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Datasheet for the decision of 7 April 2022

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Application Number: 09726974.0

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Title of invention:
TOLTRAZURIL WITH IMPROVED DISSOLUTION PROPERTIES

Patent Proprietor:
KRKA, tovarna zdravil, d.d., Novo mesto

Opponent:
Bayer Intellectual Property GmbH/Bayer Animal Health GmbH

Headword:

Relevant legal provisions:
EPC Art. 54, 56

Keyword:
Public prior use
Novelty
Inventive step

Decisions cited:

Catchword:

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Case Number: T 0603/19 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 7 April 2022

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Representative:	von Renesse, Dorothea König-Szynka-Tilmann-von Renesse Patentanwälte Partnerschaft mbB Mönchenwerther Str. 11 40545 Düsseldorf (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 19 December 2018 concerning maintenance of the European Patent No. 2276347 in amended form.**

Composition of the Board:

Chairman	M. O. Müller
Members:	S. Bertrand
	L. Bühler

Summary of Facts and Submissions

I. The appeals filed by the opponent and the proprietor lie from the opposition division's interlocutory decision that European patent No. 2 276 347 in amended form according to auxiliary request 3, filed during the oral proceedings, met the requirements of the EPC.

II. Claim 1 of auxiliary request 3, which was held allowable by the opposition division, relates to toltrazuril particles defined by a specific surface area.

III. The following documents are cited in the decision:

D2 Marketing authorisation of "Baycox® 5% oral Suspension"

D7 Declaration by Stephan Misch, 20 February 2015

D8 Declaration by Stephan Misch, 27 February 2015

D11 Delivery order of KP04XV2, dated 23 January 2008

D13 Declaration by Guido Becker

D14 Experimental report entitled "*Bestimmung der spezifischen Feststoff-Oberfläche (BET) durch Gas-Physisorption (Analog ISO 9277)*"

D15 Sample preparation of "2017-series"

D16 Experimental report entitled "*Bestimmung der spezifischen Feststoff-Oberfläche (BET) durch Gas-Physisorption (Analog ISO 9277)*"

D18 Experimental report entitled "*Verifizierung der Methode*"

D31 EP 0 147 767 A2

D34 Kim, Sung Tae, *et al*. "Microcrystallization of indomethacin using a pH-shift method" International Journal of Pharmaceutics 263 (2003), pages 141-150

D35 EP 0 130 160 B1

D36 US 4,606,939

D41 Declaration by Dr. Daniel Duff

D42 Declaration by Prof. Dr. Imre Dekany

D48 Declaration by Dr. Daniel Gondol

A051 *Hagers Handbuch der pharmazeutischen Praxis*, 5th edn., 1993, pages 411-412

IV. The opposition division came *inter alia* to the following conclusions:

- neither the subject-matter of claim 1 of the main request (patent as granted) nor that of auxiliary requests 1 and 2 filed on 1 August 2017 was novel in view of the public prior use of "Baycox® 5% oral Suspension" (hereinafter "Baycox®"), and
- the subject-matter of claim 1 of auxiliary request 3 filed on 1 August 2017 was novel and involved an inventive step over Baycox®.

V. In its statement setting out its grounds of appeal, the patent proprietor contested the opposition division's finding that the subject-matter of claim 1 of the main request was not novel. It submitted document A051 (denoted D51 by the patent proprietor) and copies of the claim sets of auxiliary requests 1 and 2.

VI. In its statement setting out its grounds of appeal, the opponent contested the reasoning of the opposition division and argued that the claims of auxiliary request 3 held allowable by the opposition division did

not involve an inventive step over Baycox® as the closest prior art.

VII. In its reply to the opponent's statement of grounds of appeal, the patent proprietor requested that the opponent's appeal be dismissed. It also submitted auxiliary requests 4 to 7.

VIII. In its reply to the proprietor's statement of grounds of appeal, the opponent asserted that neither claim 1 of the main request nor that of auxiliary request 1 or 2 was novel, and that the claims did not involve an inventive step over Baycox®, either.

IX. In a further letter, the opponent requested that auxiliary requests 3 to 7 not be admitted and argued that these requests were not allowable.

X. In preparation for the oral proceedings, scheduled at the parties' request, the board issued a communication pursuant to Article 15(1) RPBA 2020.

XI. With its letters of 7 February 2022 and 4 March 2022, the patent proprietor withdrew its appeal and informed the opponent and the board that it would not attend the oral proceedings.

XII. With its letter of 31 March 2022, the opponent also withdrew its request for oral proceedings and informed the board and the patent proprietor that it would not attend the oral proceedings.

