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Datasheet for the decision of 6 February 2025

Case Number: T 0259/23 - 3.3.07

Application Number: 16808196.6

Publication Number: 3307239

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Language of the proceedings: EN

Title of invention:
FORMULATIONS FOR SMALL INTESTINAL DELIVERY OF RSV AND NOROVIRUS ANTIGENS

Patent Proprietor:
Vaxart, Inc.

Opponent:
iosBio Ltd

Headword:
Small intestinal delivery of norovirus antigen / VAXART

Relevant legal provisions:
RPBA 2020 Art. 12(4), 13(1), 13(2)
EPC Art. 83, 56

Keyword:
Late-filed evidence - admitted (yes)
Sufficiency of disclosure - (yes)
Inventive step (yes) - no reasonable expectation of success

Decisions cited:
G 0002/21

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Case Number: T 0259/23 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 6 February 2025

Appellant: (Opponent)	iosBio Ltd Unit 6 Sovereign Business Park Albert Drive Burgess Hill West Sussex RH15 9TY (GB)
Representative:	Leonard, Thomas Charles Kilburn & Strode LLP Lacon London 84 Theobalds Road London WC1X 8NL (GB)
Respondent: (Patent Proprietor)	Vaxart, Inc. 385 Oyster Point Boulevard, Suite 9A South San Francisco, CA 94080 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2022 concerning maintenance of the European Patent No. 3307239 in amended form.**

Composition of the Board:

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

Summary of Facts and Submissions

I. European patent 3 307 239 (hereinafter "the patent") was granted on the basis of 15 claims. The independent claims of the patent as granted read as follows:

"1. An immunogenic composition for eliciting an immune response in a human comprising an immunogenic biological agent encompassed by an enteric coating that directs delivery of the immunogenic biological agent to the ileum of the human,
wherein the immunogenic biological agent is an adenoviral vector encoding the viral protein 1 of norovirus or the fusion protein (F) of Respiratory syncytial Virus (RSV),
wherein the enteric coating has a threshold pH of 5.8-6.8."

"14. The immunogenic composition of any one of the foregoing claims for use in a method for delivering the immunogenic composition to the ileum of a human comprising orally administering the immunogenic composition to the human."

"15. The immunogenic composition of any one of claims 1-13 for use in a method of eliciting an immune response in a human comprising administering the composition to the human, wherein the immune response is specific for the immunogenic biological agent."

II. An opposition was filed against the patent on the grounds that its subject-matter lacked inventive step and it was not sufficiently disclosed.

III. The opposition division took the interlocutory decision that, on the basis of the amended main request, the patent met the requirements of the EPC. The main request was filed on 8 July 2022 and contained 9 claims. The independent claims were unmodified compared to the patent as granted apart from a renumbering of claims 14 and 15 to claims 8 and 9.

IV. The decision of the opposition division, posted on 29 November 2022, cited *inter alia* the following documents:

D5: Mercier *et al.*, Vaccine, 17 December 2007, 25(52): 8687-8701
D7: US 2013/0171185 A1
D9: WO 2013/148258 A1
D14: Kim *et al.*, JCI Insight, 2018, 3(13):e121077
D20: WO 2007/100908 A2
D21: Second Declaration of Dr. Sean Tucker, 31 May 2022
D22: Huyghebaert *et al.*, Int. J. Pharm., 2005, 298, 26-37

V. The opposition division decided in particular as follows:

(a) The main request met the requirements of Rule 80 EPC as well as those of Articles 123(2), (3) and 84 EPC.

(b) The main request complied with Article 83 EPC since the application as filed (in particular example 4) combined with common general knowledge from D5 made it plausible that delivery to the ileum was achieved. The post-filed data D21 was accepted since plausibility at the effective date was

established. It confirmed achievement of ileal delivery.

(c) The main request fulfilled the requirements of Article 56 EPC. D9 represented the closest prior art. The claimed subject-matter differed from the one of D9 in the pH threshold of the enteric coating targeting delivery to the ileum and in the nature of the immunogenic biological agent. D9 did not demonstrate achievement of ileal delivery with an enteric coating having a pH threshold of 7.0 to 7.6 while it had been made credible in the patent for an enteric coating having a pH threshold of 5.8 to 6.8. Hence the patent provided a technical contribution to the art. The objective technical problem resided in the provision of an alternative immunogenic composition against norovirus or RSV that achieved ileal delivery. The skilled person would have had no reasonable expectation of success of ileum delivery with an enteric polymer having a pH threshold of 5.8 to 6.8. Also the modification of the immunogenic biological agent would not have been obvious. Adenoviral vectors were only disclosed in D5 and D20 for HIV or influenza and did not mention RSV or norovirus.

VI. The opponent (appellant) lodged an appeal against the above decision of the opposition division.

VII. With their reply to the statement setting out the grounds of appeal the patent proprietor (respondent) defended their case on the basis of the main request and of auxiliary requests 1 to 23 initially filed during the opposition proceedings on 8 July 2022 and resubmitted therewith.

VIII. Oral proceedings were held before the Board on 6 February 2025. During the oral proceedings, the respondent withdrew their main request and auxiliary request 1.

IX. The content of the claims of auxiliary request 2, upon which the present decision is based, can be illustrated as follows:

Claim 1 of auxiliary request 2 read as follows:

"1. An immunogenic composition for eliciting an immune response in a human comprising an immunogenic biological agent encompassed by an enteric coating that directs delivery of the immunogenic biological agent to the ileum of the human,
wherein the immunogenic biological agent is an adenoviral vector encoding the viral protein 1 of norovirus,
wherein the enteric coating has a threshold pH of 5.8-6.8."

Independent claims 8 and 9 of auxiliary request 2 corresponded to independent claims 14 and 15 of the patent.

X. The following items of evidence were filed by the parties during the appeal proceedings:

(a) Documents filed by the appellant with their statement setting out the grounds of appeal (D25 to D36), on 4 September 2024 (D37) and 24 January 2025 (D39), respectively:

D25: Declaration of Dr Ian Wilding

D26: Bansal *et al.*, Polimery w Medycynie, 44, 2, (2014), pages 109-118
D27: Patra *et al.*, Future Journal of Pharmaceutical Sciences, 3 (1) (2017), pages 33-45
D28: Nollenberger and Albers, International Journal of Pharmaceutics 457 (2013), pages 461-469
D29: Hardy *et al.*, Alimentary Pharmacology & Therapeutics. (1987), I, pages 209-216
D30: Hardy *et al.*, Alimentary Pharmacology & Therapeutics. (1987), I, pages 273-280.
D31: Healey, J. Chapter 7: Enteric Coatings and Delayed Release. "Drug Delivery to the Gastrointestinal Tract", Editors: Hardy, Davis & Wilson, Ellis Horwood Limited (1989)
D32: Hamman, J., Marine Drugs, 8, (2010), pages 1305-1322
D33: McGinity,JW., Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, Marcel Dekker, Inc, 2008, pages 237-277
D34: Watts P, Smith A., Expert Opinion on Drug Delivery, 2(1): (2005), pages 159-67
D35: Wilding IR *et al.*, Pharmacology & Therapeutics, 62(1-2), (1994) pages 97-124
D36: Smerud *et al.*, Nephrology Dialysis Transplantation, 26(10) (2011), pages 3237-3242
D37: Annex I - experimental report
D39: Declaration of Andrew Bacon, 24 January 2025

(b) Document filed by the respondent on 10 December 2024:

D38: Third declaration of Dr. Sean Tucker, 9 December 2024

XI. The appellant requested that the decision under appeal be set aside and that the patent be revoked. The

appellant further requested that D25 to D37 and D39 be admitted into the appeal proceedings. They also requested that D38 not be admitted.

XII. The respondent requested that the patent be maintained on the basis of one of auxiliary requests 2 to 23 filed with the reply to the statement setting out the grounds of appeal.

The respondent further requested that D25 to D37 not be admitted into the appeal proceedings, and that D38 be admitted in case D37 was admitted. They further requested that the appellant's letter dated 24 January 2025 and D39 not be admitted into the appeal proceedings.

XIII. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

(a) D25 to D37 and D39 as well as the letter dated 24 January 2025 should be admitted into the appeal proceedings. D25 was filed in direct response to the decision of the opposition division and discussed the common general knowledge evidenced by D26 to D36. D37 was submitted in response to arguments of the respondent raised in their reply to the statement of the grounds of appeal. The letter dated 24 January 2025 and D39 represented a direct response to issues raised by the appellant concerning D37 in their submission dated 30 September 2024.

D38 was not to be admitted into the appeal proceedings. Only paragraphs 33 to 38 of D38 related to D37 and could represent a response thereto. The remaining parts of the document would

represent amendments to the case of the respondent and there were no exceptional circumstances justified by cogent reasons to admit them at this late stage of the proceedings.

(b) The subject-matter defined in the claims of auxiliary request 2 was not sufficiently disclosed. In particular, the claims would cover non-working embodiments and the incomplete definition of the enteric coating in the claims prevented the skilled person from putting the invention into practice over the whole scope of the claims.

(c) The subject-matter of claim 1 of auxiliary request 2 was not inventive starting from either D5 or D7 as closest prior art.

The claimed subject-matter differed from D5 only in the nature of the immunogenic protein encoded by the adenoviral vector. The enteric coating disclosed in D5 did indeed fulfil the definition of present claim 1. No effect over the whole scope of the claim had been substantiated for this distinguishing feature. The objective technical problem to be solved was thus to be formulated as how to provide an enteric coated oral vaccine for norovirus that targeted delivery to the ileum. D5 suggested to apply the disclosed delivery system to further viral proteins. The skilled person would therefore have combined the teachings of D5 and D7, which disclosed norovirus immunogenic compositions including adenoviral vector encoding the viral protein 1 of norovirus and mentioned oral administration. The skilled person would thereby have had a reasonable expectation of eliciting some immune response since a mucosal immune response was

described in D5. The skilled person would hence have arrived at the claimed subject-matter without exercising inventive skills.

The claimed subject-matter differed from D7 in the presence of an enteric coating having a pH threshold of 5.8-6.8 and directing the delivery of the immunogenic agent to the ileum. No technical effect directly linked to this distinguishing feature had been substantiated. During the oral proceedings, the objective technical problem to be solved was defined as the provision of a norovirus vaccine having an alternative mode of administration. D7 already mentioned oral administration of the disclosed immunogenic agents. The skilled person would therefore have combined the teachings of D7 and D5 and have applied the enteric coating disclosed in D5 to the adenovrial vector of D7 with a reasonable expectation of successful immune response.

XIV. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

(a) D25 to D37 and D39 as well as the appellant's letter dated 24 January 2025 were not to be admitted into the appeal proceedings. D25 to D37 should have been filed earlier because the issues they were meant to address were already key discussion points during the opposition proceedings. Moreover D37 was not relevant. Finally the appellant's letter dated 24 January 2025 and D39 represented amendments to D37 and should not be admitted for the same reasons.

In the event that D37 be admitted into the appeal proceedings, D38 should be admitted because it was filed in direct response to D37.

(b) The subject-matter defined in the claims of auxiliary request 2 was sufficiently disclosed. The data provided in the examples of the patent substantiated that the skilled person would have been able to follow the teaching of the patent to prepare a composition that directed delivery of an adenoviral vector encoding the protein 1 of norovirus to the ileum and hence elicited a potent immune response.

(c) The subject-matter of claim 1 of auxiliary request 2 involved an inventive step starting from either D5 or D7 as closest prior art.

The claimed subject-matter differed from D5 not only in the nature of the immunogenic protein encoded by the adenoviral vector but also in the nature of the enteric coating used. D5 did not disclose the pH threshold of the enteric coating used nor the delivery of the immunogenic agent to the ileum. The claimed composition had been shown to elicit an immune response (see D14) while no efficient immunization was reported in D5. The objective technical problem to be solved resided therefore in the provision of an improved oral vaccine. The present solution was not obvious in light of the prior art. In particular, the skilled person would not have had any reasonable expectation of success of achieving a potent immune response when replacing the immunogenic protein of D5 with the viral protein 1 of norovirus disclosed in D7.

D7 did not specifically disclose any oral composition comprising an adenoviral vector encoding to the viral protein 1 of norovirus. The claimed composition had been shown to elicit an immune response upon oral administration (D14). The objective technical problem to be solved resided therefore in the provision of an improved oral vaccine for norovirus. The present solution was not obvious in light of the prior art. In particular, the skilled person would not have had any reasonable expectation of success of achieving a potent immune response when applying the enteric coating of D5 to an oral composition of the adenoviral vector encoding the viral protein 1 of norovirus of D7, due to the poor immunization results reported in D5.

Reasons for the Decision

1. Admittance of new items of evidence and submissions

1.1 D25 to D36

1.1.1 D25 to D36 were submitted by the appellant with their statement setting out the grounds of appeal.

1.1.2 D25 is an expert declaration discussing (i) common general knowledge on enteric coatings at the priority date of the patent and (ii) the results of example 4 of the patent and of D21.

1.1.3 The section of D25 discussing common general knowledge on enteric coatings refers to D26 to D34. Furthermore, D35 and D36 were cited in the statement of the grounds of appeal in a section discussing common general

knowledge on enteric coatings and ileum as a suitable site for vaccine delivery. D26 to D28 and D31 to D35 are either scientific reviews or excerpts of textbooks and constitute as such evidence of common general knowledge and D35 refers to the clinical data reported in D29 and D30. Moreover, as explained by the appellant during the oral proceedings, the passage of D36 referred to discloses common general knowledge on the location of Peyer's patches in the digestive tract (see D36, page 3237, right-hand column, 9th and 10th lines from the bottom).

1.1.4 Regarding the section of D25 discussing example 4 of the patent and D21, the Board observes that the provided arguments constitute a further development of arguments already submitted during the opposition proceedings (see in particular letter of the appellant then opponent of 11 August 2022) and represent a direct response to the decision of the opposition division on the issue of substantiation of ileal delivery.

1.1.5 Contrary to the opinion of the respondent, despite the fact that the issues of enteric coating and delivery to the ileum were already key discussion points during the opposition proceedings, the acknowledgement of a technical contribution to the art of the claimed enteric coating targeting ileal delivery by the opposition division was first made in the decision. Therefore, the filing of D25 to D36 is considered a legitimate reaction to the decision.

1.1.6 Accordingly, D25 to D36 are admitted into the appeal proceedings (Article 12(4) RPBA).

1.2 D37

1.2.1 D37 was submitted by the appellant with the letter of 4 September 2024. It contains experimental data which aims at demonstrating the threshold pH of the enteric coating of D5 and the ability of said enteric coating to target ileal delivery. According to the appellant, these experimental data were filed in response to the argument of the respondent contesting that D5 would disclose an enteric coating according to present claim 1 (raised in their reply to the statement setting out the grounds of appeal).

1.2.2 The respondent argued that the objection of lack of inventive step starting from D5, including the question of whether the coating directed delivery to the ileum, had been on file since the notice of opposition. D37 could therefore have been submitted during the opposition proceedings or at the latest with the statement setting out the grounds of appeal. Moreover, D37 would measure the release of dye while D5 would concern the release of virus particles. D37 would therefore not be relevant and even introduce unnecessary procedural complications.

1.2.3 The Board observes that the provided data are suitable to resolve the question of whether a key feature of the claims is a distinguishing feature or not with respect to the document used by both parties as closest prior art (D5). Furthermore the data support the position of the appellant already expressed in the statement of grounds of appeal (see paragraph 6.1.1) and the notice of opposition (see paragraphs 4.6.3 to 4. 6. 6). It does therefore not introduce any new development of the case. Moreover, as argued by the appellant, the data were obtained using the experimental protocol of

example 4 of the patent with a coating according to D5 and do therefore not introduce any additional complexity to the case. In this context, the Board observes that, as explained by the appellant, the complete dissolution of the tablet was the parameter measured in D37 in accordance with example 4 of the patent, not the dye release.

1.2.4 With regard to the argument of the respondent that D37 could have been filed earlier, the Board observes that, as argued by the appellant, the opposition division indicated already in its preliminary opinion that D9 was considered to represent the closest prior art and applied a strict approach based on this single document as possible closest prior art. It therefore appears that there was no compelling reason for the appellant to substantiate further their objection starting from D5 as closest prior art in response to the preliminary opinion of the opposition division. Only in the appeal proceedings did both parties agree that a different document (D5) than the one chosen by the opposition division (D9) would represent the closest prior art. In this context, the statement of the respondent in paragraph 48 of their reply to the statement of the grounds of appeal triggered the submission of D37, to clarify the issue of the difference with respect to D5. The Board is therefore of the opinion that there was no compelling reason for the appellant to submit D37 earlier. Furthermore, the submission of D37 is not detrimental to procedural economy.

1.2.5 As a result, D37 is admitted into the appeal proceedings (Article 13(1) RPBA).

1.3 D38

1.3.1 D38 is an expert declaration submitted by the respondent with the letter of 10 December 2024, *i.e.* after notification of the communication pursuant to Article 15(1) RPBA dated 4 October 2024. According to the respondent, D38 was filed in direct response to D37 and could therefore not have been filed earlier. This constituted exceptional circumstances in accordance with Article 13(2) RPBA.

1.3.2 The appellant disputed that only paragraphs 33 to 38 of D38 related to D37. The remaining parts of the document would discuss the immune response reported in D5 in a more detailed manner than before and would raise new issues.

1.3.3 The Board considers that paragraphs 33 to 38 of D38 under the heading "The experimental report in "Annex 1"" indeed represents a direct response to D37 (*i.e.* Annex 1). Moreover, the remaining paragraphs of D38 consist merely in a repetition and further development of arguments previously raised by the respondent. They do thus not represent amendments to the case of the respondent according to Article 12(4) RPBA.

1.3.4 Hence, D38 is admitted into the appeal proceedings (Article 13(2) RPBA).

1.4 Appellant's letter dated 24 January 2025 and D39

1.4.1 The appellant's letter dated 24 January 2025 contains two main sections in reply to objections raised by the respondent concerning (i) the protocol of D37 and (ii) the identity of the scientist who performed the experiments reported on D37. D39, which was submitted

together with said letter, contains a declaration of said scientist along with his CV.

1.4.2 The respondent argued that these arguments and D39 would represent amendments to D37 since they attempt to explain why a dye was used in the experiments reported therein.

1.4.3 The Board observes that the submission of the appellant dated 24 January 2025 together with D39 represent a direct response to the issues raised by the respondent concerning D37 in their submission dated 30 September 2024. These documents could hence not have been filed earlier. This represents exceptional circumstances justifying the filing of these documents at this late stage of the proceedings.

1.4.4 As a consequence, the appellant's letter dated 24 January 2025 and D39 are admitted into the appeal proceedings (Article 13(2) RPBA).

Auxiliary request 2 (main request)

2. Amendments

The appellant did not raise any objection of lack of compliance with Articles 123(2) and 123(3) EPC for auxiliary request 2. As stated by the respondent, claim 1 of auxiliary request 2 corresponds to granted claim 1 (corresponding to original claims 1 and 2) wherein the viral protein was limited to the viral protein 1 of norovirus by deletion of the alternative corresponding to the fusion protein (F) of RSV. The Board is satisfied that auxiliary request 2 meets the requirements of Articles 123(2) and 123(3) EPC.

3. Sufficiency of disclosure

3.1 Claim 1 of auxiliary request 2 relates to an immunogenic composition suitable for elliciting an immune response in a human comprising an immunogenic biological agent encompassed by an enteric coating. The enteric coating is defined in terms of a parameter (having a pH threshold of 5.8-6.8) and a functional feature, namely "that directs delivery of the immunogenic biological agent to the ileum of the human".

3.2 It is a general principle when assessing compliance with the requirements of Article 83 EPC that, when functional features are part of the claims, the suitability of the product to achieve the claimed function must be disclosed.

3.3 In the appeal proceedings, the appellant argued that the claims would cover non-working embodiments and that the skilled person would not be able to carry out the invention over the whole scope of the claims. According to the appellant it was common general knowledge that further features in addition to the pH threshold influenced the location of delivery. These features were:

- the thickness of the coating,
- the presence of additional components in the coating (*e.g.* plasticizer),
- the formulation of the tablet core,
- the available intestinal liquid to facilitate disintegration, and
- the agitation forces exerted.

The appellant concluded that the absence of a definition of the enteric coating thickness in the

claims prevented the skilled person from putting the invention into practice over the whole scope of the claims.

3.4 As recognised by the appellant, the influence of the thickness of the coating is acknowledged and discussed in the patent (see paragraphs [28] and [78] and example 4). The Board therefore considers that, as argued by the respondent, the skilled person would be able, based on the information provided in the patent together with its common general knowledge, to determine the appropriate thickness for achieving delivery to the ileum.

3.5 Regarding the other features mentioned by the appellant as having an influence on the release of the active agent, the Board observes that, as acknowledged by the appellant, the skilled person would be aware thereof from its common general knowledge. The appellant did not provide any evidence that the skilled person would not be able based on its common general knowledge to appropriately adapt the corresponding features.

3.6 Furthermore, the Board observes that the appellant did not contest the finding of the opposition division that the patent would render plausible that an enteric coating having a pH threshold of 5.8 to 6.8 could deliver the immunogenic biological agent to the ileum.

3.7 Finally, regarding the suitability to elicit an immune response in a human, the respondent referred to the examples of the patent. The Board observes that, in view of the data obtained with adenoviral vectors encoding Influenza or HIV proteins (see examples 5 and 9 of the patent as well as D5), the skilled person would have considered the claimed delivery system as

suitable to elicit some immune response in a human. Moreover, the preclinical studies in mice and ferrets reported in example 6 of the patent confirmed the immunogenic properties of an adenoviral vector encoding the viral protein 1 of norovirus. Therefore in the Board's view it is credible that the claimed composition is suitable to elicit some immune response.

3.8 Therefore, the Board comes to the conclusion that the invention according to auxiliary request 2 is sufficiently disclosed (Article 83 EPC).

4. Inventive step

4.1 The subject-matter of the claims of auxiliary request 2 relates to an immunogenic composition comprising an adenovriral vector encoding the viral protein 1 of norovirus (NV) encompassed by an enteric coating directing delivery to the ileum.

4.2 Both D5 and D7 were considered as closest prior art documents by the parties.

D5 relates to enteric polymethacrylate formulations for coating capsules containing adenoviral vectors expressing HIV-1 envelope peptides for oral administration (see abstract). The location of vector release in the gastrointestinal tract is discussed in D5 (see page 8, third paragraph and page 12, second paragraph).

D7 concerns adenoviral vector based vaccines against NV (see D7, paragraphs [0012], [0136] and [0141]).

Hence, D5 and D7 constitute suitable starting points for the assessment of inventive step.

4.3 Problem solution approach starting from D5

Distinguishing feature and related technical effect

4.3.1 It was undisputed that the claimed subject-matter differed from the one of D5 in (i) the nature of the immunogenic protein encoded by the adenoviral vector (viral protein 1 of norovirus versus HIV-1 envelope peptides in D5). However, according to the respondent, D5 would not disclose an enteric coating:
(ii) directing delivery of the immunogenic agent to the ileum, nor
(iii) having a pH threshold of 5.8-6.8.

Delivery to the ileum

4.3.2 In particular, concerning feature (ii), the respondent argued that the specific delivery point in the small intestine was not clearly specified in D5. They explained that D5 first mentioned delivery in the jejunum and ileum (page 2, second paragraph) and then a dissolution beginning in the jejunum and a release occurring prior to entry in the colon and stated that additional studies would be required to show where the delivery took place (page 8, third paragraph and page 12 second paragraph). Moreover, according to the respondent, the results obtained in D5 indicated a release too low in the intestine (low immune response, see Figures 2B and 3). Furthermore the prior art was D5, and not D37, so that the latter should not be taken into consideration. In any case, the capsules tested in D37 contained dye and dye release could not be equated to adenovirus release.

4.3.3 These arguments are not convincing.

4.3.4 As argued by the appellant, the general statements in D5 on a dissolution beginning in the jejunum and a release occurring prior to entry in the colon are consistent with an ileum directed release. The Board notes that the passages of D5 cited by the respondent do actually point to a release in the ileum.

4.3.5 Furthermore, as brought forward by the appellant, the data of Table 2A of D5 showing the release of more than 70% of dye at pH 6.5 after 100 minutes are consistent with a release in the ileum. In the context of the discussion of sufficiency of disclosure in the opposition proceedings (see decision paragraph 8.3.2.1), the respondent themselves relied on the fact that the transit time through the duodenum and the jejunum before reaching the ileum would be 2 hours with the pH increasing from 6.0 to 7.2 (see D5, table 2, first and second columns). Based on this, it is credible that the coating of D5 will have almost fully disintegrated when reaching the ileum so as to achieve delivery there.

Contrary to the opinion of the respondent, the data provided in Figure 2B reporting the release of virus over time at two different pH values do not contradict this conclusion. According to said figure, a burst in virus release is observed after 80 min at pH 7.5 while no or very limited release occurs at pH 6.0. The fact that there is a delay between dye and virus release is not unexpected, since as argued by the respondent the dye may leak from the capsule before entire disintegration thereof. However a release of virus after 80 minutes at pH 7.5 does not mean that there would be no release at all in the ileum. Furthermore, no intermediate pH value has been measured in the

experiment leading to Figure 2B of D5. A release of virus at pH 6.5 or 7.0 within 120 minutes is not excluded.

4.3.6 Moreover, the data provided by the appellant in D37 substantiate that the enteric coating of D5 directs delivery to the ileum. As from a pH around 6.4, the dissolution profile of the enteric coating of D5 is essentially the same as the one of example 4 of the patent (see D37, Figure 1). At a lower pH, both enteric coatings dissolve only very slowly and differences in dissolution in this lower pH range do not appear significant for the present issue. Furthermore, as argued by the appellant, the data of D37 (see Figure 1) indicate that the enteric coating of D5 fulfils the criteria for ileal delivery defined in D22 and referred to by the respondent himself (see D22 Abstract, fourth line, which states that "to guarantee ileal delivery, the polymer must dissolve from pH 6.8 and allow complete release within 40 minutes").

Regarding the objection of the respondent that the release of dye would be measured in D37, the appellant confirmed that the measured parameter was the time to complete disintegration of the capsules as indicated in the legend of Figure 1 and on page 1, second paragraph, eighth line of D37.

4.3.7 Finally the poor immune responses observed in D5 and referred to by the respondent may be due to other factors than a release too low down the gastrointestinal (GI) tract. There is no indication in D5 of a delivery too low down in the GI tract. Thus, this conclusion of the respondent remained unsubstantiated.

4.3.8 Accordingly, the Board considers that the functional feature (ii) does not represent a distinguishing feature over D5.

pH threshold

4.3.9 Regarding the pH threshold of the enteric coating (feature (iii) above), there is indeed no explicit disclosure thereof in D5. Nevertheless, as explained by the appellant, in view of the known pH threshold of each polymer constituting the enteric coating of D5 and their ratio therein, it is credible that the threshold of the resulting enteric coating will fall within the range defined in present claim 1.

4.3.10 As brought forward by the appellant, Eudragit Ll00 has a pH threshold of 6.0 and Eudragit Sl00 has a pH threshold of 7.0 (see e.g. D25, table 1) and a 3:1 Eudragit Ll00 : Eudragit Sl00 mixture has a pH threshold of 6.3 (see D34, page 163, section 3.2). The skilled person would thus recognise that a 4:1 Eudragit Ll00 : Eudragit Sl00 mixture (see D5, pages 4 and 11) will have a pH threshold between 6.0 and 6.3.

4.3.11 Furthermore, the disintegration data provided in D37 are consistent with a disintegration behaviour of a coating having a pH threshold of 6-6.3 and confirm that the pH threshold of the enteric coating of D5 is in accordance with the one presently claimed.

4.3.12 Therefore, in the absence of any evidence that the pH threshold of the enteric coating of D5 would be outside the claimed range, the Board comes to the conclusion that the pH threshold (feature (iii)) does not represent a distinguishing feature over D5.

Immunization against NV

4.3.13 It was undisputed that the technical effect linked to the only distinguishing feature (feature (i)) was to provide a vaccine for a different disease, namely NV.

4.3.14 The respondent argued that D14 substantiated that efficient immunization was achieved in a human clinical trial of an oral NV vaccine composition according to the present claims (see Abstract, under the heading "Conclusion" and page 9, paragraph entitled "Norovirus vaccine" under the heading "Methods").

4.3.15 During the oral proceedings, the appellant mentioned that D14 did not substantiate that efficient immunization would occur over the whole scope of the claims.

4.3.16 The Board observes that, while D14 is indeed limited to only one coating, said coating nevertheless fulfils the requirement of the claims, namely to direct delivery of the immunogenic agent to the ileum. Since D14 shows that a substantial immune response is obtained when orally administering the composition containing said coating, it is credible that such a response would be obtained for further coatings according to the claims, *i.e.* targeting delivery of the immunogenic agent to the ileum.

4.3.17 In this regard, the Board notes that it has not been disputed that this technical effect could be taken into account in accordance with G 2/21. The Board is satisfied that the technical effect of a substantial immunization against the viral protein 1 of NV was encompassed by the technical teaching and and embodied by the same originally disclosed invention.

Objective technical problem

4.3.18 Accordingly, the Board considers that the objective technical problem starting from D5 resided in the provision of an enteric coated oral immunogenic composition for a different virus, wherein delivery occurs in the ileum and wherein the composition provides a substantial immune response.

Non-obviousness of the solution

4.3.19 While D5 provides proof of principle for oral capsule delivery of adenoviral vaccines (see page 13, third paragraph, first sentence), the Board observes that results in terms of elicited immune response reported in D5 are mixed. The conclusion on effective mucosal HIV vaccination strategy is made in the context of adenoviral vector priming followed by intranasal protein/peptide boosting (see Abstract last sentence). Furthermore, as argued by the respondent, only 3 monkeys were tested without a control and using low dilutions and repeated administration of the vaccine (see page 8 paragraph entitled "Immunization of Rhesus Macaques). While some vaginal immune response is observed in all three monkeys, salivary immune response appears to be significant only in one monkey (see Figures 3A and 3B). Moreover no significant serum immune response appears to be reported. The data in Figure 3C concern indeed the response against the adenovirus vector.

4.3.20 As argued by the respondent, the development of effective orally administered vaccines is commonly known to be a difficult task. While D5 generally suggests that the delivery system disclosed therein may

be applied to other vaccines, it remains that the skilled person would not have had a reasonable expectation of success to achieve substantial immune response when applying it to NV. While the viral protein 1 of NV had been disclosed in D7 for use in NV immunogenic compositions including encoded by an adenoviral vector (see paragraphs [0012], [0141] and [0282]), no efficient oral NV vaccination had been disclosed at the priority date. As argued by the appellant, D7 generally mentions oral administration of the compositions (see paragraph [0245]). However no *in vivo* administration was performed in D7, so that D7 does not provide any indication of an actual immunization through oral administration.

4.3.21 The Board therefore concludes that, in view of the general principle disclosed in D5, the skilled person would indeed have expected some delivery of an adenoviral vector encoding the viral protein 1 of NV to the ileum when using the enteric coating of D5. However, the skilled person would not have had a reasonable expectation of success in obtaining a substantial level of immune response against the viral protein 1 of NV. This constitutes a non-obvious technical contribution over the prior art.

4.4 Problem solution approach starting from D7

4.4.1 Since the subject-matter of the claims of auxiliary request 2 is considered inventive starting from D5 as closest prior art, the inventiveness over D7 as closest prior art needs to be assessed.

4.4.2 Starting from D7 the distinguishing feature resided in the use of a specific oral delivery system.

4.4.3 As detailed under 4.3.14 to 4.3.17, D14 substantiates that efficient immunization was achieved in a human clinical trial of an oral NV vaccine composition according to the present claims (see Abstract, under the heading "Conclusion" and page 9, paragraph entitled "Norovirus vaccine" under the heading "Methods").

4.4.4 The Board hence considers that the objective technical problem starting from D7 was the provision of an oral immunogenic composition for NV providing a substantial immune response.

4.4.5 For the same reasons as detailed starting from D5 (see 4.3.19 to 4.3.21), the Board considers that in view of D7 taken in combination with D5 the skilled person would not have had any reasonable expectation of success in achieving substantial immune response when applying the delivery system of D5 to an adenoviral vector encoding the viral protein 1 of NV for oral administration.

4.5 As a result, auxiliary request 2 complies with the requirements of inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent on the basis of auxiliary request 2 filed with the reply to the statement of grounds of appeal on 18 August 2023 and a description to be adapted thereto.

The Registrar: The Chairman:

A. Vottner A. Usuelli

Decision electronically authenticated