

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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*Ex parte* LI LIANG CHIA and EILEEN FLECK WARWICK

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Appeal 2008-5698  
Application 11/070,736  
Technology Center 1600

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Decided: January 03, 2009

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Before LORA M. GREEN, RICHARD M. LEBOVITZ, and  
FRANCISCO C. PRATS, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

**DECISION ON APPEAL**

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 3-6, and 8-10. We have jurisdiction under 35 U.S.C. § 6(b).

### STATEMENT OF THE CASE

The claims are directed to an antimicrobial composition. Claims 1, 3, and 6 are representative of the claims on appeal, and read as follows:

1. An antimicrobial composition comprising:  
(a) N-(n-butyl)-1,2-benzisothiazolin-3-one; and  
(b) 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one;  
wherein said composition has a weight ratio of N-(n-butyl)-1,2-benzisothiazolin-3-one to 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one from 6000:1 to 30:1.

3. The antimicrobial composition of claim 1 in which a weight ratio of N-(n-butyl)-1,2-benzisothiazolin-3-one to 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one is from 300:1 to 35:1.

6. An antimicrobial composition comprising:  
(a) N-(n-butyl)-1,2-benzisothiazolin-3-one; and  
(b) a mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one, in a weight ratio of 5-chloro-2-methyl-4-isothiazolin-3-one to 2-methyl-4-isothiazolin-3-one up to 4:1;  
wherein a weight ratio of N-(n-butyl)-1,2-benzisothiazolin-3-one to said mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one is from 12,000:1 to 50:1.

The Examiner relies on the following references:

Whitekettle	US 5,063,217	Nov. 5, 1991
Hsu	US 5,874,476	Feb. 23, 1999
Eastwood	US 2003/0168626 A1	Sep. 11, 2003

We affirm.

## ISSUE

The Examiner concludes that claims 1 and 3-5 are obvious over the combination of Eastwood and Hsu; and that claims 6 and 8-10 are obvious over the combination of Eastwood and Whitekettle.

Appellants assert that the *prima facie* case of obviousness is rebutted by a demonstration of unexpected results.

Thus, the issue on Appeal is: Whether Appellants have demonstrated a showing of unexpected results sufficient to overcome the Examiner's *prima facie* case of obviousness?

## FINDINGS OF FACT

FF1 The present invention is drawn to antimicrobial compositions comprising mixtures of N-(n-butyl)-1,2-benzisothiazolin-3-one [n-BBIT] and (b) 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one [DCOIT]; and also to antimicrobial composition of n-BBIT and a mixture of 5-chloro-2-methyl-4-isothiazolin-3-one [CMI] and 2-methyl-4-isothiazolin-3-one [MI] (Spec. 1-2).

FF2 According to the Specification, the "compositions of the present invention unexpectedly have been found to provide enhanced antimicrobial efficacy at a combined active ingredient level lower than that of the individual antimicrobial compounds." (*Id.* at 3.)

FF3 The Specification further discusses an art "accepted" method of measuring synergy (*id.* at 7). The method uses

the ratio determined by the formula:  
$$Q_a/Q_A + Q_b/Q_B = \text{Synergy Index ("SI")}$$
  
wherein:

$Q_A$  = concentration of compound A (first component) in ppm, acting alone, which produced an end point (MIC of Compound A).

$Q_a$  = concentration of compound A in ppm, in the mixture, which produced an end point.

$Q_B$  = concentration of compound B (second component) in ppm, acting alone, which produced an end point (MIC of Compound B).

$Q_b$  = concentration of compound B in ppm, in the mixture, which produced an end point.

When the sum of  $Q_a/Q_A$  and  $Q_b/Q_B$  is greater than one, antagonism is indicated. When the sum is equal to one, additivity is indicated, and when less than one, synergism is demonstrated. The lower the SI, the greater the synergy shown by that particular mixture. The minimum inhibitory concentration (MIC) of an antimicrobial compound is the lowest concentration tested under a specific set of conditions that prevents the growth of added microorganisms.

(*Id.* at 7-8.)

FF4 The Examiner rejects claims 1 and 3-5 under 35 U.S.C. § 103(a) as being obvious over the combination of Eastwood and Hsu (Ans. 3). As Appellants do not argue claims 4 and 5 separately from claim 1, those claims stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

FF5 The Examiner also rejects claims 6 and 8-10 under 35 U.S.C. § 103(a) as being obvious over the combination of Eastwood and Whitekettle (*id.* at 6). Again, Appellants do not argue claims 8-10 separately from claim 6, thus those claims stand or fall with claim 6.

FF6 Appellants do not argue the merits of the Examiner's prima facie case of obviousness, but instead focus on demonstration of unexpected results (App. Br. 10-12).

FF7 As to the combination of n-BBIT with CMI/MI (claim 6), Appellants appear to only have tested a mixture of CMI/MI of 3:1 CMI/MI (KATHON LX) (Spec. 8).

