The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte BRENDAN MURPHY, STEVEN W. COLLIER,
ERNEST QUAN and BARBARA A. JOHNSON

Appeal 2007-1378
Application 10/327,459
Technology Center 1600

Oral Argument: None
Decided: 01 May 2007

Before: FRED E. McKELVEY, *Senior Administrative Patent Judge*, and ROMULO H. DELMENDO and SALLY GARDNER LANE, *Administrative Patent Judges*.

McKELVEY, *Senior Administrative Patent Judge*.

DECISION ON APPEAL

A. Statement of the case

This *ex parte* appeal under 35 U.S.C. § 134(a) is from rejections of claims 1, 5, 7-9, 11-14, 16-23, 25-27, 29, 31, 33-37, 39-45, 48-51, 56-58, 60-62, 64-82 (hereafter "claims on appeal").

We have jurisdiction under 35 U.S.C. § 6(b).

The application on appeal was filed on 20 December 2002.

The real party in interest is Pfizer Inc.

The Examiner rejected the claims on appeal under 35 U.S.C. § 103(a) as being unpatentable over Tenengauzer. (The reader should know that no references to *et al.* are made in this opinion.)

The Examiner also rejected the claims on appeal under 35 U.S.C. § 103(a) as being unpatentable over Singer and Curatolo.

The following prior art relied was relied upon by the Examiner.

Name	Patent Number	Issue Date
Curatolo	US 5,605,889	25 Feb 1997
Singer	US 6,365,574 B2	02 Apr 2002
Tenengauzer	US 6,764,997	20 Jul 2004

Curatolo is prior art vis-à-vis appellants under 35 U.S.C. § 102(b).

Singer is prior art vis-à-vis appellants under 35 U.S.C. § 102(e) based on Singer's filing date of 30 November 1999, appellants' filing date being 20 December 2002.

Tenengauzer is prior art vis-à-vis appellants under 35 U.S.C. § 102(e) based on Tenengauzer's filing date of 18 October 2002, appellants' filing date being 20 December 2002.

In this appeal, appellants have not attempted to antedate Singer or Tenengauzer. Accordingly, for the purpose of this appeal, Singer and Tenengauzer are prior art.

B. Record on appeal

In deciding this appeal, we have considered *only* the following documents:

1. Specification, including original claims.
2. Drawing
3. Office action entered 26 October 2005.
4. Office action entered 04 April 2006
5. Corrected Appeal Brief on appeal filed 02 August 2006
6. Examiner's Answer entered 31 August 2006
7. Tenengauzer
8. Curatolo
9. Singer
10. PTO bibliographic data sheet
11. Rouhi, *The Right Stuff*, 18 Chemical and Engineering News 26-33 (Feb. 23, 2003), a copy of which appears in the Evidence Appendix of the appeal brief.
12. Claims on appeal.

C. Issues

There are two principal issues on appeal.

The first issue is whether appellants have sustained their burden of showing that the Examiner erred in rejecting the claims on appeal as being unpatentable under 35 U.S.C. § 103(a) over Tenengauzer.

The second issue is whether appellants have sustained their burden of showing that the Examiner erred in rejecting the claims on appeal as being unpatentable under 35 U.S.C. § 103(a) over Singer and Curatolo.

D. Findings of fact

The following findings of fact are believed to be supported by a preponderance of the evidence. To the extent that a finding of fact is a conclusion of law, it may be treated as such. Additional findings as necessary may appear in the Discussion portion of the opinion.

<u>The invention</u>

The invention relates to a dry blend of non-dihydrate azithromycin which can be used to make tablets containing the azithromycin. Specification, page 3:11-14.

"Dry blend" means a generally homogeneous mixture of two or more materials in particle form. Specification, page 4:34-36.

"Non-dihydrate azithromycin" means all amorphous and crystalline forms of azithromycin, other than the dihydrate form of azithromycin (Form A). Specification, page 5:15-19.

According to appellants, flow properties of a formulation may be evaluated by a number of methods known in the art. Specification, page 13:6-7.

One way of characterizing formulation properties of a powdered material is by bulk density measurements. Specification, page 13:7-9.

A simple method to provide a description of flow characteristics by bulk density measurement is Carr's Compressibility Index. Specification, page 13:9-12.

Carr's Compressibility Index is said to be a simple test to evaluate flowability by comparing both the initial and final (tapped) bulk volumes and the rate of packing down. Specification, page 13:13-15.

