

## **REMARKS**

Favorable reconsideration is respectfully solicited in view of the following remarks.

A personal interview with the Examiner is respectfully requested prior to issuance of a first Office Action in this RCE application.

Claims 41, 61 and 62 have been amended to require that “when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride”. Support for this limitation is found, for example, in the paragraph bridging pages 3-4 of the specification; and on lines 3-7 on page 12 of the specification. Claim 64, which requires benzalkonium chloride, has similarly been amended to require that “benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation”.

Turning to the last Official Action, claims 41-42 are newly rejected as anticipated under 35 U.S.C. 102 by U.S. Patent No. 5,603,929 to Desai et al. This ground of rejection is deemed to be untenable as applied to the claims after the foregoing amendments for the following reasons.

Desai et al. teach at column 1, lines 27-34 that:

Benzalkonium chloride is a widely used preservative in ophthalmic solutions. However, benzalkonium chloride and other quaternary ammonium compounds are generally considered to be incompatible with ophthalmic compositions of drugs with acidic groups, such as nonsteroidal anti-inflammatory drugs (“NSAIDS”). These preservative [sic] lose their ability to function as they form complexes with the charged drug compounds.

As recognized by the Examiner, bromfenac used in the claimed preparation is an acidic “NSAID” drug.

Desai et al. further note at column 2, lines 1-5 that:

The use of POLYQUAD® and other polymeric quaternary ammonium compounds as a disinfectant and preservative in

contact lens care and artificial tear solutions is known. See, for example, U.S. Pat. Nos. 5,037,647; 4,525,346; and 4,407,791.

Desai et al. summarize the intended purpose of their invention at column 2, lines 18-30 as follows:

It has now been discovered that the use of a combination of a polymeric quaternary ammonium compound such as POLYQUAD® and boric acid in ophthalmic compositions of acidic drugs provides a storage-stable composition which has surprisingly good preservative efficacy. This preservative combination of a polymeric quaternary ammonium compound and boric acid is useful in ophthalmic compositions of acidic drugs such as prostaglandins, antifungals, antibacterials [sic], and diagnostic agents. This preservative combination is especially useful in ophthalmic solutions of drugs containing either a carboxyl group such as non-steroidal anti-inflammatory drugs (NSAIDS) or a sulfonamide group such as antibacterial drugs.

Desai et al. further mention at column 3, lines 30-38 that:

The compositions of the present invention may additionally include other ophthalmically acceptable components such as .... other preservatives (e.g. benzalkonium chloride) ... tyloxapol...

Thus, Desai et al. teach away from using a quaternary ammonium compound such as benzalkonium chloride as a preservative with acidic NSAID drugs like bromfenac. Desai et al. teach that the problems with benzalkonium chloride and other quaternary ammonium compounds can be avoided by using certain polymeric quaternary ammonium compounds in combination with boric acid.

Hence, an essential component of the Desai composition is a polymeric quaternary ammonium compound.

However, the instant claims as amended require that, when the claimed liquid preparation includes a quaternary ammonium compound, the quaternary ammonium compound is limited to benzalkonium chloride.

Thus the polymeric quaternary ammonium compounds disclosed in Desai et al. are excluded from the amended claims.

Therefore the amended claims 41-42 are not anticipated by Desai et al.

Claims 43-51, 53-56, 58-60 and 64-68 are newly rejected as obvious under 35 U.S.C. 103 over Desai et al. in view of U.S. Patent No. 5,475,034 to Yanni et al. and U.S. Patent No. 5,998,465 to Hellberg et al. This ground of rejection is deemed to be untenable as applied to the claims after the foregoing amendments for the following reasons.

As discussed above, each independent claim 41, 61 and 62 has been amended to require that “when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride”. In addition, independent claim 64, which requires benzalkonium chloride, has similarly been amended to require that “benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation”.

Thus, the instant claims as amended require that, when the claimed liquid preparation includes a quaternary ammonium compound, the quaternary ammonium compound is limited to benzalkonium chloride.

On the other hand, Desai et al. teach away from using a quaternary ammonium compound such as benzalkonium chloride as a preservative with acidic NSAID drugs like bromfenac. Desai et al. teach that the problems with benzalkonium chloride and other quaternary ammonium compounds can be avoided by using certain polymeric quaternary ammonium compounds in combination with boric acid.

Hence, an essential component of the Desai composition is a polymeric quaternary ammonium compound. However the polymeric quaternary ammonium compounds disclosed in Desai et al. are excluded from the amended claims.

There is no motivation or suggestion in the cited prior art to modify the Desai composition to replace the polymeric quaternary ammonium compound taught in Desai et al. with benzalkonium chloride. The intended purpose of the invention disclosed in Desai et al., as mentioned above, is to provide a storage-stable ophthalmic composition for acidic NSAID drugs,

like bromfenac, having good preservative efficacy. This preservative combination is a polymeric quaternary ammonium compound and boric acid.

The USPTO has made clear that "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." See MPEP section 2143.01 V, citing *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). Additionally, section 2143.01 VI of the MPEP plainly states: "The proposed modification cannot change the principle of operation of a reference. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." See also *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Here, a substitution of the Desai polymeric quaternary ammonium compound with benzalkonium chloride would render the Desai et al. invention unsatisfactory for its intended purpose.

Applicant therefore respectfully submits a *prima facie* case of obviousness cannot be based on the combination of Desai et al. with Yanni et al. and Hellberg et al.

In addition to the argument that the proposed modification changes the principle operation and intended purpose of Desai et al., Applicant reiterates that Desai et al. explicitly teach away from the use of a quaternary ammonium compound, such as benzalkonium chloride, as the only quaternary ammonium compound in an ophthalmic solution for an acidic NSAID drug such as bromfenac.

According to the USPTO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed. Cir. 2001) ("It is well-established that references which "teach away cannot serve to create a *prima facie* case of obviousness.") (citations omitted).

For the reasons detailed above, Applicant respectfully requests withdrawal of the rejection of all claims under 35 USC 103 as being unpatentable over Desai et al., Yanni et al. and Hellberg et al.

Lastly, claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending application Serial No. 11/755,662.

It is believed that all other grounds of rejection have been overcome in view of the instant response. Accordingly, it is respectfully submitted that this provisional ground of rejection should be withdrawn and the application passed on to allowance.

In summary, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly such allowance is solicited.

Rejoinder and allowance of the withdrawn method claims is also solicited.

Respectfully submitted,

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