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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/041,042	03/04/2011	Derek O'Hagan	PAT051223-US-CNT	4163
27476	7590	10/27/2016	EXAMINER	
NOVARTIS VACCINES at GSK 709 Swedeland Road UW2220 KING OF PRUSSIA, PA 19406-0939			TONGUE, LAKIA J	
			ART UNIT	PAPER NUMBER
			1645	
			NOTIFICATION DATE	DELIVERY MODE
			10/27/2016	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* DEREK O'HAGAN

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Appeal 2014-002707  
Application 13/041,042  
Technology Center 1600

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Before DEMETRA J. MILLS, JOHN G. NEW, and RYAN H. FLAX,  
*Administrative Patent Judges.*

MILLS, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF CASE

The following claim is representative.

1. A composition for mucosal delivery, comprising a mucosal adjuvant and two or more of the following: (a) an antigen which induces an immune response against *Haemophilus influenzae*; (b) an antigen which induces an immune response against *Neisseria meningitidis*; and (c) an antigen which induces an immune response against *Streptococcus*

*pneumonia*, wherein the mucosal adjuvant comprises a detoxified cholera or *E. coli* heat labile toxin.

*Examiner Cited References*

Lian et al.	US 2011/0045017 A1	Feb. 24, 2011 ("Lian")
Capiou et al.	WO 00/56359	Sept. 28, 2000 ("Capiou")
Rappuoli et al.	WO 01/22993 A2	Apr. 5, 2001 ("Rappuoli")

*Appellant Cited References (see Br. 9–10)*

Aucouturier et al., *Adjuvants designed for veterinary and human vaccines*, 19 VACCINE 2666–2672 (2001) ("Aucouturier").

Robert Edelman, *The Development and Use of Vaccine Adjuvants*, 21 MOLECULAR BIOTECHNOLOGY 129–148 (2002).

Wuorimaa et al., *Avidity and Subclasses of IgG after Immunization of Infants with an 11-Valent Pneumococcal Conjugate Vaccine with or without Aluminum Adjuvant*, 184 J.INFECTIOUS DISEASES 1211–1215 (2001) ("Wuorimaa").

*Grounds of Rejection*

1. Claims 1–15 and 17 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lian.

Claims 1–15 and 17 are rejected under 35 U.S.C. § 103(a) as being obvious over Capiou and further in view of Rappuoli.

## PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g., Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office).

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant.” *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted).

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

### *Rejection 1*

We vacate the Examiner’s anticipation in favor of a new ground of rejection for obviousness in view of Lian alone or in combination with Capiou.

## NEW GROUNDS OF REJECTION

Claims 1–15 and 17 are newly rejected under 35 U.S.C. § 103(e) as obvious in view of Lian.

## FINDINGS OF FACT

1. Lian disclosed HIV vaccine compositions for mucosal delivery comprising antigens which may advantageously include saccharide

antigens from *N. meningitidis* serogroup A, C, W135 and/or Y, such as the oligosaccharide; a saccharide antigen from *Streptococcus pneumoniae*; and a saccharide antigen from *Haemophilus influenzae* (see paragraphs 49–53 and 60).

2. Lian disclosed that its vaccine composition can be administered by an intranasal route; the vaccine of the invention may be in the form of a nasal spray, nasal drops, gel, or powder (see paragraph 80).
3. Lian disclosed mucosal adjuvants suitable for use in the invention include, but are not limited to, heat-labile enterotoxins or detoxified mutants thereof, such as the LTK63 or LTR72 mutants (see paragraphs 13 and 82).
4. Lian disclosed where a saccharide or carbohydrate antigen is included; it is conjugated to a carrier protein, which is bacterial toxins or toxoids, such as diphtheria (CRM<sub>197</sub>), cholera or tetanus toxoids (see paragraph 74).
5. In Lian, preferred carrier proteins are bacterial toxins or toxoids, such as diphtheria, cholera, *E. coli* heat labile or tetanus toxoids. The CRM<sub>197</sub> diphtheria toxoid is particularly preferred. (See paragraph 74).
6. Capiiau disclosed that it was well known in the art to prepare combination vaccines which provide protection against a range of different pathogens. P. 7, l. 29-p. 8, l. 4; p. 25, ll. 5-6.

#### ANALYSIS

The composition of claim 1 includes the transitional phrase “comprising,” which opens the claim up to additional elements or ingredients. Therefore, it is of no consequence that the composition of Lian is primarily directed to an HIV vaccine for mucosal delivery [¶ 13], but which also includes additional antigens. Lian’s vaccine can include additional [¶ 49] (any or all) antigens including: (a) *Haemophilus influenza* [¶ 60]; (b) an antigen which induces an immune response against *Neisseria meningitidis* [¶ 52]; and (c) an antigen which induces an immune response against *Streptococcus pneumonia* [¶ 53]; wherein the mucosal adjuvant comprises a detoxified cholera or *E. coli* heat labile toxin [¶ 14]; [¶ 74].

With respect to the anticipation rejection, Appellant argued that there was a substantial amount of picking and choosing from a laundry list of 24 disclosed additional antigens in Lian. Reply Br. 6. As explained in *Arkley*,

picking and choosing may be entirely proper in the making of a 103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness which may arise from the similarity of the subject matter which he claims to the prior art, but it has no place in the making of a 102, anticipation rejection.

*In re Arkley*, 455 F.2d 586, 587–588 (CCPA 1972). Furthermore, picking one of a finite number of known solutions to a known problem is obvious.

*KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007), states:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

Finally, “[d]isclos[ure of] a multitude of effective combinations does not render any particular formulation less obvious.” *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 807, 10 USPQ2d 1843, 1846 (Fed. Cir. 1989). Here, Lian would reasonably appear to disclose multiple effective vaccine combinations, in that Lian discloses that additional antigens (plural) may be present in the disclosed HIV mucosal vaccine. [¶49 and ¶50-74.] Moreover, this list of optional antigen components is not excessively long, but is limited to just over twenty. [*Id.*] Conceivably, while unlikely, nothing would prevent the skilled artisan from including several or all of them in a single composition. In addition, Capiou discloses that it is well known in the art to prepare combination vaccines which provide protection against a range of different pathogens. P. 7, l. 29- p. 8, l. 4; p. 25, ll. 5-6.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a vaccine composition comprising a mucosal adjuvant and any or all of the following: (a) an antigen which induces an immune response against *Haemophilus influenzae*; (b) an antigen which induces an immune response against *Neisseria meningitidis*; and (c) an antigen which induces an immune response against *Streptococcus pneumonia*, wherein the mucosal adjuvant comprises a detoxified cholera or *E. coli* heat labile toxin, in view of Lian. Lian discloses a vaccine having a mucosal adjuvant, an antigen which induces an immune response against *Haemophilus influenzae*; and an antigen which induces an immune response against *Neisseria meningitides*, in conjunction with a detoxified cholera or

*E. coli* heat labile toxin. Alternatively, Capiau motivates one of ordinary skill in the art to include multiple antigens in combination vaccines.

*Rejection 2*

Claims 1–15 and 17 are rejected under 35 U.S.C. § 103(a) as being obvious over Capiau and further in view of Rappuoli.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Answer at pages 2–14. The following facts are highlighted.

7. Capiau disclosed vaccine compositions comprising at least one *Streptococcus pneumoniae* polysaccharide antigen (preferably conjugated) and a *Streptococcus pneumoniae* protein antigen or immunologically functional equivalent thereof, optionally with an adjuvant (*see* page 8, lines 15–20).

8. The polysaccharides of Capiau may be conjugated to protein carriers, such as; diphtheria and tetanus toxoids (DT, CRM197 and TT) (*see* page 14, lines 13–18).

9. Capiau disclosed that polysaccharides to be conjugated and contemplated by this invention, include, but are not limited to meningococcal polysaccharides (including type A, C, W135 and Y) and the capsular polysaccharide from *Haemophilus influenzae* (*see* page 23, lines 5–15).

10. In one Capiau embodiment, the combination includes a vaccine that affords protection against *Neisseria meningitidis* C and Y infection

wherein the polysaccharide antigen from one or more serotypes Y and C are linked to a protein.

11. Additionally, *Haemophilus influenzae* polysaccharide based vaccine conjugated with TT, OT, or CRM197, may be formulated with the above combination vaccine. Page 23. Capiiau disclosed that many vaccines are now given as a combination vaccine so as to reduce the number of injections a subject has to receive. Thus, for Capiiau's vaccines, other antigens may be formulated with the vaccines of the current invention (*see* page 25, lines 17–29; page 26, lines 21–30; and page 27, lines 1–2).

12. Capiiau disclosed that the vaccine composition preparation is administered via a mucosal route and include intranasal administration (*see* page 18, lines 1–8), which necessarily encompasses the form of a nasal spray, nasal drops, a gel or a powder.

13. Lastly, Capiiau disclosed that suitable adjuvant systems include, but are not limited to, monophosphoryl lipid A, saponin and CPG (*see* page 15, line 27 and page 16, lines 8–14). Since Capiiau used the entire capsular polysaccharide and in light of Appellant's definition of oligosaccharide (a fragment of capsular polysaccharide), the capsular saccharide antigen of the prior art necessarily encompasses an oligosaccharide.

14. Capiiau disclosed vaccine

polysaccharides may be conjugated to protein carriers, which provide bystander T-cell help. It is preferred, therefore, that the polysaccharides utilised in the invention are linked to such a protein carrier. Examples of such carriers which are currently commonly used for the production of polysaccharide immunogens include the Diphtheria and Tetanus toxoids (DT, DT CRM197 and TT respectively), Keyhole Limpet

Haemocyanin (KLH), OMPC from *N. meningitidis*, and the purified protein derivative of Tuberculin (PPD).

Page 14.

15. Rappuoli discloses

Rappuoli et al. disclose that mucosal vaccine compositions where cholera toxin and *E. coli* heat labile toxin (LT-K63 or LT-R72) act as a mucosal adjuvant, both of which have been found to enhance antigen specific serum IgG, sIgA and local and systemic T cell responses. LT-K63 is preferred, as it has been found reliable in animal models to result in a high level of protection. Lastly, both are homologous and are interchangeable (see page 1, lines 56–27 and page 2, lines 1–7)

Ans. 4.

16. The vaccines of Rappuoli include *Bordetella pertussis*, diphtheria antigen (D), a tetanus antigen, and are for mucosal delivery. Page 1.

17. Rappuoli discloses that the detoxified form of cholera toxin (CT) or *E.coli* heat labile toxin (LT) acts as a mucosal adjuvant. CT and LT are homologous and are typically interchangeable. Page 1.

#### ANALYSIS

We agree with the Examiner's fact finding, statement of the rejection and responses to Appellant's arguments as set forth in the Answer. We find that the Examiner has provided evidence to support a prima facie case of obviousness. We provide the following additional comment to the Examiner's argument set forth in the Final Rejection and Answer. We agree with the Examiner that

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Capiou et al. with the cholera toxin and *E. coli* heat labile toxin (LT-K63 or LT-R72) of Rappuoli et al. because they act as mucosal adjuvants that are homologous and are interchangeable. Both have enhanced antigen specific serum IgG, sIgA and local and systemic T cell responses, and result in a high level of protection. One would have had a reasonable expectation, barring evidence to the contrary, that the composition, which is intended for mucosal delivery would be effective for inducing an immune response against the claimed bacterial antigens.

Ans. 4.

Appellant argues that, Capiou “never suggest[ed] that they be used together in a single composition.” App. Br. 8. Appellant argues that the art of selecting adjuvants in order to enhance immune responses to specific antigens is unpredictable as noted in the three adjuvant review articles of Aucouturier, Edelman, and Wuorimaa. App. Br. 9.

We are not persuaded. As articulated in *KSR*, “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR*, 550 U.S. at 416. We agree with the Examiner that, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Capiou with the cholera toxin and *E. coli* heat labile toxin (LT-K63 or LT-R72) of Rappuoli because they act as mucosal adjuvants that are homologous and are interchangeable.

Although Appellant argues that there is lack of predictability with respect to adjuvant selection, Appellant’s lack of predictable data from Aucouturier, Edelman, and Wuorimaa primarily relate to the unpredictability

associated with the use of alum adjuvant. Br. 10. The cholera toxin or *E.coli* heat labile toxin mucosal adjuvants of Rappuoli are appropriate for use with *Bordetella pertussis*, *diphtheria antigen (D)*, a *tetanus antigen*. FF15. Similarly, the polysaccharide vaccines of Capiou include the Diphtheria and Tetanus toxoids. FF13. Therefore, Rappuoli establishes the appropriateness of the use of cholera toxin or *E.coli* heat labile toxin mucosal adjuvants with vaccines such as that of Capiou which may also include similar antigens. Appellant has provided no contrary evidence or further evidence of unexpected results.

Capiou disclosed that it is well known in the art to prepare combination vaccines which provide protection against a range of different pathogens. P. 7, l. 29-p. 8, l. 4; p. 25, ll. 5-6. Capiou disclosed vaccine compositions comprising at least one *Streptococcus pneumoniae* polysaccharide antigen (preferably conjugated) and a *Streptococcus pneumoniae* protein antigen or immunologically functional equivalent thereof, optionally with an adjuvant (*see* page 8, lines 3–20). It would have been obvious to one of ordinary skill in the art aware of Capiou and Rappuoli to include multiple antigens in a vaccine to form a combination vaccine with an expectation of success. Appellant has provided no evidence that one of ordinary skill in the art would be unsuccessful in combining the specific antigens disclosed in Capiou.

Rejection 2 is affirmed for the reasons of record.

#### CONCLUSION OF LAW

The anticipation rejection 1 is vacated in favor of a new ground of rejection for obviousness in view of Lian. The cited references support the

Examiner's obviousness rejection 2, which is affirmed. All pending, rejected claims fall.

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b), which provides that a "new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

(1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .

(2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

Should the Appellant elect to prosecute further before the Examiner pursuant to 37 C.F.R. § 41.50(b)(1), to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection(s), the effective date of the affirmance is deferred until conclusion of the prosecution before the Examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If the Appellant elects prosecution before the Examiner and this does not result in allowance of the application, abandonment, or a second appeal,

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this case should be returned to the Patent Trial and Appeal Board for final action on the affirmed rejection, including any timely request for rehearing thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED; NEW GROUND UNDER 37 C.F.R. § 41.50(b)