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(54) **COMBINAISONS MICROBICIDES SYNERGIQUES**

**CONTENANT 4,5-DICHLORO-2-OCTYL-3-ISOTHIAZOLONE
ET CERTAINS BIOCIDES COMMERCIAUX**

(54) **SYNERGISTIC MICROBICIDAL COMBINATIONS**

**CONTAINING 4,5-DICHLORO-2-OCTYL-3-ISOTHIAZOLONE
AND CERTAIN COMMERCIAL BIOCIDES**

(57) Synergistic microbicidal compositions are disclosed, comprising 4,5-dichloro-2-octyl-3-isothiazolone and one or more known microbicides for more effective, and broader control of microorganisms in various systems.



Abstract of the Disclosure

Synergistic microbicidal compositions are disclosed, comprising 4,5-dichloro-2-octyl-3-isothiazolone and one or more known microbicides for more effective, and broader control of microorganisms in various systems.

PATENT APPLICATION OF

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for

SYNERGISTIC MICROBICIDAL COMBINATIONS
CONTAINING 4,5-DICHLORO-2-OCTYL-3-ISOTHIAZOLONE
AND CERTAIN COMMERCIAL BIOCIDES

DN89-104 MBF/JS/meb

BACKGROUND OF THE INVENTION1. Field of the Invention

This invention concerns microbicidal compositions which include an isothiazolone and one or more other biocides, and which are intended to provide more effective and broader control of microorganisms in various industrial systems and for household products, agricultural products, and biomedical products, etc. In particular, the present invention relates to the use of a composition of 2-n-octyl-4,5-dichloro-isothiazolin-3-one, hereinafter referred to as 4,5-dichloro-2-octyl-3-isothiazolone, with one or more of the following 11 compounds: 3-iodo-2-propynylbutylcarbamate, 1,2-dibromo-2,4-

dicyanobutane, p-tolyldiiodomethylsulfone, methylenebisthiocyanate,
2-thiocyanomethylthiobenzothiazole, tetrachloroisophthalonitrile, 2-n-
octyl-3-isothiazolone, bis-(trichloromethyl)sulfone, 5-bromo-5-nitro-1,3-
dioxane, 2-bromo-2-nitropropanediol, 2,2-dibromo-3-
5 nitrilopropionamide.

The term "microbicidal" (or "antimicrobial" or "biocidal") as
used herein is intended to encompass, but is not restricted to, all
bactericidal, fungicidal and algicidal activity.

2. Prior Art

10 Isothiazolones are described in U.S. Patent Nos. 3,761,488;
4,105,431; 4,252,694; 4,265,899 and 4,279,762, and elsewhere. Their use as
microbicides is well known.

15 It is the principal object of this invention to provide synergistic
compositions which overcome disadvantages of known microbicidal
compositions.

SUMMARY OF THE INVENTION

We have found that compositions formed from 4,5-dichloro-2-
octyl-3-isothiazolone and one or more of the 11 specified compounds
(supra) unexpectedly afford synergistic antimicrobial activity against a

wide range of microorganisms: the disruptive action on the organisms by the two compounds together is unexpectedly greater than the sum of both compounds taken alone. This synergy does not arise from the expected activity of the components nor from the expected improvement in activity. As a result of the synergy, the effective dose required can be lowered, which is not only more economical but also increases safety margins. The synergistic compositions of the present invention provide more effective and broader control of microorganisms in a number of systems.

The present invention thus provides a composition having microbicidal activity which includes 4,5-dichloro-2-octyl-3-isothiazolone and a second component selected from one or more of the group consisting of: 3-iodo-2-propynylbutylcarbamate, 1,2-dibromo-2,4-dicyanobutane, p-tolyldiiodomethylsulfone, methylenebisthiocyanate, 2-thiocyanomethylthiobenzothiazole, tetrachloroisophthlonitrile, 2-n-octyl-3-isothiazolone, bis-(trichloromethyl)sulfone, 5-bromo-5-nitro-1,3-dioxane, 2-bromo-2-nitropropanediol, 2,2-dibromo-3-nitrilopropionamide; wherein the

weight ratio of 4,5-dichloro-2-octyl-3-isothiazolone to the second component is from about 150:1 to 1:250.

Important applications of the synergistic antimicrobial compositions of the present invention include but are not limited to:

5 inhibiting the growth of bacteria and fungi in aqueous paints and coatings, adhesives, sealants, latex emulsions, and joint cements; preserving wood; preserving cutting fluids, controlling slime-producing bacteria and fungi in pulp and papermills and cooling towers; as a spray or dip treatment for textiles and leather to prevent

10 mold growth; protecting paint films, especially exterior paints, from attack by fungi which occurs during weathering of the paint film; protecting processing equipment from slime deposits during manufacture of cane and beet sugar; preventing microorganism buildup and deposits in air washer or scrubber systems and in

15 industrial fresh water supply systems; preserving fuel; controlling microorganisms contamination and deposits in oil field drilling fluids and muds, and in secondary petroleum recovery processes; preventing bacterial and fungal growth in paper coatings and coating processes; controlling bacterial and fungal growth and deposits during the

5 manufacture of various specialty boards, e.g., cardboard and particle
board; preventing sap stain discoloration on freshly cut wood of
various kinds; controlling bacterial and fungal growth in clay and
pigment slurries of various types; as a hard surface disinfectant to
prevent growth of bacteria and fungi on walls, floors, etc.; as a
preservative for cosmetic and toiletry raw materials, floor polishes,
fabric softeners, household and industrial cleaners; in swimming pools
to prevent algae growth; inhibiting the growth of harmful bacteria,
yeasts, fungi on plants, trees, fruits, seeds, or soil; preserving
10 agricultural formulations, electrodeposition systems, diagnostic and
reagent products, medical devices; protecting animal dip compositions
against the buildup of microorganisms, and in photoprocessing to
prevent buildup of microorganisms, and the like.

15 The compositions of the invention may be added separately to
any system or may be formulated as a simple mixture comprising its
essential ingredients, and if desired a suitable carrier or solvent, or as
an aqueous emulsion or dispersion.

The invention also provides a method of inhibiting the growth
of bacteria, fungi or algae in a locus subject to contamination by

bacteria, fungi or algae, which comprises incorporating into or onto the locus in an amount which is effective to adversely affect the growth of bacteria, fungi or algae any of the compositions defined above.

General Description of the Preferred Embodiment

5 The composition of the invention can be formulated as a solution in a wide range of organic solvents. The solutions generally contain about 5 to 30% by weight of the active composition. It is generally more convenient to provide the compositions in a water-diluted form: this may be accomplished by adding an emulsifier to the
10 organic solution followed by dilution with water.

 In general, the weight ratio of 4,5-dichloro-2-octyl-3-isothiazolone to second component in the composition may be in the range of from about 150:1 to about 1:250. The other specific and preferred ratios are given in the examples.

15 The synergism of two-component compositions is demonstrated by testing a wide range of concentrations and ratios of compounds, generated by two-fold serial dilutions in a Trypticase Soy Broth (Difco) growth medium of a microbicide in one dimension and another microbicide in the second dimension, against a bacterium Escherichia

coli (ATCC 11229), or fungi Candida albicans (ATCC 11651), Aspergillus niger (ATCC 6275), or Aureobasidium pullulan (ATCC 9348). Each test tube was inoculated to make about $1-5 \times 10^7$ bacteria per ml or $1-5 \times 10^5$ fungi per ml. The lowest concentrations of each compound or mixtures to inhibit visible growth (turbidity) at 37° for E. coli and at 30°C for the fungi for 7 days were taken as the minimum inhibitory concentration (MIC). The MIC were taken as end points of activity. End points for the mixtures of compound A (4,5 dichloro-2-octyl-3-isothiazolone) and compound B (second component microbicide) were then compared with the end points for the isothiazolone A alone and compound B alone. Synergism was determined by a commonly used and accepted method described by Kull, F.C.; Eisman, P.C.; Sylwestrowicz, H.D. and Mayer, R.L., in applied Microbiology 9:538-541 (1961) using the ratio determined by

$$Q_a/Q_A + Q_b/Q_B = \text{Synergy Index (SI)}$$

wherein

QA = concentration of compound A in parts per million (ppm), acting alone, which produced an end point.

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

QB = concentration of compound B in ppm, acting alone, which
produced an end point.

5 Qb = concentration of compound B in ppm, in the mixture,
which produced an end point

when the sum of Qa/QA and Qb/QB 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.

