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**Datasheet for the decision
of 8 April 2014**

Case Number: T 0833/11 - 3.3.01

Application Number: 01953272.0

Publication Number: 1305329

IPC: C07J31/00, C07J17/00,
A61K31/58, A61P5/44, A61P11/06,
A61P11/08

Language of the proceedings: EN

Title of invention:
6.alpha.,9.alpha.-Difluoro-17.alpha.-(2-furanylcarbonyl)-
oxy-11.beta.-hydroxy-16.alpha.-methyl-3-oxo-androst-1,4-
diene-17.beta.-carbothioic acid S-fluoromethyl ester as an
anti-inflammatory agent

Patent Proprietor:
GLAXO GROUP LIMITED

Opponent:
NORTON HEALTHCARE LIMITED

Headword:
Fluticasone furoate/GLAXO

Relevant legal provisions:
EPC Art. 100(b), 83, 100(a), 54, 56, 114(2), 111(1)
RPBA Art. 13(1), 16(1)

Keyword:

Main request, allowable
Sufficiency (yes)
Novelty (yes), specific ester
Inventive step (yes), choice of closest prior art
Admission of late-filed document (no)
Apportionment of costs (no)
Remittal (no)

Decisions cited:

T 0256/87, T 1046/97, T 0021/08, T 0967/97, T 0591/04,
T 1760/11, T 0365/07, T 0608/07, T 0593/09, T 0181/82,
G 0001/03



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Case Number: T 0833/11 - 3.3.01

**D E C I S I O N
of Technical Board of Appeal 3.3.01
of 8 April 2014**

Appellant: NORTON HEALTHCARE LIMITED
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted on
2 February 2011 concerning maintenance of the
European Patent No. 1305329 in amended form.

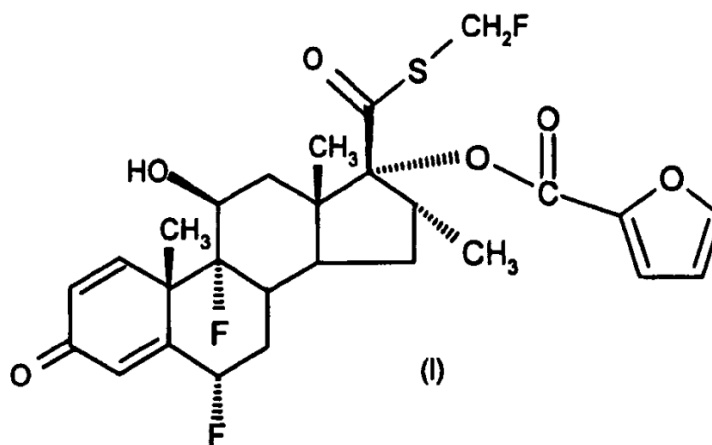
Composition of the Board:

Chairman: A. Lindner
Members: L. Seymour
D. Rogers

Summary of Facts and Submissions

I. European patent No. 1 305 329 was granted on the basis of eighty-one claims. Claims 1 to 5 read as follows:

"1. A compound of formula (1)



and solvates thereof.

2. A compound of formula (1) as defined in claim 1 in unsolvated form.
3. A compound of formula (I) in unsolvated form as defined in claim 2 in the form of Form 1 polymorph, which has an XRPD profile with a peak at around 18.9 degrees 2 Theta.
4. A compound of formula (I) in unsolvated form as defined in claim 2 in the form of Form 2 polymorph, which has an XRPD profile with a peak at around 18.4 and 21.5 degrees 2 Theta.
5. A compound of formula (I) in unsolvated form as defined in claim 2 in the form of Form 3 polymorph which has an XRPD profile with a peak at around 18.6 and 19.2 degrees 2 Theta."

II. Revocation of the patent in suit was sought pursuant to Articles 100(c), 100(b) and 100(a) EPC (lack of novelty and inventive step).

III. The following documents were cited inter alia during the opposition/appeal proceedings:

(1) WO 00/33892

(4) Difficult Asthma, Martin Dunitz 1999,
S J Szeffler et al., Chapter 21, pages 371-375

(5) Handbook of Pharmacokinetic/Pharmacodynamic
Correlation, CRC Press 1995, H Möllmann et al.,
Chapter 14, pages 323-336

(6) The United States Pharmacopeia, 23rd Ed., 1995,
pages 1843, 1844

(10) G H Phillipps et al., J. Med. Chem., 1994,
37, 3717-3729

(16) Burger's Medicinal Chemistry and Drug Discovery,
John Wiley & Sons 1997, Vol. 5, M A Avery and
J R Woolfrey, Chapter 65, pages 281-323, 326-376

(20) GB-A-2 088 877

(29) Allergy Principles & Practice, Mosby 1998,
5th ed., Vol. I, R P Schleimer, Chapter 46,
pages 638, 639

(31) US-A-5 376 359

(38) Declaration of Dr Akwete L. Adjei, dated

31 March 2014, and filed on 1 April 2014

IV. The appeal lies from the interlocutory decision of the opposition division to maintain the patent in suit in amended form based on the main request filed with letter of 13 May 2009. Claims 1 to 5 of this request were identical to those as granted (see above point I).

The opposition division considered the requirements of Article 123(2) and 123(3) EPC to be fulfilled, and the subject-matter of claims 3 to 5 to be sufficiently disclosed.

The novelty attack based on document (1) was not found to be convincing. The opposition division was of the opinion that the passage on page 4, lines 11 to 22, did not represent a technical reality with regard to furoate esters of fluticasone. Moreover, even if document (1) were considered to disclose "fluticasone furoate" in a generic sense, this could not be considered to be a disclosure of the specific individualised compound according to claim 1.

With respect to the issue of inventive step, the opposition division identified document (10) as representing the closest prior art, and fluticasone propionate as the structurally closest compound disclosed therein. Document (1) was considered to be a less suitable starting point, since it did not validly or specifically disclose any fluticasone furoate esters and did not address a problem related to the biological activity of the active agents. The problem to be solved was defined as the provision of an anti-inflammatory agent with an improved side effect profile. The opposition division was of the opinion that the comparative data described on pages 24 and 25 of the

patent in suit demonstrated that the claimed 2-furoate ester provided a solution to the problem posed. This solution was considered to be inventive since there was no indication in any of the documents provided pointing to said solution.

- V. The appellant (opponent) lodged an appeal against this decision. In its statement of grounds of appeal, the appellant disputed the analysis and conclusions of the opposition division with respect to sufficiency, novelty, and inventive step.
- VI. With its reply dated 26 October 2011, the respondent (patentee) filed three auxiliary requests.
- VII. Under cover of letter dated 1 April 2014, the appellant submitted document (38).
- VIII. In its letter dated 3 April 2014, the respondent argued against the admission of document (38) into the proceedings.
- IX. Oral proceedings were held before the board on 8 April 2014.
- X. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

The appellant requested that document (38) be admitted into the proceedings. This declaration by Dr Adjei, who was one of the two inventors named on document (1), was highly relevant, since it provided background information on this author's intention in including the disputed disclosure in document (1). Document (38) had been filed in response to the decision under appeal and the respondent's reply to the statement of grounds of

appeal. The appellant acknowledged that document (38) had been filed late in the proceedings, but denied that this could be regarded as an abuse of procedure. The document had been filed as soon as practicable after the opportunity had arisen for the appellant to speak with Dr Adjei, and its content was straightforward and could readily be dealt with within the time available. However, were the respondent to consider this to be necessary, the appellant would not resist a request for postponement of the oral proceedings.

Turning to the respondent's main request, the appellant confirmed that it did not wish to raise any objections under Articles 100(c) or 123 EPC.

The objections pursuant to Article 100(b) EPC with respect to claims 3 to 5 were maintained. In these claims, crystalline forms 1 to 3 of the compound of formula (I) were respectively defined by means of only one or two X-ray powder diffraction (XRPD) peaks. In view of the standard measurement error in the 2θ values of ± 0.2 degrees, as disclosed in document (6), it was clear that these definitions encompassed a genus of potential polymorphs. For example, the subject-matter as defined in claim 3 would also cover that of claim 5. Therefore, such definitions were insufficient to allow these particular polymorphs to be distinguished from one another, or from future unidentified polymorphs. It could be derived from document (6) that the ten strongest reflections were generally required for complete characterisation of a given polymorph. The syntheses of the three specific polymorphs disclosed in the patent in suit would not allow the skilled person to work the invention within the whole scope claimed, contrary to the requirements of Article 83 EPC. Moreover, it would represent an undue burden to the

skilled person to have to synthesise and test three reference standards each and every time an unknown sample of fluticasone furoate was to be identified. The issue of whether the skilled person would be able to establish whether a product fell within the area covered by the claims was not solely a matter of clarity to be determined under Article 84 EPC but also a consideration under Article 83 EPC, as had been made clear in the case law of the Boards of Appeal, for example, T 256/87, point 10 of the reasons.

The appellant further argued that the subject-matter of claim 1 of the main request lacked novelty with respect to document (1). The skilled person to whom this document was addressed, namely, an aerosol drug formulator, would have no difficulty understanding the phrase "fluticasone esters, such as ... furoate". Thus, prior to the publication of document (1), the term "fluticasone ester(s)" had been widely used in various patent documents directed to pharmaceutical formulations, such as document (31), in conjunction with the preferred compound "fluticasone propionate", which was known to the skilled person to be the adopted name designating fluticasone esterified at the C-17 hydroxyl group with propionic acid. It was further noted that, in disclosing fluticasone esters, document (31) referred to document (20), which, as expected, disclosed only C-17 esters of glucocorticoids such as fluticasone. This was in keeping with common general knowledge, as reflected in documents (4), (5) and (29), which all include unambiguous statements that the presence of the C-11 hydroxyl group was essential for biological activity. Contrary to the contention of the respondent, the skilled person would have no cause to consult a medicinal chemist in this context, or texts from a neighbouring field such as document (16),

since he would readily understand the phrase "fluticasone esters" appearing in document (1) to be a disclosure of the compound formed by the esterification of the C-17 hydroxyl group of fluticasone.

The appellant acknowledged that there were two possible furoic acids known to the skilled person, namely, 2-furoic acid and 3-furoic acid. However, since this was the only variable present, it followed that the skilled person reading document (1) would interpret the term "fluticasone furoate" as a direct and unambiguous disclosure, in individualised form, of each of the two compounds encompassed. In other words, there was no novelty in selecting a compound from one list, especially a list containing only two choices. The appellant argued that the case law on novelty of stereoisomers was not applicable to other areas, and also referred to decision T 1046/97.

With respect to the issue of inventive step, the appellant stated that it did not wish to challenge the analysis and positive conclusion in the decision under appeal, based on document (10) as closest prior art. However, the appellant argued that the assessment of inventive step could not be restricted to an analysis starting from a single document. It was established case law of the boards of appeal, as for instance set out in decisions T 21/08, T 967/97 and T 591/04, which were also cited in decision T 1760/11 referred to by the respondent, that, if there was a choice of several workable routes which might lead to the invention, the rationale of the problem-solution approach required that the invention be assessed relative to all these possible routes, before an inventive step could be acknowledged.

In the present case, document (1) was to be seen as constituting a feasible starting point for the assessment of inventive step. The opposition division had been wrong in its conclusion that the disputed passage in document (1) did not represent technical reality. Indeed, the skilled person reading the passage "fluticasone esters, such as phosphate, monohydrate and furoate,..." would readily identify that the term "monohydrate" was misplaced, since it was not an ester, and would simply mentally delete this as being clearly erroneous, leaving behind a scientifically meaningful sentence, disclosing plausible examples of esters of fluticasone, namely, phosphate and furoate esters.

In this context, the appellant further argued that, at the oral proceedings before the opposition division, document (1) had effectively been excluded from the discussion of inventive step. Indeed, there would have been no point in pleading on this issue, since, during the discussion of novelty, the opposition division had already taken the view that this document did not provide a valid disclosure of "fluticasone furoate", as could be seen from penultimate paragraph on page 3 of the minutes. Although the decision under appeal did mention document (1) under the heading of inventive step, this assessment was based solely on the written arguments. Under these circumstances, the appellant argued that remittal was the appropriate course of action in order to allow the appellant to present its full case before two instances. In this context, the appellant referred to decision T 365/07, in which remittal had been ordered after a new potential closest prior art document had become available.

Returning to the suitability of document (1) as a potential closest prior art, the appellant further

submitted that this document belonged to the same technical field and was directed to a similar purpose or effect as the subject-matter of the opposed patent, namely, the provision of formulations for administering active agents, for use in the treatment of inflammatory disorders, such as asthma or chronic obstructive pulmonary disease, or for use in the treatment of allergic conditions, such as allergic rhinitis. Document (1) also fulfilled the structural requirements for the selection of the closest prior art, in terms of requiring the minimum of structural and functional modifications to arrive at the claimed invention. Thus, even were it to be accepted that esterification at the C-11 position were a possibility, the term "fluticasone furoate" would cover a very small genus of structurally related compounds covering four compounds, including the subject-matter claimed. There was no evidence in the patent, or on the file, to suggest that there was any unexpected technical advantage in the specific compound of present claim 1. Hence, the problem to be solved could only be seen as lying in the provision of an alternative glucocorticoid for treating inflammation and rhinitis. No inventive step could be seen in the selection of a specific compound within the small genus taught in document (1).

XI. The respondent's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

The respondent argued that document (38) should not be admitted into the procedure in view of the fact that it had been filed extremely late without good explanation as to why Dr Adjei had not been contacted earlier. Moreover, document (38) lacked relevance, since the private intentions of one of the authors of

document (1) could not alter what was directly and unambiguously disclosed therein.

The respondent further submitted that it would be appropriate, in accordance with Article 16(1)(a), (c) and (e) of the Rules of Procedure of the Boards of Appeal (RPBA), for the appellant to bear all the respondent's costs incurred as a result of the late filing of document (38), since this constituted

- an amendment to the appellant's case,
- an act prejudicing the timely and efficient conduct of oral proceedings, as demonstrated by the appellant's readiness to accept a postponement of the oral proceedings, and
- an apparent abuse of procedure, in view of the lack of a convincing explanation for the late filing.

The appellant's objections under Article 100(b) EPC were based on mere assertions and an artificial construction of the claims. Sufficiency of disclosure should be acknowledged, since clear and complete instructions were provided in the patent in suit to enable the skilled person to synthesise and identify the claimed polymorphs.

On the question of novelty, the respondent submitted that, even were the phrase "fluticasone esters, such as ... furoate" to be regarded as part of the technical reality of the disclosure of document (1), this did not amount to a direct and unambiguous disclosure of the compound of formula (I) as claimed in claim 1 of the main request. The respondent emphasised that the claimed compound had only been assigned the name "fluticasone furoate" as its approved United States Adopted Name (USAN) and International Non-proprietary

Name (INN) some years after the filing date of the patent in suit. At the effective date of document (1), this term would not have been understood to designate an individual chemical compound. It was therefore misleading to equate said phrase with a disclosure of the compound now known as "fluticasone furoate". At best, the disputed phrase in document (1) could be read as a disclosure of a generic class of compounds in which a number of variables were left open, namely, whether the ester group was attached at the 17 α - or 11 β -position, or whether the furoate was a 2-furoate or a 3-furoate, and whether this group was further substituted. With reference to document (16), the respondent disputed the appellant's contention that esterification would necessarily be at the 17 α -position. Moreover, there would still be no direct and unambiguous disclosure that the furoate ester was a 2-furoate ester. This situation was analogous to that encountered when assessing the novelty of a single enantiomer over a prior disclosure that was sterically generic at the relevant position.

In its assessment of inventive step, the respondent maintained that document (1) was not an appropriate choice of closest prior art.

The person skilled in the art would not understand the disputed text in document (1) as disclosing a furoate ester of fluticasone as a matter of technical reality. In support thereof, the respondent pointed to internal inconsistencies within document (1), such as the fact that this document was directed to a formulation invention, and not new chemical entities; that the disputed text, which was embedded in a list of known medicaments, apparently referred to esters of fluticasone that were not known at the date of

publication of document (1); and that something had clearly gone wrong with the disputed text since "monohydrate" was listed as being an example of an ester.

Even if document (1) were held to validly disclose furoate esters of fluticasone, the respondent argued, with reference to decision T 1760/11, points 10.3.5 and 10.3.6, that this document could nevertheless be excluded as a potential starting point for assessing inventive step. Document (1) was not directed to a similar purpose or effect to the claimed invention. The former was directed to the provision of stable medicinal aerosol formulations, whereas the purpose of the patent in suit, as defined in paragraphs [0002] and [0003], was to provide new and improved corticosteroids. These were two different categories of invention, which did not belong to the same technical field. In view of the different focus of document (1) and in view of the doubts surrounding the actual disclosure of the disputed text therein, this document could not be seen as representing a promising starting point for the skilled person in the field of pharmaceutical drug research, seeking improved drug candidates. Moreover, contrary to the appellant's submission, the condition that the closest prior art must require a minimum of structural modification was not met by document (1), since the genus of compounds ostensibly disclosed therein also encompassed compounds having several structural differences with respect to the subject-matter claimed.

In contrast, document (10), like the patent in suit, was directed to the provision of novel compounds for treating inflammatory disorders such as asthma. Moreover, document (10) disclosed fluticasone

propionate (compound 13e) as the compound selected for clinical study and developed for the treatment of rhinitis and asthma. The structure of this compound only differed from that claimed in the nature of the ester group at C-17. Document (10) thus represented a suitable starting point for the purpose of assessing inventive step.

For the reasons given in the decision under appeal, the compound of formula (I) involved an inventive step over document (10). The appellant had not challenged this analysis. The question of inventive step over document (10) as the closest prior art did not therefore form part of the appeal.

- XII. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 1305329 be revoked.
- Furthermore, the appellant requested that document (38), submitted under cover of a letter dated 1 April 2014, be admitted into the proceedings. Finally, in the event that the patent were not revoked under Articles 123, 83 or 54 EPC, the appellant requested that the case be remitted to the department of first instance for reconsideration of the issue of inventive step.

The respondent (patent proprietor) requested, as a main request, that the appeal be dismissed, or alternatively that the patent be maintained on the basis of one of the auxiliary requests 1 to 3, all filed under cover of a letter dated 26 October 2011.

Furthermore, the respondent requested that document (38) not be admitted into the proceedings, and otherwise requested a postponement of oral proceedings,

and that all its costs incurred as a result of the filing of document (38) be paid by the appellant.

XIII. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Procedural requests*

2.1 *Admission of document (38) into appeal proceedings*

Document (38), which is a declaration by Dr Adjei, the inventor first designated in document (1), was filed only one week prior to oral proceedings before the board. As with all late-filed evidence, admissibility is a matter for the discretion of the board, in accordance with Article 114(2) EPC and Article 13(1) RPBA. In this context, account may *inter alia* be taken of whether a convincing case has been made as to why the evidence could not have been filed earlier and as to its *prima facie* relevance.

The appellant argued that document (38) had been submitted in reaction to the decision under appeal and to the respondent's reply to the statement of grounds of appeal. However, said decision is dated 2 February 2011, and said reply of the respondent 26 October 2011. No reasons were given by the appellant as to why several years had been allowed to elapse before Dr Adjei had been contacted. Therefore, if

considered necessary, document (38) could and should have been submitted at a much earlier stage of the proceedings.

Furthermore, it is not considered that the appellant has made a convincing case as to the relevance of document (38). The board fails to see how an account by one of the inventors outlining his intentions in relation to the wording used in document (1) can possibly throw light on the relevant question as to what is directly and unambiguously disclosed therein to the skilled person using his common general knowledge (cf. point 5 below).

Consequently, the board decided not to admit document (38) into the proceedings.

2.2 *Respondent's request for apportionment of costs*

The respondent requested that its costs incurred as a result of the late filing of document (38) be paid by the appellant, pursuant to Article 16(1) (a), (c) and (e) RPBA.

However, the board cannot recognise that the filing of document (38) constituted a change in the appellant's case. This document was intended to lend support to the position, which the appellant had held throughout the opposition appeal proceedings, that the disputed disclosure on page 4 of document (1) was intentional rather than erroneous. Moreover, the oral proceedings were not delayed as a result of the filing of document (38). Finally, the reasons given by the appellant for the late filing of document (38), although not considered to be convincing enough to sway the decision on admission (see above point 2.1), do not

point towards circumstances that would amount to an abuse of procedure by the appellant.

Consequently, the arguments of the respondent for an apportionment of costs in its favour are not considered to be convincing, and this request is rejected.

2.3 *Appellant's request for remittal*

The appellant requested remittal of the case to the department of first instance for full consideration of document (1) as potential closest prior art document.

According to Article 111(1) EPC, it is at the discretion of the board of appeal to "exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to that department for further prosecution". There is therefore no absolute right for a party to have every aspect of its case examined by two instances.

In the present case, during the oral proceedings before the opposition division, the appellant apparently did not consider it to be useful to plead on the question of whether document (1) represented a potential starting point for the assessment of inventive step (cf. penultimate paragraph of above point X). However, the board notes that this had been an issue throughout the written opposition and appeal proceedings, which had been extensively discussed by both parties, and in the decision under appeal. The board therefore concludes that the parties were in a position to present their case on this issue at oral proceedings before the board, and could be expected to do so.

The present case is not comparable to that at issue in decision T 365/07 (see point 3 of the reasons), cited by the appellant. In T 365/07, a fresh case was generated as a result of the filing of a document during the appeal proceedings, which provided previously lacking information with respect to an alleged prior use. As explained in the previous paragraph, there has been no substantial change in the factual framework of the present case during the appeal proceedings.

Under the present circumstances, the board cannot see that any constructive purpose would be served by remittal. To do so would merely unnecessarily prolong the procedure. Accordingly, the request of the appellant is refused.

3. *Main request - Amendments (Articles 100(c), 123 EPC)*

The appellant did not raise any objections with respect to the claims of the main request under Articles 100(c) or 123 EPC, and the board sees no reason to raise such objections *ex officio*.

4. *Main request - Sufficiency of disclosure (Articles 100(b), 83 EPC)*

4.1 The appellant maintained its objection of lack of sufficiency of disclosure with respect to the subject-matter of claims 3 to 5 (cf. above point I).

These claims each define a polymorph, which are designated as "Form 1", "Form 2", and "Form 3", respectively, each characterised by one or two X-ray powder diffraction (XRPD) peaks.

4.2 In order to assess whether the requirement of sufficiency of disclosure is fulfilled, it must be assessed whether the patent in suit as a whole, that is, the claims, description and figures, makes available to the skilled person, in the light of his general common knowledge, all the information necessary for obtaining the desired polymorphs without undue burden.

In the present case, it has not been contested that examples 1 to 3 of the patent in suit contain clear instructions as to how to prepare the polymorphs designated as Forms 1 to 3, respectively. Moreover, it has not been disputed that these forms are distinguishable by means of their complete XRPD patterns, as shown overlaid in Figure 1.

4.3 The appellant's case rests on the contention that, in view of the standard error in XRPD measurement for the 2θ values of ± 0.2 degrees, the one or two peaks specified in claims 3 to 5 do not properly characterise a unique crystalline form, and would not allow the skilled person to identify an unknown sample. However, this objection concerns the question of whether the claims clearly define "the matter for which protection is sought". This is a matter to be addressed under Article 84 EPC, which is not a ground for opposition (Article 100 EPC). Since claims 1 to 5 as granted have remained unamended in the main request, the board has no power to decide on this issue.

The issue of sufficiency of disclosure dealt with in decision T 256/87, cited by the appellant, related to the question of whether the information given in the patent was sufficient, in the context of the relevant general knowledge, to allow the skilled person to

identify and/or formulate the compositions as claimed (see in particular point 15 of the reasons). This is to be distinguished from the present situation where it has not been challenged that the polymorph Forms 1 to 3 can be prepared based on the methods given in the patent in suit.

On the issue of balance between Article 83 and 84 EPC, decision T 608/07 states the following (see point 2.5.2 of the reasons; cf. also decision T 593/09, point 4 of the reasons):

"... for an insufficiency arising out of ambiguity it is not enough to show that an ambiguity exists, eg at the edges of the claims. It will normally be necessary to show that the ambiguity deprives the person skilled in the art of the promise of the invention."

As explained above in point 4.2, this cannot be said to apply to the present case.

4.4 From the above it follows that a case for lack of sufficiency of disclosure has not been established. Consequently, the board has come to the conclusion that the ground of opposition under Article 100(b) EPC does not prejudice the maintenance of the main request.

5. *Main request - Novelty (Articles 52(1), 54 EPC)*

5.1 Claim 1 is directed to a specific compound, namely, fluticasone esterified at the 17 α -position with 2-furoic acid (cf. above point I).

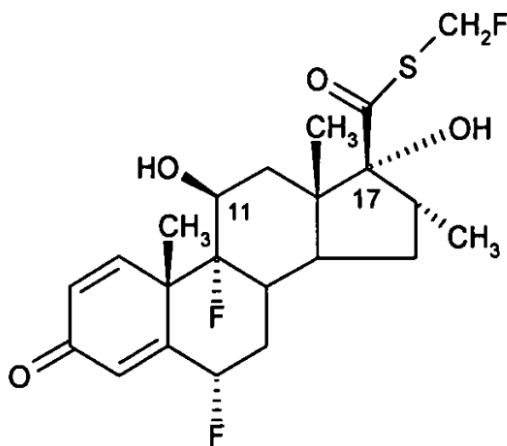
The novelty of this subject-matter was contested in view of document (1), whereby the decisive passage therein reads as follows (see page 4, lines 11 to 15):

"Particularly suitable medicaments or drugs include ... fluticasone esters, such as ... furoate, ...".

5.2 The question to be decided is therefore whether the disclosure of "fluticasone esters, such as ... furoate" in document (1), when read by the skilled person in the light of common general knowledge, amounts to a direct and unambiguous disclosure of the claimed ester in individualised form.

The board firstly notes that the appellant repeatedly used the term "fluticasone furoate" as a shorthand for the above disclosure in document (1). The board agrees with the respondent that this is misleading, since the designation "fluticasone furoate" was only assigned as the official nonproprietary name (USAN, INN) to the compound of claim 1 several years after the date of filing of the patent in suit. Prior to that, this term had not been approved as identifying a unique chemical compound.

There was no dispute between the parties that the term "fluticasone" would have been understood by the skilled person at the priority date of document (1) to uniquely identify the following compound:



However, there was disagreement as to the number of compounds encompassed by the disclosure of "fluticasone esters, such as ... furoate". The levels of potential variability advanced by the respondent included

- i) the point of attachment of the furoate group at the 17 α - or 11 β -positions; and
- ii) the regiochemistry at the furoate group (2- or 3-furoate).

5.3 Regarding the variability listed under point (i), the board notes that fluticasone comprises two free hydroxyl groups and that the position of esterification is not explicitly mentioned in document (1).

The appellant effectively argued that esterification at position 17 would be implicit to the skilled person in the sense that no other possibility would have been contemplated, based on accepted usage of the term "fluticasone ester(s)", and in view of his common general knowledge according to which the presence of the C-11 hydroxyl group was essential for biological activity.

The board is firstly not convinced that the usage of a term in the context of known structures, and patterns derived from structure-activity relationships in known structures, can be considered to provide a suitable basis for directly and unambiguously deriving a particular structural feature with respect to a previously unknown class of compound.

Additionally, the appellant's arguments are not considered to be persuasive for the following reasons:

The formulation patents, such as document (31), referred to by the appellant in order to provide support for an accepted usage of the term "fluticasone ester(s)", do not provide any definition of this term (see e.g. document (31), column 5, lines 3 to 25). In particular, it is not specified that C-17 esters are exclusively intended. Moreover, it cannot be directly and unambiguously derived from the reference therein to "fluticasone propionate" and to the "fluticasone esters" disclosed in document (20) that these are intended to indicate anything more than preferred embodiments of the more general class.

Concerning the argument based on common general knowledge, the board accepts that, as submitted by the appellant, the skilled addressee of document (1) is an aerosol drug formulator. However, the further argument of the appellant, according to which such a skilled person would be aware of certain aspects of the common general knowledge relating to structure-activity relationships in glucocorticoids and not others, is not considered to be convincing. Regardless of the level of his own common general knowledge in this respect, such a skilled person would be aware of the fact that no sound conclusion could be reached as to what was intended by a disclosure pertaining to previously unknown classes of compound without consulting the complete general knowledge in this area. This would include information provided in documents (4), (5) and (29), which are all excerpts from textbooks including short sections on structure-activity relationships in glucocorticoids, but also that provided in document (16), which is a more detailed chapter on anti-inflammatory steroids in a medicinal chemistry textbook. In documents (4), (5) and (29), it is

disclosed that the presence of the C-11 hydroxyl group is essential for activity. However, from the more detailed information provided in document (16), and in particular in section 10.13 thereof, it clearly emerges that said general trends disclosed in documents (4), (5) and (29) are not necessarily and universally applicable.

Consequently, it cannot be accepted that the skilled person would objectively understand the phrase "fluticasone esters, such as ... furoate" in document (1) to directly and unambiguously designate exclusive substitution of the furoate group at position 17 of fluticasone.

- 5.4 With respect to the "variability" referred to in point (ii) of the list in point 5.2 above, the appellant did not contest that document (1) did not specify whether the furoate was a 2-furoate or 3-furoate moiety.

The line of argument advanced by the appellant in this context according to which the disclosure of "furoate" amounted to a direct and unambiguous disclosure of each of the two specific regioisomers 2- and 3-furoate is not considered to be persuasive.

Contrary to the appellant's contention, the term "furoate" cannot be seen as a list, since this would require specific members thereof to be enumerated. It is in fact a generic term conceptually encompassing two members, but not disclosing these in individualised form.

This conclusion is in line with decision T 1046/97, cited by the appellant, wherein it was decided that the

term "optically-active forms" could not be equated to an individualised disclosure of a specific enantiomer (see point 2.1.1.6 of the reasons, penultimate paragraph).

Furthermore, the appellant did not provide any basis for its assertion that the principles developed in the case law relating to the novelty of enantiomers could not be extended to other areas. Indeed, it is noted that earlier decision T 181/82, referred to in T 1046/97 (see point 2.1.1.4 of the reasons), does not concern stereoisomers, but the expression "C₁-C₄ alkyl bromides", which was only found to disclose methyl bromide as an individual compound (OJ EPO 1984, 401, point 8 of the reasons). Moreover, the general applicability of the principle that "the description of a general concept does not disclose specific embodiments falling within the generally described area" was confirmed in decision of the Enlarged Board of Appeal G 1/03 (OJ EPO 2004, 413, see point 2.2.2 of the reasons, penultimate paragraph).

Therefore, the principle outlined above is also applicable to the regioisomers encompassed by the term "furoate".

- 5.5 Consequently, it is concluded that the phrase "fluticasone esters, such as ... furoate" encompasses a generic class, allowing for esterification at positions 11 and 17 and regioisomerism at the furoate moiety, and does not disclose the compound of claim 1 of the main request in individualised form.
- 5.6 Since the appellant did not challenge the novelty of the subject-matter of claim 1 on the basis of any of

the further documents cited, further substantiation of this matter is not considered to be necessary.

Moreover, no objection of lack of novelty was raised against any of the other claims of the main request, and the board sees no reason to differ.

Novelty is therefore acknowledged for the subject-matter of the claims according to the main request.

6. *Main request - Inventive step (Articles 52(1), 56 EPC)*

6.1 The pivotal issue in the present case is whether, as argued by the appellant, there are two feasible starting points for assessing inventive step, namely, documents (1) and (10), or whether, as argued by the respondent, document (10) is to be seen as the only realistic closest prior art.

6.2 In accordance with the problem-solution approach applied by the boards of appeal to assess inventive step, as set out in the "Case Law of the Boards of Appeal of the EPO", 7th edition 2013 (see chapter I, section D, point 2, page 165), it is necessary, as a first step, to identify the closest prior art.

As further outlined in chapter I, section D, point 3 (see in particular points 3.1 to 3.4), the aim with regard to the choice of closest prior art is to identify a starting point which the skilled person would have realistically taken under the circumstances of the claimed invention. Therefore, the first consideration in this selection is whether a prior art document discloses subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention. A further consideration is the

structural similarity with the claimed invention, in terms of common relevant technical features.

- 6.3 The field and purpose of the patent in suit are disclosed in paragraph [0002]. Here it is explained that glucocorticoids which have anti-inflammatory properties are widely used for the treatment of inflammatory disorders or diseases such as asthma and rhinitis. By way of example, "US Patent 4335121" (which belongs to the same patent family as document (20)) is further referred to as disclosing the compound known by the generic name of fluticasone propionate (cf. document (20), Example 19). Potential side effects of glucocorticoids are then elaborated. Finally, the following is stated (see paragraph [0002], last sentence, and paragraph [0003]):

"Whilst the modern steroids are very much safer than those originally introduced, it remains an object of research to produce new molecules which have excellent anti-inflammatory properties, with predictable pharmacokinetic and pharmacodynamic properties, with an attractive side effect profile, and with a convenient treatment regime.

We have now identified a novel glucocorticoid compound which substantially meets these objectives."

Thus, the patent in suit relates to the field of anti-inflammatory glucocorticoids and aims at providing new chemical entities having improved properties, for example, with respect to their side effect profile.

- 6.4 The appellant did not dispute that document (10) constitutes a suitable closest prior art.

Indeed, as is evident from the introductory paragraph of document (10), it is concerned with the same field and purpose as the patent in suit:

"The successful development of corticosteroid analogues designed to show high potency on local application to inflamed tissue has been reviewed.¹⁻⁴ Although the available [sic] compounds showed only weak undesirable systemic side effects after topical administration, we continued to seek further improvement. In this paper we describe a series of potent and novel corticosteroidal halomethyl esters of androstane-17 β -carbothioic acids with promising separations of activity."

Moreover, in document (10), the most active of the compounds tested, and chosen for more detailed examination, is disclosed as being fluticasone propionate (see page 3722, Table 1, compound 13e and right-hand column; see also page 3723, last sentence of "Biological Results and Discussion"). This compound is structurally close to the subject-matter claimed, since it only differs from the latter in the nature of the ester group at position 17.

- 6.5 Document (1) was advanced by the appellant as representing an alternative feasible starting point for the assessment of inventive step.

This document, entitled "A Medicinal Aerosol Formulation", starts with a paragraph describing the field of the invention as follows:

"This invention relates to a medicinal aerosol formulation, and more particularly, to a medicinal aerosol formulation comprising a stabilizer comprising a water addition."

The formulations according to document (1) comprise a particulate medicament or drug, which are suitable for administration by inhalation. The therapeutic categories of drugs or medicaments are listed as including "cardiovascular drugs, antiallergics, analgesics, bronchodilators, antihistamines, antitussives, antifungals, antivirals, antibiotics, pain medicaments, antiinflammatories, peptides, proteins and steroids" (page 4, lines 2 to 10).

In the following paragraph (page 4, lines 11 to 16) it is stated (emphasis added):

"Particularly suitable medicaments or drugs include albuterol (also known as salbutamol), atropine, budesonide, cromolyn, epinephrine, ephedrine, fentanyl, flunisolide, formoterol, ipratropium bromide, isoproterenol, pirbuterol, prednisolone, triamcinolone acetone, salmeterol, amiloride, **fluticasone esters, such as phosphate, monohydrate and furoate,**
(-)4-amino-3,5-dichloro- α -[[[6(2-pyridinyl)ethoxy]-hexyl]amino]methyl]benzene-methanol."

The last paragraph of the description (page 9, lines 8 to 14) reads as follows:

"The formulation of the invention can be delivered to the respiratory tract and/or lung by oral inhalation in order to effect bronchodilation or in order to treat a condition susceptible of treatment by inhalation, e.g., asthma, chronic obstructive pulmonary disease. The formulations of the invention can also be delivered by nasal inhalation in order to treat, e. g., allergic rhinitis, rhinitis, (local) or diabetes (systemic), or they can be delivered via topical (e.g., buccal)

administration in order to treat, e.g., angina or local infection."

Finally, the claims are directed to medicinal aerosol formulations, methods for the preparation and administration thereof, a method of stabilising a suspension aerosol formulation, and metered dose inhalers.

6.6 Contrary to the appellant, the board does not regard document (1) to be a feasible starting point for the assessment of inventive step.

6.6.1 As outlined above in point 6.5, the field of invention as disclosed in the description of document (1), and also reflected in the claims, is that of medicinal aerosol formulations and the stated objective is the provision of means for the stabilisation thereof. Therefore, this document differs from the patent in suit in both these aspects (cf. above point 6.3, last paragraph).

Concerning the medicaments or drugs envisaged for inclusion in the formulations according to document (1), a number of structures are listed, including the following (highlighted in bold in above point 6.5):

"... fluticasone esters, such as phosphate, monohydrate and furoate ..."

There was considerable dispute between the parties as to how this disclosure would be read by the skilled person. However, both parties agreed that it would be immediately recognisable that an error had occurred, since "monohydrate" is not an ester. The

board notes that, apart from this term, the disputed phrase cannot be said to be devoid of technical meaning, since the remaining exemplified esters listed, namely, "phosphate" and "furoate" are chemically feasible.

Nevertheless, this does not mean that the skilled person would regard this disclosure as constituting a suitable starting point for a drug discovery programme. Such programmes typically start with promising known compounds with biological properties of interest, which are then structurally modified with the aim of obtaining improvement (cf. document (10), introductory section on page 3717). Document (1) does not provide such a starting point: As explained above in points 5.3 to 5.5, "fluticasone esters, such ... furoate" can only be considered to be a disclosure of a generic class; no concrete compounds are identified that could provide a basis for further modification.

Therefore, in view of the fact that document (1) relates to a different field to the patent in suit and that the relevant disclosure of compound structures is only generic in nature, it is concluded that the skilled person would not have considered this document as a suitable starting point for his endeavour to provide improved drug candidates.

- 6.6.2 The further arguments of the appellant in favour of document (1) as closest prior art are not considered to be convincing for the following reasons:

The appellant argued that document (1) and the patent in suit were to be seen as belonging to the same technical field and having a similar purpose, owing to overlap in the disclosed diseases to be treated, the

structures envisaged, and the means of their administration (cf. e.g. document (1), page 4, lines 2 to 16 and page 9, lines 8 to 14; and patent in suit, paragraphs [0013], [0023] and [0027]). However, document (1) is not only limited to the disclosure of glucocorticoids and their use in the treatment of inflammatory and/or allergic disorders. As can be seen from the passages of document (1) cited above in point 6.5, it discloses a wide variety of compound categories suitable for incorporation in the claimed aerosol formulations, and conditions to be treated (e.g. diabetes, angina, local infection). The broad and general nature of this disclosure only serves to confirm that the focus of document (1) is on providing stable aerosol formulations, and not investigating the properties of the structures disclosed with a view to providing new pharmaceuticals.

The appellant further submitted that a minimum of structural and functional modification was required to arrive at the claimed invention, starting from document (1). However, as set out above in point 5, the disclosure "fluticasone esters, such as ... furoate" encompasses a generic class, allowing for esterification at positions 11 and 17 and regioisomerism at the furoate moiety. Therefore, the structural proximity to the claimed subject-matter depends on which part of the generic class is considered. In other words, it encompasses the subject-matter claimed but also more remote structures differing therefrom in the position of esterification and point of attachment of the furoate moiety. Therefore, the argument based on structural proximity to the claimed invention is unconvincing.

6.7 In view of the above, the board concludes that document (10) is a suitable closest prior art document, in accordance with the problem-solution approach, and that the skilled person would not have considered document (1) for this purpose.

Since the board does not regard document (1) to be a realistic, feasible, legitimate or promising starting point for the assessment of inventive step in view of the problem posed in the patent in suit, the rationale behind decisions T 21/08, T 967/97 and T 591/04 cited by the appellant is not applicable to the present case (cf. also decision T 1760/11, point 10.3.7 of the reasons).

Consequently, the board sees no reason to deviate from the starting point indicated in patent in suit for the assessment of inventive step, namely, fluticasone propionate, as disclosed in document (10).

6.8 In the decision under appeal (see paragraphs 61 to 68), the opposition division, starting from document (10) as closest prior art, held that requirements of Article 56 EPC were met (cf. also above point IV). The appellant did not challenge this aspect of the decision, and the board does not see any reason to deviate from this conclusion.

Accordingly, the subject-matter of the claims according to the main request meets the requirements of inventive step.

7. Since the main request is considered to be allowable, it is not necessary to comment on the auxiliary requests.

Order

For these reasons it is decided that:

1. The appeal is dismissed.
2. The request for apportionment of costs is rejected.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated