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Datasheet for the decision of 17 October 2019

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Language of the proceedings: EN

Title of invention:
THE USE OF SOLID CARRIER PARTICLES TO IMPROVE THE PROCESSABILITY OF A PHARMACEUTICAL AGENT

Patent Proprietor:
Gilead Sciences, Inc.

Opponents:
Teva Pharmaceutical Industries Ltd
Cooke, Richard

Headword:
Carrier particles/ GILEAD

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4)

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It can be changed at any time and without notice.

Keyword:
Late-filed evidence - submitted with the statement of grounds of appeal
Inventive step - main and auxiliary requests (no)

This datasheet is not part of the Decision.
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Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0393/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 17 October 2019

Appellant: (Patent Proprietor)	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 (US)
Representative:	Warner, James Alexander Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Appellant: (Opponent 1)	Teva Pharmaceutical Industries Ltd 5 Basel Street P.O. Box 3190 49131 Petah Tiqva (IL)
Representative:	D Young & Co LLP 120 Holborn London EC1N 2DY (GB)
Appellant: (Opponent 2)	Cooke, Richard Elkington and Fife LLP Patents Department 3-4 Holborn Circus London EC1N 2HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 11 December 2017 concerning maintenance of the European Patent No. 2296633 in amended form.**

Composition of the Board:

Chairman	J. Riolo
Members:	A. Usuelli
	Y. Podbielski

Summary of Facts and Submissions

I. Two oppositions have been filed against European patent 2 296 633 on the grounds that its subject-matter lacked novelty and inventive step, was not sufficiently disclosed and extended beyond the content of the application as filed.

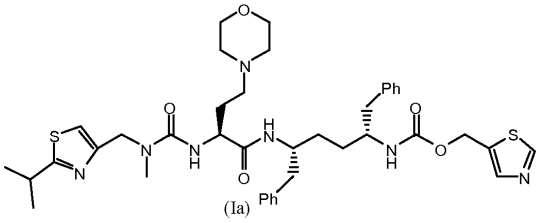
The following documents were among those cited during the first-instance proceedings:

D1: WO 2010/091197
D2: WO 03/037379
D3: Aeroperl®300/30 - Product information
D7: Ansel's pharmaceutical dosage forms and drug delivery systems, pages 42 and 43, 2005
D8: The science of dosage form design, chapter 8, 2002
D9: WO 2004/073689
D13: AAPS PharmSciTech, 9(1), March 2008
D24: WO 2008/010921
D26:Experimental report filed on 16 December 2016
D27: Handbook of pharmaceutical excipients, 4th edition, 2003, 185-188
D29: Dissertation of Abebe Endale Mengesha, Chapter 5, 2005
D30: US 7,026,507
D35: Tybost® - Summary of product characteristics

II. The appeals of the patent proprietor and of the opponents lie against the decision of the opposition division according to which the subject-matter of auxiliary request 1 met the requirements of the EPC. The decision was based on the main request filed on 16 December 2016 and on auxiliary request 1 filed during the oral proceedings held on 30 October 2017.

Claim 1 of the main request read as follows:

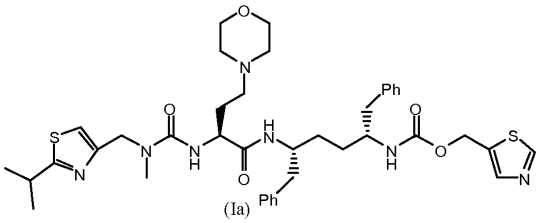
"1. A pharmaceutical composition comprising, a plurality of solid carrier particles that each comprise silicon dioxide and that each have a surface and/or pores; and a compound of formula (Ia):


(Ia)

or a pharmaceutically acceptable salt thereof in the pores or on the surface of the solid carrier particles, wherein the silicon dioxide particles have a BET surface area of at least 200 m^2/g."

Claim 1 of auxiliary request 1 read as follows:

"1. A pharmaceutical composition comprising, a plurality of silica particles that each have a surface and pores; and a compound of formula (Ia):


(Ia)

or a pharmaceutically acceptable salt thereof coated in the pores and on the surface of the silica particles, wherein the silica particles have a BET surface area of at least 200 m^2/g."