FF8 The data for the combination of n-BBIT with CMI/MI is presented below (“ITA” means isothiazoline and represents the CMI/MI mixture):

	Alone	Combinations		Organisms	Contact Time	S.I.	Ratio n-BBIT: ITA
		ITA ppm	n-BBIT ppm				
F	CMI/MI	1	28	0.03	25	<i>A. niger</i>	833:1
				0.06	25		417:1
				0.13	18		139:1
				0.28	18		64:1
				0.5	28		56:1
	CMI/MI	0.28	444	0.03	356	<i>F. moniliforme</i>	11867:1
				0.06	356		5933:1
				0.13	267		2054:1
			1	0.06	444		7400:1
				0.28	267		954:1
B	CMI/MI	5	267	1	178	<i>K. pneumoniae</i>	178:1
				0.5	267		534:1
			11	267	1		178:1
				2	178		89:1
				5	356	<i>E. coli</i>	237:1
	CMI/MI	5	356	0.3	71		106:1
				0.5	53		89:1
				1	89		142:1
			5	533	0.1		890:1
				0.3	89		297:1
				0.5	71		107:1
				1	107		45:1
				2	89		

(Spec. 11.)

FF9 No statistical analysis was presented with the data the table, so it is unclear what the margin of error may be.

FF10 The data for the combination of n-BBIT with DCOIT is presented below (“ITA” represents DCOIT):

	Alone	Combinations		Organisms	Contact Time	S.I.	Ratio n-BB1T: ITA	
		ITA ppm	n-BB1T ppm					
F	DCOIT	0.28	267	0.03	178	<i>F. moniliforme</i>	3 days	0.8 5933:1
				0.06	178			0.8 2967:1
				0.13	160			1.1 1231:1
				0.28	142			1.5 507:1
			1	0.06	267		7 days	0.8 4450:1
				0.13	267			0.9 2054:1
				0.5	124			0.8 248:1
				1	36			0.8 36:1
				0.03	356			1.0 11867:1
				0.28	356			1.3 1271:1
B	DCOIT	6	36	0.1	32	<i>S. aureus</i>	24 hr	0.9 320:1
				0.3	36			1.1 120:1
			9	0.3	36		48 hr	0.7 120:1
				0.5	53			1.1 106:1
				1	36			0.8 36:1
		11	267	2	53			1.2 27:1
				0.5	267	<i>K. pneumoniae</i>	48 hr	1.0 534:1
				1	178			0.8 178:1
				2	178			0.8 89:1
		5	267	4	267			1.4 67:1
			18	0.1	14	<i>P. mirabilis</i>	48 hr	0.9 140:1
				1	14			1.0 14:1
				0.3	18			1.1 60:1

(Spec. 12.)

FF11 Again, no statistical analysis was presented with the data in the table, so it is unclear what the margin of error may be.

#### PRINCIPLES OF LAW

The burden of demonstrating unexpected results rests on the party asserting them, and “it is not enough to show that results are obtained which differ from those obtained in the prior art; that difference must be shown to be an *unexpected* difference.” *In re Klosak*, 455 F.2d 1077, 1080 (CCPA 1972). “Mere improvement in properties does not always suffice to show unexpected results,” however “when an applicant demonstrates *substantially* improved results . . . and states that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of evidence* to the

contrary.” *In re Soni*, 54 F.3d 746, 751 (Fed. Cir. 1995) (noting further that “[g]iven a presumption of similar properties for similar composition, substantially improved properties are *ipso facto* unexpected.”). Moreover, it has been long held that “even though applicant’s modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art, unless the claimed ranges ‘produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art.’” *In re Huang*, 100 F.3d 135, 139 (Fed. Cir. 1996) (quoting *In re Aller*, 220 F.2d 454, 456, (1955), and citing *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990)).

## ANALYSIS

As to the rejection of claims 1 and 3-5 over the combination of Eastwood and Hsu, Appellants assert that the obviousness rejection may be rebutted by a showing of unexpected results, and that “[s]ynergistic interaction between molecules always is unexpected.” (App. Br. 10.) Appellants argue that “their claimed biocide combinations display synergistic activity (synergy index <1) within the claimed ranges of biocide ratios.” (*Id.* (citing Spec. 12-13).)

In response to the Examiner’s assertion that the demonstration of unexpected results is not commensurate in scope with the claimed subject matter, Appellants argue that “valid claims may include some inoperative embodiments,” and that the “practice of the Office in the past has been to allow claims to compositions exhibiting synergy at many points over the

claimed range, but not necessarily at all points.” (App. Br. 10.) Appellants assert that they “have demonstrated that most of the ratios within the claimed ranges are synergistic, and thus have provided unexpected results over the claimed ranges.” (*Id.*) Moreover, Appellants argue that claim 3 claims ratios of BBIT:DCOIT of 300:1 to 35:1, and thus excludes the points used by the Examiner to demonstrate that the unexpected results are not commensurate in scope with the claimed subject matter (*id.*).

Appellants purported unexpected results are not sufficient to overcome the Examiner’s *prima facie* case of obviousness. First, Appellants have provided no statistical analysis of the data presented (FF9 and FF11), and thus it is unclear whether the difference in activity of a mixture having an SI of 0.9 from that having an SI of 1 is statistically significant. As Appellants themselves explain, synergy is only shown with an SI less than 1, with an SI of 1 merely showing additivity (FF3). In addition, the SI data presented by the table mostly falls within the range of 0.8 to 1.1, thus it does not appear that the data within the claimed ratio recited in claim 1 presents substantially improved properties (FF10).

Moreover, even if we were to consider a SI of 0.8 and below as statistically significant and represents a substantial improvement in properties; claim 1 encompasses a ratio of n-BBIT of DCOIT of 600:1. A ratio of 507:1 with a contact time of 3 days with *F. moniliforme* had an SI of 1.5 (FF10), and there is no other data at the upper end of the ratio to support a finding of unexpected results (*id.*).

As to claim 3, claim 3 encompasses a ratio of 300:1 to 35:1. We again reiterate that we can not judge the statistical significance of the data,

and that the data is clustered between an SI of 0.7 to 1.1, thus it is unclear if there is any substantial change in the properties of the mixtures to support a finding of unexpected results for the entire claimed range (*id.*). For example, the ratio of 67:1, which falls within the claimed range, has an SI of 1.4 and therefore is not synergistic by Appellants' own definition. An SI of 0.7 was obtained for *S. aureus* at a contact time of 48 hours for a ratio of 120:1, but the same ratio at a contact time of 24 hours had an SI of 1.1 (*id.*). In addition, a ratio of 106:1, which is very close to the ratio of 120:1, produced an SI of 1.1 when contacted with *S. aureus* for 48 hours (*id.*). We therefore find that the data itself supports the uncertainty of the statistical significance of the data.

As to the rejection of claims 6 and 8-10 over the combination of Eastwood and Hsu, Appellants again assert that the obviousness rejection may be rebutted by a showing of unexpected results, and that “[s]ynergistic interaction between molecules always is unexpected, and neither its existence nor the composition ranges over which two molecules will exhibit synergistic reaction can be predicted.” (App. Br. 11.) Appellants argue that “their claimed biocide combination display synergistic activity (synergy index <1) within the claimed range of biocide ratios.” (*Id.* (citing Spec. 11).)

In response to the Examiner's finding that the unexpected results are not commensurate in scope with the claimed subject matter, as the claimed compositions display synergy against *E. coli*, at 24 hours, but not 48 hours, Appellants assert that the “fact that synergy is not observed at 48 hours does

not negate the observation of synergy at the shorter time period.” (App. Br.

12.) According to Appellants, they

have demonstrated that the claimed biocides at this ratio are synergistic against this organism over a 24-hour period, which is an unexpected result. The fact that synergy is not observed at 48 hours does not negate the observation of synergy at the shorter time period. A showing of unexpected results for a composition refutes a finding of obviousness, and does not require demonstrating that the unexpected results would be obtained for every possible measurement of the composition’s properties under every possible set of conditions. This would be impossible to prove, and to Appellant’s knowledge, has never been required. *See, e.g., In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987).

(*Id.*)

We affirm this rejection for the same reasons set forth above with respect to the rejection of claims 1 and 3-5, that is, that the statistical significance of the data is unclear (FF9), and thus it is unclear if the data supports that any of the mixtures have a substantial improvement in properties, thus supporting a finding of unexpected results.

Moreover, Appellants’ purported showing of unexpected results is not commensurate in scope with the claimed subject matter. The claims encompass a ratio of CMI/MI of up to 4:1, but Appellants only apparently tested mixtures having a ratio of CMI/MI of 3:1 (FF7).

In addition, the claim 6 encompasses a ratio of n-BBIT to CMI/MI of 12,000:1 to 50:1. However, when a ratio of 64:1 was contacted with *A. niger* for 3 days, an SI of 0.9 was obtained, while when a ratio of 56:1 was contacted with the same organism for the same amount of time, a SI of 1.5 was obtained (FF8), again demonstrating the uncertainty of the data.

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#### CONCLUSIONS OF LAW

Thus, we find that Appellants have not demonstrated a showing of unexpected results sufficient to overcome the Examiner's prima facie case of obviousness, and the rejection of claims 1 and 3-5 over the combination of Eastwood and Hsu; and the rejection of claims 6 and 8-10 obvious over the combination of Eastwood and Whitekettle; are affirmed.

#### TIME LIMITS

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

dm

ROHM and HAAS COMPANY  
PATENT DEPARTMENT  
100 INDEPENDENCE MALL WEST  
PHILADELPHIA PA 19106-2399