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Datasheet for the decision of 5 June 2025

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Language of the proceedings:	EN

Title of invention:
CALCIFEDIOL SOFT CAPSULES

Patent Proprietor:
FAES FARMA, S.A.

Opponents:
Helbig, Christian, Dr.
IP2 Patentanwalts GmbH
DSM Nutritional Products AG

Headword:
Calcifediol soft capsules / FAES FARMA

Relevant legal provisions:
EPC Art. 56, 123(2), 84
RPBA 2020 Art. 13(2), 12(4), 12(6)

Keyword:
Observations by third parties - admissibility of evidence (no)
Late-filed evidence - admitted (no)
Amendments of application - allowable (yes)
Claims - clarity (yes)
Inventive step - (yes)

Decisions cited:
G 0003/14, G 0002/21, G 0001/12, T 2717/17, T 1962/12, T 0275/11, T 0785/07

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Case Number: T 1456/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 5 June 2025

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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 12 June 2023 concerning maintenance of the European Patent No. 3204047 in amended form.**

Composition of the Board:

Chairman A. Usuelli
Members: E. Duval
L. Basterreix

Summary of Facts and Submissions

I. Three oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as filed.

II. The appeal was filed by opponent 2 (appellant) against the interlocutory decision of the opposition division finding that, on the basis of the main request with claims filed on 6 March 2023, the patent met the requirements of the EPC.

III. Claim 1 of the main request read as follows:

"An immediate release soft capsule comprising:
a) a soft capsule shell, wherein the soft capsule shell comprises:
- 40 to 80 wt% of gelatin,
- 10 to 30 wt% of glycerol, and
- 5 to 15 wt% of sorbitol,

the amounts by weight being expressed with respect to the total weight of the soft capsule shell, and wherein the soft capsule shell does not comprise less than 10 wt% nor more than 50 wt% of a plasticizer selected from the group consisting of glycerol, sorbitol, propylene glycol, polyethylene glycol, dibutyl sebacate, diethyl phthalate, dimethyl phthalate, triacetin, tributyl citrate, triethyl citrate, and mixtures thereof; and
b) a pharmaceutical composition comprising:
- calcifediol,

- an oily component selected from the group consisting of a medium chain triglyceride, isopropyl myristate, a C_{14}-C_{18} alkyl alcohol, a C_{14}-C_{18} alkenyl alcohol, lanolin alcohol and mixtures thereof, and
- a pharmaceutically acceptable organic solvent selected from the group consisting of ethanol, isopropanol, propylene glycol, polyethylene glycol, benzyl alcohol and mixtures thereof;

wherein the soft capsule shell encapsulates the pharmaceutical composition and wherein said pharmaceutical composition is devoid of waxes."

IV. The appealed decision cited in particular the following documents:

D5: applicant's submission of February 13, 2020
D11: WO 2008/134512A 1
D83: Annex V
D84: Annex VI
D85: Annex VII
D86: Izham MNM, et al., Nanomaterials, 2019, 9(1028), 1-18
D108: In vitro results (annex VIII)

V. The opposition division decided that:

(a) The main request met the requirements of Article 84 EPC. The absence of the allegedly essential feature regarding the water content of the capsule shell did not result from the amendments, and could thus not be objected to under Article 84 EPC in opposition.

(b) The main request complied with Article 123(2) EPC. The embodiments on page 9, relating to the broad

list of suitable plasticizers, and then to the preferred plasticizers glycerol and sorbitol, were not independent, but related to the same soft capsule shell, such that their combination was allowable under Article 123(2) EPC.

(c) As to inventive step, the closest prior art was Formulation 9 of D11. The claimed formulation differed in that the composition was encapsulated in a soft capsule comprising gelatin, glycerol and sorbitol in specific amounts. The technical problem was to provide a capsule composition comprising calcifediol having improved bioavailability. The claimed solution involved an inventive step.

VI. With their statement setting out the grounds of appeal, the appellant submitted documents D114-D122.

VII. With their reply to the appeal, the patent proprietor (respondent) filed documents D123-D139 and auxiliary requests 1-25.

VIII. The Board set out their preliminary opinion in a communication under Article 15(1) RPBA.

IX. Observations were filed by a third party on 14 May 2025, including a technical report comparing the bioavailability of calcifediol from soft and hard gelatin capsules. By letter dated 21 May 2025, the respondent objected to the admittance of these observations. By letter dated 23 May 2025, the appellant requested their admission.

X. Oral proceedings were held before the Board.

XI. The requests of the parties were the following:

(a) The appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety. The appellant further requested that the third party observations dated 14 May 2025 be admitted into the appeal proceedings.

(b) The respondent requested that the appeal be dismissed and that the patent be maintained on the basis of the main request upheld by the opposition division, or, alternatively, that the patent be maintained on the basis of one of the auxiliary requests 1-25 filed with the reply to the statement setting out the grounds of appeal. The respondent further requested that documents D114-D120 and D122 be not admitted into the appeal proceedings, and, in case they were admitted, that documents D123-D137 be admitted; that, in the discussion of the *in vivo* data of D83, the aspects such as dog meals and enterohepatic recirculation be not admitted; that the inventive step attack starting from the soft capsule formulation of example 7 of D11 be not admitted, and that the third party observations dated 14 May 2025 be not admitted. Should the Board admit these observations, a postponement of the oral proceedings by at least six months was requested.

(c) Neither opponent 1 nor opponent 3 made any request.

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

(a) Admittance of the third party observations

The third party observations were *prima facie* relevant, as they highlighted significant deficiencies in the

respondent's study, upon which the alleged technical effect was based. These observations were accordingly to be taken into account.

(b) Admittance of D114-D120, D122 and new arguments

The affidavit D114, and documents D115-D120 cited therein, were filed in response to the conclusions of the opposition division, where the reliability of the assays in D83 and D85 was accepted. The assay of D122 was simple and straightforward, and was *prima facie* relevant because it confirmed that there was no technical effect associated to the claimed capsules. Lastly, the dog feed topic was raised, among other shortcomings of the *in vivo* assay in dogs performed by the respondent, in the first instance proceedings. Hence these documents and arguments were to be admitted.

(c) Article 123(2) EPC

The embodiment on page 9 of the application as filed, relating to capsule shell composition of 40-80 wt% of gelatin, 10-30 wt% of glycerol, and 5-15 wt% of sorbitol, was not disclosed as linked to the previous embodiment disclosed on the same page regarding no less than 10 wt% nor more than 50 wt% of a plasticizer. The combination of these limitations in claim 1 of the main request infringed Article 123(2) EPC.

(d) Clarity

The lack of limitation as to the content of water did not fulfil the clarity requirements. This deficiency arose as a consequence of the limitation of the claims in the main request from any standard soft gelatin

capsule shell to a specific one. The amendment thus introduced non-compliance with Article 84 EPC (G 3/14).

(e) Inventive step

The immediate-release formulation in a hard gelatin capsule disclosed in Example 1 (Formulation 9) of D11 represented the closest prior art. The subject-matter of claim 1 of the main request differed in the capsule shell, namely a soft gelatin capsule shell as defined in point a) of the claim. No technical effect was derivable from such difference, let alone over the whole area claimed. The opposition division was incorrect to acknowledge some technical effects based on the documents Annex III (D5), Annex IV (D5)/(D83) and Annex VII (D85). The objective technical problem solved by the invention, starting from Formulation 9 disclosed in D11, was the provision of an alternative immediate release calcifediol formulation. The claimed solution was obvious in light of D11 alone or in combination with common general knowledge.

XIII. The respondent's arguments may be summarised as follows:

(a) Admittance of the third party observations

The third party observations could and should have been submitted at an earlier stage. No exceptional circumstances were put forward to justify their late filing. Accordingly, the third party observations were not to be admitted in the proceedings.

(b) Admittance of D114-D120 and D122

D114, documents D115-D120 cited therein, and D122 were not to be admitted as they were an amendment to the appellant's case, were not submitted in direct response to a newly raised argument, and could and should have been submitted in the first instance proceedings.

Furthermore, the aspects of dog meals and enterohepatic recirculation in the *in vivo* study in dogs of D5 and D83 had not been discussed in the opposition proceedings. They also represented an amendment to the appellant's case and were not to be admitted into the proceedings.

(c) Article 123(2) EPC

The embodiments of page 9 (namely the 10-50 wt% concentration range for the recited plasticizers, and thus implicitly the proviso of claim 1; and the capsule shell composition) were disclosed in consecutive paragraphs of the application as filed, in a convergent and narrower manner. They could thus be combined without adding new information.

(d) Clarity

The amendments made to claim 1 did not generate a lack of clarity because water was not defined in claim 1 as granted, and because the limitations made to the shell composition, in particular to the amounts of gelatin and plasticizers, were compatible with the presence of additional ingredients, such as water.

(e) Inventive step

The immediate-release formulation 9 of Example 1 of D11 could be taken as closest prior art. The distinguishing

technical feature of claim 1 was the soft capsule shell, instead of a hard capsule in D11. The effect of the differentiating feature was shown in the *in vitro* data in Annex III (D5) and *in vivo* data in Annex V (D83) among others. The objective technical problem was to provide soft capsules with improved bioavailability of calcifediol. The claimed solution involved an inventive step because D11 aimed at solving the technical problem of improved bioavailability by providing modified release formulations, and actually taught away from the claimed solution.

Reasons for the Decision

1. Admittance of the third party observations

1.1 Observations by a third party were received in the course of the appeal proceedings on 14 May 2025, i.e. three weeks before the oral proceedings before the Board, and well after notification of the Board's communication under Article 15(1) RPBA dated 30 January 2025. These observations consist in submissions regarding inventive step and a 146-page long technical report comparing the bioavailability of calcifediol from soft and hard gelatin capsules. The appellant requested that these third party observations be admitted into the appeal proceedings.

1.2 Insofar as the appellant attempts to rely on the third party observations, these represents an amendment to their case which is subject to the provisions of Article 13(2) RPBA. This amendment shall, in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the appellant. More generally, irrespective

of the appellant's request to have them admitted, the circumstance that the observations were filed under Article 115 EPC by a third party cannot subtract their admittance from the Board's discretion under Article 13(2) RPBA, because third party observations should not be given a more favourable status than submissions of a party to the proceedings to whom Article 114(2) EPC applies (see the Case Law of the Boards of Appeal, 10th edition, 2022, III.N.4.4.1). This means that the Board is to exercise their discretion taking into account the same criteria of Article 13(2) RPBA in any case.

1.3 In the case at hand, neither the third party nor the appellant justified the late filing of the observations by any exceptional circumstances, and the Board cannot identify any exceptional circumstances either. The appellant's, and third party's, arguments regarding the *prima facie* relevance of the observations fail to meet the criteria of Article 13(2) RPBA. For these reasons the Board decided to disregard the third party observations under Article 13(2) RPBA 2020.

2. Admittance of D114-D120, D122 and the new arguments

2.1 With their statement setting out the grounds of appeal, the appellant filed the affidavit D114, and the documents D115-D120 to which D114 refers, in support of their argument that the experimental data of D5, D83 and D85 were not suitable for showing the alleged technical effect.

Also with their statement setting out the grounds of appeal, the appellant filed the technical report D122. According to the appellant, D122 contains *in vitro* dissolution tests complementing those of D82/D82a and challenging those of D5, D83 and D85, and showing that

both soft and hard calcifediol capsules behave similarly once their content is dissolved/emulsified in a media containing physiological surfactants (bile salts).

2.2 D114-D120 and D122 represent an amendment to the appellant's case in the sense of Article 12(4) RPBA and may be admitted only at the discretion of the Board. D114-D120 and D122 are additionally subject to the provisions of Article 12(6) RPBA. Under Article 12(6) RPBA, the Board shall not admit evidence which should have been submitted in the proceedings leading to the decision under appeal, unless the circumstances of the appeal case justify their admittance.

2.3 In the Board's view, D114-D120 and D122 should have been filed in the first-instance proceedings, because the evidence they are supposed to counter (namely D83, D85) was submitted by the respondent as early as on 1 December 2021 with their reply to the oppositions, or even during examination proceedings in the case of D5, and also because the opposition division had already expressed the preliminary opinion that the main request involved an inventive step in the annex to the summons dated 4 May 2022 (see §26). The appellant did not justify why, despite the above circumstances, D114-D120 and D122 were not filed during the proceedings before the opposition division. The late filing of these documents can neither be regarded as responsive to developments in the first-instance proceedings nor as a reaction to the appealed decision.

2.4 In addition, the affidavit D114 raises new complex issues, in particular aspects of enterohepatic recirculation (see D114, §3) which were not discussed before the opposition division.

2.5 Likewise, the admittance of D122 would raise new complex issues, because D122 compares the dissolution behaviours of hard and soft gelatin capsules under conditions which are different from those of D5, D83 and D85 (namely, D122: in Fed State Simulated Intestinal Fluid, FeSSIF; D5 - Annex III: in Simulated Gastric Fluid without or with Pepsin; D5 - Annex IV and D83: *in vivo* in dogs; D85 - Annex VII: bioaccessibility in a tiny-TIMsg device). Assessing the relevance of D122 and its suitability to disprove the opposition division's findings would thus suppose that the experimental procedure chosen therein and its ability to discriminate soft and hard capsules be analysed.

Accordingly, the Board did not admit any of D114-D120 and D122.

2.6 Since the respondent only requested D123-D137 to be admitted in case D114-D120 and D122 would be admitted, the question of their admittance is moot.

2.7 Lastly, the appellant criticises the tests in D5 (Annex IV) and D83 on account that any information regarding the diet of the dogs, which may contain calcifediol, is missing.

The Board does not consider this argument to represent an amendment to the appellant's case, considering that it was presented in the proceedings before the opposition division (see the appellant's letters dated 18 July 2022, §23 and §30, and 16 February 2023, page 5) and briefly touched upon in the appealed decision (see §40.18). The admittance of this argument is not considered to be subject to the discretionary power of the Board.

However, the Board did not admit the aspects relating to enterohepatic recirculation in the discussion of the *in vivo* data of D83 for the same reasons as for the affidavit D114 mentioning it (see 2.4 above).

3. Main request

3.1 Article 123(2) EPC

Claim 1 of the main request combines in particular the following features disclosed in the application as filed:
- page 9 (lines 15-23) regarding the presence of 40-80 wt% of gelatin and 10-50 wt% of plasticisers selected from a list, reworded in claim 1 into a proviso excluding the presence of the plasticizers in amounts outside that range (namely "does not comprise less than 10 wt% nor more than 50 wt% of a plasticizer [...]"), and
- page 9 (lines 24-28) regarding the presence of 40-80 wt% of gelatin, 10-30 wt% glycerol and 5-15 wt% sorbitol.

The appellant contends that the two embodiments on page 9, respectively lines 15-23 and 24-28, are not unambiguously defined in the application as filed as being linked, or as one being a subset of the other. The appellant relies for confirmation on granted claim 1 in the divisional case (EP 3 689 380 B1).

The Board does not concur. The particular embodiment on page 9, lines 24-28, relating to the presence of 40-80 wt% gelatin, 10-30 wt% glycerol and 5-15 wt% sorbitol, would immediately be read as a subset of the embodiment defined immediately above (lines 15-23) and relating to

the presence of 40-80 wt% gelatin and 10-50 wt% of plasticiser selected from glycerol, sorbitol, [...] and mixtures thereof. The text proposed or accepted for grant in the divisional case has no bearing on this conclusion. Accordingly, the claimed combination of features does not extend beyond the content of the application as filed.

3.2 Clarity (Article 84 EPC)

The appellant objects that claim 1 of the main request does not fulfil the clarity requirements of Article 84 EPC, because an essential feature relating to the content of water is not specified. This lack of clarity would arise as a consequence of the limitation of the claims to a *specific* soft gelatin capsule shell in the main request, as compared with the standard soft gelatin capsule shell of the granted claims.

The Board does not share this view. It follows from G 3/14 that the claims of the main request may be examined for compliance with the requirements of Article 84 EPC only when, and then only to the extent that the amendment introduces non-compliance with Article 84 EPC. In the case at hand, the claims as granted did not specify any content of water any more than the claims of the main request. Furthermore, and contrary to the appellant's view, claim 1 as granted was not limited to a standard soft gelatine capsule, but also encompassed the specific shell defined in claim 1 of the main request. Hence, even if it were considered *arguendo* that some unknown amount of water would represent an essential feature of the specific gelatin capsule shell now claimed, the lack of clarity occasioned by the absence of this feature would in any

case also apply to the more general claim 1 as granted and would not be introduced by the amendments.

Accordingly, the limitation in claim 1 of the main request regarding the shell composition does not introduce a lack of clarity. The amendment is not open to examination under Article 84 EPC.

3.3 Inventive step

3.3.1 The invention relates to calcifediol formulations. As explained in the patent, calcifediol is known for the treatment of diseases related to vitamin D deficiency. The purpose of the invention is to address the problems of high lipophilicity and poor water solubility of calcifediol and to provide immediate release calcifediol solid oral formulations having improved bioavailability (see paragraphs [0004] and [0010]). The proposed solution is the calcifediol soft capsule according to claim 1.

The closest prior art D11 generally relates to controlled release of vitamin D compounds and mentions improved bioavailability as one of the contemplated benefits (see e.g. paragraphs [0002], [0031], and claim 1; see paragraph [0038]). D11 also discloses, for comparison, an immediate release capsule comprising 25-OH-vitamin D_3 i.e. calcifediol (see pages 30-31, example 1, formulation 9). Formulation 9 of example 1 comprises calcifediol in ethanol and caprylic/capric triglycerides (MIGLYOL 812N), filled in hard gelatin capsules, and its bioavailability is evaluated.

In appeal, the appellant takes the hard gelatin capsule of formulation 9, example 1 of D11 as sole starting point for the assessment of inventive step.

The subject-matter of claim 1 differs from formulation 9 of D11 in that the claimed capsule is a soft gelatin capsule with a soft capsule shell as defined in claim 1.

3.3.2 Technical effect

The respondent relies, among others, on D5 (Annex III and Annex IV) and D83 (Annex V) as evidence of a technical effect on bioavailability associated with the differentiating feature.

(a) The appellant contests that these post-published data can be taken into account in view of G 2/21, especially as regards an improved bioavailability associated with the mixture of sorbitol and glycerol as plasticizers in the soft gelatin capsule shell.

The application as filed mentions the problem of providing immediate release calcifediol solid oral formulations having improved bioavailability. As a solution to this problem, the application as filed proposes, in its broadest disclosure, a soft capsule comprising a further undefined soft capsule shell. The particular soft capsule shell composition of present claim 1 is however disclosed on page 9, lines 24-27 and is embodied by the single soft capsule shell prepared in the examples (see example 1(a), used with pharmaceutical composition 1-4). In example 3, the bioavailability of these soft capsules according to present claim 1 is showed to be improved compared with a reference calcifediol solution packaged in ampoules.

It is not debated that the evidence in the application as filed, comparing soft capsules with ampoules, is not suitable to show an effect over the hard capsules of D11. However, the Board considers that the skilled person, based on the application as originally filed, would derive the effect of improved bioavailability associated with the soft capsule including a soft capsule shell composition of present claim 1 as being encompassed by the technical teaching and embodied by the same originally disclosed invention. Considering the preference for and presence of the specific soft capsule shell of claim 1 in the examples studying bioavailability, the link between bioavailability and not only a soft shell generally but also, as the case may be, the now claimed specific soft shell composition, does not change the nature of the claimed invention.

Accordingly, the respondent may rely on the alleged effect if it is shown by the post-published data. For the reasons set out below, the Board concludes that this effect is shown.

(b) D5, Annex III

In D5, Annex III (see page 10), the following formulations are compared:
- sample 1: a soft gelatin capsule (corresponding essentially to example 1 with pharmaceutical composition 1 of the patent) having a soft gelatin shell comprising gelatin, sorbitol and glycerol, and a calcifediol pharmaceutical composition, both as defined in claim 1; with
- comparative sample 2: a hard gelatin capsule comprising the same calcifediol composition.

The compared samples thus differ only by the differentiating feature of claim 1 over the hard gelatin capsules of D11.

Contrary to the appellant's view, there is no reason to doubt that the tested soft capsule (i.e. sample 1) falls within the scope of the claim. The amounts of gelatin (64.5%), sorbitol (13.6%) and glycerol (20.1%) given in D5 for sample 1 fall squarely in the claimed ranges, and D5 further indicates that water is evaporated when drying the capsule. Even if it were accepted that these amounts are given with respect to the listed ingredients rather than the total weight of the soft capsule shell (including remaining water), there is no support for the respondent's allegation that the residual amount of water would bring the amounts of gelatin, sorbitol and glycerol outside the claimed ranges.

D5 (Annex III) shows the dissolution times, measured by visual inspection, in Simulated Gastric Fluid without and with Pepsin (SGF and SGFP, respectively), in a basket or paddle assembly (see §3.1, page 11). The following results are reported:

- test in SGF:

Ph. Eur. procedure	Sample	time (min)
Dissolution (Paddle assembly)	Sample 1 (soft shell)[a]	20 ± 2
	Sample 2 (hard shell)	20 ± 2
Dissolution (Basket assembly)[b]	Sample 1 (soft shell)[a]	15-25
	Sample 2 (hard shell)	20-30
Disintegration	Sample 1 (soft shell)[a]	10 ± 1
	Sample 2 (hard shell)	10 ± 1

- test in SGFP:

Ph. Eur. procedure	Sample	time (min)
Dissolution (Paddle assembly)	Sample 1 (soft shell)[a]	10 ± 1
	Sample 2 (hard shell)	25 ± 2
Dissolution (Basket assembly)[b]	Sample 1 (soft shell)[a]	15-25
	Sample 2 (hard shell)	20-30
Disintegration	Sample 1 (soft shell)[a]	10 ± 1
	Sample 2 (hard shell)	10 ± 1

The results show faster dissolution times for the claimed soft gelatin capsules in all conditions except in SGF - paddle assembly. In the Board's view, while the technical effect must be present across the scope of the claim to be taken into account, it is not required for it to be observable under all testing conditions, because some conditions may simply fail to discriminate the effect. Furthermore, the magnitude of the effect (by a ratio of 2.5 in the case of SGFP, Paddle assembly) does not support the appellant's argument that it is not significant.

The appellant emphasized that no conclusion can be drawn from the disintegration/dissolution assays of Annex III because they are defective.

The appellant firstly points out that the disintegration time is the same for both soft and hard capsules in both media, and submits that, once released, identical oily composition is available for absorption. The Board does not concur. The data in D5 show different dissolution behaviours despite the identical disintegration times.

The appellant further submits that it is not possible to determine the amount of dissolved drug (instead of the shell itself) by visual inspection, and that the

use of visual inspection in a dissolution assay does not follow the standard method set out in the European Pharmacopoeia 6.0.

The Board is not convinced. The fact that these faster dissolution times could be observed by visual inspection does not make them any less convincing. In this respect, proceedings before the EPO are conducted in accordance with the principle of the free evaluation of evidence (G 1/12). The evidence in support of the effect cannot be discarded on the sole reason that it is not in accordance with the standards set out in the Pharmacopoeia, as long as it sufficiently establishes the alleged effect.

Annex III of D5 further shows that the tested soft shells produce not only smaller globules but also an emulsion with lower polydispersity index (PDI) in comparison with hard shells, which indicates a more stable and homogeneous emulsion and an increased drug bioavailability (see §3.3 of Annex III in D5; see also D86, page 10). The same effect and formation of a stable emulsion with the soft gel capsule is observed both in the presence and absence of pepsin, which acts as surfactant. There is no support for the appellant's allegation that these globules do not contain calcifediol.

The appellant relies on D108 and D82/D82a as evidence that the claimed formulation is not a self-emulsifying drug delivery system (SEDDS), but that, once released from either soft or hard gelatin capsules, the oily composition behaves standardly. However, the appealed decision already concluded that the claimed formulations were not SEDDS (see §40.2-§40.4), but that this was not relevant as long as the improvement in

bioavailability was actually demonstrated (see §40.25). The Board concurs.

(c) D5, Annex IV and D83, Annex V

In D5, Annex IV, the same formulations as in Annex III are compared (see page 16 of D5; see (b) above).

Annex IV of D5 reports the calcifediol concentration profiles *in vivo* in dogs and shows that the curve for the soft capsule (sample 1) is above the curve for the hard capsule (comparative sample 2). A higher AUC by a ratio of 1.2 is indicated in Annex IV (see page 17).

D83, Annex V, also includes the same data, with an additional comparative sample. This data was corrected in the letter dated 27 June 2022 (see page 27). In the corrected version, the curve for the soft capsule according to claim 1 (sample 1) is still above the curve for the hard capsule (identified this time as sample 3), i.e. the area under the curve AUC is necessarily higher for sample 1 than sample 3. This is confirmed by the AUC values given in the respondent's reply to the appeal (see page 32), showing a higher AUC by a ratio of 1.4 for sample 1 compared with sample 3. While the respondent, in the course of the opposition and appeal proceedings, submitted several AUC values based on several calculations (without basal correction, or taking into account either an average basal value or individual basal values), each of these calculations lead to the same conclusion, i.e. a higher AUC for the claimed soft gel capsule, irrespective of the extent of this improvement.

The above results thus demonstrate an improved bioavailability of calcifediol when encapsulated in the

claimed soft-capsule shell, as compared with a hard-shell composition.

The appellant criticises these data for lack of scientific rigour of the experiment, in particular with respect to the number of dogs, the information on the study design or statistical significance. The respondent however provided information as to the methodology in their reply to the appeal (see page 32). In addition, the Board considers that a party filing experimental data is not under the obligation to perform any specific statistical analysis of these data, and that, in establishing whether a certain technical effect alleged by a party has been achieved, the EPO has to apply the general principle of free evaluation of evidence (see T 2717/17, point 4.3.5 of the reasons). The decisions cited by the appellant in this regard were either taken in the particular context of qualitative results in tests with a subjective character (see T 1962/12, point 1.5.1 and 1.5.2 of the reasons; T 275/11, point 3.5.2 of the reasons) or in situations where the data were considered not reliable for various reasons which do not characterise the present case, i.e. not simply on account of the small number of tested individuals (see T 785/07, point 2 of the reasons). In the case at hand, the above data are sufficiently convincing considering the information given on the methodology and the absence of demonstration to the contrary. In addition, these *in vivo* data in dogs are in line with the *in vitro* data on file (see 3.3.2(b) above). Under these circumstances, the Board considers that, even taking into account the small group of dogs tested (i.e. 3 dogs) and the alleged high inter-individual variability, the effect of improved bioavailability is shown to a sufficient degree of credibility.

The appellant submitted that the diet of the dogs may contain calcifediol. However, even if it were the case, since the daily dog feed was the same for all animals, a similar effect in all animals would be expected. Thus, this aspect does not invalidate the observed effect.

Lastly, the appellant questions the achievement of the technical effect over the whole scope of the claims. However, these doubts are speculative and not supported by any evidence. While claim 1 represents a generalisation compared with the single soft capsule composition studied in the above evidence, as regards the composition of the shell and the composition inside the capsule, the appellant did not convincingly show that a different outcome would arise for other weight ratios of the oily composition relative to the gelatin shell.

Considering the evidence in D5 and D83, the Board concludes that the problem is the provision of soft capsules with improved bioavailability of calcifediol.

3.3.3 Obviousness

The appellant's case rests on a formulation of the technical problem as the provision of an alternative immediate release calcifediol formulation, but no argument is provided in case the technical effect of improved bioavailability is acknowledged.

The appellant further states (see the grounds of appeal, page 33) that, "based on a more realistic construction of the teaching of D11 as a whole, the skilled in the art would not have taken as the starting

point for arriving at the development of the opposed patent the Formulation 9 in a hard gelatin capsule (as recited in Example 1), but rather said formulation in a soft gelatin capsule as taught in Example 7". This argument rather undermines the appellant's objection of lack of inventive step, which precisely starts from formulation 9. In any case, no reasoned objection of lack of inventive step is elaborated starting from example 7. The Board understands the appellant's argument as aiming to show that, in light of example 7, the skilled person would have incorporated the immediate release Formulation 9 in a soft gelatin capsule.

The Board does not consider that D11 contains an incentive to consider the present immediate release soft gel capsule devoid of waxes. The gist of D11 is to provide modified release formulations containing wax, and D11 further mentions as one benefit an improved bioavailability (see the abstract and paragraph [0038]). While some immediate release formulations are shown in D11, this is for comparative purposes only. The choice of D11 as starting point for the assessment of inventive step defines the framework for further developments. The skilled person, seeking to improve the bioavailability of the formulation, would not do away with the key feature of D11 pertaining to a modified release formulation. In this respect, the results reported in D11 do not point to the claimed formulation. Example 7 of D11 shows a soft gelatin capsule containing calcifediol in an immediate-release formulation (Formulation #2), however this formulation is found to perform worse than the modified release formulation #1 (see the end of paragraph [0153]). Likewise, the immediate release formulation 9 of example 1 leads to a lower calcifediol bioavailability

than the wax-comprising, modified release formulations 3 and 4 of Example 1 (see table 5 of D11). The skilled person, seeking to provide calcifediol formulations with improved bioavailability, is thus not led to the claimed solution.

The appellant expressed the view that the skilled in the art would not seek to improve the bioavailability of Formulation 9, because it already provides outstandingly good bioavailability according to Table 4 of D11. This argument ignores the finding that the claimed invention achieves better bioavailability than formulation 9 (see 3.3.2 above), and does not explain why the skilled person, faced with the above technical problem, would modify formulation 9 and arrive at the claimed invention.

Accordingly, the main request involves an inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated