



## PATENTS ACT 1977

APPLICANT	4D Pharma Research Limited
ISSUE	Whether patent application GB1809729.5 complies with the requirements of section 14(3) and 14(5)(c)
HEARING OFFICER	D L Cullen

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### DECISION

- 1 This decision concerns whether the specification of patent application GB1809729.5 entitled "*Compositions comprising bacterial strains*" ("the application") discloses the invention in a manner which is clear and complete enough to enable the invention to be performed by a person skilled in the art, as required by Section 14(3) of the Patents Act 1977 ("the Act"), and whether the claims are adequately supported by the description, as required by Section 14(5)(c) of the Act.

#### Background

- 2 The application was filed on 23 November 2016 in the name of 4D Pharma Research Limited claiming an earliest priority date of 23 November 2015. It was published as international application WO 2017/089795 on 1 June 2017 and republished as GB 2560139 on 29 August 2018, following its entry into the UK national phase.
- 3 The compliance period prescribed under Section 18(4) and Section 20(1) of the Act and further set down in Rule 30 of the Patents Rules 2007 as amended (hereafter the 'Rules') for putting this application in order for grant, originally expired on 23 May 2020. As a result of the period of interrupted days declared on 27 March 2020 under rule 110 of the Rules, this compliance date was extended to 30 July 2020 and, it was subsequently extended as-of-right under rule 108(2) to 30 September 2020 following the filing of the requisite patents form 52 (hereafter 'F52') on the final day of the qualifying period under rule 108(2)(b).
- 4 A letter from the agent dated 30 November 2020 appears to be a request for a discretionary extension to the compliance period under Rule 108(3) but there is a question over whether this was a valid request. This matter is considered further below.
- 5 An objection to lack of support was initially raised in the first examination report in the UK national phase dated 4 July 2018. An objection to insufficiency of disclosure was

first raised in the third examination report in the UK national phase dated 15 October 2019. Both objections were maintained through the further rounds of amendment and correspondence between the applicant and the examiner. As the applicant and examiner were unable to reach agreement on these issues, the applicant requested a hearing.

- 6 The examiner set out the issues to be decided in his pre-hearing report dated 30 July 2020 and the matter came before me at a hearing via video conference on 12 October 2020. The applicant was represented by Cameron Marshall of Carpmaels & Ransford. Karl Whitfield acted as assistant to the hearing officer.

### **The Invention**

- 7 This application relates to a composition comprising a bacterial strain isolated from the mammalian digestive tract and its use in the treatment of disease.
- 8 A bacterial strain is a genetic variant or subtype of a bacterial species. This intra-species diversity results mainly from genetic events such as: horizontal gene transfer, gene loss or acquisition, and recombination. This genetic diversity is the source of phenotypic variability seen in bacteria, such as geographic distribution, host specificity, pathogenicity, antibiotic resistance, and virulence.
- 9 The bacterial strain of interest in this invention is from the genus *Eubacterium*. It is identified as *Eubacterium contortum* MRX050 and the invention relates to compositions comprising this bacterial strain and other strains of *Eubacterium contortum* (hereafter *E. contortum*) and their use in a method of treating or preventing an inflammatory disease or condition mediated by the T-helper 17 cell (Th17) pathway.<sup>1</sup>
- 10 The Th17 cell pathway plays an important role in inducing the inflammatory process, the immediate protective response of the body to foreign pathogens. However, this immune response needs to be controlled to avoid injury mediated by the immune response in the form of chronic inflammation. CD4<sup>+</sup> T-cells are the first line of defence when dealing with pathogens, playing a major role in the induction and regulation of immune responses, mainly by secreting cytokines. After antigenic stimulus, naïve CD4<sup>+</sup> T cells differentiate into effector T cells. There are three main classes of such effector T cells, Th1, Th2 and Th17. While Th1 and Th2 cells provide effector responses to intracellular bacterial infections and parasitic pathogens, respectively, Th17 cells offer protection against extracellular bacterial and fungal infections and have been implicated in autoimmunity.

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<sup>1</sup> T-helper cells (Th cells), also known as CD4<sup>+</sup> cells, play an important role in the immune system, particularly in the adaptive immune system. As their name suggests, they "help" the activity of other immune cells by releasing cytokines, the small protein mediators that alter the behaviour of target cells that express receptors for those cytokines. These cells help to polarize the immune response into the appropriate kind depending on the nature of the immunological insult (virus vs. extracellular bacterium vs. intracellular bacterium vs. helminth vs. fungus vs. protist).

- 11 Th17 cells yield the Interleukin 17 (IL-17) family of cytokines.<sup>2</sup> IL-17 is required for inducing and mediating pro-inflammatory responses in the body and providing protection against pathogens. IL-17 stimulates the recruitment of neutrophils and monocytes into inflamed areas. The Th17 pathway has a major role to play in several inflammatory and autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, psoriasis, lupus, asthma and cancer (e.g., breast cancer, liver cancer). Uncontrolled activation of Th17 cells plays a significant role in the pathogenesis of such inflammatory and autoimmune disorders.
- 12 In this application, a bacterial strain of *E. contortum*, identified as MRX050, which was isolated from the digestive tract of a human volunteer, is shown to have a therapeutic effect using a mouse model of uveitis, an inflammatory condition that effects the eye. Uveitis is the term given to inflammation of the uvea, the central pigmented layer of the eye and, if untreated in humans, it can lead to cataracts, glaucoma, macular oedema and permanent vision loss. The applicants propose that the MRX050 strain and other strains of *E. contortum* can be used to treat inflammatory and autoimmune conditions, such as uveitis, that are mediated by the Th17 pathway, that they can reduce levels of cytokines that are part of the Th17 pathway, including IL-17, and they can alleviate the Th17 inflammatory response.

### **The Claims**

- 13 The set of claims currently on file consists of 29 claims. The examiner has raised no objection to claims 23 to 28 and I will not consider them further. Claims 1 and 29, as amended, are independent claims. Both claims relate to compositions for use in therapy and read as follows:

*1. A composition comprising a bacterial strain of the species Eubacterium contortum, for use in a method of treating or preventing an inflammatory or autoimmune disease mediated by the Th17 pathway.*

*29. A composition comprising a single bacterial strain of the species Eubacterium contortum, which does not contain any other bacterial strains or species, or which comprises only de minimis or biologically irrelevant amounts of other bacterial strains or species, for use in therapy.*

### **Matters to be decided**

- 14 There are two issues to be decided:
- (i) does the specification disclose the invention in a manner which is clear and complete enough, as required by Section 14(3) of the Patents Act 1977?
- and

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<sup>2</sup> The IL-17 family in humans comprises IL-17A (sometimes identified as "IL-17"), IL-17B, IL-17C, IL-17D, IL-17E and IL-17F. IL-17E is also known as IL-25. All members of the IL-17 family have a similar protein structure. Their protein sequences contain four highly conserved cysteine residues which are critical for ensuring the 3-dimensional shape of the entire molecule.

(ii) are the claims supported by the description, as required by Section 14(5)(c) of the Patents Act 1977?

15 In effect, I must determine whether, or not, there is enough information in the specification as filed that allows the invention to be performed across the entire breadth of what is claimed.

16 In dealing with this case, a question also arose in relation to whether or not the request for a discretionary extension to the compliance period under Rule 108(3) made by the applicant in their letter dated 30 November 2020 was valid.

17 I will first consider the substantive issue under Section 14 and then I will go on to consider the procedural issue in relation to Rule 108(3).

## Support and Sufficiency under Section 14

### The Law

18 Section 14 of the Act, entitled 'Making of Application', refers to certain requirements that the specification and its associated claims must meet to be allowable. In this instance, we are concerned with Sections 14(3) and 14(5).

#### *Section 14(3)*

19 Section 14(3) relates to the specification and reads as follows:

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*(3) The specification of an application shall disclose the invention in a manner which is clear enough and complete enough for the invention to be performed by a person skilled in the art.*

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20 As set down in Section 130(7) of the Act, Section 14(3) is intended to have, as nearly as practicable, the same effect as the corresponding provisions of the European Patent Convention (EPC) and the Patent Cooperation Treaty (PCT). Article 83 EPC and Article 5 PCT require the invention to be disclosed "*in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art*". An objection under this section of the Act is often referred to as "sufficiency of disclosure" or "sufficiency". This pre-grant provision concerning the patent application accords directly with section 72(1)(c) of the Act which sets out the same requirement for the validity of the granted patent. Thus, while much of the case law relating to sufficiency derives from proceedings concerning granted patents under section 72, the principles set out in these cases are pertinent to section 14(3). It is the responsibility of the applicant to ensure that, at the time of filing the application, the disclosure is clear enough and complete enough in respect of the invention defined in each of the claims. If it is not, then the application shall be refused or, if it is possible to do so, the claims must be restricted or amended to that matter which has been adequately disclosed, i.e., that for which there is an enabling disclosure. Deficiencies in the disclosure cannot be

corrected subsequently by adding matter because of the prohibition under section 76(2) of the Act.

21 The overall purpose of Section 14(3) is to prevent the patent applicant from claiming products or processes which the teaching of the specification does not enable the skilled person to perform. In effect, one is being asked to determine if there is enough information in the specification as filed by the applicant to allow the person who has a reasonable knowledge and understanding of the technical area described to carry out the invention as defined in the claims.

22 Kitchin J provided a summary of the relevant principles to be applied when assessing sufficiency (at paragraph 239) in *Eli Lilly v Human Genome Sciences*, [2008] RPC 29 (hereafter *Eli Lilly*):

*"The specification must disclose the invention clearly and completely enough for it to be performed by a person skilled in the art. The key elements of this requirement which bear on the present case are these:*

*(i) the first step is to identify the invention and that is to be done by reading and construing the claims;*

*(ii) in the case of a product claim that means making or otherwise obtaining the product;*

*(iii) in the case of a process claim, it means working the process;*

*(iv) the sufficiency of the disclosure must be assessed on the basis of the specification as a whole including the description and the claims;*

*(v) the disclosure is aimed at the skilled person who may use his common general knowledge to supplement the information contained in the specification;*

*(vi) the specification must be sufficient to allow the invention to be performed over the whole scope of the claim;*

*(vii) the specification must be sufficient to allow the invention to be so performed without undue burden."*

23 The claims are interpreted in the light of the description and the drawings as set out in Section 125 of the Act. They are construed in a purposive manner following the established principles of UK patent law.

24 For the purposes of s.14(3), the skilled person is seeking to make the patent work and does so with the common general knowledge at the time the patent was filed. The skilled worker has the patent in front of them, and thus is "*trying to carry out the invention and achieve success, ... not searching for a solution in ignorance of it.*" (see *Zipher Ltd v Markem Systems Ltd.*, [2009] FSR 1 at page 50, hereafter *Zipher*).

25 Whilst there is only one provision under the Act, it is well established in UK law that the understanding of what sufficiency is - in terms of the disclosure being clear and complete enough for the invention to be performed by the person skilled in the art - can be approached in three different ways, i.e.:

- 1) Classical insufficiency
- 2) Insufficiency by uncertainty/ambiguity
- 3) Insufficiency by excessive claim breadth

A summary of what should be understood by each of these approaches to sufficiency was provided by Floyd J (as he then was) in *Zipher* (see paragraphs 361 to 454, but especially paras 367-373 & 440-454). For the purposes of the present case we are concerned with the third approach to sufficiency outlined above.

- 26 The House of Lords in *Biogen Inc v Medeva plc* [1997] RPC 1 (hereafter *Biogen*) held that for the purposes of section 14(3) and section 72(1)(c) of the Act, the disclosure must be enough to enable the full width of the claimed invention to be performed, and that the disclosure of a single embodiment will not always satisfy this requirement regardless of the width of the claim. Lord Hoffman pointed out (at page 51, line 1 - page 52, line 8), that the extent of the patent monopoly as defined by the claims should not go beyond the technical contribution of the invention:

*“... there is more than one way in which the breadth of the claim may exceed the technical contribution to the art embodied in the invention. The patent may claim results which it does not enable, such as making a wide class of products when it enables only one of those products and discloses no principle which would enable others to be made. Or it may claim every way of achieving a result when it enables only one way and it is possible to envisage other ways of achieving that result which makes no use of the invention.”*

- 27 This type of insufficiency, arising from a disclosure which does not enable the invention to be performed across the entire width of the claim, is thus sometimes referred to as ‘*Biogen insufficiency*’.

- 28 The question of what is necessary to render an application or patent relating to a second medical use sufficient was discussed by the Supreme Court in *Warner-Lambert Company LLC v Generics (UK) Ltd (t.a. Mylan) & Anor.* [2018] UKSC 56, (hereafter *Warner-Lambert*). In its decision, the court considered a number of principles that can be used to assess the sufficiency of medical use claims. The claims of interest were in the Swiss format, but the principles outlined apply equally to the new form of medical use claims which have replaced Swiss claims following the amendments to the European Patent Convention (EPC) in 2000 (given effect in Section 4A of the Act). In the present case we are dealing with a claim in the new form, i.e. the post-EPC 2000 format.

- 29 As part of its judgment, the court in *Warner-Lambert* outlined, in paragraphs 36 and 37, how the concept of plausibility applies to the statutory requirement for sufficiency. Considering the earlier Court of Appeal judgment in this case, the Supreme Court found that there is a general principle for determining if a claim to a medical use is plausible which it set down as follows (my emphasis added in bold):

*“36. The Court of Appeal’s statement of the effect of the plausibility test has already been quoted (para 20 above). They considered that the threshold was not only low, but that the test could be satisfied by a “prediction ... based on the slimmest of evidence” or one based on material which was “manifestly incomplete”. Consistently with that approach, they considered (paras 40, 130) that the Board’s observations in SALK laid down no general principle. I respectfully disagree. The*

*principle is that the specification must disclose some reason for supposing that the implied assertion of efficacy in the claim is true. **Plausibility is not a distinct condition of validity with a life of its own, but a standard against which that must be demonstrated. Its adoption is a mitigation of the principle in favour of patentability. It reflects the practical difficulty of demonstrating therapeutic efficacy to any higher standard at the stage when the patent application must in practice be made. The test is relatively undemanding. But it cannot be deprived of all meaning or reduced, as Floyd LJ's statement does, to little more than a test of good faith. Indeed, if the threshold were as low as he suggests, it would be unlikely to serve even the limited purpose that he assigns to it of barring speculative or armchair claims.***

30 In the following paragraph of this judgment, it set out seven principles concerning the requirement for plausibility in medical use claims. These principles are discussed and listed in para 4A.29.5 of the IPO's Manual of Patent Practice.<sup>3</sup> I find this list a helpful reminder when considering the plausibility of a claim to a medical use; i.e.

- i) The proposition that a product is effective for the treatment of a given condition must be plausible.*
- ii) It is not made plausible by a bare assertion to that effect, and the disclosure of a mere possibility that it will work is no better than a bare assertion.*
- iii) The claimed therapeutic effect may be rendered plausible by a specification showing that something is worth trying for a reason; i.e. not just because there is an abstract possibility that it would work but because reasonable scientific grounds are disclosed for expecting that it might well work. The disclosure of those grounds marks the difference between a speculation and a contribution to the art.*
- iv) Although the disclosure need not definitively prove the assertion that the product works for the designated purpose, there must be something that would cause the skilled person to think that there was a reasonable prospect that the assertion would prove to be true.*
- v) That reasonable prospect must be based on a direct effect on a mechanism specifically involved in the disease, this mechanism being either known from the prior art or demonstrated in the patent per se.*
- vi) This effect on the disease process need not necessarily be demonstrated by experimental data. It can also be demonstrated by a priori reasoning.*
- vii) This evidence or reasoning must appear in the patent. The disclosure may be supplemented or explained by the common general knowledge of the skilled person. However, it is not enough that the patentee can prove that the product can reasonably be expected to work in the designated use, if the skilled person would not derive this from the teaching of the patent.*

31 The *Warner-Lambert* judgment also makes clear that the specification **as filed** must make the claimed use plausible; data filed after the filing date of the patent can only

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<sup>3</sup> The Manual of Patent Practice explains the IPO's practice under the Act and Rules and makes helpful references to relevant case law. The Manual can be viewed online at the IPO's website: <https://www.gov.uk/guidance/manual-of-patent-practice-mopp>. For the present case, paragraphs 4A.29 and 4A.29.2 - 4A.29.5 of the Manual are relevant



be used to confirm an effect made plausible in the specification or to refute a contention that the treatment does not actually work; it cannot be a substitute for sufficient disclosure in the specification.

*Section 14(5)*

32 Section 14(5) relates to the claims and reads as follows (my emphasis added):

**(5) The claim or claims shall –**

*(a) define the matter for which the applicant seeks protection;*

*(b) be clear and concise;*

***(c) be supported by the description;***

*(d) relate to one invention or to a group of inventions which are so linked as to form a single inventive concept. ....*

In the present case we are concerned specifically with Section 14(5)(c) (as highlighted above).

33 As set down in Section 130(7) of the Act, Section 14(5) is intended to have, as nearly as practicable, the same effect as the corresponding provision of the EPC, Article 84, and of the PCT, Article 6. Both provisions use essentially the same wording as section 14(5)(a)-(c).

34 It is established practice in UK law that the form of the claim is a matter for the applicant, and that any claim which fulfils the requirements of the Act is acceptable. The claims as a whole should aim to define and delimit the features of the invention, with the independent claims clearly establishing the essential features of the invention as well as providing enough details of interrelationship, operation or utility to establish that the invention achieves the intended objectives. Section 14(5)(c) requires that the scope of the invention, as defined in the claims, is consistent with what is disclosed in the specification, and not so broad that it goes beyond the invention, yet not so narrow that it deprives the applicant of a just reward for the disclosure of his invention.

35 A claim to the use of a substance or composition in therapy, surgery or diagnosis requires support by evidence of its likely efficacy in that use. This requirement follows from the decision by the Patents Court in *Prendergast's Applications [2000] RPC 446* (hereafter *Prendergast*). This case concerned support for Swiss-type second medical use claims and held that, as such claims are distinguished from the prior art by their use, this use must be supported by evidence. In this decision, Neuberger J, as he then was, emphasised that rudimentary tests would suffice and that full, detailed and rigorous testing of a drug for the proposed condition, e.g., clinical trials, was not necessary. In the absence of such evidence, the claim is considered to be speculative and to lack support.

36 The Hearing Officer in Office decision *Hoffmann-La Roche's Application (BL O/192/04)*<sup>4</sup> applied the same reasoning to claims in the first medical use format because the essential feature of such claims is the intended use and so there must be support for it. The form of evidence is not critical; the application may provide *in vivo*

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<sup>4</sup> For full text of Office decision BL O/192/04 see [Intellectual Property Office - Patents Decision \(ipo.gov.uk\)](http://www.ipo.gov.uk)



or *in vitro* data, and *in silico* modelling data may be sufficient if it is considered to provide a credible basis for support. Thus, in the case of inventions having at their heart a medical use, the description should not only identify a condition that may be treated but must show by reference to tests that the treatment is a reality and not just a possibility.<sup>5</sup> An applicant does not have to restrict their claims to the specific embodiment described, but the width of the claims must be properly supported by the description of the invention in the specification.

- 37 In *Prendergast*, the court found that support for the therapeutic use must be found in the specification. As such, later filed evidence cannot overcome the absence of any such support in the application as filed. This decision was acknowledged with approval by the House of Lords in *Conor v Angiotech* [2008] RPC 28, and the requirement for some evidence in the application to support second medical use claims was confirmed by the Patents Court decision in *El-Tawil's Application* [2012] EWHC 185.

*Relationship between Section 14(3) and Section 14(5)*

- 38 The Court of Appeal in *Genentech Inc's Patent*, [1989] RPC 147 noted that lack of support is not a ground which can be addressed after a patent is granted, unlike the provision concerning sufficiency. The comments of Dillon LJ therein (at page 236, line 50 - page 237, line 3) are a useful guide to the approach to be adopted:

*"The Patent Office ought to have very clearly in mind that it is undesirable to allow claims the object of which is to cover a wide and unexplored field or where there is no disclosure in the specification which is in any way coterminous with the monopoly indicated in the claims."*

- 39 The importance of a correct decision pre-grant on the question of lack of support was further emphasised by Aldous J in *Schering Biotech Corp.'s Application* [1993] RPC 249 (hereafter *Schering*), and he went on to point out (at page 252, line 53 - page 253, line 2) that the substance of the disclosure, rather than its form, was the key issue:

*"I do not believe that the mere mention in the specification of features appearing in the claim will necessarily be a sufficient support. The word 'support' means more than that and requires the description to be the base which can fairly entitle the patentee to a monopoly of the width claimed."*

- 40 It is often the case that the requirements of Section 14(5) of the Act overlap with those of Section 14(3) as both are concerned with the relationship between the extent of disclosure and the scope of the claims. As pointed out by Lord Walker in *Generics v Lundbeck* [2009] RPC 13 (at paragraph 20, hereafter *Generics*):

*"The disclosure must be such as to enable the invention to be performed...to the full extent of the claims. The question of whether there is sufficient enabling disclosure often interacts with a question of construction as to the extent of the claims"*.

- 41 This is particularly apparent in applications where the claims are unduly broad and speculative, as argued by the examiner in the present case, and therefore objections

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<sup>5</sup> See *Hoerrmann's Application* [1996] RPC 341; *Consultant Suppliers Ltd's Application* [1996] RPC 348.

can be raised under both Section 14(3) and Section 14(5)(c). Therefore, whilst I will deal with these sections of the Act individually below, there will inevitably be some overlap in the reasoning.

- 42 Taking all the above into account, I consider that the law requires me to determine, based on the information in the application and taking account of the views of the examiner and applicant during the examination process, whether the application provides enough detail to support the invention as claimed.

### Analysis

- 43 Taking note of the principles for assessing sufficiency set down in *Eli Lilly* (see above), the first step is to construe the claims, as it would be understood by the skilled person, interpreting them in light of the description and any drawings in the application as filed, as instructed by Section 125(1) of the Act and taking into account the Protocol to Article 69 of the EPC. To do so I first need to identify the skilled person.
- 44 Neither the examiner nor the applicant in their correspondence dwell on the identity of the skilled person. From this I take it that each considered that little turned on the point. However, sufficiency is determined based on the knowledge of the skilled person so I will deal with this point briefly. I consider the skilled person to be a team comprising a microbiologist with a knowledge of mammalian gut microbiota and a clinician having a knowledge of inflammatory and autoimmune diseases caused by bacteria and their treatment. They would be aware of the role that cytokines and interleukins play in such disease caused by bacteria. This team would be familiar with the methods to identify, isolate and culture bacterial species and strains of such species.
- 45 Turning to claim 1, it seems to me that construing the claim is straightforward. The claim refers to a composition comprising a bacterial strain of the species *E. contortum*. I consider that this means that the composition comprises a bacterial strain of *E. contortum* that has been isolated from nature, cultured and characterised. Thus, when compared to a deposited example of a strain of *E. contortum*, such as that identified in this application as being deposited with the National Collection of Industrial, Food and Marine Bacteria (NCIMB)<sup>6</sup> and identified as NCIMB 42689 or *E. contortum* MRX050, the strain being characterised is considered to be the same species as this reference sample.
- 46 This construction is also consistent for Claim 29 because ensuring that the strain present in the composition is a single strain and does not contain other bacterial strains is achieved by using an isolated pure culture to prepare the *E. contortum* strain in the composition. I consider that the alternative restriction to “only *de minimis* or biologically irrelevant amounts of other bacterial strains or species” is also consistent with this construction as it relates to the fact that one may not be able to achieve 100%

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<sup>6</sup> The National Collection of Industrial, Food and Marine Bacteria (NCIMB) is a collection of environmental and industrially useful bacterial cultures based in the UK. It has a large reference collection and has over 10,000 deposits. Deposits are made for research purposes, or for inclusion into patent submissions. NCIMB has served as a depository under the Budapest Treaty since 1982 for biological material that is the subject of patent applications.

pure bacterial strain of *E. contortum* but one can achieve a culture that has only a very small amount of other strains or species of bacteria and so, for all practical purposes, its behaviour and properties are that of the single pure strain. It indicates that the claim relates to a composition comprising a pure isolated culture rather than referring to the strain of bacteria in its natural state (i.e., the strain as present as one in a mixture of bacterial strains as occurs in nature). As the application makes clear and as mentioned above, the techniques necessary to isolate, culture and characterise such bacterial strains and to obtain them in sufficient amounts for inclusion in a composition for ingestion are known.