A useful empirical guide to flow is given by Carr's Compressibility Index: Compressibility Index (%) = [(tapped density – initial density) divided by tapped density] x 100. Specification, page 13:16-20.

Appellants tell us that it is preferred that the granules have a Carr's Compressibility Index of less than about 34%, more preferably less than about 31%, and even more preferably less than about 28%. Specification, page 14:1-5.

Claims on appeal

Since appellants do not single out any particular claim for special consideration, we will treat claim 1 on appeal as representative of the claimed invention. 37 C.F.R. § 41.37(c)(1)(vii) (2006).

Claim 1 reads:

> A dry blend, used for forming azithromycin tablets by direct compression, comprising:
>
> (a) about 1-80%, by weight, non-dihydrate azithromycin;
>
> (b) at least one pharmaceutically acceptable excipient; and
>
> (c) from about 0.25-10%, by weight, of a lubricant;

wherein the Carr's Compressibility Index, of the dry blend, is less than about 34%;

wherein said non-dihydrate azithromycin is azithromycin monohydrate hemi-ethanol solvate.

Tenengauzer

Tenengauzer relates to stabilized azithromycin compositions. Col. 1:13-14; col. 3:1-2.

One suitable particular azithromycin is azithromycin ethanolate monohydrate. Col. 3:2-6.

Pharmaceutical compositions comprising the stabilized azithromycins include dosage forms such as tablets. Col. 4:35-37.

While other dosage forms are described, according to Tenengauzer among the methods for forming preferred tablet dosage forms are dry granulation (compaction and slugging) and direct compression. Col. 4:41-43.

Singer

Singer describes azithromycin ethanolate which can be formed into tablets and compressed or coated pills. Col. 3:24-27

An Example in Singer describes preparation of azithromycin ethanolate. Col. 3:54.

Curatolo

Curatolo tells us that azithromycin is a broad spectrum antimicrobial compound. Col. 1:11-13.

Curatolo, which predates Singer, describes an oral dosage form of azithromycin. Col. 2:36-37.

Excipients and lubricants may be combined with azithromycin. Col. 6:54-57.

Curatolo, which is said to be owned by appellants' assignee Pfizer Inc., tells one the following about the level of skill in the art more than one year prior to the filing date of the application on appeal:

> As known in the art, tablet blends may be dry-granulated or wet granulated before tableting. Alternatively, tablet blends may be directly compressed. The choice of processing approach depends upon the properties of the drug and chosen excipients, for example particle size, blending compatibility, density and flowability. For azithromycin tablets, granulation is preferred, with wet granulation being most preferred. Azithromycin may be wet-granulated, and then other excipients may be added extragranularly. Alternatively, azithromycin and one or more excipients may be wet-granulated.

Col. 7:51-61.

Curatolo confirms that granulation was a known technique for use in the overall process of making azithromycin tablets.

Curatolo further confirms that the choice of processing approach depends on the properties sought to be obtained.

One of those properties is "density" which is a property of interest to appellants. *See* the various references to Carr's Compression Index in the specification generally and in the various examples.

Curatolo still further confirms that granulation is preferred as a step in making azithromycin tablets, although Curatolo expresses a preference for wet-granulation. Col. 7:56-58.

Many of the examples of Curatolo describe products with azithromycin dihydrate—which of course is outside the scope of the claims on appeal.

However, nothing in Curatolo limits the applicability of the Curatolo invention to azithromycin dihydrate.

Level of skill in the art

In addition from what we learn from Curatolo, we also learn from background of the invention as described in appellants' specification that a person having ordinary skill in the art knows that direct compression is a tableting process in which tablets are compressed directly from powder blends containing an active ingredient. Specification, page 1:5-7.

In direct compression, all the ingredients required for tableting, including the active ingredient and processing aids, are incorporated into a free flowing blend which is then tableted. Specification, page 1:7-11.

The active ingredient, excipients, and other substances are blended and then compressed into tablets. Specification, page 1:11-12.

Tablets are typically formed by pressure being applied to a material in a tablet press. Specification, page 1:13-14.

According to appellants, pharmaceutical manufacturers now prefer the use of direct compression, over wet and dry granulation processes, because of its shorter processing times and cost advantages. Specification, page 1:20-23.

What appellants tell us about the preference for direct compression, at least as of the date the application on appeal was filed (20 December 2002), is not precisely the same as what appellants' assignee said about forming tablets in Curatolo, which was filed on 29 April 1994. Apparently the art has evolved between 1994 and 2002, as is often the case.

Appellants note, in this respect, that direct compression is generally limited to those situations in which the active ingredient has physical characteristics suitable for forming pharmaceutically acceptable tablets via direct compression. Specification, page 1:23-26.

Some active ingredients, which are generally unsuitable for direct compression *per se*, can be formed into a directly compressible formulation by incorporating one or more excipients before compression. Specification, page 1:27-30.

It is known that, to form a tablet from a given formulation, the formulation must have good flow properties for precise volumetic feeding of the material [i.e., formulation,] to a die cavity and suitable compressibility, compactability, and ejection properties to form a tablet. Specification, page 2: 18-23.

The flow properties of powders are said to be critical for "efficient tableting operation." Specification, page 2:23-24.

Azithromycin A is not considered to be amenable to the production of directly compressible tablets of azithromycin formulation. Specification, page 3:1-4.

However, as Tenengauzer reveals, azithromycin ethanolate monohydrate is a suitable candidate for dry granulation tablet formation involving (1) roller compaction (Example 4; col. 15:21) and pressing (Example 4; col. 15:32) and (2) milling (Example 5; col. 18:14) and pressing (Example 5; col. 18:19).

Curatolo also tells us that azithromycin dihydrate is a suitable candidate for dry granulation or direct compression. Col. 7:51-53.

E. Principles of law

A claimed invention is not patentable if the subject matter of the claimed invention would have been obvious to a person having ordinary skill in the art. 35 U.S.C. § 103(a); *Graham v. John Deere Co. of Kansas City,* 383 U.S. 1 (1966).

Facts relevant to a determination of obviousness include (1) the scope and content of the prior art, (2) any differences between the claimed invention and the prior art, (3) the level of skill in the art and (4) any relevant objective evidence of obviousness or non-obviousness. *Graham*, 383 U.S. at 17-18.

A person having ordinary skill in the art uses known elements and process steps for their intended purpose. *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.,* 396 U.S. 57 (1969) (radiant-heat burner used for its intended purpose in combination with a spreader and a tamper and screed);

Sakraida v. AG Pro, Inc., 425 U.S. 273, 282 (1976) (the involved patent simply arranges old elements with each performing the same function it had been known to perform); *Dunbar v. Myers*, 4 Otto (94 U.S.) 187, 195 (1876) (ordinary mechanics know how to use bolts, rivets and screws and it is obvious that any one knowing how to use such devices would know how to arranged a deflecting plate at one side of a circular saw which had such a device properly arranged on the other side).

A prior art reference is not limited to its preferred embodiments or specific working examples. *In re Burckel*, 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA 1979). *See also In re Mills*, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972).

An inventor must show that the results the inventor says the inventor achieves with the invention are actually obtained with the invention and it is not enough to show results are obtained which differ from those obtained in the prior art—any difference must be shown to be an unexpected difference. *In re Klosak*, 455 F.2d 1077, 1080, 173 USPQ 14, 16 (CCPA 1972). *See also In re Geisler*, 116 F.3d 1465, 1469-70, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997) (party asserting unexpected results has the burden of proving that the results are unexpected).

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433

(CCPA 1977). *See also In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1657-58 (Fed. Cir. 1990).

F. Discussion

Examiner's § 103 rejection based on Tenengauzer

The findings support the Examiner's holding of obviousness.

One azithromycin described as useful by Tenengauzer is azithromycin ethanolate monohydrate—which is not a hydrate of azithromycin.

Lubricants said to be useful in making the Tenengauzer product are magnesium stearate and talc. Col. 5:38-39. In Example 4, magnesium stearate and talc are present in an amount of 7.6% [(32.0 + 2.0 {from Part II} + 13.6 + 15 {from Part III})/824 = 7.6%], which falls within the scope of appellants' claimed range of 0.25-10% lubricant.

Tenengauzer also describes addition of excipients. Col. 4:30.

We, like the Examiner, find it difficult to distinguish the product made by Tenengauzer from that claimed by appellants. *In re Best*, *supra*.

Appellants argue that Tenengauzer does not describe all the limitations of claim 1. However, Tenengauzer plainly reveals that a dry blend may have a non-dihydrate azithromycin, an excipient and a lubricant in an amount mentioned in claim 1.

Appellants' principal argument seems to be that Tenengauzer does not describe granules with a Carr's Compression Index of less that 34%. Appeal Brief, page 12.

With respect to the Carr's Compression Index of less than 34%, appellants' argument is not convincing.

