Intellectual Property Office

BL O/1045/24

06 November 2024

PATENTS ACT 1977

APPLICANT	DEBASISH BANERJEE
ISSUE	Whether patent application GB2201855.0 complies with sections 14(3) and 76(2) of the Act
HEARING OFFICER	Dr Rowena Dinham

DECISION

Introduction

1 This decision concerns whether patent application GB2201855.0 entitled "Enhancing Drug Activity Through Accentuated Buccal/Sublingual Administrations" complies with the requirements of the Patents Act 1977 ("the Act") with respect to added matter (Section 76(2)) and sufficiency of disclosure (Section 14(3)).

2 The application was originally filed under the Patent Cooperation Treaty ("PCT") on 28 July 2019. Amendments were made under Article 19 of the PCT on 30 August 2020, and the original application together with the amended claims was published as WO2021/019278 A1 on 4 February 2021[1]. Several further amendments to the application were made under Article 34 of the PCT, including amendments adding figure 10A on 31 May 2021.

3 The application entered the UK national phase on 12 February 2022 and was republished as GB2604037 A. Further extensive amendments to the claims, description and figures were made on 9 May 2023. The first examination report, issued on 25 May 2023, included objections to insufficiency of disclosure under Section 14(3) and added matter under Section 76(2). The amendments which were filed in response did not resolve the insufficiency issue and resulted in further added matter objections[2]. The examiner, considering that the objections were fundamental to the application and the insufficiency objection could not be overcome, then offered a hearing. Despite the offer of a hearing, further amendments to the claims were made on 2 January 2024, and in response a letter was issued on 1 March, explaining that the application would be passed to a hearing officer for a decision. This letter was a final communication in respect of substantive examination and so carried no date by which to reply. As a consequence, the amendments and

[1] WO 2021/1019278 A1
[2] Examination report dated 3 November 2023

arguments received from the attorney on 22 March 2024, dated 21 March 2024, were not considered by the examiner[3]. Further amendments were submitted directly by the applicant on 2 April 2024, which also postdate the final communication and were during a period where the applicant did not have a UK Address for Service, and these have also not been considered by the examiner.

4 During the national phase of the prosecution process, the applicant has been represented by three different attorneys with intervening periods where they were unrepresented. I further note that, when represented, the applicant has continued to file documents themselves such that, at some points, there has been significant confusion as to the authentic amended application. The present attorneys, Wilson Gunn, eventually requested, in their letter dated 20 August 2024, that the amendments to the description and claims submitted on 22 March 2024 were to be the basis of my decision. As these amendments are intended to address some of the issues outstanding, and as the attorney has so requested, I am willing to exercise discretion to take them into account when making my decision. I note however that clean copies have not been provided. Should I find that the application is in order based upon these amendments then clean copies of the amended pages will need to be filed.

5 In their letter of 20 August 2024, the present attorney also proposed a further set of amendments to the claims, requesting their consideration alongside those presently on file. As these are merely a narrowing of the scope of claim 1 by inserting the subject matter of claims 2 and 4, I will treat them as an auxiliary request and am willing to consider them. Shortly before the scheduled hearing, it was agreed that the application be forwarded for a decision on the papers, in which matter I was assisted by senior examiner Dr Graham Feeney.

The application

6 The application concerns the formulation of pharmaceutical compositions for enhanced buccal /sublingual drug delivery. It is disclosed that "permeability enhancers" may be used to increase the rate of absorption and the total drug absorbed in a given time. Two exemplar formulations are described. In the first, the sulfonylurea diabetes drug glipizide is formulated with "permeability enhancers" [4]. The identity of the "permeability enhancers" is further explained in the application at paragraph [0013] where *"The permeability enhancers used in this case were chosen from groups of alcohols, oxides, peroxides, hydroxides, esters in the minimum ratio of 1: 10 of drug to PE [permeability enhancer]"*.