XIII. Oral proceedings before the board were held on 7 April 2022 by videoconference, in the absence of both parties.

XIV. The parties' final requests were as follows:

The patent proprietor requested that:

- the decision under appeal be set aside and the opposition be rejected,

- or, alternatively, the patent be maintained in amended form on the basis of one of the claim sets of auxiliary requests 1 to 2 submitted with the statement of grounds of appeal and auxiliary requests 3 to 7 filed with the reply to the opponent's grounds of appeal, auxiliary request 3 implying that the opponent's appeal be dismissed or

- the case be remitted to the opposition division, should the subject-matter of claim 1 of any of the main request and auxiliary requests 1 and 2 be considered to be novel.

The opponent requested:

- that the decision under appeal be set aside and that the patent be revoked in its entirety, and

- that auxiliary requests 3 to 7 not be admitted into the proceedings.

XV. The patent proprietor's appeal case, where relevant for the present decision, can be summarised as follows:

Main request and auxiliary requests 1 and 2 - novelty

- It could not be concluded that the toltrazuril particles in Baycox® had a specific surface area within the claimed range of between 4 and 40 m^2/g, since the specific surface area increased with time, as shown by the values measured in 2013 in D14 and those measured in 2017 in D16. This was

explained by the degradation of the particles which became porous.

- In view of the presence of bentonite in Baycox®, there were doubts as to whether the specific surface area of the particle of toltrazuril found in the suspension was within the claimed range. The determination of the specific surface area of toltrazuril particles in Baycox® made in D14, D16 and D42 was not correct.

- Twenty-one documents were filed by the opponent to determine the specific surface area of the toltrazuril particles of Baycox®. It was not clear whether the particle size of toltrazuril in Baycox® could be determined beyond reasonable doubt from these twenty-one documents.

- It was questionable whether sample KP04XV2 measured in D16 corresponded to the batch made available to the public, because there were doubts regarding the bulk charge used to prepare sample KP04XV2.

Remittal

- The case should be remitted to the opposition division for the assessment of inventive step in the event the subject-matter of claim 1 of either the main request or auxiliary request 1 or 2 was considered to be novel. The opposition division did not decide on the inventive step of the subject-matter of claim 1 of either the main request or auxiliary request 1 or 2.

Auxiliary request 3 - inventive step

- Baycox® was the closest prior art.

- The distinguishing feature was the morphology of the particles prepared by the process referred to in claim 1 of auxiliary request 3.

- The particles of claim 1 of auxiliary request 3 dissolved faster than the toltrazuril particles present in Baycox®, as shown by the additional comparative tests submitted on 10 August 2018.

- The objective technical problem was the provision of toltrazuril particles having improved dissolution properties.

- The solution as defined in claim 1 was not obvious in view of the cited prior art.

- Claim 1 of auxiliary request 3 involved an inventive step.

Auxiliary requests 4 to 7 - inventive step

- Claim 1 of auxiliary request 4 was a process based on a pH-shift method. It was not obvious to prepare toltrazuril particles with improved dissolution properties by way of a pH-shift method.

- Claim 1 of auxiliary request 5 differed from claim 1 of auxiliary request 4 in that water was used in step a) as the solvent for suspending toltrazuril. Toltrazuril was insoluble in water and a skilled person would have expected harsh conditions to be necessary to dissolve toltrazuril in water. Thus, the alternative proposed by claim 1 of auxiliary request 5 was not obvious.

- Claim 1 of auxiliary request 6 additionally specified that the pH in step b) was maintained between 11 and 13. It was surprising that toltrazuril was stable at this pH range. For this reason, the solution proposed by claim 1 of auxiliary request 6 was not obvious.

- Claim 1 of auxiliary request 7 differed from claim 1 of auxiliary request 6 in that the precipitation of toltrazuril (step b) of claim 1 of auxiliary request 7) was achieved by adding a toltrazuril solution to an acidifying agent. This specific mixing order resulted in a higher specific surface area than the reverse order, as shown by the comparison of examples 4 and 5 with examples 1 to 3. A higher specific surface area was linked to an improved dissolution rate. Claim 1 of auxiliary request 7 involved an inventive step.

XVI. The opponent's appeal case, where relevant for the present decision, can be summarised as follows:

Main request and auxiliary requests 1 and 2 - novelty

- The subject-matter of claim 1 of these requests lacked novelty in view of the product Baycox®, as evidenced by D2, D13 to D16, D41, D42 and D48.

- The patent proprietor did not provide evidence for its allegation that the particles of Baycox® became porous and that the specific surface area of toltrazuril particles increased with time. The different washing techniques in D13 to D14 and D15 to D16 explained the different specific surface areas of the toltrazuril particles in Baycox® in D14 and D16.

- Contrary to the patent proprietor's submission, the determination of the specific surface area measured for the toltrazuril particles in Baycox® made in D14 and D16 was correct and based on the specific surface area of "Veegum" (bentonite present in Baycox®) which was measured and found to be 41.2 m^2 /g in D14 and D18.

- Even assuming that bentonite (Veegum®) had a specific surface area of 100 m^2/g, D42 showed that the specific surface area of the toltrazuril still fell within the claimed range.

- The specific surface area of charge KP04XV2, as made available to the public, was measured in D16. Thus, the patent proprietor's submission regarding the identity of the bulk charge used to prepare charge KP04XV2 was not relevant.

- The above reasoning applied to claim 1 of both the main request and auxiliary requests 1 and 2.

Auxiliary request 3

- Admittance

  - Auxiliary request 3 should not be admitted into the proceedings.

- Inventive step

  - Baycox® was the closest prior art.

  - The distinguishing feature was the morphology of the particles prepared by the process referred to in claim 1 of auxiliary request 3.

  - No effect was linked to the distinguishing feature of claim 1 of auxiliary request 3.

- The objective technical problem was the provision of alternative toltrazuril particles having a specific surface area of between 10 and 25 m^2/g.

- The solution proposed by claim 1 of auxiliary request 3 did not involve an inventive step over D31, D34, D35 or D36. The preparation of particles of organic compounds and pharmaceutically active ingredients by way of a pH-shift method to increase water solubility was known from these documents.

- Claim 1 of auxiliary request 3 did not involve an inventive step.

Auxiliary requests 4 to 7

- Admittance

  - Auxiliary requests 4 to 7 were late-filed and should not be admitted into the proceedings.

- Inventive step

  - The same reasoning as that given for claim 1 of auxiliary request 3 applied.

  - The use of water as the solvent for suspending toltrazuril, as required by claim 1 of auxiliary request 5, was obvious in view of D31, in which water was a solvent for suspending the active substance. Thus, the alternative proposed by claim 1 of auxiliary request 5 did not involve an inventive step.

  - It was expected that toltrazuril was stable at a pH between 11 and 13, as required by claim 1 of auxiliary request 6. Therefore, the subject-

matter of claim 1 of auxiliary request 6 did not involve an inventive step.

- The precipitation of toltrazuril achieved by adding a toltrazuril solution to an acidifying agent, as required by step b) of claim 1 of auxiliary request 7, was not linked to any technical effects, as shown by the comparison of examples 4 and 6 of the patent. The same reasoning as that given for claim 1 of auxiliary request 4 applied to claim 1 of auxiliary request 7.

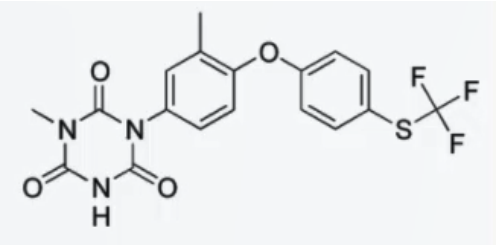
Reasons for the Decision

Main request - patent as granted

1. Claim 1 of the main request reads as follows:

"*1. Toltrazuril particles having a specific surface area between 4 and 40 m^2/g*".

Toltrazuril is represented by the following formula:



2. Novelty

2.1 The opponent objected to the novelty of the subject-matter of claim 1 of the main request in view of the public prior use of the product Baycox®. The opponent

relied, *inter alia*, on documents D2, D13 to D16, D41, D42 and D48.

2.2 Questions to be answered in relation to an instance of public prior use are when the product in question was used, under what circumstances it was used and whether the product used is as required by the relevant claims.

2.2.1 Baycox® is a commercial composition in the form of a suspension comprising toltrazuril particles as an active ingredient. This composition is referred to in paragraph [0002] of the patent.

At least document D2 shows that this commercial composition was approved at the end of 2002, i.e. before the priority date of the opposed patent (3 April 2008).

2.2.2 The charges relevant to the present instance of public prior use are KP03WGS, KP04HVR, KP02LEF and KP04XV2 (see D14 and D16). These charges were produced in 2006, 2007 and 2008, as evidenced by D7, D8 and D11 (all of which were submitted by the opponent).

D7 and D8 are declarations of an employee of a company which produced charges KP03WGS, KP04HVR and KP02LEF (particles of Baycox®). D11 is proof of shipment of KP04XV2.

D7 shows that charges KP03WGS and KP04HVR were delivered to Provet AG in August 2006 (pages 1, 3 and 4 of D7) and in March 2008 (pages 1, 5 and 6 of D7), i.e. before the priority date of the patent (3 April 2008).

According to D8 (page 15), charge KP02LEF was delivered to Schachlinger on 2 February 2004, i.e. before the priority date of the patent.

According to D11 (page 1), KP04XV2 was delivered to Cial De Servicios Agrigan, S.A. and Albet, S.A. on 23 January 2008, i.e. before the priority date of the patent.

2.2.3 The companies receiving the deliveries were not bound by secrecy agreements and thus the aforementioned charges were made available to the public (point 2.2.2 of the impugned decision). This was not disputed by the parties.

Charges KP03WGS, KP04HVR, KP02LEF and KP04XV2 were thus made available to the public before the priority date of the patent (as evidenced by D7, D8 and D11).

This was common ground between the parties.

2.2.4 Charges KP03WGS, KP04HVR, KP02LEF and KP04XV2 contained toltrazuril and bentonite (Veegum®) particles. This was also common ground between the parties.

2.2.5 What was a matter of dispute was whether the toltrazuril particles of these charges had a specific surface area as claimed.

2.2.6 During the proceedings before the opposition division, the opponent filed post-published documents D14 and D16 as evidence of the specific surface area of the toltrazuril particles of Baycox®.

D14 and D16 refer, *inter alia*, to the charges KP03WGS, KP04HVR, KP02LEF and KP04XV2 (see the column "*Bemerkung*"). The specific surface area of the toltrazuril particles of the different charges in D14 and D16 was measured in 2013 and 2017, respectively (see the column "*Messdatum*" in both documents). The preparation of the particles for the measurement in D14 and D16 is described in D13 and D15.

The results of samples of KP03WGS, KP04HVR, KP02LEF and KP04XV2 analysed in D14 and D16 are shown below:

Charge	Specific surface area determined in 2013 (D14)	Specific surface area determined in 2017 (D16)
KP03WGS	11.19 m^2/g	13.21 m^2/g
KP04HVR	9.20 m^2/g	9.44 m^2/g
KP02LEF		11.43 m^2/g
KP04XV2		10.86 m^2/g

In each case, the specific surface area of each of the charges in 2014 and 2017 falls within the range required by claim 1 of the main request (between 4 and 40 m^2/g).

2.2.7 The board has therefore concluded that the subject-matter of claim 1 of the main request lacks novelty. This conclusion is not changed by the proprietor's counter-arguments:

2.3 First, the patent proprietor disputed that the toltrazuril particles in the product that was sold before the priority date of the opposed patent had a specific surface area within the claimed range of 4 to 40 m^2/g. The reason for this was that the specific surface area increased with time. The specific surface area of three charges of Baycox® measured in D14 in 2013 had increased after four years of additional storage, as shown by D16 (measurement in 2017). The increase of the specific surface area of Baycox® was due to the degradation of the particles which became porous. It could therefore not be excluded that the Baycox® charges sold before the priority date of the

patent contained toltrazuril particles having a specific surface area smaller than the claimed range.

The board acknowledges that the surface areas of KP03WGS and KP04HVR measured in 2016 (D16: 13.21 m^2/g and 9.44 m^2/g) were larger than the corresponding values measured in 2013 (D14: 11.19 m^2/g and 9.20 m^2/g).

However, contrary to the patent proprietor's submissions, the difference between the specific surface area in D16 and that in D14 can be explained by the different methods that were used in D16 and D14 for the preparation of the samples. As submitted by the opponent (points 8 and 9 of its reply), the toltrazuril-saturated washing solution used in D15 to wash the particles characterised in D16 prevents the dissolution of the smallest particles of toltrazuril. Since these smallest particles are maintained in the sample, the specific surface area is larger in D16 when compared to the samples of D14, which were prepared in D13 with a non-saturated washing solution which dissolves even the smallest particles of toltrazuril. The different washing techniques in D13 to D14 and D15 to D16 can thus explain the increase of the specific surface area measured for particles of toltrazuril Baycox®. For these reasons, it cannot be concluded from a comparison of the results of D14 and D16 that the specific surface area of particles of toltrazuril/ Baycox® increases over time.

The above finding is corroborated by the expert declarations, i.e. D41, D42 and D48 (documents submitted by the opponent).

More specifically, the expert in D41 (second paragraph on page 3) states that the minimum durability of

Baycox® is five years, i.e. within the period between the shipment (2008) and the measurement made in D14 (2013), and that no variation of the particle size and thus the specific surface area of particles of toltrazuril is to be expected.

In D42 it is explained that the specific surface area of Baycox® is not expected to change over time (paragraphs 0014 to 0021 of D42).

D48 explains and shows that the particle size of Baycox® did not significantly change within a five-year period. This means that the specific surface area (which is inversely proportional to the particle size) did not significantly change either.

With regard to the allegation that the particles degrade and become porous, the patent proprietor did not provide evidence, as submitted by the opponent. In the absence of evidence, and in view of the above, it cannot be concluded that the particles become porous and that the specific surface area increases over time.

Thus, the patent proprietor's allegation that there is an increase of the specific surface area during storage and that Baycox® sold before the priority date of the patent contained toltrazuril particles that had a specific surface area smaller than the lower limit of the claimed range is not convincing.

2.4 Secondly, the patent proprietor submitted that in view of the presence of bentonite in Baycox®, there were doubts as to whether the specific surface area of the particle of toltrazuril found in Baycox® was within the claimed range. The calculation made in D42 took into account a specific surface area of only 100 m^2/g for bentonite. A051 showed that bentonite had a specific surface area ranging from 100 to 300 m^2/g. The

calculation made in D42 was thus incorrect and did not constitute evidence that the specific surface area of the particle of toltrazuril found in Baycox® was within the claimed range.

The board does not accept this argument.

The charges of Baycox® mentioned in D14 and D16, which include KP03WGS, KP04HVR, KP02LEF and KP04XV2, do indeed comprise bentonite particles, namely Veegum®.

In D14 and D18, the specific surface area of "Veegum" (bentonite present in Baycox®) was measured and found to be 41.2 m^2/g (see row "ZFGBR 13TolOberVN 112" in D14 and row "Veegum solo" in D18). The amount of Veegum® in the 2016 samples (D16) was reduced before the measurement by six centrifugation/washing cycles to an amount of 1.29% (see, in particular, D15, and point [58] of the opponent's reply to the proprietor's statement of grounds of appeal). Thus, the calculation of the specific surface area of the toltrazuril particles of Baycox®, obtained by measuring the specific surface area of the solid part of washed Baycox® and deducting the contribution of bentonite (present in an amount of 1.29% after six washing cycles and assuming, for bentonite, a specific surface area of 41.2 m^2/g, i.e. a deduction of 0.53 m^2/g), is the correct calculation to be carried out in the present case. For this reason alone, the patent proprietor's argument must fail.

For the sake of completeness, D42 shows that even if it is incorrectly assumed that bentonite (Veegum®) has a specific surface area as high as 100 m^2/g, the specific surface area of the toltrazuril still falls within the claimed range. The theoretical calculation in D42 was carried out on the basis of 75% of Veegum®, with a

specific surface area of 100 m^2/g, having been removed by washing the samples. The contribution in terms of specific surface area of Veegum® in each sample was then 1.72 m^2/g. Table 1 of D42 shows that the recalculated specific surface area (SSA) of toltrazuril for the samples of D14 and D16 (BET measurement minus 1.72) still falls within the claimed range of between 4 and 40 m^2/g.

Table 1 of D42 is reproduced below:

D14		
Veegum®(SSA)	no	100 m^2/g
Batch number	BET measurement	SSA of sample minus 1.72
KP03WGS	11.19	9.47
KP04HVR	9.20	7.48
D16		
Batch number	BET measurement	SSA of sample minus 1.72
KP03WGS	13.21	11.49
KP04HVR	9.44	7.72
KP02LEF	11.43	9.70
KP04XV2	10.86	9.14

2.5 Thirdly, the patent proprietor argued that twenty-one documents were filed by the opponent to determine the specific surface area of the toltrazuril particles of Baycox®. It was not clear whether the particle size of toltrazuril in Baycox® could be determined beyond reasonable doubt from these twenty-one documents.

The patent proprietor's argument is not convincing for the following reasons:

Even though the opponent filed a certain number of documents, the question to be answered is whether one or more of these documents unambiguously establishes, to the required degree of proof, that the toltrazuril particles of Baycox® correspond to those of claim 1 of the main request. As set out above, D14 and D16 constitute evidence that the specific surface area of toltrazuril from the Baycox® charges discussed above falls within the range of claim 1 of the main request. Thus, the patent proprietor's argument must fail.

2.6 Finally, the patent proprietor submitted that it was questionable whether sample KP04XV2 measured in D16 corresponded to the batch made available to the public. There was an inconsistency between D48 and D8, used by the opponent for objecting to novelty, regarding the bulk charge used to prepare KP04XV2. In D48, KP04XV2 was produced from bulk charge KP04WE4. In D8, KP04XV2 was made from bulk charge KP04X43. The specific surface area of KP04WE4 had not been tested.

The board does not agree.

As set out above, the specific surface area of charge KP04XV2 was measured in D16. This charge, and not the bulk charge used to prepare KP04XV2, was delivered to Cial De Servicios Agrigan S.A. and Albet S.A. on 23 January 2008, as identified in D11. Thus, there is no need to identify the bulk charge used to prepare KP04XV2.

2.7 The subject-matter of claim 1 of the main request therefore lacks novelty, and the main request is not allowable.

Auxiliary request 1 (claims 1 to 14 filed with the statement of grounds of appeal)

3. Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the specific surface area was restricted to a range of between 7 and 30 m^2/g.

4. Since the specific surface area of the charges identified in D14 and D16 (see point 2.2.6 above) falls within the range of claim 1 of auxiliary request 1, the reasons given for claim 1 of the main request also apply to claim 1 of auxiliary request 1. Thus, the subject-matter of claim 1 of auxiliary request 1 is not novel in view of the public prior use.

5. For this reason, auxiliary request 1 is not allowable.

Auxiliary request 2 (claims 1 to 13 filed with the statement of grounds of appeal)

6. Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the specific surface area was restricted to a range of between 10 and 25 m^2/g.

7. The specific surface areas of KP03WGS, KP02LEF and KP04XV2 (11.19 m^2/g, 13.21 m^2/g, 11.43m^2/g and 10.86 m^2 /g, respectively), identified in D14 and D16 (see point 2.2.6 above), fall within the range of claim 1 of auxiliary request 2. Thus, the subject-matter of claim 1 of auxiliary request 2 is not novel in view of the public prior use, for the same reasons as those given for the main request. Auxiliary request 2 is not allowable.

Remittal

8. The patent proprietor requested that the case be remitted to the opposition division for the assessment of inventive step in the event the subject-matter of

claim 1 of the main request or auxiliary request 1 or 2 is considered to be novel.

9. Since neither the subject-matter of claim 1 of the main request nor that of auxiliary requests 1 and 2 is novel, as set out above, the patent proprietor's conditional request is no longer relevant.

Auxiliary request 3 (claims 1 to 13 filed on 1 August 2017 before the opposition division)

10. Claim 1 of auxiliary request 3 reads as follows:

"*1. Toltrazuril particles having a specific surface area between 10 and 25 m^2/g obtainable by a process comprising the steps of:*

a) suspending toltrazuril in a solvent;

b) dissolving toltrazuril with an addition of a basifying agent to the suspension;

c) precipitation of toltrazuril with an addition of an acidifying agent to the solution or with an addition of toltrazuril solution to an acidifying agent, and

d) separation of precipitated toltrazuril from a liquid phase".

Claim 1 of auxiliary request 3 is thus defined as a product-by-process claim. The process referred to in claim 1 of auxiliary request 3 is a process of precipitating toltrazuril based on a dissolving step followed by a precipitation step, both steps being achieved by changing the pH of the solution comprising toltrazuril. This kind of process is known in the art as a pH-shift process.

11. Admittance

The opponent requested that auxiliary request 3 not be admitted into the proceedings. However, as set out above, auxiliary request 3 is the request found allowable by the opposition division. This request thus forms part of the present appeal proceedings.

12. Novelty

Novelty was not one of the opponent's objections.

13. Inventive step

13.1 The opponent made an inventive step objection in view of Baycox® as the closest prior art. The proprietor did not contest the fact that the public prior use can be considered the closest prior art and the board does not see any reason to diverge from the opponent's view either.

13.2 Distinguishing feature

The distinguishing feature is the morphology of the particles prepared by the process referred to in claim 1 of auxiliary request 3. The particles of claim 1 of auxiliary request 3 are obtained by precipitation and differ from the particles of Baycox®, which are prepared by milling. The particles of claim 1 prepared by precipitation do not exhibit the breaking edges found in milled particles.

This was common ground between the parties.

The patent proprietor submitted that the toltrazuril particles produced by the process of claim 1 of auxiliary request 3 have a different specific surface area from the toltrazuril particles of Baycox®. The specific surface area represented a further

distinguishing feature of claim 1 of auxiliary request 3 over Baycox®.

The board does not agree.

The claimed particles are characterised by a specific surface area of between 10 and 25 m^2/g. As set out above in the context of the assessment of novelty of the subject-matter of claim 1 of auxiliary request 2, the charges of Baycox® discussed above have a surface area within this range.

13.3 Technical effect and objective technical problem

The patent proprietor submitted that the claimed particles dissolved faster than the toltrazuril particles present in the above-mentioned charges of Baycox®. It referred to the additional comparative tests submitted on 10 August 2018. The objective technical problem was therefore the provision of toltrazuril particles having improved dissolution properties.

The board does not agree.

The board acknowledges that the additional comparative tests submitted on 10 August 2018 (page 6) show an increased dissolution rate of the precipitated toltrazuril particles (according to claim 1 of auxiliary request 3) in comparison to milled toltrazuril particles. However, the milled toltrazuril particles of the comparative example cannot be considered the closest prior art (Baycox®). Indeed, the milled toltrazuril particles of the comparative example have a specific surface area of 3.60 m^2/g (last full paragraph of the letter of 10 August 2018) and do not correspond to the particles present in the aforementioned charges of Baycox®, which have a

specific surface area of between 10 and 25 m^2/g, as set out in the context of the assessment of novelty of claim 1 of auxiliary request 2.

Consequently, the effect referred to by the patent proprietor cannot be taken into account when formulating the objective technical problem.

In view of the above, the objective technical problem is the provision of alternative toltrazuril particles having a specific surface area of between 10 and 25 m^2/g, as formulated by the opposition division.

13.4 Obviousness

When considering the aforementioned charges of Baycox® as the closest prior art, the opponent relied *inter alia* on D31, D34, D35 and D36 for the assessment of the obviousness of the solution proposed by claim 1 of auxiliary request 3.

D31 discloses pharmaceutical compositions comprising a poorly water-soluble active ingredient and a process of preparation for improving the bioavailability thereof. The active ingredient is characterised by a high specific surface area (abstract). The active ingredient is part of the anthelmintics group (antiparasitic drugs that expel parasitic worms and other internal parasites from the human or animal body). The particles of anthelmintics are prepared by dry milling, or by precipitation followed by wet milling. A process involving a pH-shift is also proposed in D31 (page 4, line 32, to page 5, line 16). Example 1 of D31 discloses the preparation of fenbendazole (an anthelmintic) having a specific surface area of 18.7 m^2/g by way of a pH-shift reaction.

D34 discloses a method for solubilising indomethacin (a non-steroidal anti-inflammatory drug) using a pH-shift method. D34 teaches that one way to improve the dissolution rate is to reduce the particle size, which increases the total surface area (page 141, second paragraph of the introduction).

D35 and D36 are concerned with the provision of a method for forming small particles of organic compounds by way of a pH-shift method (claim 1 of both D35 and D36). In the examples of D35 and D36, particles of sulfadiazine (an antibiotic) are prepared by way of a pH-shift method. Particle sizes smaller than 1 µm are reported in Table 1 of both D35 and D36.

The preparation of particles by way of the pH-shift method is thus known from D31, D34, D35 and D36. Hence, the skilled person looking for alternative toltrazuril particles having a specific surface area of between 10 and 25 m^2/g would have known that such particles can be prepared by way of a pH-shift method. They would therefore have arrived at the subject-matter of claim 1 of auxiliary request 3 in an obvious way.

Hence, the subject-matter of claim 1 of auxiliary request 3 does not involve an inventive step.

14. Thus, auxiliary request 3 is not allowable.

Auxiliary request 4 submitted with the reply to the statement of grounds of appeal

15. Claim 1 of auxiliary request 4 reads as follows:

"*1. A **process** for the preparation of toltrazuril particles having a specific surface area between 10 and 25 m^2/g, comprising the steps of:*

a) suspending toltrazuril in a solvent;

b) dissolving toltrazuril with an addition of a basifying agent to the suspension;

c) precipitation of toltrazuril with an addition of an acidifying agent to the solution or with an addition of toltrazuril solution to an acidifying agent;

d) separation of precipitated toltrazuril from a liquid phase; and

e) optional further maceration of toltrazuril" (emphasis added by the board).

Hence, unlike any of the higher-ranking requests, the only independent claim of auxiliary request 4 is now directed at a process of preparation.

16. Inventive step

16.1 Distinguishing features

Claim 1 of auxiliary request 4 differs from Baycox® in process steps a) to d).

16.2 Technical problem

As set out above in the context of claim 1 of auxiliary request 3, no technical advantage over Baycox® is achieved by using a pH-shift process for preparing toltrazuril particles having a specific surface area of between 10 and 25 m^2/g. Thus, no technical effect is achieved by the distinguishing features of claim 1 of auxiliary request 4. The objective technical problem is thus the provision of an alternative process for preparing toltrazuril particles having a specific surface area of between 10 and 25 m^2/g.

16.3 Obviousness

The process of claim 1 of auxiliary request 4 is obvious at least in view of D31. As set out in section 13.4 above, D31 discloses a process involving a pH-shift (page 4, line 32, to page 5, line 16). This process comprises the steps of suspending the active ingredient in a solvent, dissolving the active ingredient with the addition of a basifying agent, precipitating the active ingredient by adding an acidifying agent and implicitly separating the precipitated active ingredient from the solution. These steps of the process of D31 correspond to steps a) to d) according to claim 1 of auxiliary request 4.

Thus, the skilled person would arrive at the process of claim 1 of auxiliary request 4 by following the teaching of D31. Claim 1 of auxiliary request 4 therefore does not involve an inventive step.

17. Consequently, auxiliary request 4 is not allowable.

Auxiliary request 5 submitted with the reply to the statement of grounds of appeal

18. Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 4 in that water is used in step a) as the solvent for suspending toltrazuril. This represents a further distinguishing feature of claim 1 over the closest prior art. However, no technical effect has been shown to be achieved by this distinguishing feature. The problem underlying the subject-matter of claim 1 of auxiliary request 5 therefore remains the same as that formulated for claim 1 of auxiliary request 4, namely the provision of an alternative process for preparing toltrazuril particles having a specific surface area of between 10 and 25 m^2/g.

19. As set out above, the preparation of particles using a pH-shift method is known from D31. Furthermore, water is the solvent used in the dissolution of the active ingredient in D31 (page 5, lines 1 to 12). Thus, the subject-matter of claim 1 of auxiliary request 5 represents an obvious alternative.

Therefore, auxiliary request 5 is not allowable.

Auxiliary request 6 submitted with the reply to the statement of grounds of appeal

20. Claim 1 of auxiliary request 6 is a combination of claims 1 and 3 of auxiliary request 5, i.e. it additionally specifies that the pH in step b) is maintained between 11 and 13.

21. The fact that the pH is maintained between 11 and 13 represents a further distinguishing feature.

22. However, no technical effect has been shown to be achieved by this distinguishing feature. The problem underlying the subject-matter of claim 1 of auxiliary request 6 therefore remains the same as that formulated for claim 1 of auxiliary request 4, namely the provision of an alternative process for preparing toltrazuril particles having a specific surface area of between 10 and 25 m^2/g.

23. The patent proprietor argued that it was surprising that the active ingredient (toltrazuril) was stable at this pH range. For this reason, the solution proposed by claim 1 of auxiliary request 6 was not obvious.

24. The board does not agree. As submitted by the opponent, it is not unexpected that toltrazuril will be stable under these pH conditions and the patent proprietor did

not demonstrate that a prejudice in that regard exists in the prior art.

Thus, the skilled person considering the objective technical problem set out above would not have disregarded the use of a pH-shift method at a pH range of 11 to 13. The selection of a pH in this range represents an arbitrary choice of pH, which is part of the skilled person's routine activities.

Therefore, the subject-matter of claim 1 of auxiliary request 6 does not involve an inventive step.

25. For these reasons, auxiliary request 6 is not allowable.

Auxiliary request 7 submitted with the reply to the statement of grounds of appeal

26. Claim 1 of auxiliary request 7 differs from claim 1 of auxiliary request 6 in that the precipitation of toltrazuril (step b) of claim 1 of auxiliary request 7) is achieved by adding a toltrazuril solution to an acidifying agent. This represents a further distinguishing feature of claim 1 of auxiliary request 7 over the closest prior art in comparison to claim 1 of auxiliary request 6.

27. The patent proprietor argued that this specific mixing order resulted in a higher specific surface area than the reverse order (adding the acidifying agent to the toltrazuril solution), as shown by a comparison of examples 4 and 5 (according to claim 1 of auxiliary request 7) with examples 1 to 3 (comparative examples with the reverse order).

28. This allegation is not correct. The board acknowledges that examples 4 and 5 lead to toltrazuril particles

having a higher specific surface area in comparison with examples 1 to 3. However, as submitted by the opponent, the process of example 4, according to claim 1 of auxiliary request 7, results in toltrazuril particles having a specific surface area (15.2 m^2/g) which is lower than that obtained for the toltrazuril particles prepared in example 6 (18.8 m^2/g - comparative example with the reverse order). Thus, there is no improvement over the whole scope of claim 1 of auxiliary request 7, nor any unexpected effect, that is linked to the mixing order.

Consequently, the problem underlying the subject-matter of claim 1 of auxiliary request 7 remains the same as that formulated for claim 1 of auxiliary request 4.

The mixing order in step b) of claim 1 of auxiliary request 7 represents an arbitrary alternative in view of D31, which does not teach a specific mixing order for the precipitation of the active ingredient (page 5). The skilled person would thus add either the acidifying agent to the solution comprising the active ingredient or the solution comprising the active ingredient to the acidifying agent without having to become inventive. Choosing one of these alternatives does not involve an inventive step.

Thus, the subject-matter of auxiliary request 7 does not involve an inventive step and therefore auxiliary request 7 is not allowable.

29. Since auxiliary requests 4 to 7 are not allowable, there is no need to decide on the admittance of these requests.

30. None of the patent proprietor's requests is allowable.

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:

N. Maslin M. O. Müller

Decision electronically authenticated