We have not been told where the record would support findings to demonstrate that the 34% is an *unexpected* result. Merely because appellants achieve a Carr's Compression Index of less than 34% does not *per se* establish an unexpected result—at *best* a Carr's Compression Index of 34% is a "different" result. In any event, we cannot overlook the fact that we are told by Curatolo that granulation and direct compression are suitable methods of choice for making azithromycin tablets and that one skilled in the art looking for density properties would take into account the choice of processing. When the objective evidence of non-obviousness is balanced against the prior art and the objective evidence of obviousness which appears in this record, we have no trouble declining to credit appellants' "showing" of non-obviousness.

The Examiner made a point in the Examiner's Answer to the effect that according to the specification (page 13:30 to page 14:1), appellants indicate that formulations with a Carr's Compression Index greater than 34% "resulted in poor flow and inability to form suitable tablets on an F-press." Examiner's Answer, page 5.

In effect, what the Examiner found was that a blend has to be formulated in such a manner as to be suitable for making tablets.

Apparently that means a Carr's Compression Index of less than 34%.

What appellants have determined is precisely what we learn from Curatolo—choice of processing conditions depends on the properties of the drug and chose excipients. Col. 7:52-64.

A person skilled in the art, attempting to make a dry blend, from the ingredients set out in Tenengauzer would use ingredients and amounts to

succeed. The level of skill in the art, as revealed by this record, shows that one skilled in the art manifestly would be able to do so. To the extent that appellants limit the claims to blends which are "operable" is not surprising and reflects, we believe, nothing more than a realization of what one having ordinary skill in the art would do. Once a person sets out to follow Tenengauzer to make a tablet, one skilled in the art would be expected to use proper techniques, as shown by the level of skill on the record, to succeed—not to fail.

Appellants argue that Tenengauzer described the use of an anti-oxidant to prevent chemical degradation of azithromycin. Appeal Brief, page 13.

Appellants' argument is foreclosed by the Examiner's observation that appellants use the transition language "comprising." Examiner's Answer, page 5. See *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948).

<u>Examiner's § 103 rejection based on Singer and Curatolo</u>

The Examiner found that a person having ordinary skill in the art seeking to make the tablets of Singer would have found it obvious to use dry granulation or direct compression as described by Curatolo.

The evidence supports the Examiner's finding.

As the Examiner noted, Singer describes tablets made from azithromycin ethanolate.

To be sure, Singer does not describe precisely how one would go about making a tablet from its azithromycin—nor need Singer do so given that the prior art already describes how a tablet is to be made. *Cf. Webster*

Loom Co. v. Higgins, 15 Otto (105 U.S.) 580 (1881) ((1) "The loom itself was old. Every part of it was familiar to every loom manufacturer and to every weaver."; (2) an inventor may begin a description of an invention at the point where his invention begins, and describe what he has made that is new, and what it replaces of the old and that which is common and known is as if it were written out in the patent and delineated in the drawings).

Curatolo is a primer on what one skilled in the art knows about making tablets. *See also* the background of the invention as described in the specification.

Curatolo tells us that one skilled in the art seeking to make a tablet containing azithromycin may dry granulation or direct compression and that depending on the precise properties sought knows how to make processing choices.

On the basis of the evidence before us, we have no difficulty concluding that appellants have done nothing more than make an azithromycin dry blend using known techniques to get exactly what one skilled in the art would expect.

Appellants disagree maintaining that the art must, in appellants' words, have "some suggestion or motivation" to combine the teachings of Singer and Curatolo. Appeal Brief, page 16.

We have no trouble finding that the teachings of Singer and Curatolo can be combined—the Curatolo glove fits right on the Singer hand.

Singer is said to fail to describe all the limitations of the claims. The argument is a side show apart from the main event. If Singer described all the limitations, then the Examiner would have made an anticipation

rejection. What appellants' argument amounts to is a "divide and conquer" approach—since Singer does not show it all, then the combination of Singer and Curatolo is "no good". Sometime ago, however, binding precedent made clear that an obviousness rejection cannot be overcome by attacking references individually—which is precisely what appellants are doing. *In re Young*, 403 F.2d 754, 757, 159 USPQ 725, 728 (CCPA 1968).

Appellants go on to say that Singer does not describe any azithromycin having a Carr's Compression Index of less that 34%. Appeal Brief, page 16. Appellants are correct that there is no explicit description of Carr's Compression Index in Singer. However, making a tablet is described by Singer and any one skilled in the art would know from Curatolo precisely how to make the tablet. Not only that, but based on Curatolo, any one skilled in the art would know that through process choices, properties—including density—can be controlled. On this record, for all we know, anyone successfully making a tablet using Singer's azithromycin via the Curatolo dry granulation or direct compression process would get results similar to those of appellants. Even if not so, one skilled in the art making a granule to make the Singer tablet would obtain a granule having a Carr's Compression Index of some value. On this record we have no idea what that Index number might be.