III. In its decision, the opposition division came to the conclusion that claim 1 of the main request was not entitled to any of the priority dates claimed. This claim was therefore anticipated by document D1 which described compositions comprising the compound of formula (Ia)(cobicistat) coated on the surface of silica particles.

The subject-matter of auxiliary request 1 was considered to comply with the requirements of the EPC. Concerning the assessment of inventive step, the opposition division held that D24 was the closest prior art. The subject-matter of claim 1 differed from the disclosure of D24 in the specific formulation of cobicistat. The technical problem was the provision of a formulation of cobicistat having a reduced hygroscopicity (compared to cobicistat alone). The opposition division considered that the skilled person would have found no incentive to select the specific silica particles defined in claim 1 among the possible carriers. Therefore, the subject-matter of claim 1 was inventive.

IV. In its statement setting out the grounds of appeal filed on 20 April 2018, the appellant-patent proprietor maintained the requests filed during the proceedings before the opposition division. These requests were replaced by a new main request and 11 auxiliary requests on 6 September 2018, with the reply to the appeal of the opponents.

Claim 1 of the main request and claim 1 of auxiliary request 1 were identical respectively to claim 1 of the main request and claim 1 of auxiliary request 1 forming the basis of the decision of the opposition division (see point II above).

Claim 1 of auxiliary request 2 differed from claim 1 of the main request in specifying that the weight of the compound of formula (Ia) divided by the weight of the solid carrier particles was from 0.8 to 1.2.

Claim 1 of auxiliary request 3 differed from claim 1 of the main request in specifying that the weight percentage of the compound of formula (Ia) to the solid carrier particles was 50% ± 10%.

Claim 1 of auxiliary request 4 differed from claim 1 of the main request in that the feature "[a] pharmaceutical composition" was replaced by "[a] solid dosage form".

Claim 1 of auxiliary request 5 differed from claim 1 of the main request in that the feature "wherein the silicon dioxide particles have a BET surface area of at least 200 m^2/g" was replaced by "wherein the silicon dioxide particles have a mean particle diameter of 10 to 120 micron and a BET surface area of 40 to 400 m^2/g, and wherein the silicon dioxide particles are hydrophilic fumed silica".

Claim 1 of auxiliary request 6 was identical to claim 1 of the main request.

Claim 1 of auxiliary request 7 differed from claim 1 of the main request in that the feature "a plurality of solid carrier particles that each comprise silicon dioxide and that each have a surface and/or pores" was replaced by "a plurality of silica particles that each have a surface and/or pores".

Claim 1 of auxiliary request 8 differed from claim 1 of auxiliary request 1 in specifying that the weight of the compound of formula (Ia) divided by the weight of the silica particles was from 0.8 to 1.2.

Claim 1 of auxiliary request 9 differed from claim 1 of auxiliary request 1 in specifying that the weight percentage of the compound of formula (Ia) to the solid carrier particles was 50% ± 10%.

Claim 1 of auxiliary request 10 differed from claim 1 of auxiliary request 1 in that the feature "[a] pharmaceutical composition" was replaced by "[a] solid dosage form".

Claim 1 of auxiliary request 11 differed from claim 1 of auxiliary request 1 in that the feature "wherein the silica particles have a BET surface area of at least 200 m^2/g" was replaced by "wherein the silica particles have a mean particle diameter of 10 to 120 micron and a BET surface area of 40 to 400 m^2/g, and wherein the silica particles are hydrophilic fumed silica".

V. The following documents were submitted by appellant-opponent 1 on 23 April 2018, with its statement setting out the grounds of appeal:

D36: J. Pharm. Sci. 68(2), 197-202, 1979
D37: Journal of Pharmacy and Biological Sciences, 7(5), 20-25, 2013

In their submissions during the appeal proceedings both appellant-opponents submitted arguments as to the lack of inventive step of the requests filed by the appellant-patent proprietor.

VI. In a communication pursuant to Article 15(1) RPBA issued on 31 July 2019, the Board commented *inter alia* on inventive step starting from D24 as the closest prior art and formulating the technical problem as the provision of a cobicistat formulation that exhibits long term storage stability. It further observed that D2 appeared to indicate that silica particles were suitable to formulate substances that are difficult to handle because they are liquid or pasty and sensitive to moisture.

VII. Oral proceedings were held on 17 October 2019.

VIII. The arguments of the appellant-patent proprietor, as far as relevant to the present decision, can be summarised as follows:

(a) Admittance of document D35

D35 was filed by the appellant-patent proprietor 1 month before the oral proceedings before the opposition division and was *prima facie* relevant.

(b) Admittance of documents D36 and D37

D36 and D37 were not *prima facie* relevant and there was no justification for their late filing. Accordingly, they should not be admitted into the appeal proceedings.

(c) Inventive step

Document D24 was the closest prior art. The composition of claim 1 of the main request differed from the disclosure of D24 in that cobicistat was coated in the pores and on the surface of the silica particles.

Document D26 showed that the formulation was stable upon storage. Additional evidence of the stability of the formulation of claim 1 was provided by D35. Example 2 and Figure 2 of the patent demonstrated that by formulating cobicistat with silica particles its hygroscopicity was reduced by almost 50%. The technical problem was to provide a cobicistat formulation with enhanced handling and processability that exhibited long term chemical and physical storage stability. The first step for the skilled person trying to solve this problem would have been to characterise cobicistat by performing pre-formulation studies. In carrying out these studies, he would have found that cobicistat has a low glass transition temperature, is very hygroscopic, non-free-flowing, water-sensitive and susceptible to chemical degradation via hydrolysis. The inventive aspect of the invention did not lie however in the discovery of the cobicistat properties. It was not a "problem-invention". The real challenge for the skilled person was to provide a suitable formulation for a product presenting the properties of cobicistat. As disclosed in D27, silica was known to be a hygroscopic substance. The skilled person would have not used this material as an excipient for a formulation containing cobicistat, i.e. an active ingredient which is also hygroscopic. There was no suggestion in D24 towards using silica particles for the formulation of cobicistat. D2 disclosed the use of silica particles in pharmaceutical compositions. However, it did not suggest using these particles with hygroscopic substances. The very low hygroscopicity of the formulation of claim 1 was surprising: Figure 2 of the patent showed that both the silica particles and cobicistat were more hygroscopic than the formulation of cobicistat with silica particle. The skilled person would have not expected this effect. For instance, on

the basis of the data reported in D29 it could be established that the formulation of seeds extracts adsorbed on silica particles disclosed in D13 had a hygroscopicity which was intermediate between the hygroscopicity of the seeds extracts and the hygroscopicity of the silica particles.
The subject-matter of claim 1 of the main request was therefore inventive. The same arguments applied to claim 1 of the auxiliary requests.

Claims 1 of auxiliary requests 2, 3, 8 and 9 were inventive also in view of the features defining the amount of silica particles in relation to the amount of cobicistat. Document D36, referred to on page 2 of D2, disclosed compositions containing only 3% of silica. Low amounts of silica particles were disclosed also in D27. The relative amount of silica particles in the compositions of auxiliary requests 2, 3, 8 and 9 was much higher than the amount disclosed in the prior art documents.

IX. The arguments of the appellant-opponents, as far as relevant to the present decision, can be summarised as follows:

(a) Admittance of document D35

D35 was late-filed, not *prima facie* relevant and there was no decision of the opposition division to admit it into the proceedings. Therefore, it did not form part of the appeal proceedings either and the appellant could not rely on it.

(b) Admittance of documents D36 and D37

These documents had been filed with the statement of grounds of appeal and they were in response to the decision of the opposition division. They should be admitted into the appeal proceedings.

(c) Inventive step

The closest prior art document D24 described the product cobicistat in claim 37 and in example S. The subject-matter of the main request differed from the disclosure of D24 in that cobicistat was on the surface and in the pores of silica particles. The technical problem was to provide a stable formulation for cobicistat. By carrying out the routine pre-formulation studies described in D7 and D8, the skilled person would have noticed that cobicistat had a low glass transition temperature, was hygroscopic and difficult to process due to its non free-flowing nature. Document D2 taught the use of silica particles to formulate active ingredients whose flow behaviour was insufficient, were moisture-sensitive, liquid or pasty and therefore difficult to handle. Silica particle formulations containing hygroscopic substances were disclosed for instance in D13, D29 and D30. The data reported in Figure 2 of the patent were not surprising: they merely showed that silica particles could be used to lower the hygroscopicity of an active ingredient. This was in line with the teaching of the prior art documents describing formulations containing silica particles. Thus, the skilled person would have considered obvious to provide cobicistat formulations in which the active ingredient was on the surface or in the pores of silica particles.

There were no effects associated with the features introduced in some auxiliary requests concerning the amount of silica particles in relation to the amount of cobicistat. Moreover, this amount was included in the general range disclosed on page 21 of D2. Furthermore, claim 1 of auxiliary requests 2 and 8 covered also compositions in which the ratio of silica particles to cobicistat was 1:1. However, the same ratio was used also in example 1 of D13.

Thus, none of the requests complied with the requirements of Article 56 EPC.

X. The appellant-patent proprietor requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed on 6 September 2018 or one of auxiliary requests 1 to 11 filed on the same date. It also requested that documents D36 and D37 filed with the grounds of appeal of appellant opponent 1 not be admitted into the proceedings.

XI. The appellant opponents requested that the decision under appeal be set aside and that the patent be revoked. They also requested that document D35 not be admitted into the appeal proceedings.

Reasons for the Decision

1. Admittance of documents D35 to D37

1.1 Document D35 was filed by the appellant-patent proprietor about 1 month prior to the oral proceedings before the opposition division. As D35 was not relevant to the appealed decision, the opposition division did

not decide on whether to admit the document into the proceedings (point 2.4 of the decision). In the appeal proceedings the appellant-patent proprietor did not rely on D35 in its statement setting out the grounds of appeal but in its reply to the appeals of the opponents (letter of 6 September 2018 paragraph 4.17).

The Board considers D35 to be *prima facie* relevant as it gives a summary of the characteristics of Tybost® which contains cobicistat and silica particles. Document D35 is thus admitted into the proceedings.

1.2 Documents D36 and D37 have been filed by appellant-opponent 1 with its statement setting out the ground of appeal to support the argument that the skilled person would have used the silicon dioxide carrier described in D2 with moisture-sensitive and hygroscopic active ingredients, such as aspirin (see paragraph 50 of the statement of grounds of appeal). The filing of these documents is in response to the considerations made by the opposition division in point 5.6 of the decision, according to which the skilled person would have not considered using silicon dioxide particles to reduce the hygroscopicity of a hygroscopic substance such as cobicistat.

1.2.1 According to Article 12(4) RPBA the Board may hold inadmissible documents presented for the first time in appeal proceedings if these documents should have been presented already during the first instance proceedings. This is not the case for documents D36 and D37 since, as explained above, they have been filed in response to the decision under appeal. Therefore, documents D36 and D37 are admitted into the appeal proceedings.

Main request

2. Inventive step

2.1 Closest prior art

2.1.1 The patent-in-suit relates to the provision of a formulation for the compound cobicistat, an inhibitor of cytochrome P450 monooxygenase. In paragraph [0002] of the description it is explained that the compound is difficult to handle and to process on a large scale because it has a low glass transition temperature, is hygroscopic, lacks crystallinity and is non free-flowing.

2.1.2 Document D24, considered by the opposition division as the closest prior art, describes a broad class of inhibitors of cytochrome P450 monooxygenase (see formula (I) on page 2). Cobicistat is included in this general class of compound and is specifically disclosed on page 216 (example S) and in claim 37. D24 does not disclose any specific formulation containing cobicistat. Hence, the subject-matter of claim 1 differs from the disclosure of D24 in that cobicistat is in the pores or on the surface of solid carrier particles of silicon dioxide (also referred to as silica particles in the patent, see paragraphs [0015] and [0017]).

2.2 Technical problem

2.2.1 Example 2 and Figure 2 of the patent shows that Aeroperl®300 (fumed silica) loaded with cobicistat adsorbs 2.4% moisture. Cobicistat alone and Aeroperl®300 alone adsorb 4.8% and 9.3% moisture respectively.

The experimental report D26 demonstrates that the formulation of claim 1 is stabile upon storage. Document D35, a summary of the characteristics of the product Tybost® containing cobicistat and silica particles, indicates that the medicinal product has a shelf life of 4 years and does not require any special storage conditions.

2.2.2 Although no evidence has been filed by the appellant-patent proprietor to substantiate an enhancement of the processability of cobicistat, it is accepted that this effect is achieved having regard to the reduction of the hygroscopicity of the compound. Thus, having regard to the data disclosed in the patent, in D26 and D35, the Board agrees with the appellant-patent proprietor that the technical problem is the provision of a cobicistat formulation with enhanced handling and processability that exhibits long term chemical and physical storage stability.

2.3 Obviousness

2.3.1 It is undisputed by the parties that the skilled person seeking to provide a formulation of cobicistat would as a first step characterise the compound by performing pre-formulation studies. The appellant-opponents referred in this regard to the extracts from textbooks filed as documents D7 and D8 that explain the necessity of carrying out stability tests at various temperatures and relative humidity (D7, page 43, left-hand column) and to determine certain fundamental physical and chemical properties of the drug molecule (D8, page 114, left-hand column). These properties include stability, hygroscopicity and powder flow behaviour (D8, pages 129 to 134).

The parties also agree in concluding that by carrying out these pre-formulation studies the skilled person would observe that cobicistat has a number of properties that renders difficult its processing into a pharmaceutical formulation. In particular, it is very hygroscopic, non-free-flowing and susceptible to chemical degradation via hydrolysis. In this respect the parties explicitly agreed during the oral proceedings that the patent-in-suit was not based on a "problem invention". In other words it is common ground that the observation of the problems arising from the chemical and physical properties of cobicistat does not provide any contribution to the inventive merit of the solution claimed.

The Board sees no reason to deviate from the common position of the parties. Therefore, it concludes that the skilled person would establish, without any inventive effort, that cobicistat is hygroscopic, non-free-flowing and susceptible to chemical degradation via hydrolysis.

2.3.2 It needs therefore to be established what the skilled person would do in order to provide a stable formulation of cobicistat having regard to the chemical and physical properties of this substance.

Document D2 describes the use of silicon dioxide as carrier of active ingredients in pharmaceutical compositions (page 4, lines 16 to 28 and page 18, lines 13 to 24). Silicon dioxide is in the form of a granular material having a BET surface area of 40 to 400 m^2/g (page 4, lines 30 to 33). The document indicates that this granular material is suitable in particular to formulate substances that are difficult to handle

because they are liquid or pasty, are sensitive to moisture, have an insufficient flow behaviour and can be processed only with difficulty as a result of a too low melting point (page 19, lines 7 to 24). On page 13 (lines 13 onwards) D2 explains that the silicon dioxide granular material can be used with a wide range of active ingredients without providing any restriction as to their chemical structure or therapeutic application. The long list of suitable substances includes ritonavir (page 16, line 5), a molecule structurally similar to cobicistat.

The teaching of D2 is confirmed by several other prior art documents. Document D9 indicates that silica particles such as Aeroperl®300 (i.e. the same particles used in example 2 of the patent) can be used to adsorb oil or oily-like materials or materials that are unstable in aqueous medium (see paragraph linking pages 10 and 11). D13 describes the use of Aeroperl®300 as carrier for liquid and pasty active ingredients (page 31, right-hand column). Document D30 indicates that the flowing properties of 3-hydroxy-3-methylbutyrate can be improved if the compound is applied to silica particles (column 1, lines 42 to 48).

2.3.3 Document D2 does not indicate whether the silicon dioxide particles described therein may be useful also with hygroscopic active ingredients. This aspect was underlined by the appellant-patent proprietor in its submissions to support the presence of an inventive step.

However, as discussed above, D2 indicates that the silicon dioxide particles are suitable for products which are difficult to handle, are non-free flowing, sensitive to moisture and have a low melting point.

These physical properties which render difficult the preparation of stable formulations, match to a large extent to those discussed in paragraph [0002] of the patent is respect of cobicistat. In the Board's view, even in the absence in D2 of any mention to the issue of hygroscopicity, the skilled person would readily remark that the active ingredients for which the silicon dioxide particles are recommended in D2 have many properties in common with cobicistat. That would already constitute a strong incentive to prepare a formulation of cobicistat coated on silicon dioxide particles.

In any case, the usefulness of silica particles in reducing the hygroscopicity of active ingredients is described in other prior art documents. Thus, document D13 shows that the percentage of water adsorbed by a dry extract of the seeds of G linus lotoides decreases by increasing the amount of Aeroperl®300 in the formulation (see Figure 3). D30 explains that the hygroscopic and storage-unstable compound 3-hydroxy-3-methylbutyrate, can be brought into a low-hygroscopic, free-flowing and readily handleable form by formulating it with silica (column 1, lines 30-52).

2.3.4 The Board is also not persuaded by the appellant-patent proprietor's argument that the skilled person would avoid combining a hygroscopic substance such as cobicistat with another hygroscopic material such as silica.

Indeed no prior art document has been cited supporting the existence of a prejudice in this regard. Quite to the contrary, D13 and D30 indicate that silica is used as an excipient in formulations containing a hygroscopic active ingredient.

2.3.5 Commenting on Figure 2 of the patent, the appellant-patent proprietor observed that the formulation of claim 1 has a water uptake that is less than the uptakes of cobicistat alone and Aeroperl®300 alone. This result is in its view surprising since the formulation of seeds extracts adsorbed on silica particles disclosed in D13 has a hygroscopicity which is intermediate between that of the seeds extracts and that of the silica particles.

As discussed above, D13 and D30 teach that when an active substance is combined with silica particles, the resulting product has a hygroscopicity which is less than the one of the active substance alone. The data reported in Figure 2 of the patent confirms this finding, i.e. cobicistat loaded on Aeroperl®300 is less hygroscopic than cobicistat alone. The extent of the reduction of the hygroscopicity or the observation that the hygroscopicity of the loaded product falls between those of the separated substances is an observation that may be of theoretical interest, but has no impact on the decision making process of the skilled person seeking to reduce the hygroscopicity of cobicistat. The prior art suggests solving this problem by coating the active ingredient on silica particles. The exact value of the hygroscopicity of cobicistat loaded on Aeroperl®300 may possibly be better than what expected but it still remains the result of the implementation of the teaching of the prior art.

2.4 Therefore, the subject-matter of claim 1 of the main request does not comply with the requirements of Article 56 EPC.

Auxiliary requests 1, 4-7, 10 and 11

3. The appellant-patent proprietor did not submit any argument on inventive step specific to these auxiliary requests but referred to the submissions made in respect of the main request.

The Board agrees that the considerations set out above in relation to the main request apply also to auxiliary requests 1, 4-7, 10 and 11 for the following reasons.

3.1 Claim 1 of auxiliary request 1 refers to "silica particles" whereas the main request refers to "carrier particles that each comprise silicon dioxide".

The Board notes that in the description of the patent various expressions such as "silicon dioxide", "silica particles" or "fumed silica" are used indistinctively to define the silica carrier (see paragraphs [0016] to [0020]). Thus, the carrier particles defined in claim 1 of auxiliary request 1 are the same particles of the main request. Hence, this modification does not modify the assessment of inventive step.

Claim 1 of auxiliary request 1 also indicates that cobicistat is "coated in the pores and on the surface" of the silica particles whereas claim 1 of the main request indicates that the active ingredient is "in the pores or on the surface" of the particles. This modification was apparently introduced to align the wording of the claim with the wording used in the priority documents. This modification does not alter the considerations set out above in respect of the main request as to the relevance of the documents disclosing active ingredients loaded on silica particles, in particular D2, D13 and D30. Indeed, the

appellant-patent proprietor did not submit any comment in this regard.

3.2 In claim 1 of auxiliary request 4 the expression "pharmaceutical composition" used in the main request has been replaced by "a solid dosage form". The Board notes that also the silica particles of D2 can be formulated as solid dosage forms (see paragraph linking pages 12 and 13).

3.3 Claim 1 of auxiliary request 5 specifies that the silicon dioxide particles have a mean particle diameter of 10 to 120 micron and a BET surface area of 40 to 400 m2/g, and the silicon dioxide particles are hydrophilic fumed silica.

The Board observes that the silica described in D2 is based on pyrogenically produced silicon dioxide and has the same particle size and BET surface area (page 4, lines 30 to 33). The same considerations apply to the hydrophilic fumed silica Aeroperl®300 disclosed in D3 and used in the formulation described in D13.

3.4 Claim 1 of auxiliary request 6 is identical respectively to claim 1 of the main request.

3.5 Claim 1 of auxiliary request 7 refers to "silica particles" whereas the main request refers to "carrier particles that each comprise silicon dioxide". As explained in point 3.1 above, this modification has no impact on the assessment of inventive step.

3.6 Claims 1 of auxiliary requests 10 and 11 are based on claim 1 of auxiliary request 1 and differ therefrom on account of the same features introduced in claims 1 of auxiliary requests 4 and 5 in respect of the main

request. As explained in points 3.2 and 3.3 above, these features do not provide any inventive contribution to the subject-matter of the claims.

3.7 For the above reasons it is concluded that auxiliary requests 1, 4 to 7, 10 and 11 do not comply with the requirements of Article 56 EPC.

Auxiliary request 2

4. Claim 1 of this request establishes a relationship between the amount of cobicistat and the amount of silica carrier by specifying that the weight of cobicistat divided by the weight of the solid carrier particles is from 0.8 to 1.2.

4.1 In the appellant-patent proprietor's opinion the skilled person would not consider to prepare cobicistat formulations in which the weight ratio cobicistat to silica particles is as defined in claim 1 since he would be led by the teachings of D27 and D36 to prepare compositions containing lower amounts of silica particles.

4.1.1 Document D27 suggests in Table 1 to use low concentrations of silicon dioxide (from 0.1 to 1.0%) when the product is used as glidant. This teaching is therefore of no relevance in the present case in which silicon dioxide is used as a carrier of an active ingredient. Moreover, Table 1 does not provide an information as to the BET surface area of the product.

Document D36 describes a solid dosage form comprising aspirin and silica (see abstract). In section "Summary and conclusions" (page 202) the authors state that silica provides the maximum stabilisation when used in

an amount of 3%. Document D2 briefly discusses document D36 in the last paragraph of page 2, in the context of describing the background of the invention. Starting from the third paragraph of page 3, D2 explains that the silica-based products used in the prior art, including D36, present several drawbacks. The objective of D2 is therefore to provide a new granular material based on silicon dioxide having improved properties. This product is described starting from the third paragraph of page 4 of D2. Thus, the silica used in the preparation of the aspirin formulation disclosed in D36 is not the same silica used for the pharmaceutical formulations described in D2. Therefore, the skilled person confronted with the problem of providing a formulation containing cobicistat coated on the surface of the silica particles of D2, would not refer to D36 to decide on the amounts of silica and active ingredient. He would rather consider the teaching of D2 itself that suggests using 10 to 150 g of active ingredient per 100 g of silicone dioxide (page 21, lines 1-2). This proportion covers for instance a weight ratio active ingredient to silica particle of 1, which is included in the range of claim 1 of auxiliary request 2.

4.1.2 The appellant-patent proprietor did not submit any evidence to show that the weight ratio specified in claim 1 of auxiliary request 2 is associated with any particular technical effect. Since this ratio falls inside the general teaching of D2, it does not provide any inventive contribution to the subject-matter of the claim.

4.2 Therefore, auxiliary request 2 does not fulfil the requirements of Article 56 EPC.

Auxiliary request 3

5. Claim 1 of auxiliary request 2 also includes a feature establishing a relationship between the amount of cobicistat and the amount of silica carrier. In this case the claim specifies that the weight percentage of the active ingredient to the solid carrier particles is 50% ± 10%.

5.1 The appellant-patent proprietor argued on inventive step by referring to the same arguments submitted in respect of auxiliary request 2.

The Board notes that the general proportion of active ingredient to silica carrier disclosed in D2 (10 to 150 g of active ingredient per 100 g of silicone dioxide, see point 4.1.1 above) also covers formulations in which the amount of active ingredient is 50% ± 10% of the amount of silicon dioxide (e.g.50 g of active ingredient per 100 g of silicon dioxide).

Hence, the considerations set out in respect of auxiliary request 2 apply also to auxiliary request 3. Hence, this request also does not fulfil the requirements of Article 56 EPC.

Auxiliary requests 8 and 9

6. Claims 1 of auxiliary requests 8 and 9 are based on claim 1 of auxiliary request 1 and differ therefrom essentially on account of the same features introduced in claims 1 of auxiliary requests 2 and 3 in respect of the main request. As explained in points 4 to 5.1 above, these features do not provide any inventive contribution to the subject-matter of the claims.

Therefore, auxiliary requests 8 and 9 do not fulfil the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

G. Rauh J. Riolo

Decision electronically authenticated