- 47 It is clear and accepted by both the examiner and the applicant that the application discloses only one study using one bacterial strain to treat one inflammatory disease. More specifically, Example 1, described on pages 29 to 32 of the application as filed, details the administration of *Eubacterium contortum* strain MRX050 to mice with uveitis and the effects of this composition on relieving the uveitis. The conclusions from the study are described in the application (page 32 line 12-18) as follows:

*“Clinical scores determined by TEFI [topical endoscopic fundal imaging] increased from Day 14, as expected in this model of IRBP-induced [interphotoreceptor retinoid-binding protein-induced] uveitis. By Day 28, a striking and statistically significant reduction in disease incidence and disease severity was observed in the MRX050-treated group, which was comparable to that seen for the positive control group. In particular, these data indicate that treatment with the strain MRX050 reduced retinal damage, optic disc inflammation and/or retinal tissue infiltration by inflammatory cells (see TEFI retinal image scoring system above). These data indicate the strain MRX050 may be useful for treating or preventing uveitis.”*

- 48 Returning to the wording of claim 1:

*A composition comprising a bacterial strain of the species Eubacterium contortum, for use in a method of treating or preventing an inflammatory or autoimmune disease mediated by the Th17 pathway.*

This leads me to consider two aspects of the issue of support in this application. The first aspect being whether there is support for a composition for treating conditions other than uveitis and the second aspect being whether there is support for the use of a composition comprising any strain of *E. contortum* other than MRX050.

#### *Treatment of Conditions other than Uveitis*

- 49 According to the examiner the evidence in the application does not demonstrate any direct effect on the Th17 pathway, which given its nature is often also referred to as the Th17 cascade. It does not demonstrate that this is the mechanism by which the treatment is effective or show that this cascade is involved in achieving the therapeutic outcome observed in Example 1. Without direct evidence of an effect on an underlying mechanism he feels that there is not support across the full breath of claim 1. In a similar fashion his view is that test results relating to the single bacterial strain MRX050 cannot be generalised to all strains of *E. contortum*, not least since there is no common general knowledge as to how *E. contortum* might work mechanistically.

- 50 For their part the applicants argue that treatment of uveitis must involve an effect on Th17/IL-17 pathway since there is no other mechanism suggested by which the effects could be produced and that it is plausible to extrapolate from that point. They have identified the relevant prior art that shows that uveitis can be mitigated by targeting the Th17 cascade (see page 10, line 28 to page 11 line 7 and references 27-34 cited therein). The results of the mouse study show that the MRX050 strain of *E. contortum* has brought about some therapeutic relief. As uveitis is caused by IL-17 and the Th17 cascade, then the relief of uveitis is achieved by interfering with IL-17 and the Th17 cascade in some way. At the hearing the applicants described their claim to treating diseases mediated by the Th17 pathway as being plausible, considering the uveitis treatment results and given that it is known that uveitis is, itself, a disease that is caused by the Th17 cascade.
- 51 The *E. contortum* MRX050 is not applied directly to the eye in order to exert its therapeutic effect, it is ingested. Thus, the presence of the *E. contortum* in the mice has brought about a physiological change within the animal tested that has resulted in the relief of uveitis. Their proposal is that this change is exerted through the Th17 cascade.
- 52 From the prior art identified by the applicant in the specification as filed, it seems to be accepted that the uveitis in the mouse model of Example 1 in the application results from Th17 mediated inflammation and in my view the skilled person would realise this. It seems to me plausible for the applicant to argue as a working hypothesis that the results of the study reported in the application indicate that the MRX050 strain has an effect on reducing inflammation caused by the Th17 pathway. In his pre-hearing report, the examiner expressed his view that the observation that the disease is treated does indeed support the possibility of a direct effect on Th17/IL-17, but it also does not exclude any other possibility of how the reduction in inflammation may be achieved.
- 53 Given what is, in the view of the Supreme Court in *Warner-Lambert*, the relatively undemanding test for plausibility, I think that it would be setting the bar too high to demand the exclusion of other possibilities before accepting the argument of an applicant for their working hypothesis. It is true that a direct effect on Th17/IL-17 is not shown definitively to be the case by the information in the application. Nevertheless, in the absence of specific evidence undermining or contradicting this effect, I feel that the applicant's argument that the method of action for the systemic effect reported in the study is inhibition of Th17 mediated inflammation cannot be dismissed as speculative or mere assertion. It is a working hypothesis with support from the literature that explains the observed effect in the animal model. As discussed at the hearing, although the application does not provide any experimental data demonstrating a specific mechanism, it does provide information from the prior art to show that IL-17 and the Th17 pathway mediate the inflammatory process in arthritis, cancer, asthma and multiple sclerosis. As the Supreme Court pointed out in the *Warner-Lambert* decision, the effect on the disease process can be demonstrated by *a priori* reasoning, it does not necessarily need experimental data. Here we have some experimental data in relation to uveitis which shows that the MRX050 strain ingested into and residing in the gut has a systemic effect on a condition in the eye. The proposed basis for this systemic effect is mediation of the IL-17/Th17 pathway. This pathway is known to be involved in a number of other conditions from the prior

art, thus the person skilled in the art would consider it is reasonable to expect that this strain will also have an effect on these other conditions.

- 54 As further support for this view, the applicants argue that the skilled person will not be surprised that drugs which treat one inflammatory or autoimmune condition can also have efficacy against other inflammatory or autoimmune conditions. The applicant referred to adalimumab, an antibody, and methotrexate, a chemotherapy drug, as examples of active agents which are effective against uveitis but are also effective in treating a number of other inflammatory or autoimmune conditions. While both these examples are very different to the whole bacterial cells of *E. contortum* MRX050, it is reasonable to consider that if it shows a useful activity against uveitis it is not just an assertion to say that it will be likely to show activity against other inflammatory or autoimmune conditions.
- 55 While absolute proof of efficacy or clinical trial data is not required for the grant of a claim to a medical use, if such data does later emerge to show that such a use is not justified, then the claim will be insufficient. In *Eli Lilly & Co v Janssen Alzheimer Immunotherapy* [2013] EWHC 1737, evidence obtained after the filing date (the failure of subsequent clinical trials) was held to show that the teaching of the patent was insufficient. In the absence of evidence to show that the proposed therapeutic use does not work, I consider that it is not unreasonable for the applicant to propose this claim to “*treating or preventing an inflammatory or autoimmune disease mediated by the Th17 pathway*”.

#### *Inclusion of other Bacterial Strains*

- 56 The applicants also argued that a claim is supported if it can be reasonably predicted that the invention will work across the scope of the claim. In other words, whether a skilled person could reasonably expect that other strains of *E. contortum* would show similar efficacy to MRX050. More specifically they argued that the skilled person would appreciate that different strains belonging to the same species demonstrate a high level of identity, both genetically and phenotypically (this is after all why they are grouped together under the same species!). Therefore, different strains of the same bacterial species typically share phenotypic properties, including, the ability to treat the same diseases. They further made the point that MRX050 is naturally occurring rather than being genetically modified and hence would be considered by the skilled person to be similar to other isolated *E. contortum* strains.
- 57 The agent confirmed at the hearing that the MRX050 strain was isolated from a single human volunteer and is not genetically modified or altered in any way. Consequently, they consider that it can serve as an example of how other *E. contortum* strains will behave. To reinforce their argument that other strains of *E. contortum* would be expected to exert a similar therapeutic response, the applicant filed further evidence to show that multiple *E. contortum* strains including MRX050 all are very similar and that there is nothing special or particular about the MRX050 strain to suggest that it behaves in a manner different to other *E. contortum* strains. Firstly, seven *E. contortum* strains were shown to have very similar abilities to activate the NF- $\kappa$ B<sup>7</sup> promoter (see data provided with response from Agent dated 3 February 2020). Secondly, three of

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<sup>7</sup> Nuclear factor kappa-light-chain enhancer of activated B cells, NF- $\kappa$ B

these seven strains, including MRX050, were also analysed by MALDI-TOF mass spectrometry and shown to produce very similar profiles (the same mass fragments and very similar intensities). I consider this evidence supports the view put forward by the applicant that MRX050 is an example of an *E. contortum* strain that is very similar to other strains of *E. contortum*. The two review articles provided by the applicant in addition to this further evidence also confirms that prior to the application date for the patent, it was known that NF- $\kappa$ B is a transcription factor particularly associated with the differentiation of Th17 cells and the upregulation by IL-17 of pro-inflammatory chemokines and cytokines.<sup>8</sup> The fact that these 5 strains including MRX050 all give a similar response in terms of activation of NF- $\kappa$ B is further support that such strains will likely have a similar mitigating effect on the IL-17/Th17 pathway as claimed in the specification as filed.

58 Thus, I consider that, on the balance of probabilities, it is acceptable to argue that, given the MRX050 strain is similar to other strains of *E. contortum*, then, in the absence of specific evidence to the contrary, these strains will likely have similar properties. I consider that a person skilled in the art would be satisfied that it is not just assertion on behalf of the applicant to propose that *E. contortum* strain MRX050 can serve as an example of how other strains of *E. contortum* will behave.

59 The examiner suggested that *E. contortum* may itself show pro-inflammatory effects citing the documents from *Severijnen et al.*<sup>9</sup> and *Hazenberg et al.*<sup>10</sup> in support of this view. If so, this would suggest the opposite to that proposed by the applicant – that strains of *E. contortum* could cause inflammation rather than mitigate it as claimed. Both papers discuss the inflammatory effect arising from the injection of bacterial cell wall fragments of strains of *E. contortum* into animal models, specifically a rat model. *Severijnen et al.* shows that the cell wall fragments from *E. contortum* can induce an inflammatory response – in this case chronic arthritis. In *Hazenberg et al.*, the authors explored the role of *E. contortum* strains in Crohns disease. They found that the injection of dead cells of *E. contortum* into conventional rats resulted in an antigenic response producing antibodies, although when live cells of *E. contortum* were added into the intestine of germ-free rats, the resultant colonisation of the intestine by *E. contortum* did not result in an antigenic response or produce antibodies.

60 The applicant countered by arguing that in contrast to these papers, the invention as claimed relates to a different physical form and to administration to a different site. In particular, the invention relates to properties of whole *E. contortum* cells and not cell wall fragments and to their impact in the intestine where they normally reside rather than arising from direct injection into the body cavity of the rats tested. The latter injection step avoids the need to pass through the wall of the intestine into the blood system, for wider distribution in the body. In operation, even though the *E. contortum* bacteria will grow, live and die in the gut and so may produce fragments as part of their life cycle, they do not cross into the body cavity. The invention relates to a systemic effect that arises from the presence of the whole bacterial cells in the gut

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<sup>8</sup> See for example, J. F. Zambrano-Zaragoza et al., International Journal of Inflammation, 2014, pages 1-12, in particular, page 2, paragraph 2 (section entitled '2. Th17 Cells: Who Are They?' and page 3, paragraph 2.3 (sub-section entitled '2.3. IL17 Signalling')

<sup>9</sup> (see <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC258488/>)

<sup>10</sup> (see <https://academic.oup.com/femsle/article/13/1/117/761249>)

which results in a positive therapeutic change in the eye. The proposal that this general physiological change is caused by the Th17/IL-17 pathway is thus plausible. Given the contrast between the antigenic properties of the cell wall fragments and the lack thereof of the live cells of *E. contortum* discussed in *Hazenberg et al.*, I find that I agree with the applicant on this point.

- 61 Thus, in the absence of evidence to show that different *E. contortum* strains demonstrate different behaviour and effects and bearing in mind the relatively low threshold for plausibility as discussed above, it does not seem reasonable for me to reject the applicant's contention that it is plausible for the skilled person to suppose strains of *E. contortum* other than MRX050 will show similar effects on inflammatory or autoimmune diseases mediated by the Th17 / IL-17 pathway.
- 62 As noted above, there is no dispute that the application as filed does provide experimental evidence to show that the MRX050 strain of *E. contortum* has a therapeutic effect on uveitis in rats. However, citing *Prendergast*, the examiner considers that this is not enough to support the claim to treatment of a other diseases where the Th17 cascade also plays a significant role, given that there is no direct evidence that the mechanism of action by which *E. contortum* MRX050 achieves the systemic outcome seen in the rats with uveitis is via the Th17 cascade. I consider that this is too strict an interpretation. It is not necessary in my view to provide experimental evidence in support of all the conditions claimed if it can be reasonably predicted from the demonstrated activity that the substance would likely treat the diseases in question. The skilled team taking account of the experimental evidence provided in the application as filed and the further reasoning provided therein would, in my view, consider that the description does offer a working or plausible hypothesis for a mechanism common to all the conditions proposed. Thus, a claim to include other conditions in addition to uveitis is supported. Similarly, given that the MRX050 strain of *E. contortum* was isolated from a human volunteer and is not modified or manipulated further, it is reasonable to suggest that other strains of this species will behave in a similar manner. This is further supported by the late filed evidence discussed above. Thus, I am satisfied, that, on the balance of probabilities, this is more than speculation or mere assertion.

### **Discretionary Extension to the Compliance date under Rule 108(3)**

- 63 A question has arisen in relation to whether or not the request for a discretionary extension to the compliance period under Rule 108(3) made by the applicant on 30 November 2020 was valid.
- 64 If this request was not valid, I would need to consider whether or not the application was in order when the compliance period expired on 30 September 2020.
- 65 If the request was valid, I will then consider whether discretion can be exercised to allow this request for an extension to the compliance period. The subsequent requests for successive further extensions to the compliance period under rule 108(3) filed on 4 January 2021 and on 27 January 2021 can then also be considered in that circumstance.



## The Relevant Law

- 66 The regime for acquiring extensions of time to prescribed periods is set out in rule 108 of the Rules and Schedule 4 to those Rules.
- 67 I have previously considered this regime in an earlier Office decision *Optinose AS's Application* (BL O/144/12)<sup>11</sup> which sets out what is required for a valid request for an extension to the compliance period under rule 108(3).
- 68 The relevant parts of rule 108 for the present case read (my emphasis added in **bold**):

[...]

*(2) The comptroller shall extend, by a period of two months, any period of time prescribed by the provisions listed in Part 2 of Schedule 4 where—*

*(a) a request is filed on Patents Form 52;*

*(b) no previous request has been made under this paragraph; and*

*(c) that request is filed before the end of the period of two months beginning with the date on which the relevant period of time expired.*

***(3) The comptroller may, if he thinks fit, extend or further extend any period of time prescribed by the rules listed in Part 2 of Schedule 4 where—***

***(a) a request is filed on Patents Form 52; and***

***(b) the person making the request has furnished evidence supporting the grounds of the request, except where the comptroller otherwise directs.***

[...]

*(6) An extension may be granted under paragraph (1) or (3) notwithstanding the period of time prescribed by the relevant rule has expired.*

***(7) But no extension may be granted in relation to the periods of time prescribed by the rules listed in Part 3 of Schedule 4 after the end of the period of two months beginning immediately after the period of time as prescribed (or previously extended) has expired.***

For the purposes of this decision, it is relevant to note that the compliance period (as prescribed in rule 30) is listed in Parts 2 and 3 of Schedule 4. Thus, the limitation in Rule 108(7) applies to this time period.

- 69 Rule 4 of the Rules is entitled 'Forms and Documents' and reads as follows (my emphasis added in **bold**):

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<sup>11</sup> See full text of decision BL O/144/12 at <https://www.ipo.gov.uk/p-challenge-decision-results/o14412.pdf>

4.—(1) *The forms of which the use is required by these Rules are those set out in directions under section 123(2A) and are referred to in these Rules as Patents Forms.*

**(2) *Such a requirement to use a form is satisfied by the use of a form which is acceptable to the comptroller and contains the information required by the form as so set out.***

(3) *Such directions must be published in accordance with rule 117(c).*

(4) *Unless the comptroller otherwise directs, to file any form or other document under the Act or these Rules only one side of each sheet of paper must be used and the other side must remain blank.*

**(5) *But where the information is delivered in electronic form or using electronic communications—***

**(a) *a requirement under these Rules to use a form; and***

**(b) *the requirements in paragraph (4),***

***do not apply.***

(6) .....

For the purposes of this decision, it is relevant to note that F52 concerning a request for extension of the compliance period is one of the patents forms established in directions under Section 123(2A) of the Act.

70 The Manual of Patent Practice explains the IPO's practice under the Act and Rules and provides helpful references to relevant case law. The Manual can be viewed online at the IPO's website:

<https://www.gov.uk/guidance/manual-of-patent-practice-mopp>.

71 Paragraphs 123.33.1–123.36.1; 123.36.5; 123.36.7-123.36.10; 123.36.12-123.41 of the Manual, which relate to *Time Limits*, are relevant to the present case.

## **Analysis**

72 In a letter dated 30 November 2020, the agent requested an extension to the compliance period as follows:

*"I request a further extension to the compliance period under Rule 108(3)."*

and went on to state that the reason for this request was:

*"A hearing was scheduled and took place on 12th October 2020 (i.e. after the extended compliance period) and we are still awaiting the decision from the hearings officer. Accordingly, we request a further extension of four months to allow sufficient time for a decision to be issued. Should a decision not be issued within this extended time frame, we further request the option of extending the compliance period further in the future.*

- 73 The date (30 November 2020) that this request was made corresponds to the final day of the two-month period set down in Rule 108(7) beginning with the date on which the compliance period expired (30 September 2020). There was no F52 filed with this request.
- 74 The request in this letter was made within the period 30 July 2020 to 31 March 2021, when the temporary amendments to the Patents (Fees) Rules 2007 are in effect as part of the Office response to the impact of the Coronavirus pandemic.<sup>12</sup> As a consequence, the fee for an application for an extension of time to a prescribed time limit, in this case for an extension of the compliance period, which accompanies the Form 52 is reduced to nil.
- 75 The above letter dated 30 November 2020 was filed electronically with the office by the agent as confirmed by the electronic filing receipt on file (see IPSUM).<sup>13</sup> This receipt indicates that the documents were filed by the agent in the afternoon.
- 76 A letter from the Office to the agent dated 4 January 2021 pointed out that the request for an extension to the compliance date could not be accepted because no F52 had been filed with the agent's letter dated 30 November 2020. It confirmed that no fee was required. This letter also explained that an extension to the compliance period can only be granted for a period of two months although it is possible, as referred under rule 108(4), to request two such extensions for the same application using the same form. This letter also suggested that discretion could be exercised to accept the late filing of the F52 because the agent had (i) stated that they sought an extension in the letter dated 30 November 2020 which corresponds to the last date in which such a request could be made, and (ii) that it had been their intention to extend the compliance date for the reason given in this letter (while awaiting the outcome of the hearing that took place on 12 October 2020). Unfortunately, this offer that discretion could be exercised to allow late filing of the F52 was in error. Rule 108(7) cannot be interpreted this flexibly. It is a hard deadline. Rule 108 already allows for a period of time after the expiry of the compliance date for a retrospective request to be filed, i.e., the two-month period referred to in rule 108(7). This period cannot be extended further once this two-month period has passed.
- 77 While it is accepted that a request for such an extension to the compliance date can be made on the last day of this two-month period, this assumes that the request is a valid one. If, for some reason, it is not a valid request, there is no time left to allow the applicant to correct the request before this period ends. Clearly this is a possibility that may arise if the applicant, or the agent acting for the applicant, waits until the final day of the two-month period to make such a request.
- 78 While the putative request for a discretionary extension was made on the last day possible, it did not include a F52 which is a requirement for such a request under rule 108(3), even though at present the fee associated with this form has been waived.

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<sup>12</sup> See (a) UK statutory instrument 2020 no 644 entitled 'The Patents, Trade Marks and Registered Designs (Fees) (Coronavirus) (Amendment) Rules 2020' [here](#) and (b) related UKIPO Press Release dated 1 July 2020 concerning the temporary fee changes [here](#).

<sup>13</sup> See IPSUM [Intellectual Property Office - Patent document and information service \(Ipsum\) \(ipo.gov.uk\)](#) record for this application

This error could only have been corrected on the 30 November but once the two-month period passes, no correction or adding of missing documents can take place.

- 79 The request made on 30 November 2020 should have included a F52 and the fact that it did not was an error. Unfortunately, this was the final day on which a further retrospective extension could have been requested. When filed at the office, the documents relating to such a request must be uploaded to the correct patent file, notified to and considered by the appropriate formalities, patent examination and hearings staff for any issues with the request to be identified and a possible course of action determined. This must then be communicated to the agent dealing with the case, in order for them to deal with the issue and, in this particular circumstance, to file the missing form. Even allowing for the greater speed of electronic communication in today's world, it is not possible for all this to be done in a single working day, still less in part of a day as in this instance.
- 80 The Office wrote to the applicant in a letter dated 25 February 2021, on behalf of the hearing officer, to explain the above situation and to seek their views on this matter. The letter explained that it was not possible to exercise discretion to accept a F52 filed after 30 November 2020. This letter also set out that the preliminary view of the hearing officer was, having considered all the correspondence on file, the arguments presented at the hearing and the materials provided after the hearing, that this application did disclose the invention in a manner which is clear and complete enough to enable the invention to be performed by a person skilled in the art and that the claims, as amended on 8 July 2020, are adequately supported by the description as required under Section 14 of the Act.
- 81 The applicant responded in a letter dated 8 March 2021 indicating that the non-filing of the F52 was an "*unintended oversight*" on their part and that it was always their intention to do so in the same way as they had done in relation to the extension of the compliance period requested on 30 September 2020. They indicated that it was not clear how this error had occurred. Given that the error was wholly unintentional, they requested the "*Hearing officer to exercise their discretion in favour of the applicant in respect of this procedural issue, given that the non-filing of the F52 was wholly unintentional*".
- 82 As I have indicated above, an exercise of discretion such as that requested by the applicant is not possible in this case. However, as the letter filed on 30 November 2020 was filed electronically, I consider that Rule 4 of the Rules applies in this instance, in particular, part (5) of this rule. Thus, a form need not be provided by the applicant as long as all the necessary information is available to the office in the communication provided electronically. As part (2) of Rule 4 indicates, as long as all the information necessary is set out in the communication, it can be considered as acceptable to the comptroller. This is facilitated by the fact that under the temporary waiver of fees in response to the impact of the COVID-19 pandemic no fee was necessary.<sup>12</sup> While it is more likely for a situation such as this to arise for those unfamiliar with the patent application process who are acting on their own behalf, often referred to as private applicants, there is no reason why the same approach cannot apply in this instance.
- 83 I am satisfied – as I have indicated above – that the letter dated 30 November 2020 included all the necessary information, i.e., a request for a discretionary extension to

the compliance period, an appropriate reason for doing so and that all of this information was provided before the end of the two-month period under rule 108(7). Because of the temporary arrangements in relation to the fees discussed above<sup>12</sup>, no fee was necessary to accompany this request and so it only needed to include the relevant information.

- 84 Thus, I deem that a valid request for an extension of time under rule 108(3) was made on the 30 November 2020. I am further satisfied that discretion can be exercised to accept the request for an extension to the compliance period for the reason requested.

### **Conclusion**

- 85 Taking into account all of the above and having considered the correspondence on file including the amended claims dated 8 July 2020, the arguments presented to me at the hearing, and the materials submitted following the hearing, it is my view that patent application GB1809729.5 does disclose the invention in a manner which is clear and complete enough to enable the invention to be performed by a person skilled in the art. Thus, I am satisfied that the application complies with Section 14(3) of the Act.
- 86 Furthermore, taking into account all of the above and having considered the correspondence on file including the amended claims dated 8 July 2020, the arguments presented to me at the hearing, and the materials submitted following the hearing, it is also my view that the claims in patent application GB1809729.5 are adequately supported by the description. Thus, I am satisfied that the application complies with Section 14(5)(c) of the Act.
- 87 The request for a discretionary extension to the compliance period under rule 108(3) did not include a F52, but in the absence of the need for the appropriate fee, the letter associated with this request which was filed electronically included all the necessary information. I therefore deem that a valid request to extend the compliance period was made on the final day of the two-month period for doing so under rule 108(7). I note that the applicant has filed two further successive requests under rule 108(3) – in each case including a F52, but not including a fee, given that the temporary arrangements where no fee is required are still in force until 31 March 2021. I am satisfied that these requests can be accepted for the reasons outlined above. The period for putting this application in order under Section 20 now expires on 30 March 2021.
- 88 As the examiner reported in his pre-hearing report dated 30 July 2020, there are some matters still outstanding in relation to this application. I therefore remit this application back to the examiner to complete the examination and grant process under Section 18.

D L Cullen

Deputy Director, acting for the Comptroller