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# Datasheet for the decision of 17 November 2021

**Case Number:** T 1487/19 - 3.3.01

**Application Number:** 09767450.1

**Publication Number:** 2307011

**IPC:** A61K31/4035, A61P25/00

**Language of the proceedings:** EN

**Title of invention:**
USE OF ISOINDOLES FOR THE TREATMENT OF NEUROBEHAVIORAL DISORDERS

**Patent Proprietor:**
Afecta Pharmaceuticals, Inc.

**Opponent:**
Regimbeau

**Relevant legal provisions:**
EPC Art. 100(c), 123(2)

**Keyword:**
Amendments - extension beyond the content of the application as filed (yes)

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**Case Number: T 1487/19 - 3.3.01**

# D E C I S I O N
# of Technical Board of Appeal 3.3.01
# of 17 November 2021

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Afecta Pharmaceuticals, Inc.<br>2102 Business Center Drive<br>Irvine, CA 92612 (US) |
| **Representative:** | Hutter, Anton<br>Venner Shipley LLP<br>5 Stirling House<br>Stirling Road<br>The Surrey Research Park<br>Guildford GU2 7RF (GB) |
| **Respondent:** (Opponent) | Regimbeau<br>20, Rue de Chazelles<br>75847 Paris Cedex 17 (FR) |
| **Representative:** | Regimbeau<br>20, rue de Chazelles<br>75847 Paris Cedex 17 (FR) |
| **Decision under appeal:** | **Decision of the Opposition Division of the European Patent Office posted on 15 February 2019 revoking European patent No. 2307011 pursuant to Article 101(3)(b) EPC.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairman** | A. Lindner |
| **Members:** | R. Hauss |
| | R. Romandini |

## Summary of Facts and Submissions

I. European patent No. 2 307 011 (patent in suit) was granted with a sole claim, which reads as follows:

> *"1. Mazindol, or a pharmaceutically acceptable salt thereof, for use in the treatment of inattention, hyperactivity and impulsivity caused by attention deficient hyperactivity disorder (ADHD) in a mammalian patient, wherein the mazindol, or the pharmaceutically acceptable salt thereof is the only active agent, and wherein mazindol is administered as a daily dose of 2.5 mg."*

II. The patent was opposed under Article 100(a) and (c) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step and extended beyond the content of the application as filed.

III. The patent proprietor requested as its **main request** that the opposition be rejected, and also filed three amended versions of claim 1 as its first to third auxiliary claim requests.

The sole claim of the **first auxiliary request** is identical to claim 1 as granted (main request), except that it specifies that the patient is a human child.

The sole claim of the **second auxiliary request** is identical to claim 1 as granted, except that it further specifies that the patient is a human between 11 and 14 years of age.

The sole claim of the **third auxiliary request** is identical to claim 1 as granted, except that it further

specifies that the patient is a male human between 11 and 14 years of age.

IV. In the discussion concerning the issue of added subject-matter (Articles 100(c) and 123(2) EPC), the patent proprietor relied, *inter alia*, on Example 3 in paragraph [0123] of the application as filed as the basis for the dosage regimen of 2.5 mg daily, recited in the claims of all the requests. Example 3 reads as follows:

> *"Example 3: P. M. is a 14 year old male. At 4 years of age a diagnosis of ADHD was made and he was treated with Ritalin (methylphenidate) with some improvement in attention span but little effect on several other neurobehavioral symptoms, including abusive behavior and depression. At age 9 years of age, he was also being treated with risperidone which continued for 2 years. At 13 years of age the patient was started on Mazindol at 2.5 mg BID and the Ritalin was discontinued. Within 2 months he reported improved attention span, loss of hyperactivity and his bad behavior as a result of his impulsivity significantly improved. Subsequently, the risperidone was then completely discontinued without any recurrence of symptoms of ADHD (i.e. poor attention span, hyperactivity, or inappropriate behavior). The patient was then maintained on Mazindol at 2.5 mg/day as the sole agent without the return of any symptoms of ADHD over the next 3 years."*

V. The decision under appeal is the opposition division's decision revoking the patent, announced on 17 January 2019 and posted on 15 February 2019.

VI. According to the decision under appeal, the subject-matter of claim 1 as granted (main request) was a generalisation from Example 3 of the application as filed. As the example concerned an individual patient with a specific treatment history, this generalisation was not allowable as it extended beyond the content of the application as filed. Analogous objections applied to the subject-matter of claim 1 of each of the first to third auxiliary requests (Articles 100(c) and 123(2) EPC).

VII. The patent proprietor (appellant) filed an appeal against this decision.

VIII. With the statement setting out the grounds of appeal, the appellant re-submitted the claims according to the main request and first to third auxiliary requests considered in the decision under appeal.