Appellants, of course, maintain that the Carr's Compression Index of less that 34% is unexpected. We have already addressed why appellants' proofs fall short of those required by law to establish the "unexpected" nature of the results.

Appellants also maintain that the Examiner has engaged in hindsight. We totally disagree and appellants have failed to explain why one skilled in the art would not have used the Curatolo process choices to make the Singer tablet. Binding precedent tells us that obviousness judgments are necessarily based on hindsight, but so long as judgment takes into account only knowledge known in the art, there is no hindsight error. *In re McLaughlin*, 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971). The Examiner's rejections are based squarely on the prior art. There is no impermissible hindsight in this case.

Appellants rely on Rouhi in an attempt to "catch" the Examiner contradicting herself. The Examiner initially had held that the claimed invention was based on a non-enabling description because, according to appellants, the Examiner initially felt that there was some question whether azithromycin (presumably Form F) would maintain its crystalline structure when granulated. Basically, what the Examiner was investigating was whether appellants on the one hand had an enabling description and if so whether the invention would have been obvious. The Examiner's technique is a proper and often used technique to accomplish the examination required by 35 U.S.C. § 131 and 37 C.F.R. § 1.104 (2006) in pharmaceutical and organic chemistry cases. In support of a first blush non-enabling rejection, the Examiner mentioned Rouhi—as she should have to support the rejection. Upon consideration of appellants' arguments, ultimately the Examiner became convinced that there was an enabling description and so the lack of enablement rejection was withdrawn. But, what appellants seek to do is create an "estoppel" against the Examiner from forever changing her mind

when becoming convinced an applicant has a point with respect to one of numerous rejections. If the Examiner, at the Examiner's Answer stage, had harbored any doubt about enablement, we would have had both an enablement and obviousness rejection before us. Moreover, on the merits of the rejections before us, Rouhi seems to be a "generic" discussion about numerous problems and concerns in the pharmaceutical field. While paroxetine hydrochloride and cefadroxil are mentioned (see page 30), neither are azithromycins—a fact which immediately can be confirmed by reference to the 2001 Physicians' Desk Reference at pages 1003 and 3114. Appellants' reliance on Rouhi is not persuasive when weighed against the explicit azithromycin teachings of Curatolo—a patent said to be owned by appellants' assignee. Curatolo convincingly shows that one skilled in the art uses dry granulating or direct compression techniques to make azithromycin tablets. Rouhi does not appear to mention azithromycin. For the reasons given, as applied to the facts of this case, we credit the more relevant teachings of Curatolo over the less relevant "teachings" of Rouhi.

Appellants maintain that the Examiner has used an "obvious to try" standard. According to appellants an "obvious to try" standard is not an appropriate standard. Appeal Brief, pages 12-13 and 16-17. This argument goes nowhere. The Examiner did not make an obviousness holding based on "obvious to try." Moreover, an "obvious to try" argument is often made when there is an issue of whether the evidence supports a finding that there is a reasonable chance of success. *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). *See also* (1) *In re Eli Lilly & Co.*, 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990) (an "obvious-to-try" situation exists

when a general [prior art] disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the [prior art] disclosure, but the [prior art] disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued) and (2) *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1365, 82 USPQ2d 1321, ____ (Fed. Cir. 2007). There is no legitimate "obvious to try" issue in this case since the prior art tells one skilled in the art precisely how to make "operable" tablets. Not only is there a reasonable chance of success in this case—there is no doubt a skilled artisan would be successful.

G. Conclusions of law

Appellants have not sustained their burden on appeal of showing that the Examiner erred in rejecting the claims on appeal as being unpatentable under 35 U.S.C. § 103 over (1) Tenengauzer or (2) the combination of Singer and Curatolo.

On the record before us, appellants are not entitled to a patent containing the claims on appeal.

H. Decision

ORDERED that the decision of the Examiner rejecting the claims on appeal under 35 U.S.C. § 103(a) over Tenengauzer is *affirmed*.

FURTHER ORDERED that the decision of the Examiner rejecting the claims on appeal under 35 U.S.C. § 103(a) over the combination of Singer and Curatolo is *affirmed*.

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED

mv

cc (via First Class mail)

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