Appeal Nos. CA-2024-002325 & CA-2024-002295

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 (The Hon Mr Justice Meade)

Claim No: HP-2022-000022

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

AND BETWEEN:

Claim No: HP-2022-000027

(1) PFIZER INC.
(2) BIONTECH SE

Claimants / Appellants

– and –

MODERNATX, INC.

Defendant / Respondent

PFIZER / BIONTECH'S SKELETON ARGUMENT ON THE RESPONDENT'S NOTICE

References to the Appeal Bundles are in the form [Bundle/Tab/Page]

12 June 2025

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1. This skeleton argument responds to Moderna's skeleton argument on its Respondent's Notice dated 17 April 2025 ("**Moderna's RN Skeleton**"). Defined terms used in Pfizer/BioNTech's main appeal skeleton argument (our "**Main Skeleton**") are adopted herein. It is also necessary to respond to a couple of points in Moderna's skeleton argument served on 5 June 2025 ("**Moderna's Main Skeleton**") which Moderna accepts are newly raised. [CORE/20] [CORE/19] [CORE/21]

Dr Enright

2. We addressed the Judge's errors concerning Dr Enright's background in our Main Skeleton at §§90-107. In particular, the Judge was wrong to characterise Dr Enright as a *"pure, basic scientist"* and/or to rely upon that finding (whether or not it was wrong) as a reason to support the finding that Prof Rosenecker was a more useful witness than Dr Enright in helping him to understand how the skilled person would think and reason. [CORE/19/298-301]

3. Similarly, the additional reasons advanced by Moderna relating to Dr Enright's work on modified nucleosides and microRNAs (§§2(a) & (b) of Moderna's RN Skeleton), cannot assist Moderna, even were they correct. It is well-established that the function of expert witnesses is to educate the court and that it does not matter whether or not they approximate the skilled person (see *Rockwater* [12]; §94 our Main Skeleton). The reliance by Moderna on the details of Dr Enright's work is therefore misplaced as a matter of law. [CORE/20/309] [JA/4/172-173] [CORE/19/299]

4. But a further problem arises for Moderna on the relevance of Dr Enright's work as a matter of fact, because the Judge made a finding that Dr Enright's group was an example of a real-world team working in an area where a solution to the problem addressed by EP949 could be useful, namely studying gene expression and the efficacy of RNA platforms (see §§260-263 Judgment and in particular item (iv) §260). The work of Dr Enright's group was reflected in (by way of example) the zebrafish publications, including the Giraldez 2006 paper. It follows that Dr Enright *can* fairly be said to approximate the skilled person. [CORE/5/102-103] [SUPP/4]

5. Moderna tries to explain away the obvious inconsistency in the Judge's approach by making a new point in its Main Skeleton at §§120-123 to the effect that the Judge cannot have been intending to include Dr Enright's team within his characterisation of real teams in the field but instead intended to exclude teams doing work of the type reported in Giraldez 2006. [CORE/21/332-333] [SUPP/4]

6. This makes no sense. The Judge's §260 list was taken directly from Pfizer/BioNTech's closing submissions at §§48-77 (headings A to G corresponding to sub-paragraphs (i) to (ix) in §260 Judgment), which referred to a number of real research teams in those areas, as illustrated by their published literature. One sub-paragraph expressly included was "*Studying gene expression and the efficacy of RNA platforms*", and the Giraldez 2006 paper co-authored by Dr Enright was one of three papers referred to in §65(a) of Pfizer/BioNTech's closing submissions which established this as an area where a solution to the problem identified by EP 949 could be useful. [CORE/5/102-103] [SUPP/20/295-305] [CORE/5/102-103] [SUPP/20/300]

7. Had the Judge wished to exclude the Giraldez paper (and thus Dr Enright's work in this area), he would have had to do so expressly and explain why. Moderna cannot be right that one must read into §260 of the Judgment that the Judge had specifically excluded the Giraldez work because it was towards the basic research end of the spectrum (Moderna's Main Skeleton §§122-123), particularly when a significant number of the other examples of real-world teams identified by Pfizer/BioNTech in its closing submissions similarly had basic research goals in mind – see for example §§50, 67, 69, 70-73 &74-75 of Pfizer/BioNTech's closing submissions. In the light of this, it is plain that the mistake made by the Judge was to sideline Dr Enright's evidence on the basis of an incorrect assumption about his experience. [CORE/21/333] [SUPP/20/295-297, 301, 302-304]

8. Given that there is no requirement as a matter of law that an expert approximates the skilled person, there is certainly no basis upon which to go further and require that an expert must have been actively working on seeking to solve the specific problem that the patent addresses in order to assist the Court, which is the proposition that Moderna's additional reasons at §§2(a) & (b) of its RN Skeleton seek to support. Nevertheless: [CORE/20/309]

   (a) As to (a), Dr Enright's work on modified nucleosides was concerned with their natural incidence in mRNA and how they regulate mRNA expression, which illustrates his necessarily deep understanding of mRNA biology (see T1/110$_9$-111$_2$). [SUPP/15]

   (b) As to (b), and as explained in our Main Skeleton at §102, whilst microRNAs are not themselves translated, they function by binding to mRNAs and regulating their translation. Dr Enright was asked about the Giraldez 2006 paper and explained that it used mRNA encoded reporter genes (T1/82$_8$-85$_{23}$) and that mRNA that is [CORE/19/300] [SUPP/15/253-254]

translated effectively would have been useful in such work (T1/116$_{19}$-117$_{8}$). The fact that microRNA binding typically downregulates mRNA translation is irrelevant, since Dr Enright's work (as exemplified by the Giraldez paper) involved assessing mRNA translation. So, the Judge rightly found that a solution to the problem of increasing the translation and reducing the immunogenicity of such mRNA would have been useful in that work (see §§257-263 Judgment). Further, Dr Enright explained that microRNAs were "*on the way*" to therapeutics and that all his work on RNA and mRNA biology was directed towards helping understand and prevent human disease (T1/130$_{3\text{-}16}$). It was therefore wrong to describe him as a "*pure, basic scientist*". [SUPP/15] [CORE/5/102-103] [SUPP/15/257]

(c) Finally, we note that Moderna's expert, Prof Rosenecker, was not himself making the decisions in his team about which modified nucleosides to use around the priority date – see §§43 & 255 Judgment. So if it was a requirement that an expert must have been actively working on seeking to solve the problem that the patent addresses in order to assist the Court, then his evidence should also have been rejected. [CORE/5/57 & 101]

Routes 1 and 2

9. We addressed the correct construction of Example 31 of UPenn in our Main Skeleton at §§60-62 & 69. It teaches the skilled reader to make additional nucleoside modifications and test them for both immunogenicity and translation. This is clear from at least the following (emphases added): [CORE/19/292-293 & 294]

(a) The Example is entitled "*Testing the effect of additional nucleoside modifications on RNA immunogenicity and efficiency of translation*"; [SUPP/2/160]

(b) Having cross-referred back to the Examples describing how to make the RNAs (Examples 2 and 7) and test for immunogenicity (Examples 1-8) and translation efficiency (Examples 9-15), Example 31 then states that *"Certain additional modifications are found to decrease immunogenicity and enhance translation"*; and [SUPP/2/131-134 & 139-140] [SUPP/2/128-141] [SUPP/2/140-146]

(c) It was CGK that modified nucleosides could reduce the immunogenicity of mRNA (e.g., from Karikó 2005), so the skilled reader would understand that the advance being taught by UPenn was modifications that could not only reduce

immunogenicity but also enhance translation, i.e. do both (see Judgment §§221(iii), 231 & 377). [CORE/5/96-97, 98 & 126]

10. Whilst it is right to say that Example 31 proposes testing for immunogenicity and that testing for immunogenicity does not require the use of mRNA (see §3 of Moderna's RN Skeleton), Example 31 is teaching the skilled reader to test for both, and testing for both requires RNA that can be translated i.e. mRNA. [CORE/20/309]

11. As for §4 of Moderna's RN Skeleton, we have addressed why the Judge was wrong to find that m1Ψ was not individually described in our Main Skeleton at §§71-75. Given that Example 31, properly construed, provides instructions to go back and perform Example 2 with each of the additional modifications from [00291] (see our Main Skeleton §§67-70 & 76), it follows that [00290] individually describes the use of Example 2 with m1Ψ. [CORE/20/309] [CORE/19/294-295] [CORE/19/293-294 & 295]

12. These references in our Main Skeleton also demonstrate that Moderna is wrong to suggest that we have not challenged the Judge's finding in the second sentence of §324 (Moderna's Main Skeleton §§90, 97-98). That being said, even if Example 31 does *not* teach the skilled reader to go back and perform Example 2 with the exact RNAs disclosed there, the use of the method in Example 2 to synthesise *any mRNA* with m1Ψ to test for immunogenicity and translation will hit claim 3. The Judge's finding in §324 must be read alongside his finding at §379(v) that Example 31 was *"a positive teaching to look for other, better, nucleosides… which is a technical teaching"*. [CORE/5/117] [CORE/21/326 & 328] [CORE/5/117 & 127]

13. As for §5 of Moderna's RN Skeleton, we have addressed why the Judge was wrong to find that even if m1Ψ was individually described then Routes 1 and 2 still required a selection from lists at §§60-69 of our Main Skeleton; see also §§9-10 above. If, contrary to Pfizer/BioNTech's primary case, a selection from lists is required, claim 3 lacks novelty on this basis too since there are sufficient pointers to mRNA and/or to m1Ψ for the reasons given at §§75 & 77-78 Main Skeleton and §§9-10 above. [CORE/5/312] [CORE/19/292-294] [CORE/19/295]

[0056]

14. We have addressed the correct construction of [0056] of UPenn at §§21-31 of our Main Skeleton. It would be understood to disclose the Ψ-like nucleosides of particular interest. [0069] is the only other short list of nucleosides, but the skilled person would recognise they had already been tested in UPenn and had not performed as well as Ψ [CORE/19/286-288]

(§375 Judgment). That only serves further to support the skilled reader's interest in the list of Ψ-like nucleosides in [0056], each of which is explicitly described in [0056] of UPenn as a "*[p]seudouridine*". Moderna suggests in §§56-58 of its Main Skeleton that it was not argued at trial that m1Ψ was "individualised" in [0056]. This submission is not understood as it is clear from Pfizer/BioNtech's Novelty Chart at trial that it was relying on the disclosure of m1Ψ in [0056] as a preferred pseudouridine residue within the scope of claim 1/[004]. [CORE/5/125] [CORE/21/320-321]

100% Replacement

15. Moderna raises a new point in §68 of its Main Skeleton about 100% replacement. This point was not run before the Judge and does not appear in Moderna's Respondent's Notice. It is said (at §66) that this is in response to new arguments run by Pfizer/BioNTech on appeal, but this is incorrect – the points at §§64-66 of Moderna's Main Skeleton reflect the reliance by Pfizer/BioNTech on Examples 2, 7 and the CGK at trial (which Moderna acknowledges at §61) – see the third column of Pfizer/BioNTech's novelty chart. However, neither party wishes to trouble the Court with a "pleading point" and so we deal with it below. [CORE/21/322-323] [CORE/21/320-322] [CORE/21/322] [CORE/21/321]

16. Moderna's argument is that because the data in UPenn show that there are other modifications which do not work in terms of translation (m^5C, m^5U and m^6A), the skilled reader would be discouraged from trying 100% replacement of uridine with a pseudouridine. This is a complete non-sequitur and neither of the experts suggested this in their evidence at trial. The experiments to which Moderna refers were not designed to test the optimum % of replacements and, like the other experiments in UPenn, 100% replacement was the default for all (except the 5% m^6A which performed no better than unmodified mRNA). There is therefore no basis for Moderna to rely on this material in relation to the point about 100% replacement, and, even if it could, it does nothing to undermine Pfizer/BioNTech's case on novelty. As explained in our Main Skeleton at §51, Example 2 of UPenn teaches 100% replacement and Example 7 (see Figure 5) teaches that 100% replacement, as opposed to some lesser % replacement, results in the greatest effect in terms of a reduction in innate immune response, which was consistent with the CGK (see §§51(a)-(c) of our Main Skeleton). [CORE/19/291] [SUPP/2/138-140 & 174] [CORE/19/291]