10 The test results for demonstration of synergism of microbicide
combinations are shown in Tables 1 to 11. Each table concerns the
combination of 4,5-dichloro-2-octyl-3-isothiazolone and one other
microbicide, and shows:

1. the identity of the second microbicide (compound B);
- 15 2. test against E. coli, C. albicans (C. alb), A. niger or A.
pullulan (A. pullul)

3. the end-point activity in ppm measured by MIC for compound A alone (QA), for compound B alone (QB), for compound A in the mixture (Qa), or for compound B in the mixture (Qb);
- 5 4. the calculation of synergy index (SI) based on the formula $SI = Qa/QA + Qb/QB$, and the weight ratio of 4,5-dichloro 2-n-octyl-3-isothiazolone (compound A) to compound B in the particular combination (A:B);
- 10 5. the range of weight ratios for synergism and the preferred weight ratios. It will be appreciated by those skilled in the art that the ratios given are approximate only.

The MIC values of each compound tested alone (QA or QB) are end-point activities except where the value is expressed as x.10. In these cases, the end-point activity was not seen at the highest tested concentration. For purpose of calculation of the synergy index and for operational definition of MIC, the reported value is twice the highest tested concentration. The value could be an underestimate of the true MIC; thus, the true synergy index could be even lower.

15

TABLE 1

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 3-iodo-2-propynylbutylcarbamate

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
A. niger	16.10	4.00	4.00	2.00	0.25	0.50	0.75	2:1
	16.10	4.00	8.00	0.50	0.50	0.13	0.62	16:1
A. pullul	16.10	2.00	8.00	0.25	0.50	0.13	0.62	32:1
C. alb	16.00	4.00	8.00	2.00	0.50	0.50	1.00	4:1
C. alb	2.00	8.00	0.25	4.00	0.13	0.50	0.63	1:16
C. alb	4.10	16.10	2.00	4.00	0.49	0.25	0.74	1:2
C. alb	32.10	16.00	4.00	8.00	0.12	0.50	0.62	1:2
	32.10	16.00	16.00	2.00	0.50	0.13	0.62	8:1
E. coli	16.00	250.00	8.00	125.00	0.50	0.50	1.00	1:16
E. coli	8.00	250.00	4.00	62.00	0.50	0.25	0.75	1:16

Synergistic ratios of compound A:compound B range from 32:1 to 1:16; preferred ratios are in the range 32:1 to 1:2.

TABLE 2

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 1,2-dibromo-2,4-dicyanobutane

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	16.00	62.00	1.00	31.00	0.06	0.50	0.56	1:31
	16.00	62.00	8.00	16.00	0.50	0.26	0.76	1:2
C. alb	4.00	32.00	1.00	8.00	0.25	0.25	0.50	1:8
	4.00	32.00	2.00	1.00	0.50	0.03	0.53	2:1
C. alb	4.10	31.00	2.00	8.00	0.49	0.26	0.75	1:4
C. alb	32.10	125.00	16.00	16.00	0.50	0.13	0.63	1:1
E. coli	16.00	62.00	8.00	16.00	0.50	0.26	0.76	1:2
E. coli	8.00	62.00	4.00	31.00	0.50	0.50	1.00	1:8
A. niger	16.10	64.10	8.00	16.00	0.50	0.25	0.75	1:2

Synergistic ratios of compound A:compound B range from 2:1 to 1:31, preferred ratios are in the range of 2:1 to 1:2.

TABLE 3

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone

Compound B = p-tolyldiiodomethylsulfone

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	4.10	10.00	2.00	2.50	0.49	0.25	0.74	1:1.25
C. alb	4.00	4.00	2.00	0.50	0.50	0.13	0.63	4:1
E. coli	16.00	1000.10	8.00	125.00	0.50	0.12	0.62	1:16
E. coli	8.00	1000.10	4.00	31.00	0.50	0.03	0.53	1:8
A. niger	16.10	16.00	8.00	8.00	0.50	0.50	1.00	1:1
A. pullul	16.10	8.00	8.00	4.00	0.50	0.50	1.00	2:1

Synergistic ratios of compound A: compound B range from 4:1 to 1:16; preferred ratios are in the range 4:1 to 1:1.25

TABLE 4

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = methylenebisthiocyanate

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Ob</u>	<u>Qa/QA</u>	<u>Ob/OB</u>	<u>SI</u>	<u>A:B</u>
C. alb	16.00	125.10	8.00	62.00	0.50	0.50	1.00	1:8
C. alb	4.00	32.00	2.00	2.00	0.50	0.06	0.56	1:1
C. alb	32.10	62.00	16.00	8.00	0.50	0.13	0.63	2:1
C. alb	4.10	31.00	2.00	16.00	0.49	0.52	1.00	1:8
E. coli	16.00	125.00	0.50	62.00	0.03	0.50	0.53	1:125
A. pullul	16.10	32.00	4.00	16.00	0.25	0.50	0.75	1:4
	16.10	32.00	8.00	8.00	0.50	0.25	0.75	1:1

Synergistic ratios of compound A:compound B range from 2:1 to 1:125; preferred ratios are in the range of 2:1 to 1:4.

TABLE 5

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 2-thiocyanomethylthiobenzothiazole

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	32.10	8.00	16.00	4.00	0.50	0.50	1.00	4:1
C. alb	2.00	8.00	0.25	4.00	0.13	0.50	0.63	1:16
A. niger	16.10	32.10	2.00	16.00	0.12	0.50	0.62	1:8
	16.10	32.10	8.00	2.00	0.50	0.06	0.56	4:1
A. pullul	16.10	8.00	4.00	4.00	0.25	0.50	0.75	1:1
	16.10	8.00	8.00	2.00	0.50	0.25	0.75	4:1

Synergistic ratios of compound A:compound B range from 4:1 to 1:16; preferred ratios are in the range of 4:1 to 1:8.

TABLE 6

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone

Compound B = tetrachloroisophthalonitrile

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	0.50	16.00	0.25	2.00	0.50	0.13	0.63	1:8
A. niger	16.10	32.10	0.25	16.00	0.02	0.50	0.51	1:64
	16.10	32.10	8.00	0.50	0.50	0.02	0.51	16:1
A. pullul	16.10	16.00	2.00	8.00	0.12	0.50	0.62	1:4
	16.10	16.00	8.00	1.00	0.50	0.06	0.56	8:1
C. alb	2.00	32.10	1.00	1.00	0.50	0.03	0.53	1:1

Synergistic ratios of compound A:compound B range from 16:1 to 1:64; preferred ratios are in the range of 8:1 to 1:8.

TABLE 7

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 2-n-octyl-3-isothiazolone

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	16.00	4.00	0.25	2.00	0.02	0.50	0.52	1:8
	16.00	4.00	0.50	1.00	0.03	0.25	0.28	1:2
C. alb	4.00	1.00	1.00	0.50	0.25	0.50	0.75	2:1
	4.00	1.00	2.00	0.06	0.50	0.06	0.56	32:1
C. alb	4.10	1.00	2.00	0.50	0.49	0.50	0.99	4:1
C. alb	32.10	2.00	16.00	1.00	0.50	0.50	1.00	16:1
E. coli	16.00	250.00	4.00	125.00	0.25	0.50	0.75	1:32
E. coli	16.00	125.00	8.00	31.00	0.50	0.25	0.75	1:4
A. pullul	16.10	8.00	4.00	4.00	0.25	0.50	0.75	1:1
	16.10	8.00	8.00	1.00	0.50	0.13	0.62	8:1

Synergistic ratios of compound A:compound B range from 32:1 to 1:32; preferred ratios are in the range of 8:1 to 1:2.

TABLE 8

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = bis-(trichloromethyl)sulfone

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	16.00	16.00	4.00	4.00	0.25	0.25	0.50	1:1
C. alb	16.00	250.10	8.00	125.00	0.50	0.50	1.00	1:16
E. coli	16.00	125.00	0.50	62.00	0.03	0.50	0.53	1:125
	16.00	125.00	4.00	31.00	0.25	0.25	0.50	1:8
	16.00	125.00	8.00	16.00	0.50	0.13	0.63	1:2
E. coli	16.00	1000.00	1.00	62.00	0.06	0.06	0.12	1:62
	16.00	1000.00	2.00	31.00	0.13	0.03	0.16	1:16
	16.00	1000.00	4.00	16.00	0.25	0.02	0.27	1:4
	16.00	1000.00	8.00	1.00	0.50	0.00	0.50	8:1

Synergistic ratios of compound A:compound B range from 8:1 to 1:125; preferred ratios are in the range of 8:1 to 1:8.

TABLE 9

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 5-bromo-5-nitro-1,3-dioxane

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	4.10	50.00	1.00	25.00	0.24	0.50	0.74	1:25
	4.10	50.00	2.00	6.20	0.49	0.12	0.61	1:3.1
C. alb	16.00	100.00	0.25	50.00	0.02	0.50	0.52	1:200
	16.00	100.00	0.50	25.00	0.03	0.25	0.28	1:50
	16.00	100.00	2.00	12.50	0.13	0.13	0.25	1:6.2
E. coli	8.00	100.00	1.00	50.00	0.13	0.50	0.63	1:50
	8.00	100.00	4.00	25.00	0.50	0.25	0.75	1:6.2
E. coli	16.00	50.00	2.00	25.00	0.13	0.50	0.63	1:12.5
	16.00	50.00	8.00	12.50	0.50	0.25	0.75	1:1.6

Synergistic ratios of compound A:compound B range from 1:1.6 to 1:200; preferred ratios are in the range of 1:1.6 to 1:12.5.

TABLE 10

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone

Compound B = 2-bromo-2-nitropropanediol

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	4.10	100.10	0.50	50.00	0.12	0.50	0.62	1:100
	4.10	100.10	1.00	25.00	0.24	0.25	0.49	1:25
	4.10	100.10	2.00	12.50	0.49	0.12	0.61	1:6.2
C. alb	16.00	200.10	4.00	100.00	0.25	0.50	0.75	1:25
	16.00	200.10	8.00	25.00	0.50	0.12	0.62	1:3.2
E. coli	16.00	25.00	4.00	12.50	0.25	0.50	0.75	1:3.2
	16.00	25.00	8.00	3.10	0.50	0.12	0.62	1:0.4
E. coli	16.00	25.00	4.00	12.50	0.25	0.50	0.75	1:3.2
	16.00	25.00	8.00	6.20	0.50	0.25	0.75	1:0.8

Synergistic ratios of compound A:compound B range from 1:0.4 to 1:100; preferred ratios are in the range of 1:0.4 to 1:6.2.

TABLE 11

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
 Compound B = 2,2-dibromo-3-nitrilopropionamide

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	4.10	250.00	0.50	125.00	0.12	0.50	0.62	1:250
	4.10	250.00	2.00	16.00	0.49	0.06	0.55	1:8
C. alb	32.10	250.00	16.00	16.00	0.50	0.06	0.56	1:1
E. coli	16.00	250.00	1.00	125.00	0.06	0.50	0.56	1:125
	16.00	250.00	8.00	16.00	0.50	0.06	0.56	1:2
E. coli	8.00	250.00	1.00	125.00	0.13	0.50	0.63	1:125
	8.00	250.00	2.00	62.00	0.25	0.25	0.50	1:31

Synergistic ratios of compound A:compound B range from 1:1 to 1:250; preferred ratios are in the range of 1:1 to 1:125.

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As can be seen by review of Tables 1-11, the compositions of the invention demonstrate synergistic microbicidal activity as measured by minimum inhibitory concentrations (MIC) and show surprisingly greater activity than the algebraic sum of the individual components which make up each composition.

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In contrast, an example of non-synergistic combination of 4,5-dichloro-2-octyl-3-isothiazolone and sodium dichlorophene is shown

in Table 12. In this example of non-synergism, the microbial activities of either component as measured against E. coli and C. albicans are not affected by the presence or the absence of the other component in the combination. It is also not antagonistic because no loss of activity of either component in the combination was detected.

The synergistic activities of the compositions of the invention in most cases are applicable to bacteria, fungi, and a mixture of bacteria and fungi. Thus, the combinations not only lower the use-level of biocide but also broaden the spectrum of activity. This is especially useful in situations where either component alone does not achieve the best results due to weak activity against certain organisms.

TABLE 12 (comparative)

Compound A = 4,5-dichloro-2-octyl-3-isothiazolone
Compound B = Sodium dichlorophene

<u>ORGANISM</u>	<u>end-point activity in ppm</u>				<u>calculations</u>			
	<u>QA</u>	<u>QB</u>	<u>Qa</u>	<u>Qb</u>	<u>Qa/QA</u>	<u>Qb/QB</u>	<u>SI</u>	<u>A:B</u>
C. alb	4.10	16.00	No effect					
C. alb	16.00	32.00	No effect					
E. coli	16.00	62.00	No effect					

What is claimed:

1. A microbicidal composition the first component of which is 4,5-dichloro-2-octyl-3-isothiazolone and the second component of which is selected from one or more of the following 11 compounds: 3-iodo-2-propynylbutylcarbamate, 1,2-dibromo-2,4-dicyanobutane, p-tolyldiiodomethylsulfone, 2-thiocyanomethylthiobenzothiazole, tetrachloroisophthlonitrile, 2-n-octyl-3-isothiazolone, bis-(trichloromethyl)sulfone, 5-bromo-5-nitro-1,3-dioxane, 2-bromo-2-nitropropanediol;

wherein the weight ratio of first component to second component is in the range of from about 150:1 to about 1:250.

2. The composition of claim 1, wherein the ratio of the first component to the second component, 3-iodo-2-propynylbutylcarbamate, is in the range of from about 32:1 to about 1:16.

3. The composition of claim 1, wherein the ratio of the first component to the second component, 3-iodo-2-propynylbutylcarbamate, is in the range of from about 32:1 to about 1:2.

4. The composition of claim 1, wherein the ratio of the first component to the second component, 1,2-dibromo-2,4-dicyanobutane is in the range of from about 2:1 to about 1:31.

5. The composition of claim 1, wherein the ratio of the first component to the second component, 1,2-dibromo-2,4-dicyanobutane is in the range of from about 2:1 to about 1:2.

6. The composition of claim 1, wherein the ratio of the first component to the second component, p-tolyldiiodomethylsulfone, is in the range of from about 4:1 to about 1:16.

7. The composition of claim 1, wherein the ratio of the first component to the second component, p-tolyldiiodomethylsulfone, is in the range of from about 4:1 to about 1:1.25.

8. The composition of claim 1, wherein the ratio of the first component to the second component, 2-thiocyanomethylthiobenzothiazole, is in the range of from about 4:1 to about 1:16.

9. The composition of claim 1, wherein the ratio of the first component to the second component, 2-thiocyanomethylthiobenzothiazole, is in the range of from about 4:1 to about 1:8.

10. The composition of claim 1, wherein the ratio of the first component to the second component, tetrachloroisophthalonitrile, is in the range of from about 16:1 to about 1:64.

11. The composition of claim 1, wherein the ratio of the first component to the second component, tetrachloroisophthalonitrile, is in the range of from about 8:1 to about 1:8.

12. The composition of claim 1, wherein the ratio of the first component to the second component, 2-n-octyl-3-isothiazolone, is in the range of from about 32:1 to about 1:32.

13. The composition of claim 1, wherein the ratio of the first component to the second component, 2-n-octyl-3-isothiazolone, is in the range of from about 8:1 to about 1:2.

14. The composition of claim 1, wherein the ratio of the first component to the second component, bis-(trichloromethyl)sulfone, is in the range of from about 8:1 to about 1:125.

15. The composition of claim 1, wherein the ratio of the first component to the second component, bis-(trichloromethyl)sulfone, is in the range of from about 8:1 to about 1:8.

16. The composition of claim 1, wherein the ratio of the first component to the second component, 5-bromo-5-nitro-1,3-dioxane, is in the range of from about 1:1.6 to about 1:200.

17. The composition of claim 1, wherein the ratio of the first component to the second component, 5-bromo-5-nitro-1,3-dioxane, is in the range of from about 1:1.6 to about 1:12.5.

18. The composition of claim 1, wherein the ratio of the first component to the second component, 2-bromo-2-nitropropanediol, is in the range of from about 1:0.4 to about 1:100.

19. The composition of claim 1, wherein the ratio of the first component to the second component, 2-bromo-2-nitropropanediol, is in the range of from about 1:0.4 to about 1:6.2.

20. A microbicial product containing from about 5 to about 30% of the composition of claim 1.

21. A microbicial product containing a composition according to claim 1, an emulsifier and water.

22. A method for inhibiting the growth of bacteria, fungi, or algae in a locus subject to contamination by bacteria, fungi, or algae, which comprises incorporating onto or into the locus, in an amount which is effective to adversely affect the growth of bacteria, fungi, or algae, the composition of claim 1.

23. The method of claim 22 wherein the locus is an aqueous medium, and the composition additionally contains an emulsifier and water.