Hence, the sole claim of the main request is identical to claim 1 as granted (see points III. and I. above), and the claims of the auxiliary requests are as set out in point III. above.

IX. By letter of 20 October 2021, the appellant advised that it would not be attending the oral proceedings scheduled for 17 November 2021 and requested that a decision be issued in its absence. As a consequence, the board cancelled the oral proceedings and the appeal proceedings continued in writing.

X. The appellant's arguments may be summarised as follows:

The feature in claim 1 as granted that required mazindol to be administered as a daily dose of 2.5 mg was based on paragraphs [0050] and [0052] or on Example 3 of the application as filed, or on all of these passages taken in combination.

The subject-matter as claimed in the main request met the criteria for a permissible intermediate generalisation on the basis of Example 3.

In particular:

- the claim feature "for use in the treatment of inattention, hyperactivity and impulsivity caused by attention deficit hyperactivity disorder (ADHD) in a mammalian patient" meant that the patient to be treated must suffer from all three symptoms;

- the patient in Example 3 had suffered from all three symptoms, which had been successfully treated with 2.5 mg/day mazindol as the sole agent;

- the patient's previous treatment history with other medication was irrelevant. This was because:

  - the symptoms of ADHD could not be cured but had to be treated by regularly administering a suitable medicament,
  - any previously administered medication (methylphenidate, risperidone) would have been eliminated from the patient's body within a matter of days after discontinuation and would not have affected the subsequent treatment.

This reasoning also applied to the claims of all the auxiliary requests. Moreover, the definitions of the patient in the auxiliary requests took further clinical circumstances of the patient in Example 3 into account.

The definition of the patient as "a human child" in the first auxiliary request was based on paragraphs [0022] and [0027] of the application as filed and on the fact that the patient in Example 3 was a child.

The definitions of the patient in the second and third auxiliary requests, too, were based on Example 3. In this context, the person skilled in the art would

understand that Example 3 contained an obvious error in the sentence *"At 13 years of age the patient was started on Mazindol at 2.5 mg BID"*, which should instead read: *"At 11 years of age (...)"*.

XI. The opponent's (respondent's) arguments may be summarised as follows:

Paragraphs [0050] and [0052] of the application as filed did not disclose a daily dose of 2.5 mg mazindol.

Example 3 of the application as filed concerned an individual case with a specific treatment history involving other medicaments. On that basis, the dosage regimen of 2.5 mg mazindol daily could not be interpreted as an effective ADHD treatment by itself, let alone for patients of any age. It was not apparent from Example 3 that monotherapy with 2.5 mg mazindol alone treated the ADHD symptoms, or that the absence of returned symptoms was unrelated to the age of the patient and his progression into adulthood, which in some patients could have a beneficial effect.

The same reasoning applied to the auxiliary requests. Furthermore:

- the patient in Example 3 was not a child (as defined in claim 1 of the first auxiliary request);
- contrary to the appellant's assertion, it was not apparent from the text of Example 3 that the patient's treatment with mazindol must have started at 11 years of age. Even if it were obvious to a reader that an error had occurred (which was, however, disputed), it was far from obvious how such an error should be corrected.

XII. The appellant requested that the decision under appeal be set aside and that the opposition be rejected (main request), or, in the alternative, that the patent be

maintained in amended form on the basis of the claims of one of the first to third auxiliary requests, all filed with the statement setting out the grounds of appeal.

XIII. The respondent requested that the appeal be dismissed.

## Reasons for the Decision

1. Admissibility of the appeal

The appeal complies with Articles 106 to 108 EPC and Rule 99 EPC; it is admissible.

2. Amendments - main request

2.1 For the purposes of Article 100(c) EPC, it must be established whether the application as filed provides a direct and unambiguous disclosure of the subject matter set out in claim 1 of the main request, i.e. all the technical features of claim 1 in combination.

2.2 The application as filed concerns isoindole compounds of formula (I), which also covers mazindol, and their usefulness in the treatment of various neurobehavioural disorders.

*Claims in the application as filed*

2.3 The claims as originally filed concern:

- mazindol, but not its salts (see independent claims 21, 38, 54 and 59)
- for the treatment of ADHD or at least one of its symptoms, but not necessarily the specific combination of the three symptoms "inattention,

hyperactivity and impulsivity" mentioned in claim 1 as granted (see dependent claims 24, 41 and 57).

2.4 The dependent claims referring back to claims 21, 38 or 54 do not mention a mammalian patient or a daily dose of 2.5 mg mazindol, nor do they specify that mazindol is used as the only active agent. The daily dose mentioned in claims 25, 26, 42 and 58 is lower, namely between 1 and 2 mg mazindol.

