific candidate change, including $m^1\Psi$. The fundamental reason for this is that the plan of experiments proposed by Pfizer/BioNTech would be taking place in a situation where the reason for the success of Ψ was unknown and where any small change could make a big difference. The central motivation for the approach Dr Enright advocated was, at the end of the day, to try to work out why Ψ had been successful by empirical trial and error, supported by the logic that negative results would be informative, and hoping that some changes would be positive, but not having any real idea in advance which they would be. And it should not be forgotten that Dr Enright's approach had narrowed the inquiry right at the outset by going straight to the [0056] list.

410. I also bear in mind that while the effort involved in these sorts of experiments might not be huge once set up, they include both *in vitro* and animal model experiments, hoping that the former would limit and guide the need for the latter. So the work in its nature would not be lightly undertaken without a real, reasoned expectation of success.

411. Pfizer/BioNTech relied heavily on paragraph 40 of Prof Rosenecker's second report, which said:

> 'In relation to the second step, and on the assumption that the Skilled Person had indeed turned to the RNA Modification Database, I agree that it would have been logical to search for modifications similar to Ψ and thereby arrive at the results in Dr Enright's Exhibit AJE-08, namely the entries for Ψ, Ψm, $m^1\Psi$, $m^1acp^3\Psi$ and $m^3\Psi$. I also agree the Skilled Person would derive as much information as possible from the entries on the RNA Modification Database. However, if Dr Enright is suggesting in paragraph 6.50 that the Skilled Person would only be interested in each compound's structural similarity to Ψ, biological origin and synthesis, I disagree. If the Skilled Person was seeking to prioritise Ψm, $m^1\Psi$, $m^1acp^3\Psi$ and $m^3\Psi$, they would also be interested in any comments or literature cited in the Database that might be relevant to the exercise.'

412. He said this in the context of Karikó 2008, from which it would be necessary to go to the RNAMD to obtain the list of naturally occurring pseudouridines, but similar logic could be applied to UPenn where the list is in [0056] (plus m^5D) and could be verified in the RNAMD.

413. I agree that this evidence does help Pfizer/BioNTech, but in my view only modestly, and not nearly to the extent that Pfizer/BioNTech argued. Prof Rosenecker clearly was not resiling from his view that the skilled person would not start the exercise of making modified nucleosides other than Ψ: he said as much in paragraph 39 (he also said in paragraph 38 that the skilled person would want to work out why Ψ worked before trying modifications). Nor, plainly, was he saying that there was any logic or understanding to think this shortlist would work. Paragraph 40 does not say that, and he was consistent in his oral evidence that it does not. Nor was he saying that a focus on [0056] in UPenn was justified (he was not talking about UPenn) and I do not think he meant, either, that in the context of Karikó 2008 the skilled person would be led *only* to this shortlist from the RNAMD. I think what he said can only assist Pfizer/BioNTech to the extent of the naturally occurring pseudouridines being a subset of modified nucleosides which potentially *could* be tested. He plainly did not say they would be, and this evidence said nothing about prospects of success.

414. I should mention also that Moderna argued that the skilled person would think that changing away from Ψ would risk increased toxicity, because Ψ is widely found in nature and there are metabolic pathways to deal with it. I agree this would be another factor against obviousness, but it is not central to my reasons.

415. I must assess all these matters in the round. Doing so, I find that Pfizer/BioNTech's attack of obviousness fails, and it is not a close call, either. There is no special pointer in UPenn to try other pseudouridine modifications and the focus on [0056] is artificial and hindsight-driven. But even leaving that aside, the fundamental exercise proposed by Dr Enright is one of blind trial and effort with no idea of what is likely to succeed or why, uninformed by any concrete expectation of success and without any incentive of some immediate practical application. The one concrete piece of information that the skilled person would come across in considering what to do along the lines proposed by Pfizer/BioNTech is Charette & Gray, and that is a pointer away, for reasons given above. I also prefer Moderna's position because of my finding that hindsight entered into Dr Enright's evidence.

> 416. None of this is to say that the sort of thing that Dr Enright proposed would be scientifically unmeritorious if a very well-resourced basic research group wanted to do it. Perhaps they would have some insight into why Ψ worked that is not present in UPenn, or perhaps they would be content to aim to publish a paper with a sort of initial SAR for Ψ. That does not make such work obvious for the notional skilled person, however. Pfizer/BioNTech submitted that if the ordinary skilled person were deterred by the uncertainty or lack of prospects of success relied on by Moderna then science would never progress. That overlooks that science may progress by people making inventions, and/or by ordinary skilled people making small incremental changes when their effects can be predicted and there is a good chance of a practical result."

Test on appeal

94. Since the assessment of obviousness involves a multi-factorial evaluation by the judge, this Court is only entitled to intervene if the judge erred in law or principle: see *Actavis v ICOS* at [78]-[81]. See also *Lifestyle Equities CV v Amazon UK Services Ltd* [2024] UKSC 8, [2024] Bus LR 532 at [46]-[50] (Lord Briggs and Lord Kitchin) and *Iconix Luxembourg Holdings SARL v Dream Pairs Europe Inc* [2025] UKSC 25 at [94]-[95] (Lord Briggs and Lord Stephens).

PBNT's grounds of appeal

95. PBNT contend that the judge erred in law or principle in four respects. First, they contend that the judge erred in his identification of the skilled person to whom EP949 is addressed, and therefore wrongly sidelined Dr Enright's evidence. Secondly, they contend that the judge erroneously interpreted [0056]. Thirdly, they contend that the judge wrongly found that Dr Enright's evidence was tainted with hindsight. Fourthly, they contend that the judge erred in his assessment of the skilled person's motivation and expectation of success.

The skilled person

96. The person skilled in the art is, as Hoffmann LJ noted *in Société Technique de Pulverisation STEP v Emson Europe Ltd* [1993] RPC 513 at 519, adopting the phrase of Lord Radcliffe in *Davis Contractors Ltd v Foreham UDC* [1956] AC 696 at 728, one of the "anthropomorphic conceptions" devised by the law. Although Hoffmann LJ expressed scepticism about the value of such anthropomorphic conceptions, this one is firmly rooted in statute, which gives effect to Article 56 of the European Patent Convention (among other provisions). Like many anthropomorphic conceptions in the law, the skilled person is partly an empirical and partly a normative creature. It is an empirical concept in that, as discussed below, the skilled person should embody the skills and experience of real scientists working in the relevant field at the relevant time. It is a normative concept in that the skilled person has qualities which do not correspond to that of any real person, such as being deemed to be aware of any item of prior art which has been made available to the public, and in that it provides a benchmark for the assessment of issues such as obviousness.

97. The judge considered the law as to the identification of the skilled person at [103]-[117]. There is no dispute as to the accuracy of that account. For present purposes it is sufficient to note two points which were and remain common ground. The first is that, as Henry Carr J succinctly summarised the position in *Garmin (Europe) Ltd v Koninklijke Philips NV* [2019] EWHC 107 (Pat) at [85](i):

> "A patent specification is addressed to those likely to have a real and practical interest in the subject matter of the invention (which includes making it as well as putting it into practice)."

98. The second is that the correct approach to the identification of the skilled person or team for the purposes of obviousness in a case like the present one is that set out by Birss J (as he then was) in *Illumina Cambridge Ltd v Latvia MGI Tech SIA* [2021] EWHC 57 (Pat), [2021] RPC 12 at [68]:

> "i) To start by asking what problem does the invention aim to solve?
>
> ii) That leads one in turn to consider what the established field which existed was, in which the problem in fact can be located.
>
> iii) It is the notional person or team in that established field which is the relevant [person or] team making up the person skilled in the art."

This statement is unaffected by the appeal in that case [2021] EWCA Civ 1924, [2022] RPC 14.

99. As will appear, in the present case the issue concerning the correct identification of the skilled person is closely related to a question concerning the role of expert witnesses in patent cases. In general, expert witnesses may perform three main roles in patent cases. First and foremost, they educate the court as to the relevant technology and put it in possession of the skilled person's common general knowledge. This is required in almost all patent cases, although it would be possible in some cases for the court to proceed on the basis of an agreed statement of common general knowledge. Secondly, in many cases expert witnesses are required to give evidence concerning one or more of the substantive issues in the case, and in particular obviousness. Thirdly, in some cases expert witnesses are required to interpret the results of experiments, which may be experiments performed for the purposes of the litigation (for example, experiments to prove an issue on infringement).

100. So far as the second of these roles is concerned, Sir Donald Nicholls V-C giving the judgment of the Court of Appeal in *Mölnlycke AB v Procter & Gamble Ltd (No. 5)* [1994] RPC 49 said at 113:

> "The Act requires the court to make a finding of fact as to what was, at the priority date, included in the state of the art and then to find again as a fact whether, having regard to that state of the art, the alleged inventive step would be obvious to a person skilled in the art.

> In applying the statutory criterion and making these findings the court will almost invariably require the assistance of expert evidence. The primary evidence will be that of properly qualified expert witnesses who will say whether or not in their opinions the relevant step would have been obvious to a skilled man having regard to the state of the art. All other evidence is secondary to that primary evidence."

101. In *Technip France SA's Patent* [2004] EWCA Civ 381, [2004] RPC 46 Jacob LJ, having discussed the concept of the person skilled in the art at [6]-[10], went on:

> "11. … sometimes the requirement that the skilled man be uninventive is used by counsel for a patentee in an attempt to downgrade or dismiss the evidence of an expert called to say that a patent is obvious—'my witness is more nerdlike than his' is the general theme. I do not find this a helpful approach. It is frequently invoked and Mr Waugh Q.C. invoked it in this case in an effort to downgrade Rockwater's expert evidence on obviousness given by Professor Witz. Mr Waugh said his witness, Mr Nash, was more appropriately qualified than Professor Witz, and that the latter, because he had patents in his name, 'was of an inventive turn of mind'.
>
> 12. I must explain why I think the attempt to approximate real people to the notional man is not helpful. It is to do with the function of expert witnesses in patent actions. Their primary function is to educate the court in the technology—they come as teachers, as makers of the mantle for the court to don. For that purpose it does not matter whether they do not approximate to the skilled man. What matters is how good they are at explaining things.
>
> 13. But it also is permissible for an expert witness to opine on an 'ultimate question' which is not one of law. I so held in *Routestone Ltd v Minories Finance Ltd* [1997] B.C.C. 180 and see s.3 of the Civil Evidence Act 1972. As regards obviousness of a patent Sir Donald Nicholls V.C. giving the judgment of the Court of Appeal in *Mölnlycke AB v Procter & Gamble Ltd (No.5)* [1994] R.P.C. 49 at p.113 was explicit on the point: [citing the passage quoted above]
>
> 14. But just because the opinion is admissible,
>
> > 'it by no means follows that the court must follow it. On its own (unless uncontested) it would be 'a mere bit of empty rhetoric' Wigmore, *Evidence* (Chadbourn rev) para.1920. What really matters in most cases is the reasons given for the opinion. As a practical matter a well-constructed expert's report containing opinion evidence sets out the opinion and the reasons for it. If the reasons stand up the opinion does, if not, not. A rule

> of evidence which excludes this opinion serves no practical purpose. What happens if the evidence is regarded as inadmissible is that experts' reports simply try to creep up to the opinion without openly giving it. They insinuate rather than explicate' (*Minories* at p.188).
>
> 15. Because the expert's conclusion (*e.g.* obvious or not), as such, although admissible, is of little value it does not really matter what the actual attributes of the real expert witness are. What matters are the reasons for his or her opinion. And those reasons do not depend on how closely the expert approximates to the skilled man."

102. In considering this passage, it is important to distinguish between two questions. The first question is whether the witness is uninventive. The second question is whether the witness is properly qualified to opine on the question of obviousness.

103. So far as the first question is concerned, it needs to be borne in mind that expert witnesses in patent cases often appear to be overqualified. There are at least two reasons for this. First, it is common for the experts to be called to address the state of the art 10-20 years earlier. In the present case, for example, the experts gave evidence at a trial in 2024 about the state of the art in 2010. It is inevitable that a witness who was in the relevant field at the relevant time will subsequently have gained more experience. Frequently, they will have become more senior, been promoted and so on. The second reason is that it is sometimes more practical, for reasons of independence and availability, to call witnesses who have recently retired. Prior to their retirement such witnesses will typically have been at the apex of their careers.

104. As Jacob LJ explained, in most cases it is unprofitable to attempt to compare the extent to which two expert witnesses reflect the requirement that the skilled person be uninventive. Typically, both witnesses will be leading scientists who have some degree of creativity. In most cases there is no clear metric by which to assess the relative "inventiveness" of two witnesses, and any attempt to do so will often confront the court with questions it is not in a position to answer. For example, being a named inventor on a number of patent applications does not necessarily indicate a high degree of inventiveness: it depends on the quality of the applications which in turn depends on the filing policy of the applicant. Furthermore, publishing scientific papers may or may not indicate just as much inventiveness, again depending on the quality of the papers which in turn depends on factors such as the reputation of the journals in which they are published.

105. So far as the second question is concerned, it is axiomatic that expert witnesses must be, in Nicholls V-C's words, "properly qualified". Not only was *Mölnlycke* binding on the Court in *Technip*, but also Jacob LJ cannot have intended to depart from that statement since he cited it. In order to be properly qualified, an expert witness must be in a position to speak to the common general knowledge of the skilled person at the relevant date. A witness who cannot do that is not properly qualified, no matter how expert that witness may be in other ways and no matter how good a witness the person in question is. It necessarily follows that it may be relevant in some cases to determine which of two expert witnesses more closely reflects the skills and experience of the

skilled person. A witness whose expertise closely reflects that of the skilled person is better placed, all other things being equal, to assist the court to assess whether a particular step would be obvious to the skilled person than a witness whose expertise does not closely reflect that of the skilled person. By contrast with "inventiveness", this is an assessment which the court is in a position to undertake applying objective criteria.

106. For this reason, it is commonplace for judges hearing patent cases to assess the extent to which the parties' expert witnesses embody the attributes of the skilled person. I shall confine myself to one example of this. In *MedImmune v Novartis Pharmaceuticals UK Ltd* [2011] EWHC 1669 (Pat), one of the expert witnesses was a Professor Brammer. As I explained at [116]-[117], he was a model witness whose evidence was of considerable assistance to me in understanding the technical issues, but his evidence did not reflect the perspective of a member of the skilled team. In his own words, he was "looking in from the outside". This assessment was not questioned on the appeal in that case [2012] EWCA Civ 1234, [2013] RPC 27.

107. In my judgment Jacob LJ cannot have intended in *Technip* to preclude, or even discourage, judges from making assessments of this kind. As Jacob LJ himself subsequently said in *SmithKline Beecham plc v Apotex Europe Ltd* [2004] EWCA Civ 1568, [2005] FSR 23 at [53]:

> "… in weighing the views of rival experts as to what is taught or what is obvious from what is taught, a judge should be careful to distinguish his views on the experts as to whether they are good witnesses or good teachers—good at answering the questions asked and not others, not argumentative and so on, from the more fundamental reasons for their opinions. Ultimately it is the latter which matter—are they reasons which would be perceived by the skilled man?"

108. Turning to the present case, PBNT rely on the judge's finding at [260] that there were real teams working in each of nine sub-fields where a solution to the problem addressed by EP949 could be useful, and his finding at [263] that the skilled person was someone with a knowledge of RNA biology, with a practical interest in improving the use of mRNA in relation to translation and immunogenicity in any of those sub-fields.

109. PBNT contend that the judge then fell into error when he found at [259] and [266] that the skilled person would not be "a basic scientist interested in fundamental research" and when he found at [265] that Dr Enright was "not from any of the subfields but rather a pure, basic scientist". PBNT argue that there is a gap or inconsistency in the judge's reasoning for three reasons. First, there is no sharp dividing line between fundamental research and therapeutic research. Secondly, sub-fields (iv), (v), (vii) and (viii) are towards the fundamental end of the spectrum. Thirdly, and most importantly, one real-world team working in sub-field (iv) (studying gene expression and the efficacy of RNA platforms) was Dr Enright's group, which used mRNA encoding reporter proteins to analyse microRNA binding in zebrafish.

110. I do not accept this argument. The first two points can be taken together. The judge did not suggest that there was a sharp dividing line between fundamental research and therapeutic research. As I read the judgment, this is part of the reason why the judge did not accept the dichotomy postulated by the parties between transcript therapy and fundamental research. Equally, it may well be correct to say that sub-fields (iv), (v), (vii) and (viii) are more towards the fundamental end of the spectrum than the other sub-fields, but that does not detract from the judge's point that what the sub-fields have in common is that they are all areas in which the invention potentially has practical application.

111. As for the third point, there is no gap or inconsistency in the judge's reasoning. It is clear that the judge was well aware that Dr Enright had carried out research in sub-field (iv). The judge's assessment was that Dr Enright's research in that sub-field was of a fundamental character rather than research into practical applications. That was a matter for his evaluation having heard Dr Enright give evidence. It is an assessment which the judge was fully entitled to make.

112. PBNT also contend that the judge erred in law when he concluded at [66] that, because Dr Enright was a pure, basic scientist interested in fundamental research, "Prof Rosenecker was a more useful witness in helping [the judge] to understand how the skilled person would think and reason at the EP949 Priority Date". PBNT submits that this is contrary to *Technip* at [15]. I do not accept this submission. For the reasons given in paragraphs 100-107 above, the judge was entirely correct to consider how closely the witnesses' experience corresponded to that of the skilled person. As the judge explained at [266] and [416], this has a significant impact on the assessment of obviousness.

113. Finally, although it is not a ground of appeal, PBNT suggest that it is odd that the judge said at [259] that "the upshot is more in favour of Moderna" when on the face of it the judge's formulation of the skilled person is closer to PBNT's than to Moderna's. As counsel for Moderna pointed out, however, the upshot of the judge's determination did favour Moderna when it came to the assessment of obviousness, which is precisely why PBNT complain about it.

Interpretation of [0056]

114. This ground of appeal recapitulates part of PBNT's argument on lack of novelty by route 3. PBNT contend that the judge should have interpreted [0056] as presenting a list of Ψ-like nucleosides of particular interest as a technical teaching. I disagree for the reasons given in paragraph 63 above.

Hindsight

115. The interpretation of [0056] feeds into PBNT's third ground. PBNT contend that the judge's conclusion at [63] that Dr Enright's approach was materially affected by hindsight was unfair and wrong because what Dr Enright said about m^5D is factually correct (it is the most structurally similar to $m^1\Psi$ of the modified nucleosides listed in [0056]) and there was nothing hindsight-driven in his focus on [0056] given that, as discussed in context of novelty, the definition applies to [004]/claim 1.

116. I do not accept this argument. The judge accepted at [58] that m^5D is in fact particularly similar to $m^1\Psi$. That does not undermine his view that the phraseology of paragraph 7.16 of Dr Enright's first report was indicative of hindsight. As for [0056], I have already held that the judge was right about its interpretation. In those circumstances the judge was entitled to conclude that Dr Enright's heavy focus on [0056] was another indication of hindsight. Furthermore, as counsel for Moderna pointed out, the judge's conclusion was also based on Dr Enright's reliance upon Brand, but PBNT do not challenge that aspect of his reasoning.

117. PBNT also question the relevance of Dr Enright's supposed hindsight given that his approach involved testing all five of the modified nucleosides listed in [0056], albeit that he had an order of preference. PBNT argue that this is the antithesis of hindsight. As to this, the judge explained the relevance of Dr Enright's hindsight repeatedly, in particular at [379](ii), [404], [409] and [415]. The judge made no error in taking that view.

Motivation and expectation of success

118. PBNT's fourth ground is largely, if not entirely, premised on acceptance of the first three grounds. PBNT contend that, if the judge had not mischaracterised the skilled person, wrongly sidelined Dr Enright, wrongly interpreted [0056] and wrongly found that Dr Enright's evidence was tainted with hindsight, he would and should have accepted Dr Enright's evidence that it would be obvious to the skilled person to explore other modified nucleosides, that they would start by examining modifications similar to Ψ and that they would want to test all five of those listed in [0056]. Since the premises for this contention have not been established, it does not get off the ground. The same goes for PBNT's argument that Dr Enright's evidence demonstrates that the skilled person would be motivated to test these modified nucleosides.

119. In addition, PBNT criticise the judge's reliance upon his finding at [266], [382], [409] and [415] that the skilled person would have no concrete or positive expectation of success if they considered whether to test $m^1\Psi$. PBNT do not challenge that finding as such, but they argue that this would have been a routine experiment in an empirical field, and therefore it is immaterial if the skilled person had no expectation of success, relying upon *Actavis v ICOS* at [65]. The short answer to this argument is that the judge was not persuaded that it would have been a routine experiment for the skilled person to undertake, so that they would do it without any expectation of success, unless the skilled person was a pure scientist engaged in fundamental research like Dr Enright, who was as interested in negative results as he was in positive results. The judge made no error in reaching that conclusion.

Conclusion

120. For the reasons given above the judge made no error of law or principle in concluding that claim 3 of EP949 was not obvious in the light of UPenn.

Overall conclusion

121. I would dismiss the appeal.

Lord Justice Snowden:

122. I agree.

Lord Justice Moylan:

123. I also agree.