7 The second example discloses the formulation of the benzodiazepine tranquilizer alprazolam and "permeability enhancers" in sublingual tablets / sprays[5]. At claim 7 as originally filed, an alprazolam formulation is defined wherein the *"…permeability*

[3] These amendments do not constitute an allowable response to the examination report of 3 November 2023, firstly because a response had already been received and secondly because the reply by date of 3 January 2024 had passed, with no permissible or as-of-right request for extension.
[4] "Glipizide - 7.5 mg, **Permeability Enhancers - 300 mg**, Cyclamate Sodium - 1.5 mg, Methyl Cellulose 15 cps - 6 mg, Magnesium Stearate - 3 mg, Talcum - 5mg" at paragraph [0014] on page 4.
[5] "Alprazolam - 250 mg, **Permeability Enhancers - 15 mg**, Lactose - 10 mg, Talcum - 1.5 mg, Magnesium Stearate - 500 mg, Dry Starch - 1.5 mg, PVP – 1 mg, Alcohol to granulate - q.s." at paragraph [0019] on page 5.

enhancer which could be chosen from a group of sugars selected from poly and monosacchides [sic], trioses, tetroses pentoses, hexoses both aldo and keto, preferably from hexoses…".

8 As amended on 22 March 2024, claim 1, the sole independent claim, reads as follows:

> *A process for increasing the activity of drugs by increasing their active site concentration comprising of: combining a pharmacologically active drug capable of sublingual/buccal means of administration; and adding an ASPE (active site permeability enhancer) capable of rapid transfer of the drug to the active site, resulting in increased active site concentration, leading to faster onset, higher efficacy, and longer duration of action.*

9 The proposed amendments to the claims provided with the attorney's letter of 20 August 2024 simply add the subject matter of claims 2 and 4 to that of claim 1 such that the scope of the invention is narrowed to specifically defining the glipizide and alprazolam formulations. The issue of added matter does not turn on the proposed amendments to the claims. However, I will assess their relevance to the insufficiency issue.

10 In considering this application, I note that the description has been substantially rewritten from that originally filed. For the avoidance of doubt, it should be noted that the terms *"permeability enhancers"*, *"receptor site permeability enhancers"*, *"RSPE's"* [sic], *"active site permeability enhancers"* and *"ASPE"*, whilst not clearly terms of the art, have been treated as being synonymous when read and understood by the skilled person in the context of the application itself.

The law

11 The relevant law is defined in the Patents Act 1977 (as amended) and can be viewed online at the IPO's website:

The Act: https://www.gov.uk/guidance/the-patent-act-1977

12 The Manual of Patent Practice explains the IPO's practice under the Act 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 10

13 I have indicated below the sections of the Act which apply to each of the examiner's objections. There is no dispute concerning the relevant law and its application to the facts of this case.

Issues for decision

14 There are many issues of contention between the applicant and the examiner, each relating to substantive requirements of the Act that need to be satisfied before the patent may be granted. Specifically, in their pre-hearing report, the examiner sets out

that the application fails to meet the requirements for added matter[6], sufficiency[7], novelty[8], inventive step[9] and clarity[10]. They have also deferred other matters, including updating of the search.

15 I have carefully considered the documents on file, and I shall address the objections set out in the detailed pre-hearing report to the extent necessary to resolve the question of whether the application meets the requirements and conditions for grant of a patent.

Added matter- Section 76(2)

16 Objections to added matter have been raised throughout the prosecution of this application and it is worthwhile reiterating that under Section 72(a)(d), the presence of added matter is a very clear and unambiguous grounds for the revocation of a granted patent. A patent containing added matter is invalid, and amendments which add matter to an application for a patent are not allowable under Section 76(2). As summarised by Jacob J. (as he then was) in *Richardson-Vicks Inc.'s Patent*[11], (at page 576 line 34-37)*:*

> *"the test of added matter is whether a skilled man would, upon looking at the amended specification, learn anything about the invention which he could not learn from the unamended specification."*

17 In *Bonzel and Schneider (Europe) AG v Intervention Ltd* ("*Bonzel*") [12] Aldous J (as he then was) described a three-step analysis to determining whether there was added matter in a patent (at page 574):

> *(1) to ascertain through the eyes of the skilled addressee what is disclosed, both explicitly and implicitly in the application;*
>
> *(2) to do the same in respect of the patent as granted;*
>
> *(3) to compare the two disclosures and decide whether any subject matter relevant to the invention has been added whether by deletion or addition. The comparison is strict in the sense that subject matter will be added unless such matter is clearly and unambiguously disclosed in the application either explicitly or implicitly.*

18 I note the strictness of the third step, with no allowance whatsoever for adding details that may be merely obvious.

19 In the pre-hearing report, the examiner identified additional subject matter at paragraph [0038] on amended pages 6-7 of the specification; in the formulation for alprazolam the reference to *"Permeability Enhancers – 15mg"*[13] was replaced by

---

[6] Section 76(2)
[7] Section 14(3)
[8] Section 1(1)(a)
[9] Section 1(1)(b)
[10] Section 14(5)(b)
[11] Richardson-Vicks Inc.'s Patent [1995] RPC 568
[12] Bonzel and Schneider (Europe) AG v Intervention Ltd [1991] RPC 553
[13] See the top of page 5 of the WIPO pamphlet.

"*Dextrose – 20 mg (RSPE)*". Later in the same amended paragraph [0038] new statements are made that "*Here dextrose a hexose is used as RSPE"* and that *"The RSPE's were sugars".* The examiner also identified that matter was added by the inclusion of figure 10A and the description thereof[14], which presented additional data concerning the efficacy of the glipizide formulation of the invention.

20 Subsequently, in the amendments dated 22 March 2024, figure 10A and references to it were deleted, and the quantity of dextrose to be used in the alprazolam formulation was reverted to 15mg. Thus, the sole issue of added matter to be decided concerns the replacement of "Permeability Enhancers" (now expressed as ASPEs) with "dextrose", which is found at paragraphs [0037] and [0037.1]. I will now follow the three-step test set out in *Bonzel*.

Step 1: to ascertain through the eyes of the skilled addressee what is disclosed, both explicitly and implicitly in the application [as filed]:

21 I note that the examiner has identified the skilled person as part of their analysis of inventive step, whereas the applicant has not suggested any alternative during their response. For the purposes of assessing both inventive step and added matter, the skilled person would be the same. The skilled person is a formulation scientist with expertise in pharmaceutical formulations, tabletting and delivery. Their common general knowledge would consequently include standard pharmaceutical formulation techniques and substances, including those known as being suitable for various modes of administration such as sublingual/buccal administration. It would be desirable for them to improve the efficiency of delivery of a drug, but they would be aware that they would need to balance that with concerns regarding safety, potential drug abuse and the palatability of the formulation.

22 The application as originally filed discloses a method to enhance buccal /sublingual drug delivery by the addition of "permeability enhancers" to the formulations. Two examples are provided. The first provides formulations for increasing the permeability of glipizide, with reference to figures 1-10. At paragraph [12] a reference is made to figure 10, with paragraph [13] going on to state that "*the permeability enhancers used in this case were chosen from groups of alcohols, oxides, peroxides, hydroxides, esters in the minimum ratio of 1:10 drug to PE",* presumably an indication that the formulation for which the results of figure 10 were provided comprised a compound which was an alcohol, oxide, peroxide, hydroxide, or ester. Paragraph [14] goes on to provide an example composition for administration of the drug glipizide:

> *"Example: Glipizide 7.5mg,* ***Permeability Enhancers 300mg****, Cyclamate Sodium 1.5mg, Methyl Cellulose 15 cps 6mg, Magnesium Stearate 3mg, Talcum 5mg".*

23 The second example provides formulations for increasing the permeability of alprazolam, with reference to figures 11-13. An example composition is provided at paragraph [19]:

[14] See page 12 of the figures and description paragraph [0016] as amended 2 January 2024

"*Examples [sic]: Alprazolam 25mcg,* ***Permeability Enhancers 15mg****, Lactose 10 mg, Talcum 1.5mg, Magnesium Stearate 500 mcg, Dry Starch 1.5mg, PVP 1mg, Alcohol to granulate q.s."*

24 What constitutes the "permeability enhancers" in the compositions for alprazolam is disclosed in claim 7 of the application as filed, and is from a selection "*which could be chosen from a group of sugars selected from poly and monosacchides [sic], trioses, tetroses, pentoses, hexoses both aldo and keto, preferably from hexoses"*[15].

25 Therefore, in terms of explicit disclosure of a specific "permeability enhancer", there is nothing other than any compound selected from the broad group of alcohols, oxides, peroxides, hydroxides, or esters, for glipizide compositions, or from the broad group of sugars selected from poly and monosaccharides, trioses, tetroses, pentoses, hexoses both aldo and keto for alprazolam compositions.

26 When it comes to what has been implicitly disclosed, prevailing practice is that matter may be regarded as having been disclosed if the skilled reader would realise that it was implicit in the original document[16]. The applicant submitted, based upon our published guidance[17], that the list of suggested permeability enhancers should be treated as being a range that *"implicitly discloses every item falling within that range, and accordingly any subrange can be claimed"*.

27 I disagree with this. Whilst the skilled person would understand what constitutes a "sugar" *per se*, in the absence of any indication of any specific sugars, they would not understand which, if any, of the sugars that fall within the group of sugars selected from "poly and monosaccharides, trioses, tetroses, pentoses, hexoses both aldo and keto" would be capable of acting as a "permeability enhancer". This is further confused by the presence of "lactose 10mg" in the alprazolam formulation provided in example 2, in addition to the "permeability enhancer 15mg". Lactose is a disaccharide and thus falls within the scope of what constitutes a "sugar" yet apparently not one which is a "permeability enhancer" in the formulation of example 2. As such I cannot see how the skilled person would take from the disclosure of the application as filed which specific sugars are intended to implicitly have the desired effect of a "permeability enhancer".

Step 2: to do the same in respect of the patent [application as amended];

28 The application as now amended explicitly discloses that the alprazolam formulation specifically comprises dextrose as the "permeability enhancer"[18].

Step 3: to compare the two disclosures and decide whether any subject matter relevant to the invention has been added whether by deletion or addition.

---

[15] See claim 7 as filed, which reads: *"Buccal/sublingual Alprazolam formulation comprising of Alprazolam and a permeability enhancer which could be chosen from a group of sugars selected from poly and monosacchides [sic], trioses, tetroses pentoses, hexoses both aldo and keto, preferably from hexoses…."*

[16] See DSM NV's Patent [2001] RPC 35 at paragraphs 197-200.

[17] see the Manual of Patent Practice, April 2024, at 18.69.1

[18] See paragraph [0037] at page 6 of the description as now amended.

29 In the amended specification the skilled person is newly taught that the exemplified alprazolam formulation comprises **dextrose** as the "permeability enhancer", rather than one selected from the generic list comprising *"a group of sugars selected from poly and monosacchides [sic], trioses, tetroses pentoses, hexoses both aldo and keto, preferably from hexoses"*.

30 The application as filed has no detail of what the specific "permeability enhancers" may be; the formulation for alprazolam is merely exemplified as comprising "*permeability enhancers-15mg*", with no further disclosure other than the generic list of sugars. There is no instruction to the skilled person of which hexoses (or indeed any of the sugars) might act as "permeability enhancers" and nothing pointing them towards dextrose as that sugar. As such the skilled person learns something additional that is relevant to the alprazolam invention, i.e. that rather than using (or indeed testing, as the case may be here) any generic sugar as a permeability enhancer for alprazolam, they should use dextrose. This is not taught either explicitly or implicitly in the application as originally filed.

31 Therefore, this identification of added subject matter contrary to Section 76(2) is grounds to refuse this application under Section 18(3).

Sufficiency-Section 14(3)

32 The examiner has objected that Section 14(3) is not satisfied as the application does not enable the skilled person to perform the invention without undue burden. It is their opinion that the skilled person would need to enter into a prolonged trial-and-error process in order to identify suitable permeability enhancer and drug combinations. This amounts to an invitation to conduct a research programme.

33 The applicant's counter argument is best summarised from the letter submitted by their then attorney on 21 March 2024. In this letter, it is asserted that the claims define the invention in functional terms, and that the amendments that were made to the description serve as guidance to the skilled person in determining which substances may be used as permeability enhancers without having to embark upon a research program and thus without undue burden[19].

34 There is significant case law that deals with the issue of sufficiency. In recent years, the reasoning used to assess whether an application satisfies section 14(3) of the Act has relied predominantly on *Eli Lilly v Human Genome Sciences* [20] ("*Eli Lilly")* particularly at paragraph [239] wherein Kitchen J gave the following summary of the relevant principles to be applied:

> *(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;*

[19] The argument put is that "A range of sugars having 3 to 6 carbon atoms, has been disclosed, and dextrose with 6 carbon atoms implicitly belongs to that range…"
[20] *Eli Lilly v Human Genome Sciences [2008] RPC 29*

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

(iv) 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.

35 In *Regeneron Pharmaceuticals v Kymab*[21] it was held that the skilled person can use common general knowledge to perform the invention and make any obvious necessary changes but that any work involved must not be undue. In *Zipher Ltd v Markem Systems Ltd* [22] ("*Zipher*") at paragraph [363] it was stated that *"…a patent can also be insufficient if the steps can be characterised as prolonged research, enquiry or experiment."*. These judgments share common themes in how they formulate the question of what constitutes a sufficient disclosure.

36 Following the principles set down in *Eli Lilly*, arguably the first step of the test is to identify the skilled person and their relevant common general knowledge, although in the analysis of sufficiency of disclosure, I further note that the skilled person would be capable of making routine workshop developments and that the skilled person is *"trying to carry out the invention and achieve success…not searching for a solution in ignorance of it* [23]*".*

37 In my construction of claim 1, I have removed the desirable results to be achieved requiring that the permeability enhancers result in "*increased active site concentration*" of the drug, "*leading to faster onset, higher efficacy, and longer duration of action*". I therefore construe claim 1 as follows:

A process suitable for increasing the activity of a drug intended for a sublingual/buccal means of administration by increasing its active site concentration by formulating it with an ASPE (active site permeability enhancer).

38 In assessing whether the invention is sufficiently disclosed to the skilled person such that it can be performed, the key question is whether the skilled person, using their common general knowledge and trying to work the invention, would be able to identify the specific active site "permeability enhancers" to include in a pharmaceutical formulation, and specifically be able to identify which "permeability enhancers" could be used in the glipizide and alprazolam formulations.

---

[21] *Regeneron Pharmaceuticals v Kymab Ltd [2018] EWCA Civ 671*
[22] *Zipher Ltd v Markem Systems Ltd & ANOR [2009] FSR 1, [2008] EWHC 1379 (Pat)*
[23] Zipher at paragraph [366]

39 In the application as originally filed and published by WIPO the guidance regarding "permeability enhancers" is couched in terms of broad classes of compounds. Having carefully read the original specification (thus disregarding any added matter), it is my view that the skilled person would not be able to identify, without undue burden, how a "permeability enhancer" might be chosen for any particular drug. Indeed, it remains unclear which suitable "permeability enhancer" should be used to formulate either alprazolam or glipizide. The only guidance for the glipizide formulation appears at paragraph [0013][24], whilst that for the alprazolam formulation appears at original claim 7[25]. The range of potential compounds to choose from is enormous, no principles are taught with which to narrow that list down, and so I do not see how the skilled person can reasonably predict which of the compounds can be considered to act as "permeability enhancers". I also note that whilst the application provides "results" by way of figures 1-13, there is no indication in any of these figures what "permeability enhancers" are used to obtain these "results", and so I see no evidence of a single workable example within the application as filed.

40 The skeleton arguments provided in the attorney's letter of 15 August 2024 point out that the introduction of dextrose into the description now provides a workable embodiment, thus overcoming the sufficiency objection. Notwithstanding the fact that I have already considered that the introduction of dextrose amounts to unallowable additional subject matter, even if it were allowable this single "embodiment" would not be adequate to support the breadth of the claim. There is no indication why dextrose was selected as a specific "permeability enhancer", and so the skilled person would not be able to use this additional information to aid them in their search for other similar compounds. Therefore, once again the skilled would be embarking upon a research project to identify "permeability enhancers" defined in the claims.

41 I must therefore agree with the examiner that the application does not disclose the claimed invention clearly enough and completely enough to be able to work it without the undue burden of embarking upon a research project.

42 To summarise, I have followed the reasoning set down in *Eli Lilly* to determine whether or not the invention is sufficiently disclosed. I am unable to identify subject matter appearing in the application as originally filed that teaches the skilled person how to choose specific, suitable "permeability enhancers" for any drug, including glipizide or alprazolam. The proposed amendments to the claims, provided with the attorney's letter dated 20 August 24, do not remedy this issue.

43 I therefore conclude that the specification does not allow the invention to be performed without undue burden. The requirements of Section 14(3) of the Act are not met, this alone also being grounds to refuse the application under Section 18(3).

Other issues

44 The examiner has raised further objections to clarity, novelty and inventive step, which I consider to be justified from a cursory view. However, having already found that the application does not comply with the requirements of Section 76(2) and Section 14(3), I do not consider it necessary or proportionate for me to consider any

[24] See paragraph 6 above.
[25] See paragraph 7 above.

other issues identified by the substantive examiner, or arising from the newly amended claims.

Conclusion

45 The application contains added matter contrary to Section 76(1) of the Act and the application does not meet the sufficiency requirements of Section 14(3) of the Act. The application is therefore refused under Section18(3).

Appeal

46 Any appeal must be lodged within 28 days after the date of this decision.

DR ROWENA DINHAM

Patent Examination Group Head acting for the Comptroller