*Description as filed*

2.5 The statement in paragraph [0013] of the application, according to which the prior art does not disclose that mazindol alone would be useful in treating the specific symptoms of inattention, hyperactivity and impulsivity, is not a positive and direct disclosure of this use.

2.6 The parties restricted their submissions to discussing the possible basis for the specified daily dose of 2.5 mg. In this regard, the appellant relied on paragraphs [0050] and [0052] or Example 3 (paragraph [0123]) of the application as filed.

2.7 The board considers that paragraphs [0050] and [0052] do not disclose treatment with a daily dose of 2.5 mg mazindol.

- Paragraph [0050] states that isoindole compounds of formula (I) may be administered to adult humans at a daily dosage in the general range of 0.01 to 2000 mg to treat a neurobehavioural disorder. This is a rather general statement covering a broad range of compounds, therapeutic indications and dosages, without any mention of mazindol or a dosage of 2.5 mg. Hence, this statement cannot be regarded as a specific disclosure of treatment with a daily dose of 2.5 mg mazindol.

- Paragraph [0052] states that mazindol is available in certain countries in the form of round tablets containing 1.0, 2.5 or 5.0 mg mazindol. There is no direct and unambiguous disclosure that a 2.5 mg tablet is provided as a daily dose, let alone one that is effective for treating symptoms of ADHD in mammalian patients. As set out in paragraph [0013], mazindol was known only for the treatment of different disorders and symptoms.
- This assessment does not change by reading paragraph [0052] together with paragraph [0050], as suggested by the appellant. While, on this basis, a reader would not rule out the possibility that a daily dose of mazindol in an unspecified medical indication might be 2.5 mg, there is no actual explicit or implicit disclosure of a daily dose of 2.5 mg.

2.8 While Example 3 does disclose a daily dose of 2.5 mg mazindol, this example relates to just one individual human patient, but does not disclose the treatment of mammalian patients in general with this dosage regimen. For that reason alone, Example 3 cannot provide an adequate basis for the subject-matter of claim 1 of the main request.

2.9 As set out in paragraph [0111] of the application as filed, when administered to an individual, effective amounts will, for example, depend on the particular condition being treated, the severity of the condition, individual patient parameters including age, physical condition, size and weight, concurrent treatment, frequency of treatment, and the mode of administration. Even if the appellant's argument that prior treatment with methylphenidate and risperidone could not have had any impact were to be accepted, the statements in

Example 3 still apply to just one individual patient with a specific case history and unknown individual parameters which may have affected the treatment and health status of that patient. The treatment described in the example was tailored to that specific patient.

2.10 For these reasons, the ground of opposition according to Article 100(c) EPC prejudices the maintenance of the patent in suit according to the main request.

3. Amendments - auxiliary requests

3.1 Claim 1 of each auxiliary request is identical to claim 1 of the main request, except that the following features were added (see point III. above):

- first auxiliary request: the patient is a human child
- second auxiliary request: the patient is a human between 11 and 14 years of age
- third auxiliary request: the patient is a male human between 11 and 14 years of age

3.2 The same reasoning set out in section 2 above for the main request also applies to all the auxiliary requests. The more specific amended definitions of the patient group do not overcome the objection that the dosage regimen in Example 3 is disclosed only for a single individual and not for a more general patient group.

3.3 For the sake of completeness, the amendments made in the claims of the auxiliary request are not supported by the application as filed either:

3.3.1 While the statement that the patient may be a child is found in the general part of the description (paragraphs [0022] and [0027] of the application as

filed relied on by the appellant), children are not specifically disclosed in combination with a dosage regimen of 2.5 mg mazindol per day.

3.3.2 Example 3 mentions that the patient was 14 years old at the time of writing, and also mentions that at 13 years of age he was started on mazindol at 2.5 mg BID and later was maintained at 2.5 mg per day mazindol for three years.

The appellant argued that, because of the discrepancy in this statement between the one-year difference (14-13 years of age) and the three-year maintenance treatment, it was obvious for the reader to conclude that the patient must have been 11 rather than 13 years old when starting the mazindol treatment. This is the basis proposed by the appellant for the age range of 11 to 14 years mentioned in claim 1 of the second and third auxiliary requests.

The board considers that, while it may be evident to the reader that there was an error in Example 3, replacing 13 with 11 would not be the only possible correction (see also the decision under appeal, point 4.2 of the Reasons). Therefore, the age range of 11 to 14 years is not directly and unambiguously disclosed.

Even if it were, this would not amount to a disclosure of a patient group of humans, or male humans, between 11 and 14 years of age, but still only to the disclosure of one individual (see point 2.8 above).

3.4 For these reasons, the definition of claim 1 of each of the auxiliary requests extends beyond the content of the application as filed (Articles 100(c) and 123(2) EPC).

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated